Enantioselective Conjugate Additions to Meldrum's Acid Acceptors for the Synthesis of Quaternary Centres and Studies on Persistent Intramolecular C–H•••X (X = O, S, Br, Cl, and F) Hydrogen Bonds Involving Benzyl Meldrum's Acids

by

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I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

The construction of benzylic quaternary stereocentres via the enantioselective copper-catalyzed 1,4-addition of dialkylzinc reagents to Meldrum's acid acceptors in the presence of a phosphoramidite ligand is reported. Meldrum's acid acceptors can be easily accessed and numerous derivatives have been prepared to investigate the scope of the enantioselective 1,4-addition. The reaction is tolerant to a wide range of heteroaromatic and functional groups. The significance of substituting the position *para*, *meta*, and *ortho* to the electrophilic centre is also highlighted. Primary and secondary organozinc reagents are shown to be compatible in this reaction.

A highly enantioselective synthesis of carboxylic acid derivatives having an α-quaternary centre through copper-catalyzed 1,4-addition of dialkylzinc reagents to aryl acetate derivatives is also described. This method employs a commercially available phosphoramidite ligand and readily accessible Meldrum's acid acceptors. A brief insight into the observed selectivity is also discussed. The significance of this method was established by the expedient preparation of chiral diesters, succinimides, γ-butyrolactones, and isocyanates from highly functionalized benzyl Meldrum's acids.

In addition to 1,4-addition, the enantioselective asymmetric synthesis of benzylic tertiary and quaternary stereogenic centres via 1,6-addition of dialkylzinc reagents to Meldrum's acid acceptors is outlined. This work represents one of the early examples of 1,6-asymmetric conjugate addition reactions and discussions on the regioselectivity of the process are disclosed.

On a different subject matter, the occurrence and persistence of C–H•••X (O, S, Br, Cl, and F) bond in solution using ^{1}H NMR spectroscopy is discussed for a large number of benzyl Meldrum's acids. The latter are novel and reliable probes for the evaluation of this type of non-classical interactions in solution. The persistence of the C–H•••X bond in solution is demonstrated to be dependent upon structural features present on the aromatic moiety and the benzylic position of the benzyl Meldrum's acid derivatives. The observations presented highlight the large potential of Meldrum's acid in developing an understanding of the function and nature of C–H•••X interactions.

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List of Abbreviations

Ac	acetyl
acac	acetylacetonate
ACCN	azobis(cyclohexanecarbonitrile)
aq	aqueous
Ar	aryl
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
BINOL	2,2′-dihydroxy-1,1′-binaphthyl
BINPO	2-diphenylphosphinyl-2′-diphenyl-phosphin-1,1′-binaphthalene
Bn	benzyl
br	broad
Bu	butyl
c	concentration (g per 100 mL)
c-	cyclohexyl
calc'd	calculated
cat	catalytic
CuTC	copper(I) thiophene-2-carboxylate
Cy	cyclohexyl
d	doublet
DCC	N,N′-dicyclohexyl carbodiimide
DCE	1,2-dichloroethane
DMAP	4-*N*,*N*-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	*N*, *N*-dimethylformamide
DMSO	dimethyl sulfoxide
dppa	diphenylphophoryl azide
ee	enantiomeric excess
EI	electron impact
equiv	equivalent(s)
Et	ethyl
ether	diethyl ether
EtOAc	ethyl acetate
F-C	Friedel-Crafts
GC-MS	tandem gas chromatography-mass spectrometry
h	hour
hex	hexyl
HMDS	hexamethyldisilazide

HMPA	hexamethylphosphoric amide
HPLC	high performance liquid chromatography
HRMS	high-resolution mass spectrometry
Hz	Hertz
i-	iso-
IBX	2-iodoxybenzoic acid
J	spin coupling constant
JMOD	*J*-modulated ^{13}C-decoupled NMR
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
lit	literature
m	multiplet
m-	meta
M	molar (mole per litre)
M	metal
max	maximum
Me	methyl
Meldrum's acid	2,2-dimethyl-1,3-dioxane-4,6-dione
min	minute
mL	millilitre
mmol	millimole
mol	mole
M.p.	melting point
MS	molecular sieves
Ms	methanesulfonyl
MTBE	methyl *tert*-butyl ether
m/z	mass/charge
N/A	not available
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
nOe	nuclear Overhauser effect
N/R	no reaction
Nu	nucleophile
o-	ortho
p-	para
PCC	pyridinium chlorochromate
Ph	phenyl
Piv	pivaloyl (trimethylacetyl)
PMB	*para*-methoxybenzyl

ppm	parts per million
Pr	propyl
Py	pyridine
q	quartet
quant	quantitative
quint	quintet
R	alkyl group
rac	racemic
rt	room temperature
s	singlet
t	triplet
t-	tert
TBDMS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin-layered chromatography
TMS	trimethylsilyl
TMTHF	2,2,5,5-tetramethyltetrahydrofuran
t_R	retention time
triflate	trifluoromethanesulfonate
Ts	*para*-toluenesulfonyl (tosyl)
wt	weight

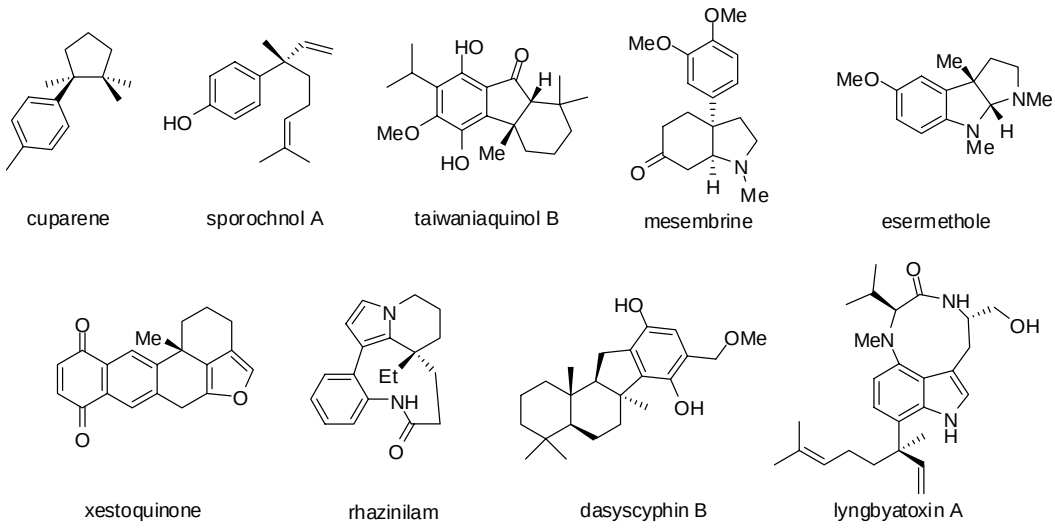
Chapter 1

Introduction and Background

(A) Introduction

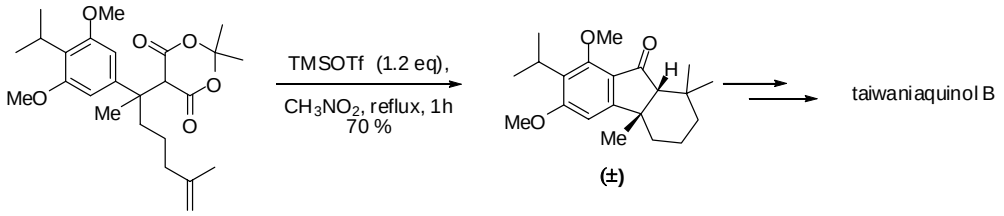
The asymmetric construction of molecules with quaternary stereocentres represents a challenging aspect of organic synthesis, with a growing number of methodologies available to access this demanding motif.[1] The importance of this structural moiety is exemplified by their appearance in biologically active molecules and/or natural products. Figure 1.1 illustrates a selected list of natural products with such stereocentres.[2]

Figure 1.1: Selected list of natural products with one or more quaternary stereocentres



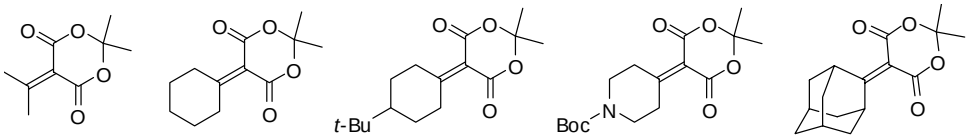
Inspired by the total synthesis of (±)-taiwaniaquinol B[3] in which Meldrum's acid[4,5] was used to participate in a domino intramolecular Friedel-Crafts acylation followed by carbonyl α-tert-alkylation (Scheme 1.1), our group became interested in the enantioselective synthesis of quaternary stereocentres.

Scheme 1.1: Domino intramolecular F-C acylation/α-tert-alkylation reaction for the synthesis of the cyclic core of taiwaniaquinol B



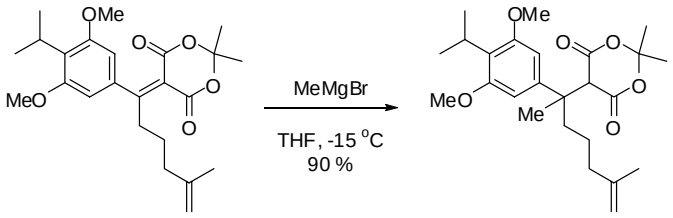
The difficulty for the asymmetric formation of stereocentres is highlighted in the area of 1,4-additions, where there is a dearth of methods able to form quaternary stereocentres in an enantioselective manner while analogous reactions to form tertiary centres are numerous and well-established.[6] More specifically, the formation of quaternary centres via the conjugate addition to 5-(1-arylalkylidene) Meldrum's acids was unprecedented even in a racemic fashion; however, 1,4-additions of aryl Grignard and organocopper reagents to symmetrical 5-(1-alkylalkylidene) Meldrum's acids were reported (Figure 1.2).[7] This results in achiral Meldrum's acid derivatives for any nucleophile in the 1,4-addition reaction.

Figure 1.2: All reported symmetrical alkylidene Meldrum's acids used in 1,4-addition reactions



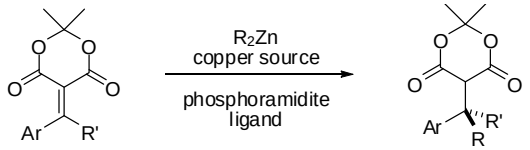
Consequently the total synthesis of (±)-taiwaniaquinol B was completed; the benzylic quaternary centre was introduced via a 1,4-addition of MeMgBr to an unsymmetrical, and for the first time, 5-(1-arylalkylidene) Meldrum's acid (Scheme 1.2).

Scheme 1.2: 1,4-Addition of MeMgBr to an alkylidene Meldrum's acid



The development of an enantioselective variant of this 1,4-addition to alkylidene Meldrum's acids was promising, as exemplified by the use of carbon-metal nucleophiles for the generation of either chiral or achiral quaternary carbons. In this thesis, our efforts and successes in the formation of quaternary stereocentres via the enantioselective copper-catalyzed 1,4-addition of dialkylzinc reagents to alkylidene/benzylidene Meldrum's acids in the presence of a phosphoramidite ligand is presented (Scheme 1.3).

Scheme 1.3: Enantioselective 1,4-addition to Meldrum's acid acceptors for the formation of quaternary stereocentres



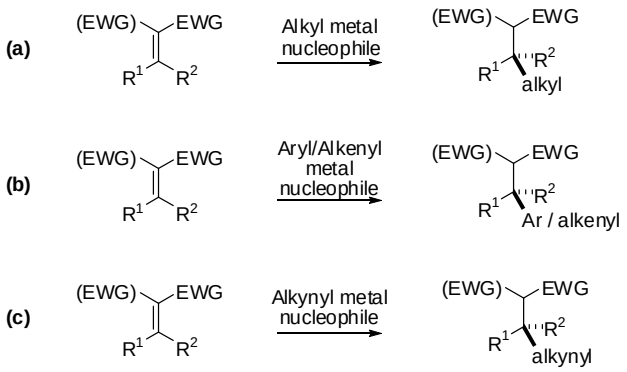
Although there were no literature precedents at the outset of this project, this lack was noted by other groups as well, as during our investigation, and subsequently, examples of enantioselective 1,4-addition yielding quaternary centres have been reported and are outlined in the next section.

(B) Literature precedents on the enantioselective metal-catalyzed, 1,4-addition of carbon-metal nucleophiles to olefin acceptors for the formation of quaternary stereocentres

The general strategy for the formation of quaternary stereocentres involves the addition of different carbon nucleophiles, with varying hybridized carbons, to an olefin acceptor. Although the 1,4-addition of sp^3-hybridized (alkyl, Scheme 1.4a) and sp^2-hybridized (aryl and alkenyl, Scheme 1.4b) carbon nucleophiles has been reported, to

date there are no reports on the formation of quaternary stereocentres via the addition of sp-hybridized (alkynyl) carbon nucleophiles (Scheme 1.4c).[8] The alkene itself can be monoactivated or diactivated, trisubstituted or tetrasubstituted, and either cyclic or acyclic.

Scheme 1.4: Approaches in the 1,4-addition reaction for the formation of quaternary stereocentres

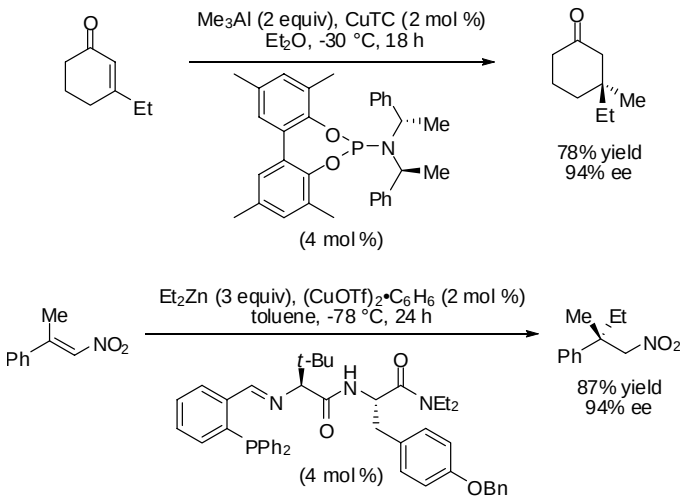


R^1, R^2 = Aryl, alkyl, alkenyl or alkynyl, carbonyl group

(I) Alkyl Nucleophiles

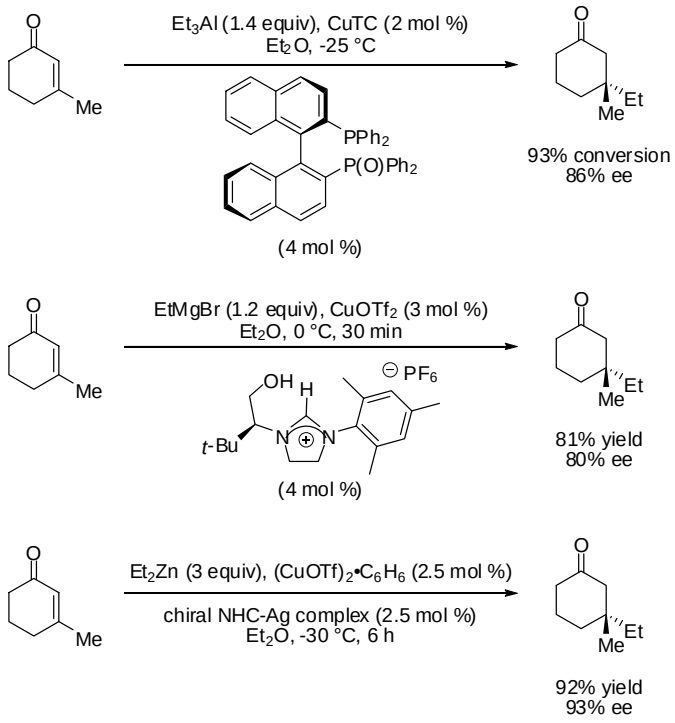
The first two reports on the asymmetric conjugate addition of alkyl nucleophiles to olefin acceptors for the formation of quaternary stereocentres were independently reported by the groups of Alexakis and Hoveyda in 2005. Alexakis has shown the successful copper-catalyzed 1,4-addition of trialkylaluminum reagents, $(alkyl)_3Al$ hereafter, to cyclic enones in the presence of a phosphoramidite ligand,[9,10] while Hoveyda has shown the copper-catalyzed addition of dialkylzinc reagents,[11] $(alkyl)_2Zn$ hereafter, to acyclic nitroalkenes in the presence of a peptide ligand (Scheme 1.5).[12]

Scheme 1.5: First reports on enantioselective 1,4-addition of $(alkyl)_3Al$ and $(alkyl)_2Zn$ to cyclohexenones and nitroalkenes for the formation of quaternary stereocentres



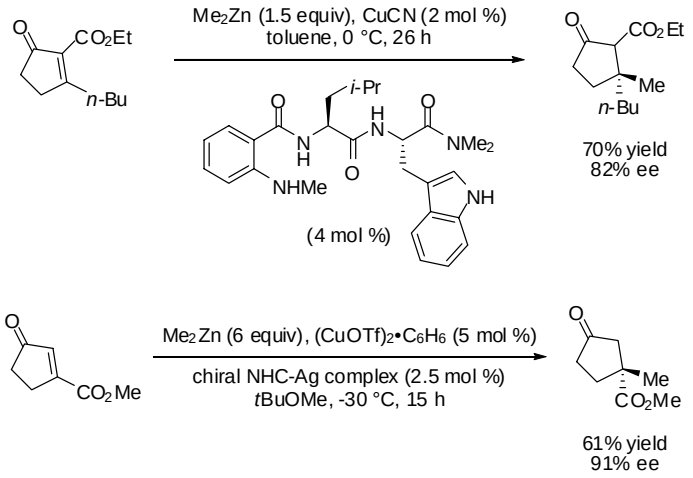
These two reports showed the diversity of alkyl nucleophiles, substrates, and chiral ligands that can be used for copper-catalyzed addition for the formation of quaternary stereocentres. Soon after, more reports in this area emerged from both groups. Alexakis and Gladiali reported the use of 2-diphenylphosphinyl-2′-diphenyl-phosphin-1,1′-binaphthalene (BINPO) as ligand in place of a phosphoramidite[13] and the copper-catalyzed asymmetric conjugate addition of Grignard reagents to cyclic enones employing *N*-heterocyclic carbenes (NHCs) as ligands (Scheme 1.6).[14] Hoveyda also reported the use of a NHC-complex in the asymmetric 1,4-addition of organozinc reagents to β-substituted cyclic enones for the formation of quaternary stereocentres (Scheme 1.6).[15]

Scheme 1.6: Use of BINPO and NHC ligands in the enantioselective 1,4-addition of aluminum, Grignard, and zinc reagents to cyclic enones for the formation of quaternary stereocentres



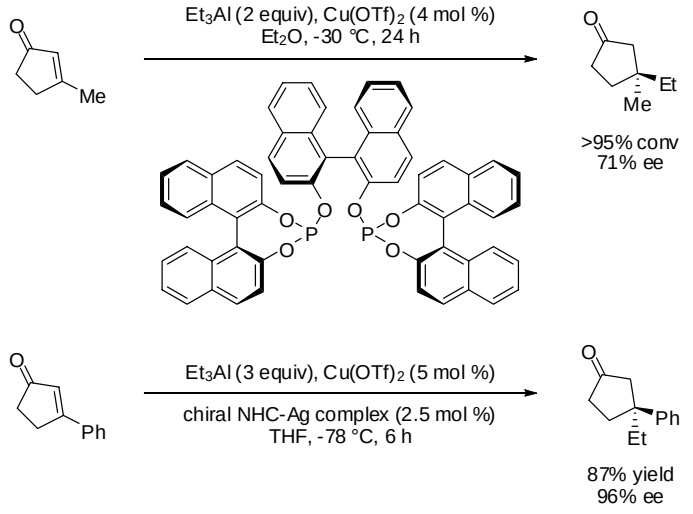
A shortcoming on those published reports was the transformations of β-substituted cyclopentenones to quaternary stereocentres, a less efficient process[16] but an important one that can be used in the formation of a variety of biologically active products.[17] To address this issue, Hoveyda showed that the dialkylzinc reagents can react with highly activated cycloalkenones bearing a carboxylate group at the 2- or 3-position (Scheme 1.7).[18,19] It was clearly stated in the former that the described protocol is "ineffective with the less activated but also less sterically hindered β-substituted cyclic enones".

Scheme 1.7: Advancement in the 1,4-addition to cyclopentenones for the formation of quaternary stereocentres



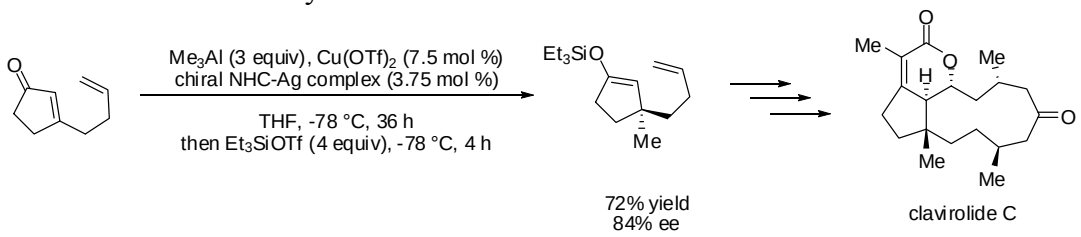
Alexakis later showed that the copper-catalyzed conjugate addition of $(alkyl)_3Al$ reagents to 3-substituted cyclopent-2-enones in the presence of diphosphite ligands is generally superior to the use of phosphoramidite ligands but nevertheless only modest yields and enantioselectivities were observed (Scheme 1.8).[20] To circumvent the use of activated cyclopentenones while still maintaining high conversions and enantioselectivities, Hoveyda developed the addition of aluminum reagents to β-substituted cyclic enones in the presence of a NHC-complex (Scheme 1.8).[21]

Scheme 1.8: Further improvements in the enantioselective 1,4-addition of aluminum reagents to cyclopentenones for the formation of quaternary stereocentres



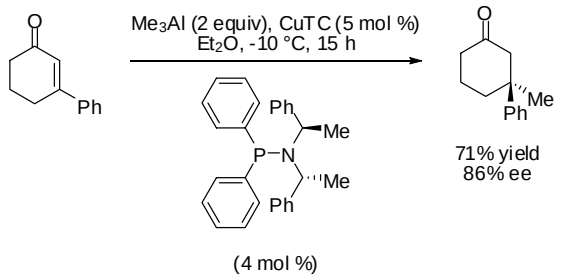
This method was later used in the total synthesis of clavirolide C employing the asymmetric 1,4-addition as the first step in this synthesis (Scheme 1.9).[22]

Scheme 1.9: Application of asymmetric 1,4-addition for the formation of quaternary stereocentres in the total synthesis of clavirolide C



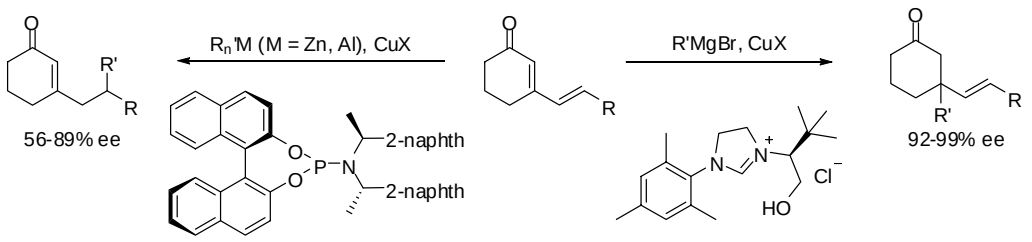
Other reports on the asymmetric 1,4-addition of alkyl nucleophiles were also reported. Alexakis has shown the use of SimplePhos as an efficient ligand for the copper-catalyzed 1,4-addition of Me_3Al to β-cyclic enones (Scheme 1.10).[23] Tomioka has studied a variety of chiral NHC ligands for the construction of this motif by the addition of Grignard reagents to 3-substituted cyclohexenones.[24]

Scheme 1.10: Use of SimplePhos as ligand in the asymmetric 1,4-addition to 3-phenyl-2-cyclohexenone



A regiodivergent 1,4 versus 1,6-asymmetric copper-catalyzed conjugate addition was reported by Alexakis' group when employing 3-alkenylcyclohexen-2-ones as electrophiles (Scheme 1.11).[25] Depending on the alkyl nucleophile used, 1,4- or 1,6-addition was obtained. For example the use of either Et_2Zn or Et_3Al affords 1,6-product, while EtMgBr affords the 1,4-product exclusively. Mixed results were observed when the size of the nucleophile was increased.

Scheme 1.11: A regiodivergent 1,4- versus 1,6-asymmetric copper-catalyzed conjugate addition employing 3-alkenyl cyclohexen-2-ones

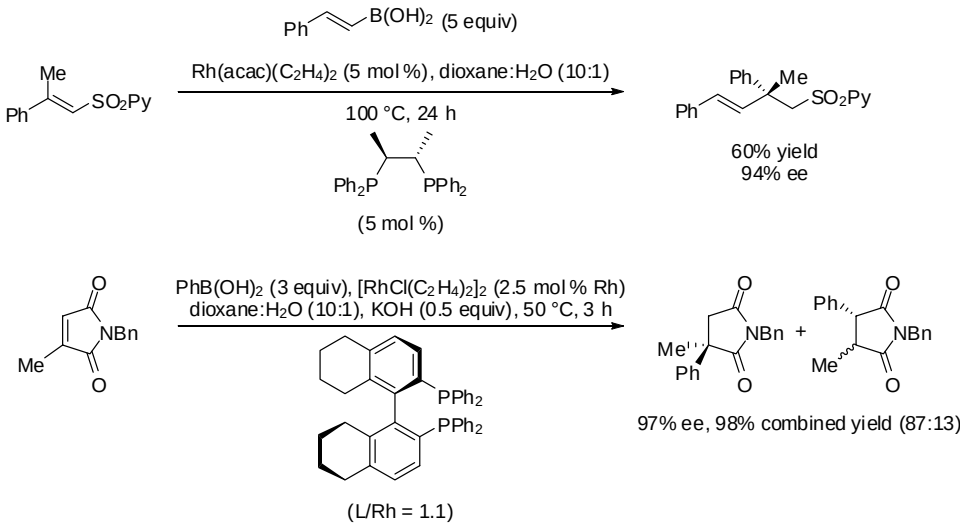


The possibility of adding alkyl groups via 1,4-addition to olefin acceptors was further extended to the addition of aryl and alkenyl groups. This is presented in the next section.

(II) Aryl/Alkenyl Nucleophiles

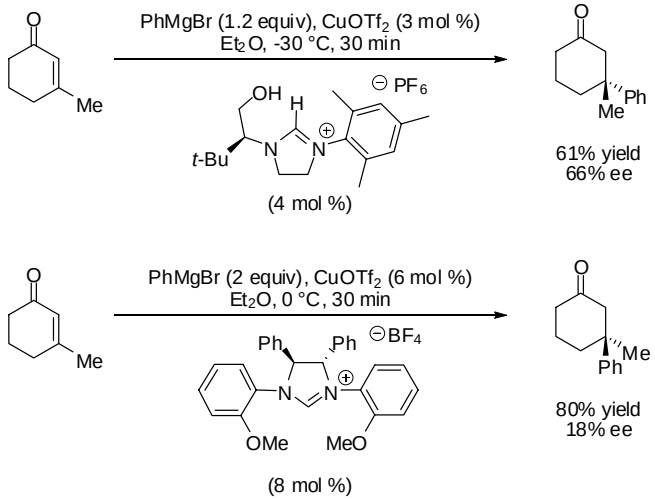
The asymmetric 1,4-addition of aryl/alkenyl carbon nucleophiles to activated acceptors for the generation of quaternary stereocentres offers an alternative approach to the conjugate addition of alkyl carbon nucleophiles discussed above. Carretero's group has reported the first sp^2-hybridized carbon nucleophile for the enantioselective construction of this type of stereocentres (Scheme 1.12).[26] Although all reported catalysis for alkyl delivery was done with copper, this report represents the first Rh-catalyzed asymmetric 1,4-addition for the formation of quaternary stereocentres. The addition of alkenylboronic acids to α,β-unsaturated pyridylsulfones was achieved in modest to good conversions, and enantioselectivities. Similarly, Hayashi employs the use of rhodium catalysis for the asymmetric construction of benzylic quaternary stereocentres via 1,4-addition of arylboronic acids to 3-substituted maleimides, furnishing 3,3-disubstituted succinimides in high regio- and enantioselectivities (Scheme 1.12).[27]

Scheme 1.12: Rh-catalyzed addition of alkenyl and aryl boronic acids to olefin acceptors for the formation of quaternary stereocentres



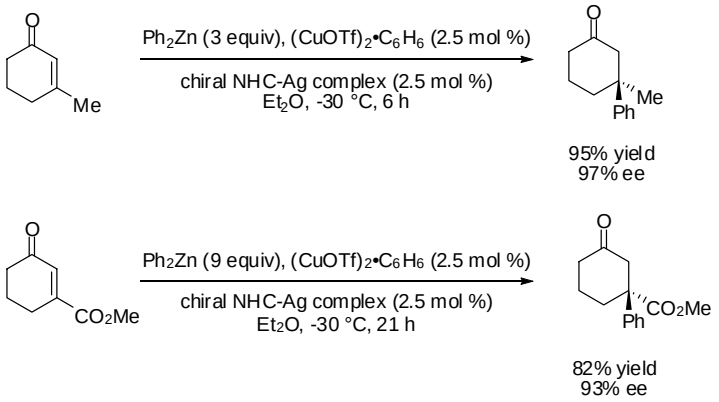
In contrast, both Alexakis[14] and Tomioka[24] reported a single example of the asymmetric synthesis of benzylic quaternary stereocentres via the copper-catalyzed 1,4-addition of PhMgBr to 3-substituted cyclohexen-2-one in the presence of chiral NHC ligands to afford chiral 1,4-products in poor to modest yields and enantiomeric excess (Scheme 1.13).

Scheme 1.13: Asymmetric Cu-catalyzed 1,4-addition of PhMgBr to 3-methyl-cyclohexenone in the presence of NHC ligands for the formation of quaternary stereocentres



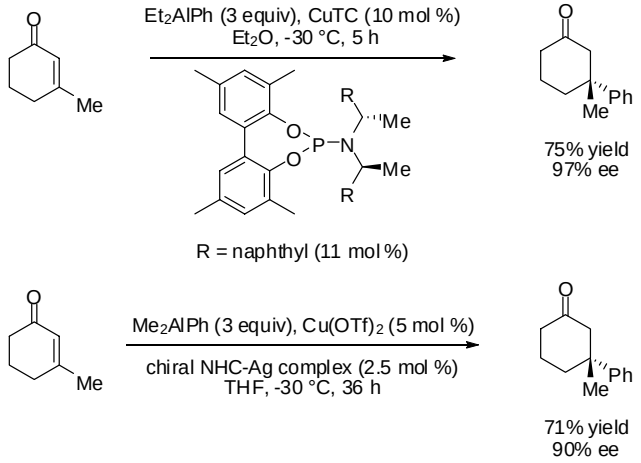
Hoveyda has also shown that diarylzinc reagents can be added successfully to both activated and non-activated cyclic enones in the presence of a NHC-complex to obtain 1,4-conjugate products in high to excellent yields and enantioselectivities (Scheme 1.14).[15,19]

Scheme 1.14: Asymmetric 1,4-addition of diarylzinc reagents to activated and non-activated cyclic enones in the presence of NHC-complex as ligands



Also, both Hoveyda[21] and Alexakis[28] have independently reported the copper-catalyzed asymmetric 1,4-addition of aryl aluminum reagents to these cyclic trisubstituted enones in excellent yields and selectivities (Scheme 1.15).

Scheme 1.15: Asymmetric 1,4-addition of $ArAlR_2$ to cyclic enones for the formation of quaternary stereocentres



As this represents a complete literature survey on metal-catalyzed 1,4-addition of carbon-metal nucleophiles to olefin acceptors for the formation of quaternary centres to date, this thesis presents a complementary route to access these stereocentres via the addition to Meldrum's acid acceptors.

(III) Alkylidene/Benzylidene Meldrum's acids in the asymmetric 1,4-addition for the formation of quaternary stereocentres

The above reports on the formation of benzylic quaternary stereocentres represent a great advancement in the area of asymmetric conjugate addition. However, despite the incredible expansion of compatible catalysts, ligands, and nucleophiles, the published reports of this reaction encompass a relatively small range of electrophiles. The substrates used for these conjugate additions can be summarized in four categories: (a) α,β-unsaturated pyridylsulfones (one report), (b) nitroalkenes (one report), (c) maleimides (one report), and the majority (d) tri- and tetrasubstituted cyclic 5, 6, and 7-membered enones.

Trisubstituted, acyclic olefins such as nitroalkenes and α,β-unsaturated pyridylsulfones are excellent acceptors in the asymmetric 1,4-addition to generate quaternary stereocentres (Scheme 1.5 and 1.12). However, the preparation of such precursors either requires the separation of (*E*)/(*Z*) isomers or entails a more difficult preparation of one of the two geometrical isomers.[29] With the exception of maleimides (Scheme 1.12), all other olefin acceptors can be summarized into cyclic, trisubstituted olefins of various ring sizes, offering a narrow selection of products containing an benzylic quaternary stereocentres. Of note are diactivated, cyclic, tetrasubstituted olefins subjected to asymmetric 1,4-addition reactions generating quaternary stereocentres in good to excellent yields and enantioselectivities, but providing products as mixtures of diastereomers (Scheme 1.7).[18]

Complementing these reports and broadening the scope of available electrophiles, this thesis outlines our investigations into alkylidene/benzylidene Meldrum's acids as acceptors for the synthesis of benzylic quaternary stereocentres. The usefulness of Meldrum's acid in a variety of chemical transformations and the advantageous features of alkylidene/benzylidene Meldrum's acids such as (a) olefin geometrical symmetry, which

avoids difficult substrate preparation/separation of (*Z*)/(*E*) isomers, (b) the doubly activated olefin which allows mild reaction conditions, (c) a relatively easy and general means of preparation by Knoevenagel condensation with a variety of ketones, and (d) their crystalline nature, which permits purification by crystallization/trituration, prompted us to investigate these electrophiles for the formation of quaternary stereocentres.

(C) Summary

The formation of quaternary stereocentres is an important aspect in organic chemistry. Many natural products and biologically active molecules contain this structural motif. The enantioselective 1,4-addition to activated acceptors for the construction of these stereocentres began emerging by 2005 with a growing number of reports to date; however the olefin acceptors constitute a very narrow range of substrates. It is therefore desirable to access these stereocentres by broadening the type of electrophile and maintaining excellent yields and enantioselectivities for the asymmetric conjugate addition.

The purpose of this research is to examine alkylidene/benzylidene Meldrum's acids as electrophilies in the asymmetric conjugate addition for the formation of quaternary stereocentres.

Chapter 2 of this thesis presents a full account of our findings on the asymmetric copper catalyzed 1,4-addition of organozinc reagents to alkylidene and indenylidene Meldrum's acids.

Chapter 3 presents a full account of our findings on the asymmetric copper catalyzed 1,4-addition of organozinc reagents to functionalized benzylidene Meldrum's acids. The highly functionalized quaternary stereocentres were subjected to numerous chemical transformations to obtain carboxylic acid derivatives, lactones, and succinimides.

Chapter 4 of this thesis presents our findings on the asymmetric copper catalyzed 1,6-addition to Meldrum's acid acceptors for the formation of both quaternary and tertiary stereocentres. The competition between 1,6- versus 1,4-addition reactions is discussed with reference to literature precedents.

On a different subject area, Chapter 5 outlines a detailed study on benzyl Meldrum's acids as excellent probes for intramolecular C–H•••X hydrogen bonds in solution. Numerous models were prepared for this study and analysis of the hydrogen bonding

properties of Meldrum's acids were determined by ^{1}H NMR. X-ray analyses of selected benzyl Meldrum's acids were obtained and compared to postulated solution structures.

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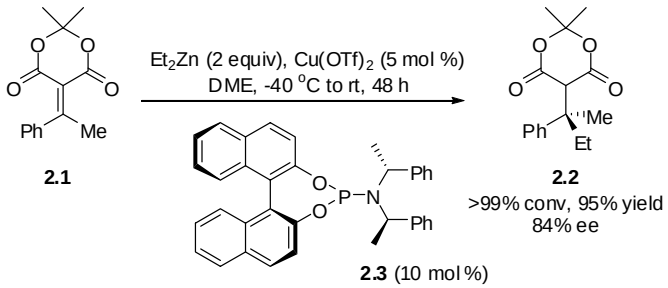
Chapter 2*

The Catalytic Asymmetric 1,4-Addition to Alkylidene Meldrum's Acids: Synthesis of Benzylic Quaternary Stereocentres

(A) Introduction

In Chapter 1 the asymmetric synthesis of quaternary stereocentres via the metal catalyzed 1,4-addition of organozinc, Grignard and aluminum reagents to electron deficient acceptors as reported in literature was summarized. Despite the growing number of reports in literature in this area, not a single report was published at the initiation of our investigations. Consequently, we decided to investigate the copper-catalyzed conjugate addition of dialkylzinc reagents to alkylidene Meldrum's acids for the formation of benzylic quaternary stereocentres. The investigations were initiated using 5-(1-phenylethylidene) **2.1** to probe the reactivity of these tetrasubstituted alkenes. Treating Meldrum's acid **2.1** with diethylzinc in the presence of catalytic amounts of copper(II) triflate and phosphoramidite ligand **2.3**[1] furnished the desired product **2.2** in >99% conversion, 95% yield, and 84% enantiomeric excess and this represents the optimized, developed reaction conditions for this investigation (Scheme 2.1).

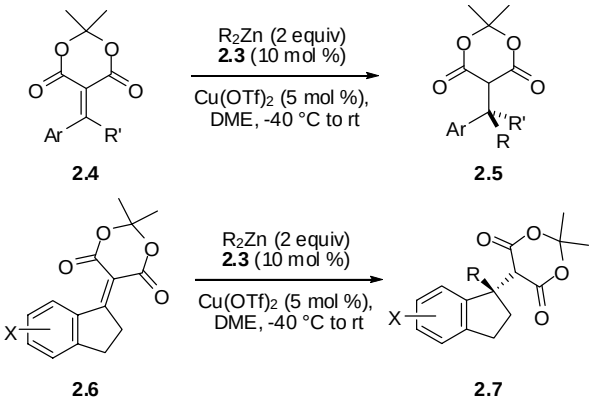
Scheme 2.1: Developed conditions for the asymmetric copper-catalyzed 1,4-addition of diethylzinc to alkylidene Meldrum's acid **2.1**



* Reproduced in part with permission from [Fillion, E.; Wilsily, A. *J. Am. Chem. Soc.* **2006**, *128*, 2774-2775]. Copyright [2006] American Chemical Society and Wilsily, A.; Lou, T.; Fillion, E. *Synthesis* **2009**, 2066-2072. Special Issue on Phosphoramidite Ligands.

In this chapter, along with the optimization studies, a systematic study outlining the asymmetric 1,4-addition of dialkylzinc reagents to alkylidene and indenylidene Meldrum's acids is presented (Scheme 2.2). Various heteroaromatic, *para*, *meta*, and *ortho* substituted aryl groups have been subjected to the conjugate addition reaction to determine the scope of this reaction. The use of NMR, x-ray crystallography, and various models are used to demonstrate how enantioselectivity is influenced by substitution at the *ortho*-, *meta*-, and *para* positions of the aromatic ring attached to the electrophilic centre. Also, the use of various organozinc reagents is outlined along with difficulties encountered during our investigations. This chapter represents our investigation on the asymmetric 1,4-addition of carbon nucleophiles to generate benzylic quaternary stereocentres.

Scheme 2.2: Asymmetric copper-catalyzed 1,4-addition of dialkylzinc reagents to alkylidene and indenylidene Meldrum's acids **2.4** and **2.6**

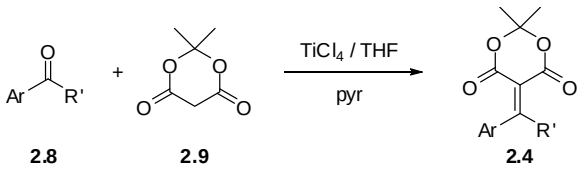


(B) Results and Discussion

(I) Optimization of Asymmetric 1,4-Addition

The synthesis of alkylidene Meldrum's acids was accomplished via the Knoevenagel condensation of ketones and Meldrum's acid giving generally crystalline solids and allowing access to study the asymmetric 1,4-addition reaction (Scheme 2.3).[2]

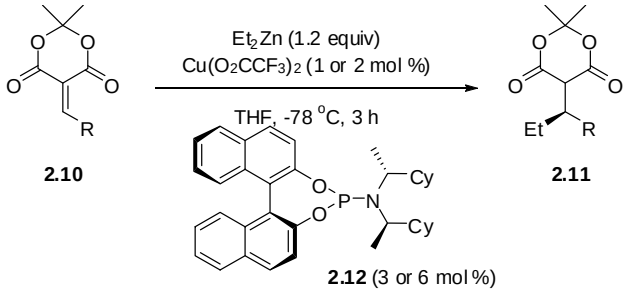
Scheme 2.3: Knoevenagel condensation of ketones with Meldrum's acid



2.8 **2.9** **2.4**

The investigations were initiated using 5-(1-phenylethylidene) **2.1** and the initial conditions began with first surveying the literature on the asymmetric 1,4-addition to olefin acceptors. An important contribution to this area was the asymmetric 1,4-addition of Et_2Zn to benzylidene Meldrum's acids **2.10** reported by Carreira and coworkers (Scheme 2.4).[3]

Scheme 2.4: Asymmetric 1,4-addition of Et_2Zn to benzylidene Meldrum's acids



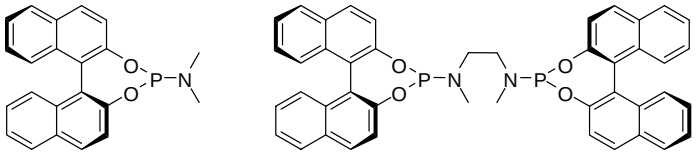
2.10 **2.11**

2.12 (3 or 6 mol %)

We were excited by the possibility of employing both organozinc reagents and phosphoramidite ligands for the asymmetric 1,4-addition to alkylidene Meldrum's acids for the formation of quaternary stereocentres. Although these conditions were a good starting point for the initiation of our studies, there are a few things worth mentioning. First, studies on copper salts for the asymmetric conjugate addition of Et_2Zn to cyclohexenones have shown that copper(I) triflate, or CuOTf, is a superior catalyst as a result of its high solubility in most organic solvents.[4] This study was later verified by Alexakis and coworkers by examining a variety of copper sources and solvents for the same reaction.[5] In fact, Alexakis suggested that the use of $Cu(OTf)_2$ had an added advantage of cost and being easier to handle. Consequently, $Cu(OTf)_2$ was chosen as the starting copper catalyst for our investigations knowing that a number of solvents were going to be tested, and solubility problems of other salts need to be avoided, for optimal asymmetric 1,4-addition reaction for the formation of quaternary stereocentres.

Secondly, the catalytic loadings involved in the reaction developed by Carreira and coworkers involves the use of 3:1 phosphoramidite ligand to copper while literature reports have shown an important 2:1 phosphoramidite ligand to copper ratio for the asymmetric 1,4-addition reaction.[4] The crystal structure of the complex of CuI and phosphoramidite ligand **2.13** (Figure 2.1) shows three phosphoramidite ligands bound through the phosphorus to the copper. The iodide occupies the last site giving a tetrahedral geometry of the copper.

Figure 2.1: Phosphoramidite ligands **2.13** and **2.14**



2.13 **2.14**

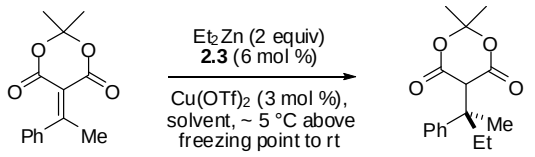
The authors postulated from the x-ray structure that during the conjugate addition two phosphoramidite ligands are bound to the copper, one site is occupied by the olefin, and the other is bound to the alkyl moiety that was transferred from the organozinc reagent. This was supported by the synthesis of bidentate ligand **2.14**. The use of bidentate ligand **2.14** and copper salt (1:1) achieved the same ee values as found for ligand **2.13** (2:1), which supports the phenomenon that two ligands are bound to the copper ion. Furthermore, Zhan and Gschwind have shown that at least 1.5:1 ligand to copper salt is necessary when identifying the structure of precatalytic copper phosphoramidite complex in solution.[6]

Finally, the phosphoramidite ligand **2.12** was not commercially available and we decided to develop the asymmetric conjugate addition reaction employing a commercially available phosphoramidite ligand **2.13** or **2.3**. The use of ligand **2.3** rather than **2.13** was shown to give superior enantioselectivities for the asymmetric 1,4-addition and was chosen as the initial ligand for the optimization studies.[7]

With this information in mind, the initiation of asymmetric 1,4-addition to alkylidene Meldrum's acid was probed (Scheme 2.5). 5-(1-Phenylethylidene) **2.1** was treated with a mixture of $Cu(OTf)_2$ (3 mol %), phosphoramidite ligand **2.3** (6 mol %), Et_2Zn (2 equiv)

in THF (0.1 M) which afforded benzyl Meldrum's acid **2.2** in a gratifying 59% yield and 63% ee after 24 h (Table 1 entry 1).

Table 2.1: Representative sample of solvents surveyed for the optimization of Et_2Zn addition to alkylidene **2.1**



2.1 **2.2**

Entry	Solvent	Time	Yield (%)	ee (%)
1	THF	24	59	63
2	Et_2O	48	91	59
3	1,4-dioxane	24	21	36
4	MTBE[a]	24	62	53
5	TMTHF[a]	24	NR	N/A
6	Benzene	24	100	50
7	Toluene	24	99	57
8	Anisole	24	53	24
9	CH_2Cl_2	48	NR	N/A
10	EtOAc	72	32	81
11	DMF	96	15	19
12	DME[a]	48	93	84
13	***DME***	***48***	***95***	***84***[b]

[a] MTBE = methyl *t*-butyl ether; TMTHF = 2,2,5,5-tetramethyltetrahydrofuran; DME = 1,2-dimethoxyethane [b]Cu : **2.3** = 5 mol % : 10 mol %

Other ethereal solvents such as diethyl ether afforded **2.2** in similar ee with higher yields after 48 hours, while solvents such 1,4-dioxane or methyl *t*-butyl ether were inferior (entries 2-4). Alkylidene Meldrum's acid **2.1** showed poor solubility in 2,2,5,5-tetramethyltetrahydrofuran as solvent (entry 5). Aromatic solvents generally showed excellent conversions with similar enantioselectivities with the exception of anisole (entries 6-8). The use of dichloromethane as solvent afforded no product after 48 hours (entry 9). More polar solvents showed varying levels of enantioselectivity with consistent poor yields (entries 10-11). The use of 1,2-dimethoxyethane was far superior to all other solvents tested both for yields and enantioselectivities (entry 12-13). Increased

conversion to **2.2** was observed when the copper catalyst was increased to 5 mol % and the phosphoramidite ligand was increased to 10 mol % as observed by ^{1}H NMR analysis of the crude mixture; the conversion increased from 96 to >99% over the same time period. Of note, other nucleophilies such as Et_3Al, EtMgBr, and Et_2Mg were inferior for yields/or enantioselectivities. Also, comparable results were obtained with 5 mol % of $Cu(OAc)_2 \bullet xH_2O$ (90%, 88% ee), $Cu(acac)_2 \bullet xH_2O$ (91%, 88% ee), and $Cu(O_2CCF_3)_2 \bullet xH_2O$ (99%, 88% ee), but CuCN gave **2.2** in 80% yield and 48% ee. We were satisfied with the formation of benzylic quaternary stereocentre with this level of conversion and enantioselectivity, and decided to investigate the scope of the 1,4-addition reaction with the optimized conditions at hand.

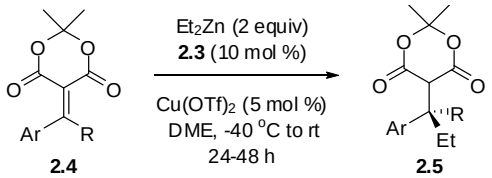
(II) Scope of Substrates in the Asymmetric Copper-Catalyzed, 1,4-Addition of Dialkylzinc Reagents to Alkylidene and Indenylidene Meldrum's Acids.

(1) Varying the Aryl Group.

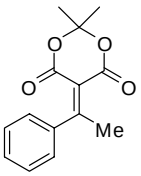
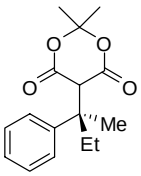
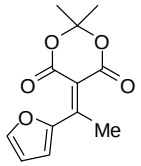
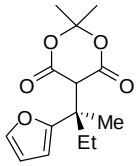
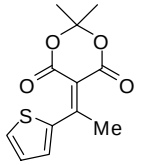
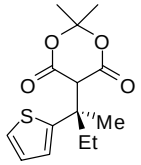
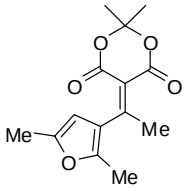
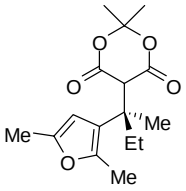
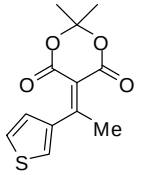
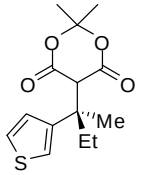
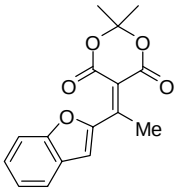
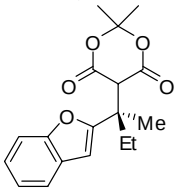
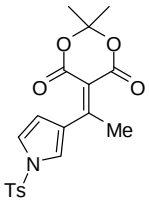
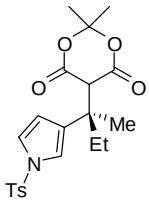
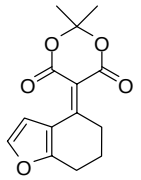
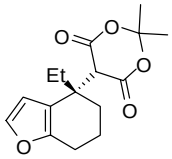
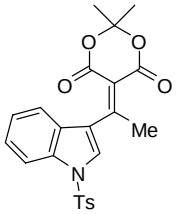
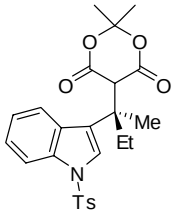
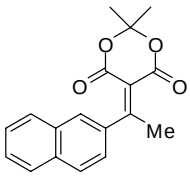
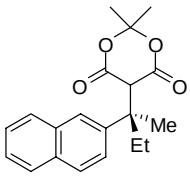
The importance of heteroaromatic ring systems in pharmaceutical compounds inspired us to examine the scope of these important ring systems in the asymmetric conjugate addition reaction (Table 2.2). Furthermore, these heteroaromatic rings can be subjected to numerous chemical transformations providing access to a diversity of compounds.[8]

Substituting the phenyl group with 2-thiophene increased the enantioselectivity from 84 to 92% ee (Table 2.2, entries 1-2). The 3-thiophene heteroaromatic moiety led to improved enantiomeric excess over the structurally similar 2-thiophene moiety (entry 3). Tosylated pyrrole and indole give excellent enantioselectivities and yields (entries 4 and 5); however it was necessary that the nitrogen substituent be electron-withdrawing to prevent decomposition of isolated products (protonation of the nitrogen and elimination of the heteroaromatic ring generating dialkyl substituted alkylidenes). Several furyl substituted alkylidenes were also subjected to the reaction conditions with good to excellent yields and enantioselectivities (entries 6-9). Benzo- or fused furyl groups were also tolerated with good enantioselectivities (entries 8 and 9). Although 1-naphthyl substituted alkylidene led to complete recovery of starting material, possibly due to steric interactions, 2-naphthyl substituted alkylidene gave excellent enantioselectivity in moderate yield (entry 10).

Table 2.2: Heteroaromatic Variations



2.4 2.5

entry	substrate	product	entry	substrate	product
1			6		
	2.1	**2.2**, 95% yield, 84% ee		**2.23**	**2.24**, 97% yield, 91% ee
2			7		
	2.15	**2.16**, 77% yield, 92% ee		**2.25**	**2.26**, 92% yield, 84% ee
3			8		
	2.17	**2.18**, 95% yield, 96% ee		**2.27**	**2.28**, 63% yield, 77% ee
4			9		
	2.19	**2.20**, 99% yield, 96% ee		**2.29**	**2.30**, 77% yield, 76% ee
5			10		
	2.21	**2.22**, 74% yield, 96% ee		**2.31**	**2.32**, 66% yield, 95% ee

(2) *Para*- and *Ortho*-Substitution in Aryl Ring.

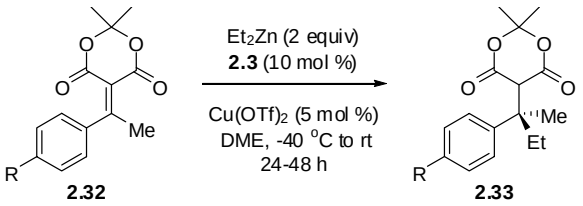
To demonstrate substrate scope and functional group tolerance in the asymmetric 1,4-addition of dialkylzinc reagents to 1-arylethylidene Meldrum's acids, *para* substitution of the aromatic moiety relative to the electrophilic centre was investigated. It was first postulated that electron-donating substituents and electron-withdrawing substituents would have opposite effects on the enantioselection of this reaction due to the electronic differences between these substituents.

After numerous *para* substituted 1-phenylethylidene Meldrum's acids were synthesized, they were subjected to the optimized reaction conditions using Et_2Zn. Electron-withdrawing halogen containing groups at the *para* position on the aromatic moiety relative to the electrophilic centre resulted in enantioselectivities between 92-95% enantiomeric excesses (Table 2.3, entries 1-4). Similarly, phenol derivatives with varying electronic donating abilities, furnished products with enantiomeric excesses ranging between 92-96% in good to excellent yield (entries 5-10). The reaction shows tolerance towards benzyl and alkyl ethers (entries 5 and 8), including acid-sensitive *t*-butyl ether (entry 9). Silyl ethers and acetyl groups are also well tolerated with no removal of these groups observed (entries 6, 7, 10).

Substituents bearing sp^2 carbons such as phenyl, alkene, or ester group gave excellent yields and ee's up to 95% (entries 11-13). A silyl protected alkyne furnished the conjugate addition product in superior enantioselectivity of 97% ee (entry 14).

Inductively donating alkyl groups showed a significant increase in enantioselectivities with increasing size furnishing products with up to 99% ee and 91% yield (entries 15-17). Introducing an analogous silicon derivative for a *t*-butyl group furnishes product in excellent enantioselectivity, although it was inferior to the *t*-butyl group (entry 18).

Table 2.3: Substituting the *para*-position

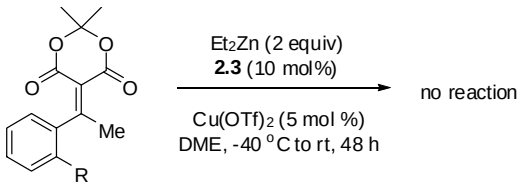


entry	substrate	product	yield (%)	ee (%)
Halogens				
1	X = Cl (**2.34**)	**2.35**	88	95
2	X = Br (**2.36**)	**2.37**	84	92
3	X = F (**2.38**)	**2.39**	83	92
4	X = CF_3 (**2.40**)	**2.41**	87	92
Phenol derivatives				
5	R = Bn (**2.42**)	**2.43**	75	93
6	R = TIPS (**2.44**)	**2.45**	81	94
7	R = TBDMS (**2.46**)	**2.47**	74	96
8	R = *i*-Pr (**2.48**)	**2.49**	84	95
9	R = *t*-Bu (**2.50**)	**2.51**	87	95
10	R = Ac (**2.52**)	**2.53**	87	93
sp and sp^2 Hybridized carbon substituents				
11	R = Ph (**2.54**)	**2.55**	76	95
12	R = $CHCH_2$ (**2.56**)	**2.57**	90	94
13	R = CO_2Me (**2.58**)	**2.59**	99	93
14	R = CCTIPS (**2.60**)	**2.61**	95	97
Inductively donating groups				
15	R = Me (**2.62**)	**2.63**	82	89
16	R = *i*-Pr (**2.64**)	**2.65**	88	98
17	R = *t*-Bu (**2.66**)	**2.67**	91	99
18	R = TMS (**2.68**)	**2.69**	90	93

The synthesis of *ortho*-substituted 1-arylalkylidenes was then targeted to probe the steric influence of the substitutent on the enantioselection of the conjugate addition. A number of *ortho* substituted 1-arylethylidenes were subjected to the reaction conditions (Scheme 2.5). Electron-donating benzyloxy group (**2.70**), electron-withdrawing chloro group (**2.71**), and σ-donating methyl (**2.72**) groups at the *ortho* position on the aromatic ring relative to the electrophilic centre all had the same outcome: complete recovery of starting material after 48 h.

It was speculated that the close proximity of the aromatic substituent to the olefin electrophilic carbon likely blocks the delivery of the alkyl group. Interestingly, *ortho*-substituted 3-furyl alkylidene surprisingly gives a benzylic quaternary stereocentre in 92% yield and 84% ee (Table 2.2, entry 7).

Scheme 2.5: Asymmetric 1,4-addition of Et_2Zn to *ortho*-substituted benzylidene Meldrum's acids



R = OBn (**2.70**), Cl (**2.71**), Me (**2.72**)

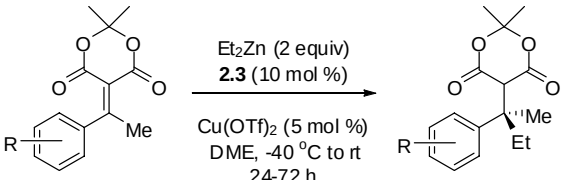
The lack of reactivity of *ortho*-substituted alkylidene Meldrum's acids while the excellent conversions, yields and enantioselectivities of benzylic quaternary stereocentres derived from the *para*-substituted alkylidene Meldrum's acids interested us to investigate the remaining *meta*-substituted alkylidene Meldrum's acids in the asymmetric conjugate addition reaction.

(3) *Meta*- and Multi-Substitution in Aryl Ring.

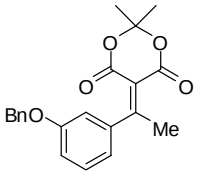
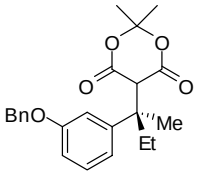
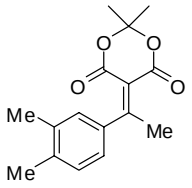
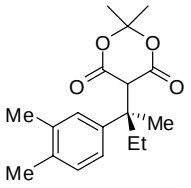
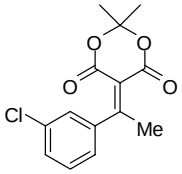
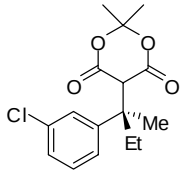
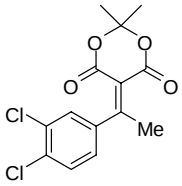
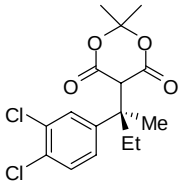
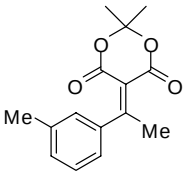
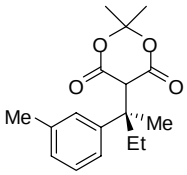
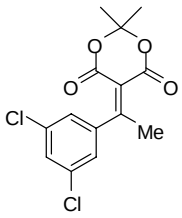
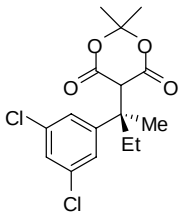
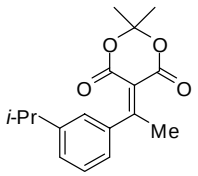
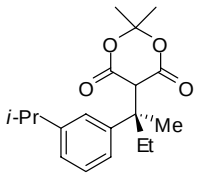
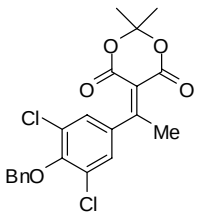
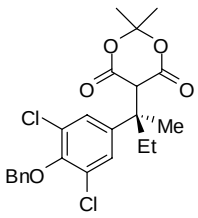
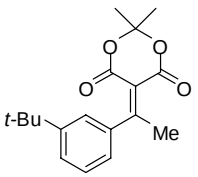
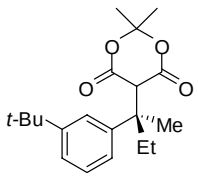
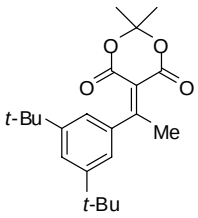
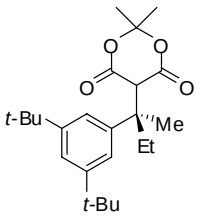
Substituents at the *meta* position to the electrophilic centre were also considered in the asymmetric, copper-catalyzed 1,4-addition of dialkylzinc reagents. While *meta*-substituted alkylidene Meldrum's acids did participate in the reaction, the enantioselectivites of the observed products were contrastingly different to the outcome resulting from the identical *para* substitution. For example, chloro, benzyloxy, and methyl groups furnished benzylic quaternary stereocentres in 89-95% ee when substituted at the *para* position but when moved to the *meta* position the ee decreased to between 74-79% ee (Table 2.3, entries 1, 5, 15 versus Table 2.4, entries 1-3).

To further examine these results, large groups such as *i*-Pr and *t*-Bu groups, which caused a large increase in ee at the *para* position, were placed at the *meta* position. Surprisingly, these substituents showed the most promising results, giving enantioselectivities of 97% and 98% ee and high yields (Table 2.4, entries 4-5). Of note, these two models also led to an increased reaction rate in comparison to inductively donating yet smaller methyl group (entries 4-5).

Table 2.4: Substituting the *meta*-position



2.32 **2.33**

entry	substrate	product	entry	substrate	product
1			6		
	2.73	**2.74**, 97% yield, 79% ee		**2.83**	**2.84**, 98% yield, 91% ee
2			7		
	2.75	**2.76**, 96% yield, 74% ee		**2.85**	**2.86**, 88% yield, 95% ee
3			8		
	2.77	**2.78**, 93% yield, 78% ee		**2.87**	**2.88**, 91% yield, 50% ee
4			9		
	2.79	**2.80**, 91% yield, 97% ee		**2.89**	**2.90**, 82% yield, 59% ee
5			10		
	2.81	**2.82**, 99% yield, 98% ee		**2.91**	**2.92**, 31% yield, 26% ee

Entries 8-10 conditions: 8 mol % $Cu(OTf)_2$ and 16 mol % of **2.3** were used for complete conversion

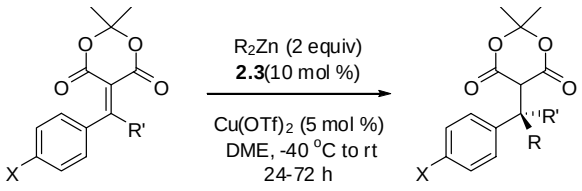
The combined effects of multi-substitution were also investigated. Mono-*meta* chloro substitution results in decreased enantiomeric excess in comparison to the parent unsubstituted alkylidene (74% versus 84% ee, Table 2.4, entry 2). In addition, 3,5-dichloro-substituted alkylidene results in yet additional decrease in the enantioselectivity (entry 8, 50% ee). An increase of about 10% ee was observed when benzyloxy group was included at the 4-position of the 3,5-dichlorosubstituted system (59% ee versus 50% ee, entries 8-9). Similar to the dichloro-substituted alkylidene, 3,4-dimethyl alkylidene resulted in product with high enantioselectivity, indicating a predominance of the *para* position over the *meta* (entry 6). Of note, a substantial decrease in rate is observed when alkylidene Meldrum's acids are disubstituted at the meta positions, therefore requiring higher catalyst loading and prolonged reaction times to obtain good conversions (entries 8-10).

(4) Chain Substitution and Dialkylzinc Reagents.

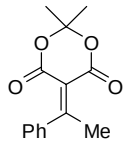
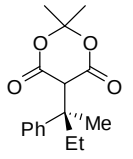
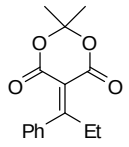
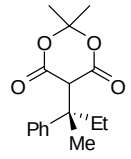
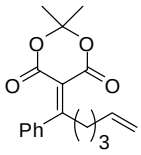
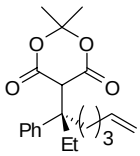
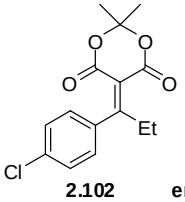
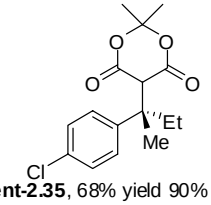
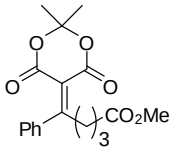
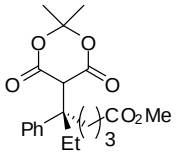
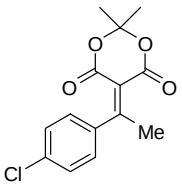
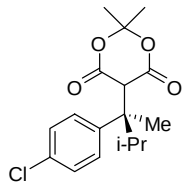
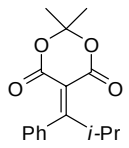
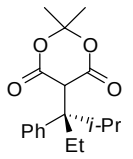
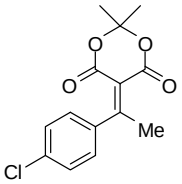
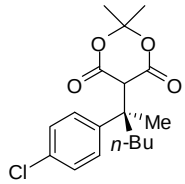
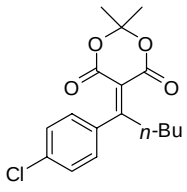
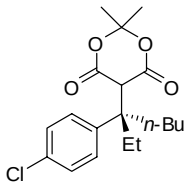
The previous sections examined the effects of phenyl ring substitution on enantioselectivity for 5-(1-aryl)ethylidene Meldrum's acids using Et_2Zn giving access to stereocentres bearing methyl and ethyl groups. In order to provide a more diverse range of products, the alkyl substituents of this stereocentre should be variable. In this section, two strategies were used to achieve this: using non-ethylidene Meldrum's acid derivatives and adding nucleophiles other than diethylzinc.

Primary alkyl groups give good enantioselectivities when Et_2Zn is used for the asymmetric conjugate addition (Table 2.5, entries 1 versus 2-3, and 5). Of note, an alkene or an ester in the chain are well tolerated while providing a modest increase in enantioselectivity in comparison to shorter alkyl chains (entries 2-3 versus 1). In contrast, secondary alkyl groups such as isopropyl (entry 4) or cyclohexyl (not shown), inhibit the delivery of the alkyl group in the asymmetric conjugate addition reaction. Et_2Zn addition to *para*-chloro substituted alkylidene Meldrum's acid **2.99** giving product **2.100** shows that the reaction not only tolerates long primary butyl chain, but demonstrates generality to substituted aryl groups as well (entry 5).

Table 2.5: Chain Modification and Dialkylzinc Reagent Additions



2.4 **2.5**

entry	substrate	product	R_2Zn	entry	substrate	product	R_2Zn
1			Et_2Zn	6			Me_2Zn
	2.1	**2.2**, 95% yield, 84% ee			**2.101**	**ent-2.2**, 93% yield, 76% ee	
2			Et_2Zn	7			Me_2Zn
	2.93	**2.94**, 60% yield, 89% ee			**2.102**	**ent-2.35**, 68% yield 90% ee	
3			Et_2Zn	8			$i\text{-}Pr_2Zn$
	2.95	**2.96**, 67% yield, 89% ee			**2.34**	**2.103**, 99% yield, 65% ee	
4			Et_2Zn	9			$n\text{-}Bu_2Zn$
	2.97	**2.98**, NR, N/A			**2.34**	**2.104**, 87% yield, 87% ee	
5			Et_2Zn				
	2.99	**2.100**, 78% yield, 94% ee					

Entries 6-7 conditions: **2.125** (10 mol %), $Cu(O_2CCF_3)_2 \cdot xH_2O$ (5 mol %); see next section for details

Alternatively, the alkyl groups at the benzylic position can be changed by addition of other dialkylzinc reagents. For example, the enantiomers of addition products **2.2** and **2.35** (formed in 84 and 95% ee by addition of Et_2Zn to **2.1** and **2.34**, respectively; Table 2.5, entry 1 and Table 2.3, entry 1) can be synthesized by addition of Me_2Zn to **2.101** and **2.102**, respectively, in good to excellent ee (Table 2.5 entries 6-7). The problem of low conversion in addition reactions using Me_2Zn has been noted by others,[9] and our efforts to overcome this poor reactivity was the subject of a recent study (next section). Addition of *n*-Bu_2Zn proceeded smoothly to give **2.104** in excellent yield and enantioselectivity (Table 2.5, entry 9). The secondary dialkylzinc reagent *i*-Pr_2Zn added with high conversion, but afforded product of lower ee than the other nucleophiles (entry 8). However, this does provide a means to access sterically hindered quaternary centres not accessible by addition to branched alkylidene Meldrum's acids of the type **2.98** (entry 8 versus 4).

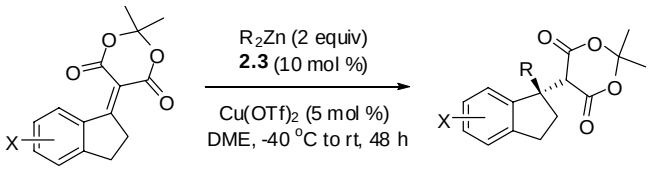
In this section, an overview of chain variations was described. Also, the use of various dialkylzinc reagents was outlined. In the next section, optimization studies towards the addition of dimethylzinc are discussed below. But first, the asymmetric 1,4-addition to indenylidene Meldrum's acids is presented.

(5) Indenylidene Meldrum's acids.

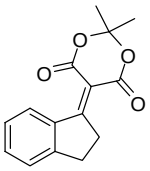
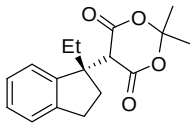
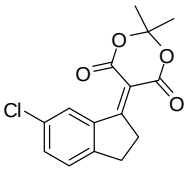
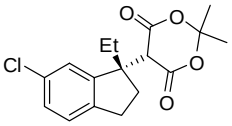
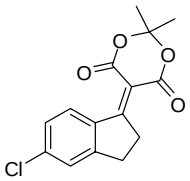
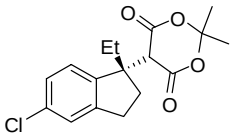
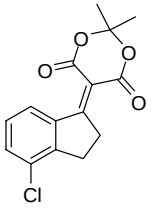
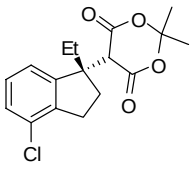
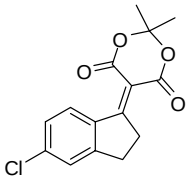
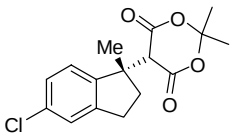
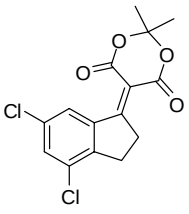
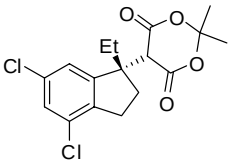
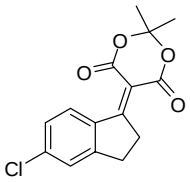
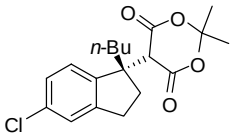
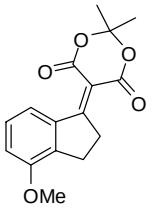
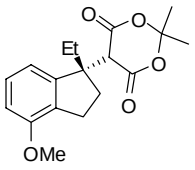
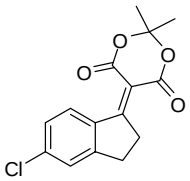
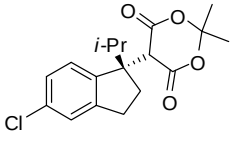
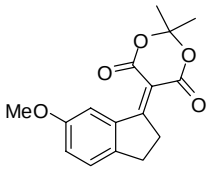
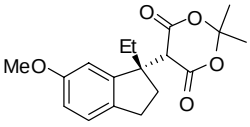
As a continuation of addition reactions employing electrophiles with alkyl chains other than methyl, we investigated a cyclic variant by preparing indenylidene Meldrum's acids via the condensation of indanones with Meldrum's acid. Recently, there have been a number of reports on the synthesis of 1-substituted chiral indanes, including examples of quaternary stereocentres.[10] As shown below, indenylidene Meldrum's acids are excellent acceptors for the preparation of this motif (Table 2.6).

Subjecting indenylidene Meldrum's acid **2.105** to the optimized reaction conditions furnished indane **2.106** in 96% ee, a substantial increase in enantioselectivity from the analogous, non-fused 1-phenylethylidene **2.1** which furnished benzylic Meldrum's acid in 84% ee (Scheme 2.1).

Table 2.6: Formation of Indanes via Asymmetric 1,4-Addition to Indenylidene Meldrum's Acids



2.6 **2.7**

entry	substrate	product	entry	substrate	product
1	 **2.105**	 **2.106**, 96% yield, 96% ee	6	 **2.112**	 **2.113**, 87% yield, >99% ee
2	 **2.107**	 **2.108**, 94% yield, 99% ee	7	 **2.114**	 **2.115**, 99% yield, 79% ee
3	 **2.107**	 **2.109**, 98% yield, 99% ee	8	 **2.116**	 **2.117**, 86% yield, 97% ee
4	 **2.107**	 **2.110**, 97% yield, 97% ee	9	 **2.118**	 **2.119**, 91% yield, 75% ee
5	 **2.107**	 **2.111**, 99% yield, 57% ee	10	 **2.120**	 **2.121**, 99% yield, 99% ee

Entries 3 conditions: 5 equivalents of Me_2Zn

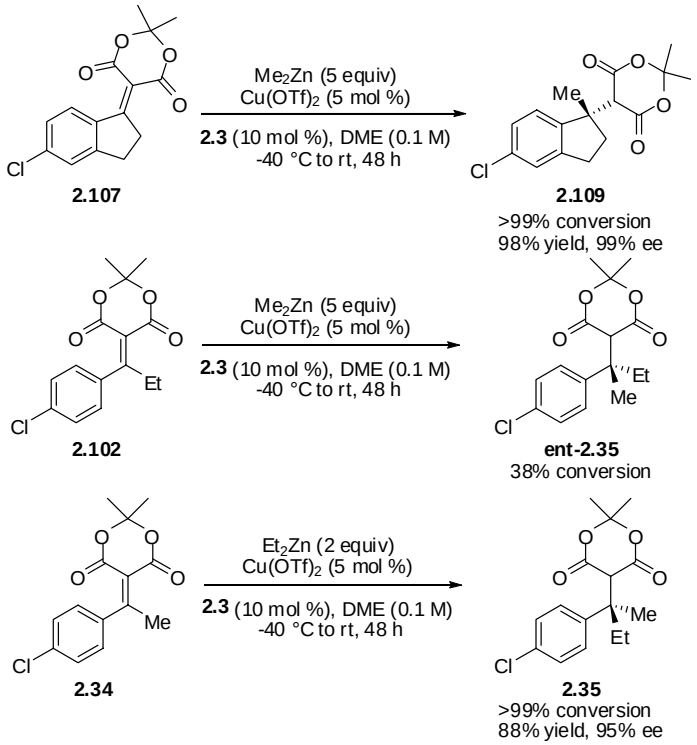
Furthermore, substitution at the *para* position on the aromatic moiety relative to the electrophilic centre also enhances the enantioselection, which is consistent with the non-fused alkylidene Meldrum's acid (Table 2.6, entry 2). Dialkylzinc reagents including Me_2Zn, *n*-Bu_2Zn, *i*-Pr_2Zn give excellent yields, with the former two yielding excellent enantioselectivities (entries 2-5). Chloro-substituted indenylidene Meldrum's acids **2.112** and **2.114** provided indanes with excellent yields, however, indenylidene Meldrum acid **2.114** provided indane **2.115** in superior enantioselectivity in comparison to **2.112**, despite being both meta to the electrophilic stereocentre (entries 6 and 7). Indenylidene Meldrum's acids **2.118** and **2.120**, substituted with methoxy groups provided the same results as electron withdrawing chloro group (entries 9 and 10). Of note, dichloro substituted indenylidene Meldrum's acid **2.116** furnished indane **2.117** in excellent yield and enantiomeric excess (entry 8).

In the next section, dimethylzinc addition to alkylidene versus indenylidene Meldrum's acids is discussed and the optimization studies towards alkylidene Meldrum's acids are discussed.

(6) Dimethylzinc Addition to Alkylidene Meldrum's Acids

In previous sections of this chapter, it was shown that alkylidene Meldrum's acids **2.4** are excellent electrophiles to access benzylic quaternary stereocentres through enantioselective copper-catalyzed conjugate addition of organozinc reagents in the presence of commercially available chiral phosphoramidite ligand **2.3**. Excellent conversions, yields and enantioselectivities in the formation of **2.5** were achieved. Despite the superior electrophilicity of alkylidene Meldrum's acids **2.4** towards organozinc reagents, the addition of Me_2Zn lacked generality. The conjugate addition of Me_2Zn to Meldrum's acid indenylidene **2.107** gave >99% conversion, 98% isolated yield and 99% ee. However, less reactive alkylidene **2.102** led to a poor 35% conversion, an inferior result in comparison to Et_2Zn addition to alkylidene Meldrum's acid **2.34** (Scheme 2.6).

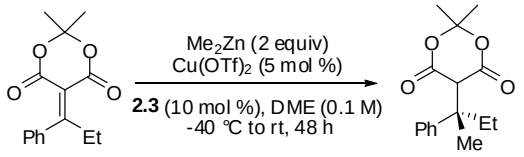
Scheme 2.6: Dimethylzinc addition to alkylidene Meldrum's acids and comparison to diethylzinc addition



The commonality of methyl-containing quaternary stereocentres in bioactive natural products prompted us to optimize the enantioselective methyl delivery to alkylidene Meldrum's acids **2.4**. A limited number of reports have appeared in the literature regarding asymmetric addition of methyl groups for the formation of quaternary carbons. Hoveyda showed that the poorly nucleophilic Me_2Zn reacted with highly activated alkenes such as nitroalkenes,[11] and cycloalkenones bearing a carboxylate group at the 2- or 3-position,[12] in the presence of a copper catalyst, to yield quaternary stereocentres in good yields and enantioselectivities. We also obtained limited success on the addition of Me_2Zn to 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)aryl acetates (Chapter 3).[13] The addition of MeMgBr catalyzed by copper salts was also reported.[14] To date, the copper-catalyzed addition of Me_3Al to cyclic enones has provided the best selectivity, as independently reported by the Alexakis[15] and Hoveyda[16] groups. In this section, an optimized 1,4-addition of Me_2Zn to tetrasubstituted alkenes **2.4** is outlined along with substrate scope and limitations.

The asymmetric conjugate addition was optimized using 2,2-dimethyl-5-(1-phenylpropylidene)-1,3-dioxane-4,6-dione (**2.101**) (Table 2.7). Subjecting **2.101** under our previously developed conditions, 2 equiv of Me_2Zn (10 wt% solution in hexane), 5 mol % of $Cu(OTf)_2$, in DME (final concentration of 0.08 M) from –40 °C to room temperature, gave a 32% conversion to Meldrum's acid **ent-2.2** after 48 h (Table 2.7 entry 1). Strongly Lewis acidic nucleophiles were then investigated to promote the addition to the alkylidenes with good conversions. Grignard reagents MeMgI, MeMgBr, and MeMgCl gave excellent conversions but nearly racemic product **ent-2.2** (entries 2-4). The use of the (R,S)-Josiphos ligand also gave excellent conversions with nearly racemic products (not shown in Table). Conjugate addition involving organoaluminum reagents led to improved conversions in comparison to Me_2Zn. However, poor enantioselectivities were observed (entries 5 and 6). The nearly racemic product **ent-2.2** observed for these reactions suggested that the uncatalyzed addition of the nucleophiles towards alkylidene Meldrum's acid **2.101** was the predominant pathway.

Table 2.7: Survey of Organometallic Reagents in the Conjugate Addition to Alkylidene Meldrum's Acid **2.101**



2.101 **ent 2.2**

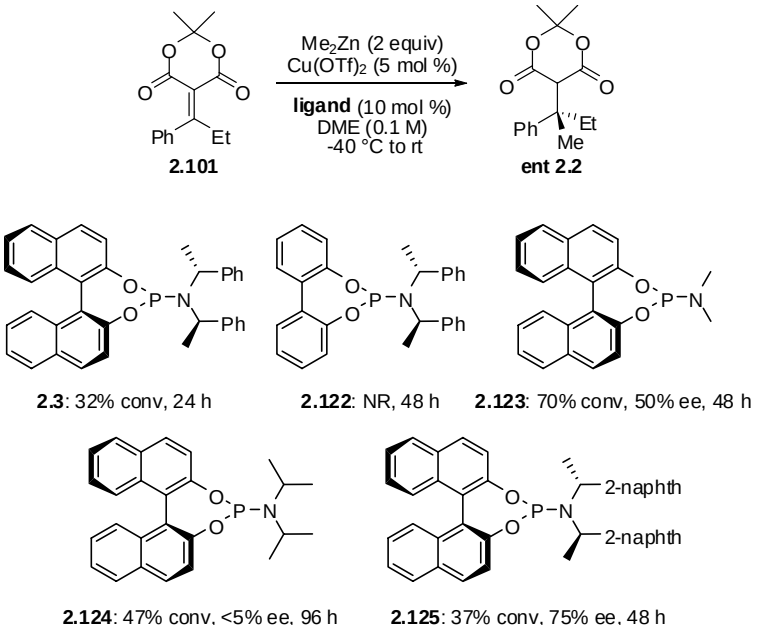
Entry	Me_nM	Time (h)	Conversion (%)	ee (%)
1	Me_2Zn	48	32	n/a
2	MeMgI	72	63	<5
3	MeMgBr	72	88	<5
4	MeMgCl	72	97	<5
5	Me_2AlCl	96	64	<5
6	Me_3Al	48	96	<5

The consistency of Grignard reagents and Me_3Al to give excellent conversion but racemic material led us to reexamine the asymmetric conjugate addition of Me_2Zn. We decided to systematically study the phosphoramidite ligand and copper sources to improve conversions. Ligand **2.122** containing a biphenyl rather than an axially chiral

BINOL moiety found in ligand **2.3**, led to complete inhibition of the conjugate addition (Figure 2.2). In contrast, leaving the BINOL moiety intact while replacing the chiral amine on the phosphorus atom with a dimethylamino group (**2.123**) gave 70% conversion and 50% ee after 48 h. Increasing the steric hindrance around the amine moiety by having a diisopropyl amine (**2.124**) had a detrimental effect on both conversion and enantioselectivity. The substitution of the phenyl moiety on the chiral amine with the 2-naphthyl moiety (**2.125**) gave only slight improvement of conversion with an enantioselectivity of 75% ee.

From this survey of phosphoramidite ligands, decreasing the size of the amine moiety increased the conversion, while decreasing enantioselectivity. These results showed that phosphoramidite ligand **2.3** and 2-naphthyl substituted ligand **2.125** led to optimal enantioselectivities despite lower conversions.

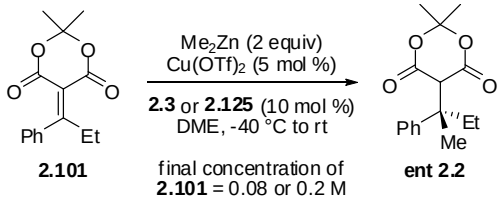
Figure 2.2: Phosphoramidite ligands



To promote the addition of Me_2Zn to alkylidene Meldrum's acids **2.4**, a bimolecular process, the concentration of the reaction mixture was increased. Two approaches were used to run the reaction at higher concentration; either utilizing a more concentrated solution of Me_2Zn, or diminishing the quantity of DME. Considering the total volume of solvent DME and hexanes from the 10% wt% solution of Me_2Zn, the reactions discussed

above were carried out at a final concentration of 0.08 M for **2.101**. Gratifyingly, conversion improved substantially by decreasing the amount of DME used in half, for a final concentration of 0.2 M. As depicted in Table 2.8, when ligand **2.3** was used, conversion increased from 32% to 78%, and 37% to 82% with ligand **2.125**. Of note, the decrease in the relative quantity of DME versus hexane did not result in a loss in enantioselectivity.

Table 2.8: Concentration Studies

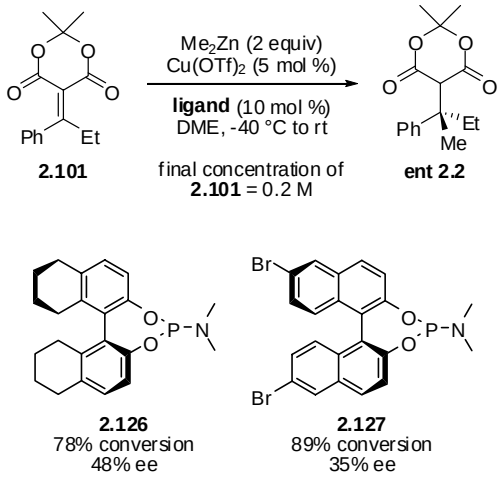


2.101 **ent 2.2**

Entry	Ligand	Final concentration of 2.101	Conversion (%)	ee (%)
1	**2.3**	0.08 M	32	n/a
2	**2.3**	0.2 M	78	77
3	**2.125**	0.08 M	37	75
4	**2.125**	0.2 M	82	75

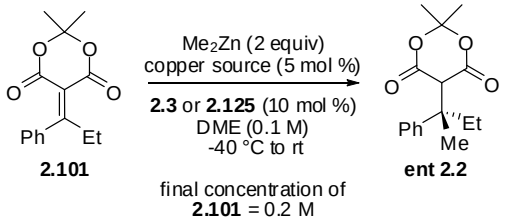
Further ligands with modifications to the BINOL backbone were tested to increase the conversion and the enantioselectivity (Figure 2.3). Ligand **2.126**, with a partially hydrogenated BINOL moiety, led to enantioselectivity similar to **2.123**. Finally, 6,6'-dibrominated phosphoramidite ligand **2.127** gave improved conversion but decreased enantioselectivity in comparison to **2.123**. Based on these results, phosphoramidites **2.3** and **2.125** were the best ligands in the Me_2Zn addition for obtaining high yield and enantioselectivity.

Figure 2.3: Varying the phosphoramidite ligands



Copper sources were then explored to further optimize conversion and enantioselectivity. After testing a few copper sources, it was shown that consistent enantioselectivities were achieved regardless of the copper source for both ligands **2.3** (Table 2.9 entries 1-5) and **2.125** (Table 2.9 entries 6-8). However, the source of copper had a bigger influence on conversion. $Cu(OTf)_2$ gave the lowest conversion compared to all other copper sources tested (entries 1 and 6), while $Cu(O_2CCF_3)_2 \bullet xH_2O$ led to the best results (entry 7). This time, the final concentration was increased by using a more concentrated solution of Me_2Zn. The conversion was increased to near completion by using a 2.0 M solution of Me_2Zn in toluene (2 equiv) (entry 8), for a final concentration of 0.33 M.

Table 2.9: Optimization of the Copper Source

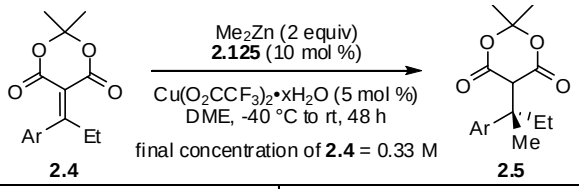


Entry	Ligand	Copper Source	Conversion (%)	ee (%)
1	**2.3**	$Cu(OTf)_2$	78	77
2	**2.125**	$Cu(OTf)_2$	82	75
3	**2.3**	$Cu(OAc)_2 \bullet H_2O$	94	75
4	**2.3**	$Cu(acac)_2$	88	75
5	**2.3**	CuTC[a]	90	74
6	**2.3**	$Cu(O_2CCF_3)_2 \bullet xH_2O$	87	73
7	**2.125**	$Cu(O_2CCF_3)_2 \bullet xH_2O$	95	77
8	**2.125**	$Cu(O_2CCF_3)_2 \bullet xH_2O$	98[b]	76

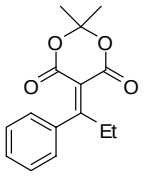
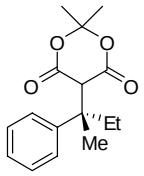
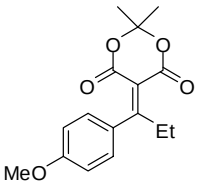
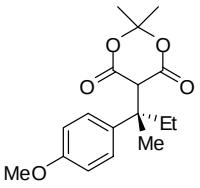
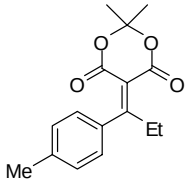
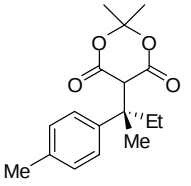
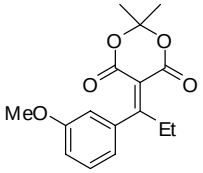
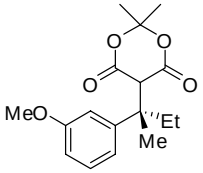
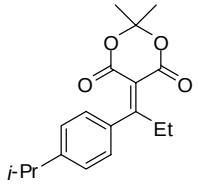
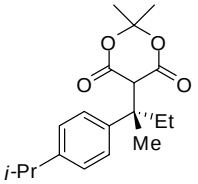
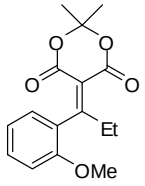
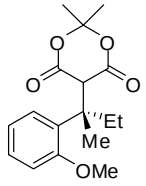
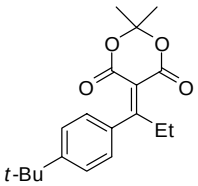
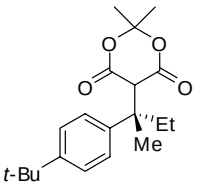
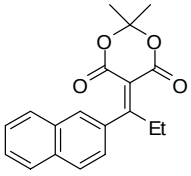
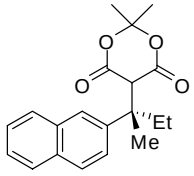
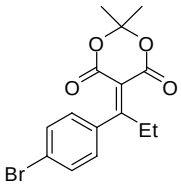
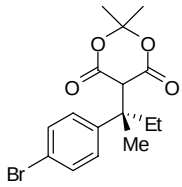
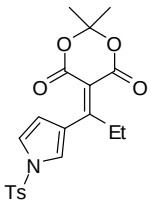
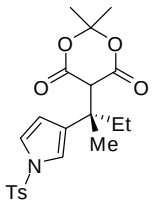
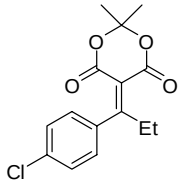
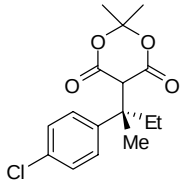
[a] CuTC: copper(I) thiophene-2-carboxylate. [b] Me_2Zn (2.0 M in toluene) was used rather than Me_2Zn (10 wt% in hexane). Final concentration of **2.101** was 0.33 M.

With the optimal conditions in hand, the scope of the Me_2Zn addition to alkylidene Meldrum's acids was investigated (Table 2.10). Electron-donating groups positioned para to the electrophilic site furnished products in excellent yields and enantioselectivities (Table 2.10 entries 2-4, 7). Electron-withdrawing groups at the 4-position also provide products with good yields and enantioselectivities (entries 5-6). Substituting the meta position yielded diminished selectivities, while *ortho*-substitution led to full recovery of starting material. These results are consistent with our previously reported Et_2Zn addition to similar alkylidenes. Interestingly, 3-*N*-tosylated pyrrole substituted **2.139** gives product **ent-2.20** in excellent yield and enantioselectivity (entry 11).

Table 2.10: Scope of the Conjugate Addition of Me_2Zn



2.4 **2.5**

entry	substrate	product	entry	substrate	product
1			7		
	2.101	**ent-2.2**, 93% yield, 76% ee		**2.132**	**2.133**, 93% yield, 85% ee
2			8		
	2.128	**ent-2.63**, 85% yield, 83% ee		**2.134**	**2.135**, 79% yield, 69% ee
3			9		
	2.129	**ent-2.65**, 99% yield, 94% ee		**2.136**	**2.137**, no rxn, n/a
4			10		
	2.130	**ent-2.67**, 84% yield, 97% ee		**2.138**	**ent-2.32**, 82% yield, 79% ee
5			11		
	2.131	**ent-2.37**, 68% yield, 91% ee		**2.139**	**ent-2.20**, 93% yield, 97% ee
6					
	2.102	**ent-2.35**, 68% yield, 90% ee			

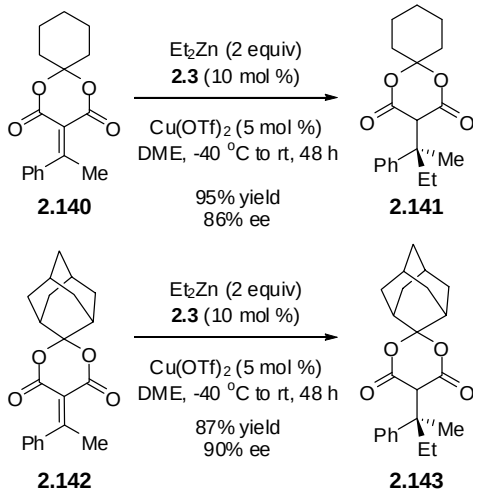
It is noteworthy to comment on the experimental procedure. A typical reaction involves the addition of Me_2Zn to a precooled solution containing copper source and the chiral phosphoramidite ligand. After five minutes, a solution of the substrate in DME is added to the reaction mixture. Although this procedure works with a number of these alkylidenes, it became a problem for some substrates insoluble in DME at high concentration. To overcome this problem, a solution of copper, phosphoramidite ligand, and dimethylzinc was added to a concentrated mixture of the substrate in DME. This "reverse" addition allowed for better conversion and isolated yields while not affecting the enantioselectivities.[15b]

In summary, the asymmetric conjugate addition of Me_2Zn to alkylidene Meldrum's acids has been achieved in good to excellent yields and enantioselectivities.

(7) Varying the Acetal Group in Alkylidene Meldrum's Acids.

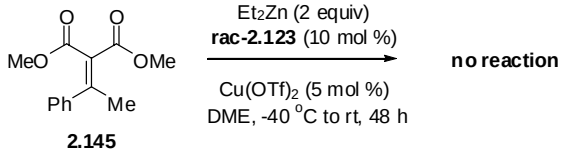
A last possible variation of the alkylidene Meldrum's acid electrophile is to use cyclic malonates derived from condensation of malonic acid with ketones other than acetone. We have found that using alkylidenes containing a cyclohexyl (**2.140**) or adamantyl (**2.142**) group provide conversion and ee similar to standard Meldrum's acid (Scheme 7). Although the adamantyl substituted **2.142** does provide a slight improvement in ee over **2.1**, this gain does not justify the use of a more expensive and non-commercially available starting material.

Scheme 2.7: Addition to alkylidene Meldrum's acids **2.140** and **2.142**



We have also made an interesting observation regarding the overall superior electrophilicity of alkylidene Meldrum's acids compared to their structurally similar alkylidene dialkylmalonates.[17] That is, under conditions in which alkylidene Meldrum's acid **2.1** is alkylated in >99% conversion, the alkylidene malonate **2.145** is completely unreactive (Scheme 2.8). Considering that electrophiles of the type **2.145** are more difficult to prepare[18] than alkylidene Meldrum's acids and are inferior electrophiles, we hope this comparison will reinforce the privileged nature of Meldrum's acid-based acceptors.

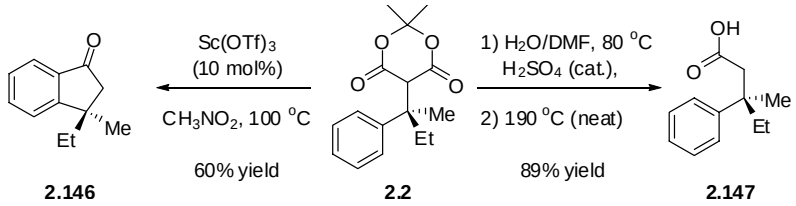
Scheme 2.8: Addition to alkylidene malonate **2.145**



(III) Rationalization of the Observed Enantioselectivity

Alkylidene Meldrum's acids were shown to be excellent electrophiles in the asymmetric 1,4-addition of organozinc reagents for the formation of benzylic quaternary stereocentres. Although *ortho*-substitution was detrimental to the reaction, substitution at the *para* or *meta* position of alkylidene Meldrum's acids led to excellent conversions and yields of the desired products, with the former generally having consistently high enantioselectivities. The absolute stereochemistry of the quaternary stereocentres was determined by transforming benzyl Meldrum's acid **2.2** into known (*R*)-3-ethyl-3-methyl-1-indanone[19,20] using a protocol previously developed in our group.[21] In addition, the stereochemistry of the conjugate addition adduct **2.2** was verified when it was hydrolyzed to the known *β,β*-disubstituted pentanoic acid.[19] The stereochemistries of other benzyl Meldrum's acid derivatives **2.4** were assigned by analogy to **2.2** (Scheme 2.9).

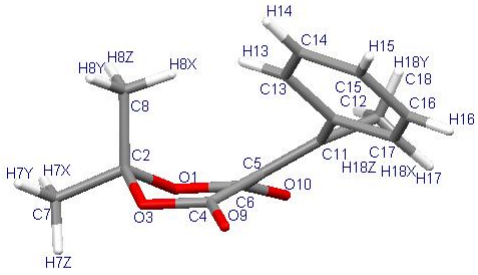
Scheme 2.9: Chemical transformations for absolute stereochemistry determination

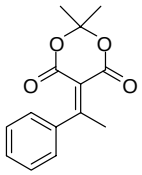


2.146 **2.2** **2.147**

The conformation of Meldrum's acid and the related derivatives has been the discussion of several reviews, crystallographic publications, and theoretical discussions.[22] While a number of reports discuss the conformation of alkylidene Meldrum's acids that are trisubstituted olefins from the analyses of x-ray structures, to the best of our knowledge, there has been no report on the crystal structures of aryl-substituted alkylidene Meldrum's acids that are tetrasubstituted olefins. To gain some insight on the observed enantioselectivities, x-ray structures of alkylidene and indenylidene Meldrum's acids **2.1**, **2.34**, **2.66**, **2.71**, **2.75**, **2.77**, **2.81**, **2.105**, **2.107**, **2.112**, **2.114**, and **2.317** were obtained, beginning with unsubstituted 5-(1-phenylethylidene) Meldrum acid **2.1** (Figure 2.4).

Figure 2.4: X-ray structure of **2.1**





2.1

The crystal structure reveals a boat conformation, consistent with published crystallographic data for alkylidene Meldrum's acids that are trisubstituted alkenes.[22b] Furthermore, the phenyl ring is not in conjugation with the activated olefin. As a result, it was postulated that the absence of conjugation between the aryl moiety and the

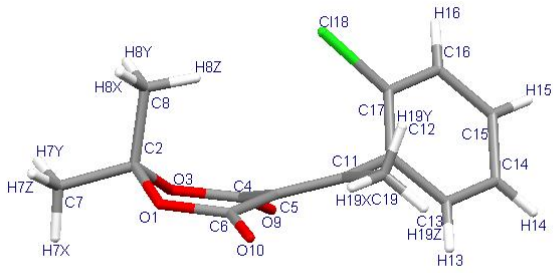
electrophilic centre in the olefin may explain the various enantioselectivities observed when the phenyl moiety is substituted at the *ortho*, *meta*, and *para* positions. This section addresses some of the possible factors influencing the observed enantioselectivities with discussions related to x-ray structures and NMR spectra of alkylidene Meldrum's acids.

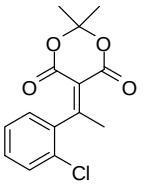
(1) *Ortho*- Substitution

1-Arylalkylidenes substituted at the ortho position were subjected to optimized 1,4-addition reaction but resulted in recovery of starting material after 48 h, regardless of the electronic nature of the substituent (Scheme 2.5). At room temperature, substrates with a methyl, benzyloxy, or chloro groups in the *ortho* position all exhibited two well separated singlets in the ^{1}H NMR spectrum corresponding to the methyl groups on the Meldrum's acid moiety. This suggests that these molecules have hindered rotation about the aryl-alkene C-C bond, and exist as racemic atropoisomers.[23] X-ray analysis of 2-chloro and 2-methoxy substituted alkylidene Meldrum's acids (**2.71** and **2.148**) show both the boat conformation of the Meldrum's acid moiety and the absence of conjugation of the aryl moiety with the olefin acceptor (Figure 2.5).

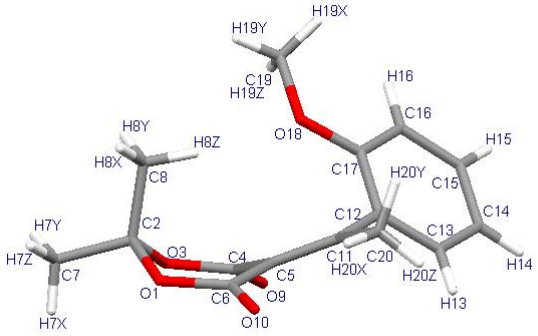
It was speculated that the close proximity of the aromatic substituent to the olefin electrophilic carbon likely blocks the delivery of the alkyl group. Due to the significantly smaller size of fluorine versus other halogens, carbon or oxygen substituents, 1-(2-fluorophenyl)-5-ethylidene Meldrum's acid **2.149** was synthesized. This substrate is distinguished from the other *ortho* substituted 1-phenylethylidenes in that the atropiosomers slowly interconvert at room temperature as depicted by the broad singlet of the corresponding Meldrum's acid methyl groups. In addition to recovering some of the alkylidene Meldrum's acid in the optimized conjugate addition reaction, hydride addition to the alkylidene Meldrum's acid **2.149** was also observed (Scheme 2.10).[24] Therefore, intrinsic steric encumbrance of the substrate itself due to *ortho* substitution on the aromatic moiety blocks the ability of the alkyl group to be delivered.

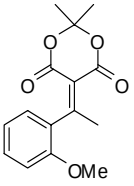
Figure 2.5: X-ray structures of **2.71** and **2.148**





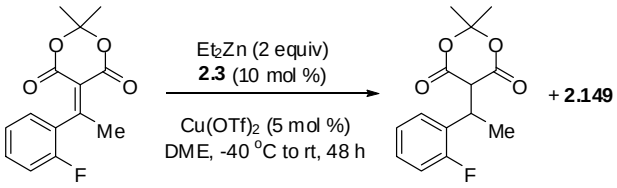
2.71





2.148

Scheme 2.10: Conjugate addition to alkylidene Meldrum's acid **2.149**



2.149 **2.150**

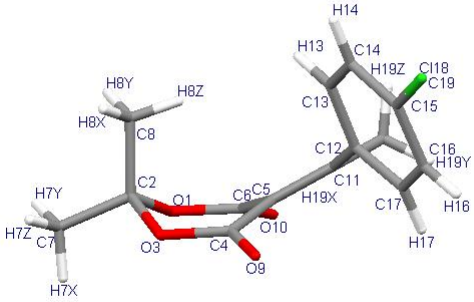
(2) *Para*- Substitution

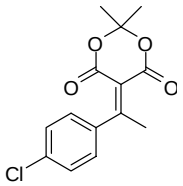
It was observed that any substituent at the *para*-position increases the enantioselectivity of the reaction regardless of the electronic nature of the substituent. The absence of any correlation between ^{13}C chemical shift of the electrophilic carbon of these 1-arylethylidenes **2.4** and observed enantioselectivities also suggests that electronic

factors are not significant. For example, electron-withdrawing *para*-chlorophenylethylidene **2.34**, electron-donating *para*-benzyloxyphenylethylidene **2.42**, and unsubstituted 5-(1-phenylethylidene) **2.1** gave 95, 93, and 84% ee, respectively, while the chemical shifts of the olefin acceptor attached to the aromatic ring are 173.3, 172.9, and 173.1 ppm, respectively. With these observations in hand, the influence of the electronic nature of the *para* substituent on the aromatic moiety and the observed enantiomeric excess can be discounted.

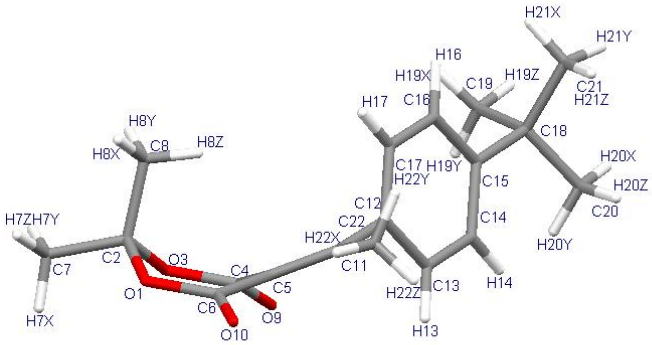
Crystallographic data for an electron-withdrawing *para*-chloro and for sigma-donating *para tert*-butyl substrates **2.34** and **2.66** were obtained. The x-ray structures for both alkylidenes show the adoption of a boat conformation (Figure 2.6).

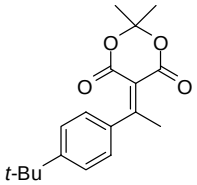
Figure 2.6: X-ray structures of **2.34** and **2.66**





2.34





2.66

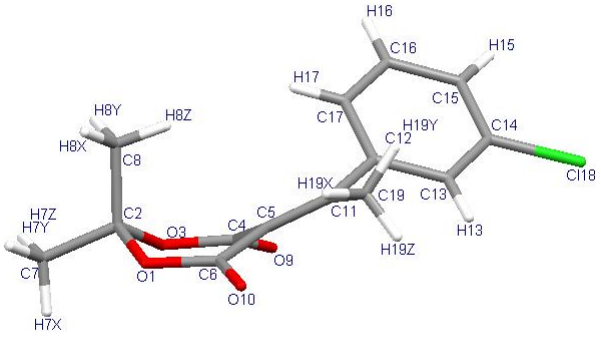
Consistent with the unsubstituted alkylidene **2.1**, the aryl group for electron-withdrawing *para* chloro substituted (**2.34)** and inductively-donating *para* *t*-butyl (**2.66**) groups show that the aromatic group is not in conjugation with the electron deficient olefin. Since the aryl moiety is not in conjugation with the electrophilic centre, reasons other than electronic components must be considered. Substituents at the *para*-position, regardless of their electronic nature, share one thing in common: they are larger in size than a hydrogen atom. The size of the substituent was postulated to have a positive impact on the enantioselection of the conjugate addition, despite the distance of the *para* position from the electrophilic centre. Supporting this argument is the increase in enantioselectivity as a function of the size of the groups within a class of substituents (Table 2.3). For example, with alkyl groups moving from a smaller Me to CF_3 to *i*-Pr to the largest *t*-Bu group, the ee increased from 89% to 92% to 98% to 99%, respectively; a similar trend was observed between the trialkylsilyl OTIPS and larger OTBDMS (94% to 96% ee). Interestingly, the silicon analogue of *t*-Bu, TMS, gave inferior ee to *t*-Bu presumably due to the longer C-Si bond.[25]

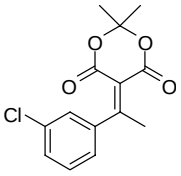
(3) *Meta*- Substitution

Substituents at the position *meta* to the electrophilic centre was shown to have detrimental effects on the enantioselectivity for substituents such as methyl, benzyloxy, or chloro. Exceptionally high enantioselectivites were observed however when the meta position was substituted with large groups such as *i*-Pr and *t*-Bu (Table 2.4 entries 4-5).

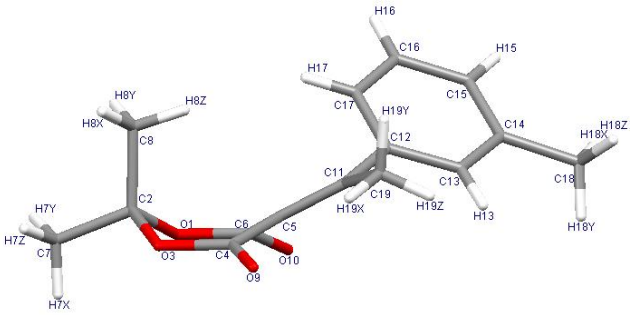
To gain further insight on rationalizing the enantioselectivity observed for *meta*-substituted alkylidenes, crystallographic data for *meta* substituted alkylidenes chloro, methyl and *t*-Bu groups **2.75**, **2.77**, and **2.81** were obtained (Figure 2.7).

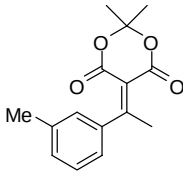
Figure 2.7: X-ray structures of **2.75**, **2.77**, and **2.81**



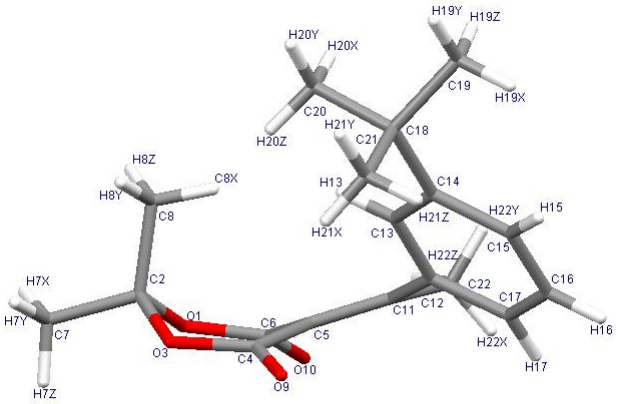


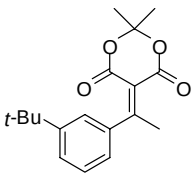
2.75





2.77





2.81

These crystal structures show features consistent with unsubstituted alkylidene **2.1**, in that all have boat conformations and non-conjugation of the aryl ring with the olefin. Interestingly, however, the 3-chloro and the 3-methyl substituted alkylidenes **2.75** and **2.77** which give similar enantioselectivity in the asymmetric conjugate addition reaction also show a similar "exo" conformation of the substituent relative to the olefin.[26] In contrast, 3-*t*-butyl substituted alkylidene **2.81**, which gives the quaternary benzylic stereocentre in excellent enantioselectivity has a different, "endo" conformation.

We postulated that the relative orientations in space of the meta substituents are playing a role in the enantiodetermining step. That is, an "exo" disposed group is detrimental to the ee while an "endo" oriented group is beneficial. This was validated experimentally by the reaction of Et_2Zn and 3,5-di-*t*-Bu alkylidene **2.91**, in which the "exo" orientation is filled. Not surprisingly, the product formed in low conversion and ee (Table 2.4, entry 10).

In a similar manner, the difference in selectivities between chlorinated indenylidenes **2.112** and **2.114**, wherein the Cl group in each is meta to the electrophilic carbon but is of fixed relative orientation due to the attachment via a fused ring, is interesting. In **2.112** the chlorine occupies the "endo" position and the ee increases versus the unsubstituted indenylidene **2.105**; this contrasts with **2.114**, where the chlorine is "exo", which provides a substantial decrease in enantioselectivity. It should be noted that while some trends between alkylidene and indenylidene Meldrum's acids may be shared, their differing rotational flexibilities makes a direct comparison inexact. For example, the reaction of bis-*meta* dichloro- substituted indenylidene **2.116** gives addition product in high enantioselectivity while, as mentioned, bis-*meta* dichloro-substituted alkylidene **2.87** is significantly less selective than **2.75** (Table 2.6, entries 6-8 and Table 2.4, entries 2, 8).

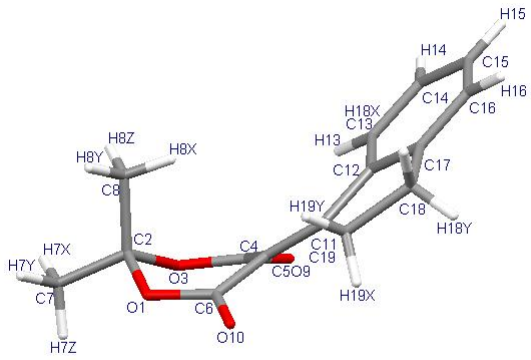
(4) Indenylidene Meldrum's acids

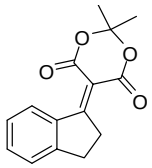
Indanes were obtained in high yields and enantioselectivities from the conjugate addition to indenylidene Meldrum's acids. Apart from substituting the 4-position of the indenylidene substrates, substituents at the 5 or 6-position relative to the olefin acceptor displayed superior enantioselectivities than alkylidene Meldrum's acids. Consequently,

we obtained x-ray structures of indenylidene Meldrum's acids to gain further insight of these different acceptors.

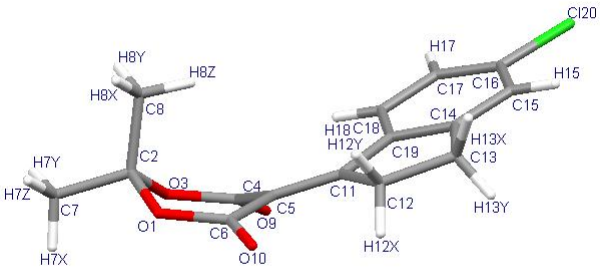
Two important features of indenylidene Meldrum's acids were noted by obtaining x-ray structures of **2.105**, **2.107**, **2.112**, and **2.114** (Figure 2.8).

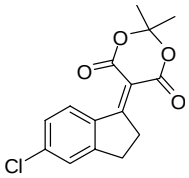
Figure 2.8: X-ray structures of **2.105**, **2.107**, **2.112**, and **2.114**



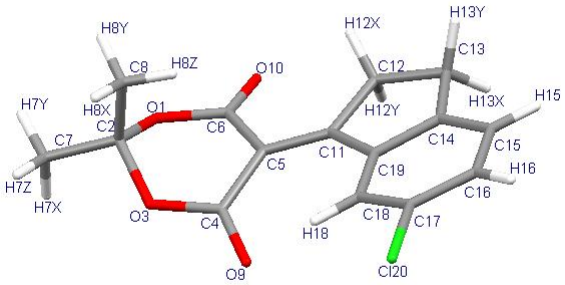


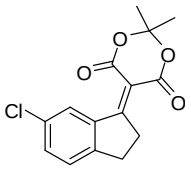
2.105



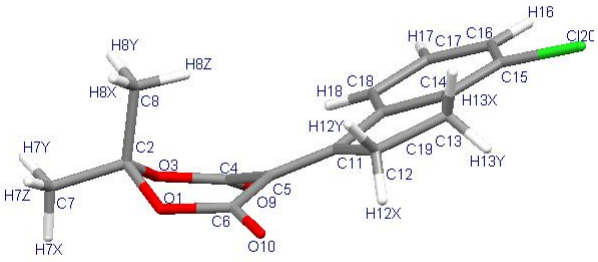


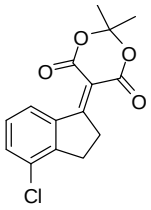
2.107





2.112



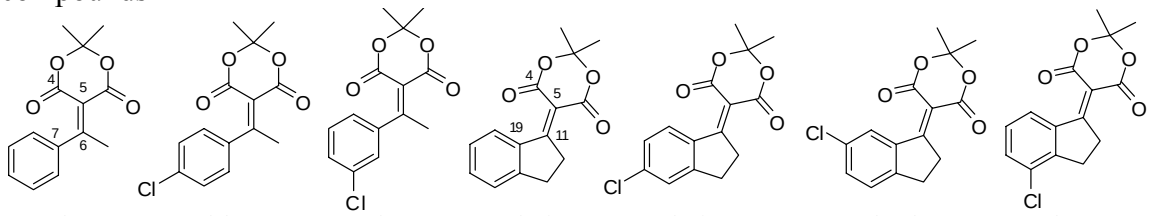


2.114

There is significant elongation of the C=C bond length of the indenylidene Meldrum's acids versus the C=C bond lengths of the alkylidene Meldrum's acids (Table 2.11). Furthermore, examination of the cis-substituents around the olefin acceptor shows the out-of-plane arrangement of these groups as demonstrated by measuring the C4–C5–C11–C19 (indenylidenes) and C4–C5–C11–C12 (alkylidenes) dihedral angles. The dihedral angle for the indenylidene Meldrum's acids are greater than the analogous alkylidene Meldrum's acids with differences as high as 4.6°. The only exception to this observation was 4-chloro substituted indenylidene derivative **2.114** having much lower dihedral angle than all the x-ray structures in this series, due to hydrogen bonding between H12X and O10. The combination of single bond character attributable to the olefin bond length and the higher dihedral angle of indenylidene Meldrum's acids may be

contributing factors for the observation of high enantioselectivities in the conjugate addition in comparison to alkylidene Meldrum's acids. Furthermore, 4-chloro indenylidene Meldrum acid **2.114** possessing the lowest dihedral angle in this series also demonstrates the lowest enantioselectivity in the conjugate addition reaction.

Table 2.11: Bond length and dihedral angle data for selected x-rays structures of selected compounds



2.1 **2.34** **2.75** **2.105** **2.107** **2.112** **2.114**

Entry	Compound	C=C Bond length (Å)	Dihedral Angle (°)
1	**2.1**	1.343	10.8[a]
2	**2.34**	1.344	10.0[a]
3	**2.75**	1.345	10.9[a]
4	**2.105**	1.367	15.4[b]
5	**2.107**	1.364	14.0[b]
6	**2.112**	1.367	13.1[b]
7	**2.114**	1.361	5.4[b]

[a] C4–C5–C11–C12; [b]C4–C5–C11–C19

(C) Summary

The scope and limitations of the asymmetric synthesis of benzylic quaternary stereocentres via copper-catalyzed 1,4-addition of dialkylzinc reagents to alkylidene and indenylidene Meldrum's acids has been studied. The reaction is tolerant of a wide range of heteroaromatic and functional groups. The significance of substituting the position para, meta, and ortho to the electrophilic centre was also highlighted. Substituting the ortho position leads to recovery of conjugate addition precursor while substituting the para position leads to increased enantioselectivities. Small substituents at the meta position yield lower ee while large groups provide a substantial increase in facial selectivity. Steric interactions rather than electronic factors related to the substituents on the aryl group likely cause the observation of reactivity and enantioselectivity differences

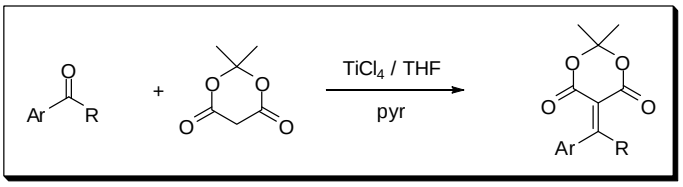
in the asymmetric conjugate addition of organozinc reagents to alkylidene Meldrum's acids. It was also shown that primary and secondary organozinc reagents are compatible with good to excellent results.

(D) Experimental Section

(I) General Methods

All reactions were carried out in flame-dried glassware under a dry argon atmosphere. 1,2-Dimethoxyethane was distilled from sodium-benzophenone ketyl under nitrogen and degassed via the freeze-pump-thaw method. All copper sources were obtained from commercial sources and used without further purification. $(Alkyl)_2Zn$ reagents were also obtained from commercial sources and used without further purification. Chiral phosphoramidite ligand can be obtained from commercial sources or prepared following a literature procedure.[27] ^1H NMR spectra were referenced to residual ^1H shift in $CDCl_3$ (7.24 ppm). $CDCl_3$ (77.0 ppm) was used as the internal reference for ^{13}C NMR spectra. Flash chromatography was performed using 230-400 mesh silica gel unless indicated otherwise. Optical rotations were recorded in cells with 1 dm path length. Chiral HPLC analyses were performed using a Chiralcel OD, OD-H, OJ-H or AD-H column. All columns are 250 x 4.6 mm. High resolution mass spectra were run at the University of Waterloo with a source temperature of 200 °C, mass resolution of 9000, and electron energy of 70 eV. The late Dr. Nicholas J. Taylor, University of Waterloo, is gratefully acknowledged for X-ray structures determinations.

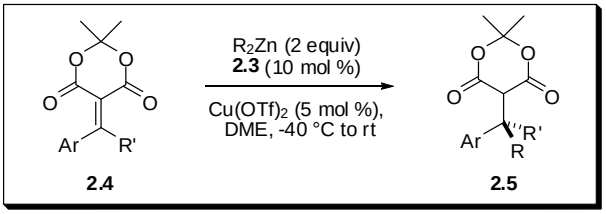
(II) General Procedure A: Preparation of Alkylidene Meldrum's Acids



Alkylidene Meldrum's acids were prepared by the Knoevenagel condensation of Meldrum's acid with ketones using Brown and coworkers' method.[2] In a typical reaction, a solution of $TiCl_4$ (2.1 equiv) in CH_2Cl_2 (3 M) was added dropwise under nitrogen to dry THF (0.3 M), which was cooled at 0 ºC, resulting in a yellow suspension. A solution containing the ketone (1.0 equiv) and Meldrum's acid (1.0 equiv) in dry THF (0.7 M) was added dropwise via a syringe to the $TiCl_4$•THF complex. The flask containing the solution of ketone and Meldrum's acid was rinsed with THF (2X) and added to the

reaction mixture. Subsequently, pyridine (5.0 equiv) was added to the reaction mixture dropwise at 0 ºC. The reaction was allowed to warm up slowly to room temperature and stirred until completion of reaction or for 24 h. The reaction was quenched by the addition of water and diluted with either Et_2O or EtOAc. After the solid was dissolved, the layers were partitioned. The aqueous layer was extracted was Et_2O or EtOAc (2X), and the combined organic layers were washed with $NaHCO_3$ saturated solution (2X), brine (1X), dried over $MgSO_4$, filtered and concentrated. Purification by either crystallization/trituration and/or flash chromatography provided the alkylidene Meldrum's acids.

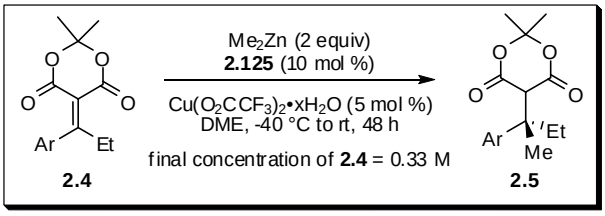
(III) General Procedure B: 1,4-Addition of $(alkyl)_2Zn$ to Alkylidene Meldrum's Acids



Reactions were typically carried out using 0.12 mmol of substrate. In a glove box, copper source (5 mol %) and phosphoramidite chiral ligand (10 mol %) were charged in a flame-dried resealable Schlenk tube. DME (0.5 mL) was then added to the Schlenk tube to wash down any residual solids to the bottom. The reaction mixture was allowed to stir at ambient temperature for 30 minutes, outside the glove box, and then cooled to -40 ºC. In the dry box, $(alkyl)_2Zn$ solution (2.0 equiv) was transferred to a round-bottom flask equipped with a septum. This solution was added to the Schlenk tube dropwise via a syringe and the resulting solution was stirred for 5 min. A solution of alkylidene Meldrum's acid (1.0 equiv) in DME (0.5 mL) was then added dropwise via a syringe. Finally, DME (0.2 mL) was added to wash down the remaining solid on the sides of the Schlenk tube. The reaction mixture was allowed to warm up slowly to room temperature. After stirring for 48 h, the reaction mixture was cooled to 0 ºC, 5% HCl and EtOAc were added to the reaction mixture. The layers were partitioned and the aqueous layer was extracted with EtOAc (3X). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude residue was purified by

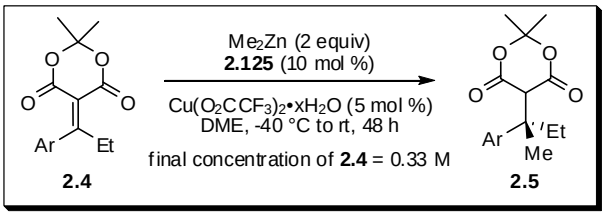
flash column chromatography on silica gel using hexanes in EtOAc to yield the desired product. HPLC using a chiral column OD-H or AD-H was used to measure the enantiomeric ratio of the products.

(IV) General Procedure C: 1,4-Addition of Me_2Zn to Alkylidene Meldrum's Acids



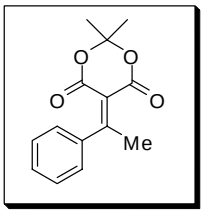
Reactions were typically carried out using 0.4 mmol of substrate. In a glove box, copper source (5 mol %) and **2.125** (10 mol %) were charged in a flame-dried resealable Schlenk tube. DME (0.3 mL) was then added to the Schlenk tube to wash down any residual solids to the bottom. The reaction mixture was allowed to stir at ambient temperature for 30 minutes, outside the glove box, and then cooled -40 °C. In the dry box, Me_2Zn solution (2.0 equiv) was transferred to a round-bottom flask equipped with a septum. This solution was added to the Schlenk tube dropwise via a syringe and the resulting solution stirred for 5 min. A solution of alkylidene Meldrum's acid (1.0 equiv) in DME (0.3 mL) was then added dropwise via a syringe. Finally, DME (0.2 mL) was added to wash down the remaining solid on the sides of the Schlenk tube. The reaction mixture was allowed to warm up slowly to room temperature. After stirring for 48 h, the reaction mixture was cooled to 0 ºC, 5% HCl and EtOAc were added to the reaction mixture. The layers were partitioned and the aqueous layer was extracted with EtOAc (3X). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude residue was purified by flash column chromatography on silica gel using hexanes in EtOAc to yield the desired product. HPLC using a chiral column OD-H or AD-H was used to measure the enantiomeric ratio of the products.

(V) General Procedure D: "Reverse" 1,4-Addition of Me_2Zn to Alkylidene Meldrum's Acids

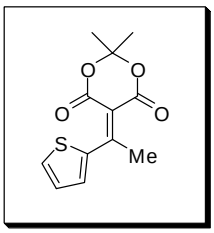


Reactions were typically carried out using 0.4 mmol of substrate. In a glove box, copper source (5 mol %) and **2.125** chiral ligand (10 mol %) were charged in a flame-dried flask equipped with a stir bar. DME (0.4 mL) was then added to the Schlenk tube to wash down any residual solids to the bottom. The reaction mixture was allowed to stir at ambient temperature for 30 minutes, outside the glove box, and then cooled to -40 °C. In the dry box, Me_2Zn solution (2.0 equiv) was transferred to a round-bottom flask equipped with a septum. Me_2Zn solution was added to the reaction mixture at -40 °C. After stirring for 5 minutes, the resulting mixture was added to a -40 °C, pre-cooled Schlenk tube charged with alkylidene Meldrum's acid (1.0 equiv) in DME (0.2 mL) dropwise via a syringe. DME (0.2 mL) was used to wash the flask and transfer remaining residue into the Schlenk tube. The reaction mixture was allowed to warm up slowly to room temperature. After stirring for 48 h, the reaction mixture was cooled to 0 °C, 5% HCl and EtOAc were added to the reaction mixture. The layers were partitioned and the aqueous layer was extracted with EtOAc (3X). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude residue was purified by flash column chromatography on silica gel using hexanes in EtOAc to yield the desired product. HPLC using a chiral column OD-H or AD-H was used to measure the enantiomeric ratio of the products.

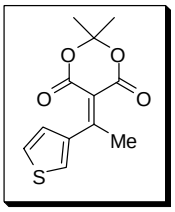
(IV) Substrate Specific Information



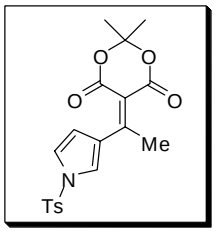
2,2-Dimethyl-5-(1-phenylethylidene)-1,3-dioxane-4,6-dione (2.1):[2] Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 49% yield. M.p. 107-109 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40-7.38 (m, 3H), 7.19-7.15 (m, 2H), 2.71 (s, 3H), 1.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.1, 161.1, 160.2, 141.7, 129.4, 128.4, 125.8, 116.8, 103.8, 27.3, 26.2; HRMS(EI) *m/z* calc'd for $C_{14}H_{14}O_4$ (M^+): 246.0892. Found: 246.0898.



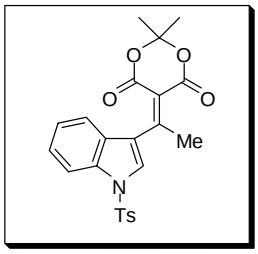
2,2-Dimethyl-5-(1-(thiophen-2-yl)ethylidene)-1,3-dioxane-4,6-dione (2.15): Prepared according to general procedure A. Recrystallization from MeOH afforded a dark yellow solid in 43% yield. M.p. 78-81 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.58 (d, J = 5.0 Hz, 1H), 7.45 (d, J = 3.7 Hz, 1H), 7.09 (t, J = 4.4 Hz, 1H), 2.80 (s, 3H), 1.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.1, 161.3, 161.1, 141.7, 131.5, 131.3, 127.9, 115.2, 103.8, 27.2, 26.3; HRMS(EI) *m/z* calc'd for $C_{12}H_{12}O_4S$ (M^+): 252.0456. Found: 252.0464.



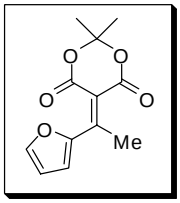
2,2-Dimethyl-5-(1-(thiophen-3-yl)ethylidene)-1,3-dioxane-4,6-dione (2.17): Prepared according to general procedure A. Recrystallization from MeOH afforded a dark beige solid in 59% yield. M.p. 117-118 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49-7.48 (m, 1H), 7.30 (dd, J = 5.1, 3.0 Hz, 1H), 7.02 (dd, J = 5.1, 1.0 Hz, 1H), 2.71 (s, 3H), 1.79 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.8, 161.3, 160.8, 141.1, 127.3, 126.9, 125.7, 115.8, 103.7, 27.2, 25.7; HRMS(EI) *m/z* calc'd for $C_{12}H_{12}O_4S$ (M^+): 252.0456. Found: 252.0449.



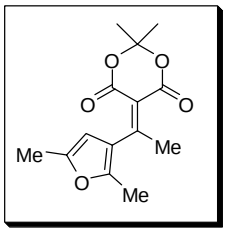
2,2-Dimethyl-5-(1-(1-tosyl-*1H*-pyrrol-3-yl)ethylidene)-1,3-dioxane-4,6-dione (2.19): Prepared according to general procedure A. Recrystallization from MeOH afforded a dark yellow solid in 30% yield. M.p. 137-138 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.63 (t, *J* = 1.8 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.09 (t, *J* = 2.7 Hz, 1H), 6.40 (dd, *J* = 3.2, 1.6 Hz, 1H), 2.63 (s, 3H), 2.39 (s, 3H), 1.74 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.4, 161.5, 161.1, 145.8, 135.0, 130.3, 127.2, 123.9, 120.8, 114.5, 113.8, 103.6, 27.0, 24.6, 21.6; HRMS(EI) *m/z* calc'd for $C_{16}H_{13}NO_5S$ (M^+-acetone): 331.0514. Found: 331.0527.



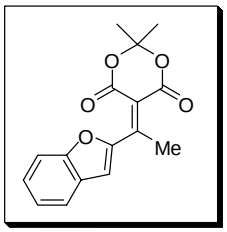
2,2-Dimethyl-5-(1-(1-tosyl-*1H*-indol-3-yl)ethylidene)-1,3-dioxane-4,6-dione (2.21): Prepared according to general procedure A. Purified using flash chromatography on Davisel (100-200 mesh, 60 Å) eluting with 3:1 hexanes/EtOAc, crystallized from MeOH and acetone affording a light yellow solid in 23% yield. M.p. 153-154 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.91 (d, *J* = 8.1 Hz, 1H), 7.82 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.37-7.28 (m, 3H), 7.24 (d, *J* = 7.5 Hz, 2H), 2.81 (s, 3H), 2.31 (s, 3H), 1.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.5, 161.2, 159.9, 145.5, 134.7, 134.5, 130.1, 127.9, 127.1, 127.0, 125.1, 123.8, 122.0, 120.4, 116.9, 113.9, 103.7, 27.3, 25.9, 21.6; HRMS(EI) *m/z* calc'd for $C_{23}H_{21}NO_6S$ (M^+): 439.1090. Found: 439.1090.



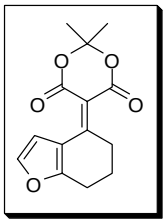
5-[1-(2-Furyl)ethylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.23): Prepared according to general procedure A. Recrystallization from MeOH afforded a yellow solid in 65% yield. M.p. 137-138 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.60 (d, *J* = 1.1 Hz, 1H), 7.27 (d, J = 3.6 Hz, 1H), 6.59-6.57 (m, 1H), 2.70 (s, 3H), 1.78 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.6, 161.0, 153.3, 151.6, 146.6, 120.1, 113.2, 112.7, 103.7, 26.9, 20.8; HRMS(EI) *m/z* calc'd for $C_{12}H_{12}O_5$ (M^+): 236.0685. Found: 236.0690.



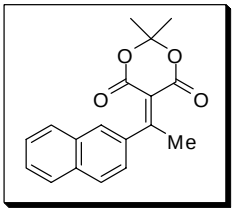
5-(1-(2,5-Dimethylfuran-3-yl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.25): Prepared according to general procedure A. Recrystallization from MeOH afforded a yellow solid in 69% yield. M.p. 121-122 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.87 (s, 1H), 2.62 (s, 3H), 2.23 (s, 6H), 1.75 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.4, 161.5, 160.4, 150.7, 122.7, 114.5, 106.6, 103.3, 27.2, 26.0, 14.3, 13.2; HRMS(EI) *m/z* calc'd for $C_{14}H_{16}O_5$ (M^+): 264.0998. Found: 264.0999.



5-(1-(Benzofuran-2-yl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.27): Prepared according to general procedure A. Recrystallization from MeOH afforded an orange solid in 43% yield. M.p. 132-134 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 0.7 Hz, 1H), 7.47 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.40 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.27 (dt, *J* = 7.3, 1.1 Hz, 1H), 2.80 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 160.7, 155.7, 153.7, 152.8, 127.9, 127.8, 123.8, 122.5, 115.7, 115.0, 111.8, 104.1, 27.1, 21.2; HRMS(EI) *m/z* calc'd for $C_{16}H_{14}O_5$ (M^+): 286.0841. Found: 286.0848.

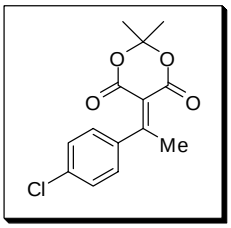


5-(6,7-Dihydrobenzofuran-4(5*H*)-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.29): Prepared according to general procedure A. Recrystallization from MeOH afforded a pink solid in 66% yield. M.p. 153-154 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.26 (d, *J* = 2.0 Hz, 1H), 6.83 (d, *J* = 1.7 Hz, 1H), 3.20 (t, *J* = 6.0 Hz, 2H), 2.80 (t, *J* = 6.4 Hz, 2H), 2.02 (quintet, *J* = 6.3 Hz, 2H), 1.71 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 162.7, 161.8, 141.6, 117.9, 110.0, 109.5, 103.3, 29.7, 26.8, 23.9, 22.3; HRMS(EI) *m/z* calc'd for $C_{14}H_{14}O_5$ (M^+): 262.0841. Found: 262.0839.

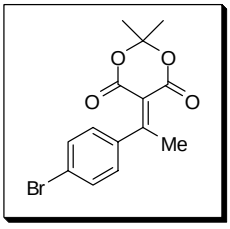


2,2-Dimethyl-5-[1-(2-naphthyl)ethylidene]-1,3-dioxane-4,6-dione (2.31): Prepared according to general procedure A. Recrystallization from MeOH afforded a yellow solid in 55% yield. M.p. 157-158 ºC

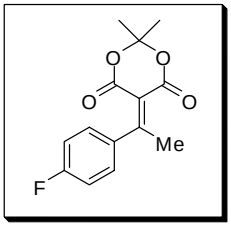
(MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.86-7.83 (m, 3H), 7.67 (s, 1H), 7.51 (t, *J* = 4.4 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 1H), 2.81 (s, 3H), 1.86 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.2, 161.2, 160.4, 139.2, 133.4, 132.7, 128.4, 128.1, 127.8, 127.1, 126.7, 125.4, 123.8, 116.9, 103.9, 27.4, 26.5; HRMS(EI) *m/z* calc'd for $C_{18}H_{16}O_4$ (M^+): 296.1049. Found: 296.1042.



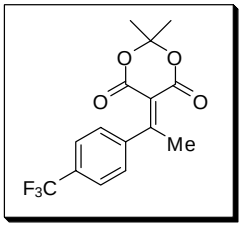
5-[1-(4-Chlorophenyl)ethylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.34): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 48% yield. M.p. 94-95 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 2.68 (s, 3H), 1.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.7, 161.9, 160.1, 140.0, 135.5, 128.8, 127.3, 117.2, 104.0, 27.4, 26.3; HRMS(EI) *m/z* calc'd for $C_{14}H_{13}{}^{35}ClO_4$ (M^+): 280.0502. Found: 280.0508.



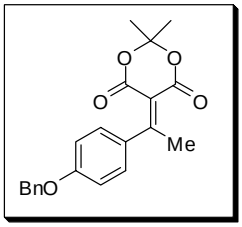
5-[1-(4-Bromophenyl)ethylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.36): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 62% yield. M.p. 111-113 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52 (d, *J* = 8.5 Hz, 2H), 7.04 (d, *J* = 8.5 Hz, 2H), 2.68 (s, 3H), 1.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.7, 160.9, 160.1, 140.5, 131.8, 127.5, 123.8, 117.2, 104.0, 27.4, 26.2; HRMS(EI) *m/z* calc'd for $C_{14}H_{13}{}^{79}BrO_4$ (M^+): 323.9998. Found: 323.9988.



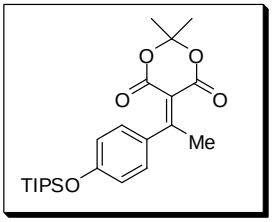
5-[1-(4-Fluorophenyl)ethylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.38): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 61% yield. M.p. 88-89 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.19-7.17 (m, 2H) 7.09-7.03 (m, 2H), 2.68 (s, 3H), 1.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.8, 162.0 (d, *J* = 248.5 Hz), 160.9, 160.2, 137.5 (d, *J* = 3.5 Hz), 128.1 (d, *J* = 8.5 Hz), 117.0, 115.6 (d, *J* = 21.9 Hz), 103.8, 27.3, 26.3; HRMS(EI) *m/z* calc'd for $C_{14}H_{13}FO_4$ (M^+): 264.0798. Found: 264.0790.



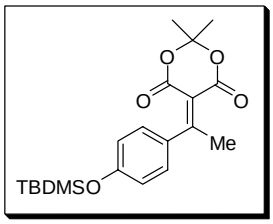
2,2-Dimethyl-5-1-[4-(trifluoromethyl)phenyl]ethylidene-1,3-dioxane-4,6-dione (2.40): Prepared according to general procedure A. Recrystallization from toluene afforded a beige solid in 15% yield. M.p. 113-114 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 2.74 (s, 3H), 1.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.3, 160.7, 159.8, 145.3 (d, *J* = 1.0 Hz), 130.9 (q, *J* = 32.6 Hz), 125.9, 125.6 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 270.7 Hz), 117.6, 104.1, 27.4, 26.2; HRMS(EI) *m/z* calc'd for $C_{14}H_{10}F_3O_4$ (M^+-CH_3): 299.0531. Found: 299.0534.



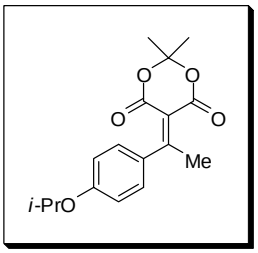
5-1-[4-(Benzyloxy)phenyl)]ethylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (2.42): Prepared according to general procedure A. Recrystallization from toluene afforded a light yellow solid in 31% yield. M.p. 173-174 ºC (toluene); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43-7.32 (m, 5H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.98 (d, *J* = 8.6 Hz, 2H), 5.07 (s, 2H), 2.72 (s, 3H), 1.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.9, 161.3, 160.9, 160.4, 136.3, 133.9, 128.6 (2C), 128.2, 127.5, 115.6, 114.7, 103.6, 70.1, 27.3, 26.1; HRMS(EI) *m/z* calc'd for $C_{21}H_{20}O_5$ (M^+): 352.1311. Found: 352.1318.



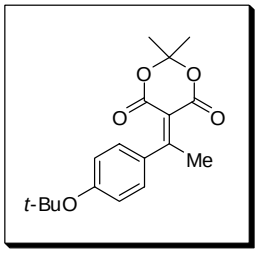
2,2-Dimethyl-5-(1-(4-(triisopropylsilyloxy)phenyl)ethylidene)-1,3-dioxane-4,6-dione (2.44): Prepared according to general procedure A. Purified using flash chromatography on Davisel (100-200 mesh, 60 Å) eluting with 9:1 hexanes/EtOAc, afforded a light yellow oil in 30% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.12 (d, *J* = 7.1 Hz, 2H), 6.86 (d, *J* = 6.9 Hz, 2H), 2.70 (s, 3H), 1.81 (s, 6H), 1.27 (septet, *J* = 7.3 Hz, 3H), 1.08 (d, *J* = 7.3 Hz, 18H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.1, 161.4, 160.9, 158.1, 134.0, 128.6, 119.8, 115.5, 103.5, 27.2, 26.0, 17.8, 12.6; HRMS(EI) *m/z* calc'd for $C_{23}H_{34}O_5Si$ (M^+): 418.2176. Found: 418.2178.



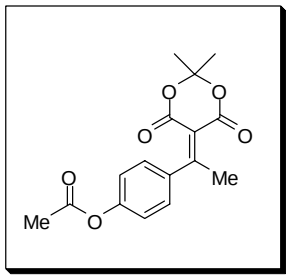
5-(1-(4-(*tert*-Butyldimethylsilyloxy)phenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.46): Prepared according to general procedure A. Purified using flash chromatography using a gradient on Davisel (100-200 mesh, 60 Å) eluting with 9:1, followed by 3:1 hexanes/EtOAc to afford a yellow oil. For an analytically pure sample, crystallization of the yellow oil in hexanes affords a light yellow solid in 33% yield. M.p. 76-78 ºC (hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.12 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 2.70 (s, 3H), 1.81 (s, 6H), 0.96 (s, 9H), 0.21 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.0, 161.4, 160.9, 157.6, 134.2, 128.5, 119.9, 115.6, 103.6, 27.3, 26.1, 25.5, 18.2, -4.4; HRMS(EI) *m/z* calc'd for $C_{20}H_{28}O_5Si$ (M^+): 376.1706. Found: 376.1715.



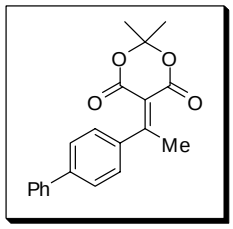
5-(1-(4-Isopropoxyphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.48): Prepared according to general procedure A. Recrystallization from MeOH afforded a bright yellow solid in 63% yield. M.p. 125-128 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.18 (d, *J* = 6.8 Hz, 2H), 6.86 (d, *J* = 6.8 Hz, 2H), 4.56 (septet, *J* = 6.1 Hz, 1H), 2.71 (s, 3H), 1.81 (s, 6H), 1.33 (d, *J* = 6.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.0, 161.4, 161.1, 159.8, 133.1, 128.8, 115.2, 103.6, 70.0, 27.3, 26.1, 21.9; HRMS(EI) *m/z* calc'd for $C_{17}H_{20}O_5$ (M^+): 304.1311. Found: 304.1308.



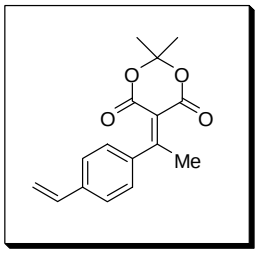
5-(1-(4-*tert*-Butoxyphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.50): Prepared according to general procedure A. Purified using flash chromatography using a gradient on Davisel (100-200 mesh, 60 Å) eluting with 5:1 then 3:1 hexanes/EtOAc affording a bright yellow oil in 43% yield. For an analytically pure sample, the yellow oil was crystallized in MeOH to afford a light yellow solid. M.p. 76-78 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.12 (d, *J* = 8.2, 2H), 6.96 (d, *J* = 8.2 Hz, 2H), 2.70 (s, 3H), 1.80 (s, 6H), 1.36 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.9, 161.3, 160.7, 157.4, 135.7, 127.7, 122.9, 115.9, 103.6, 79.2, 28.8, 27.3, 26.1; HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_5$ (M^+): 318.1467. Found: 318.1476.



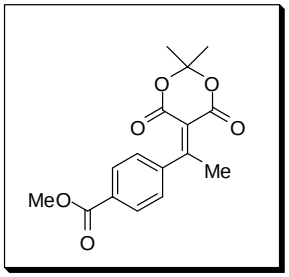
4-(1-(2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)ethyl) phenyl acetate (2.52): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 68% yield. M.p. 144-145 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.19 (d, *J* = 8.7 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 2.68 (s, 3H), 2.27 (s, 3H), 1.79 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.0, 168.9, 161.0, 160.2, 151.3, 138.8, 127.3, 121.6, 116.9, 103.8, 27.2, 26.2, 21.1; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_6$ (M^+): 304.0947. Found: 304.0943.



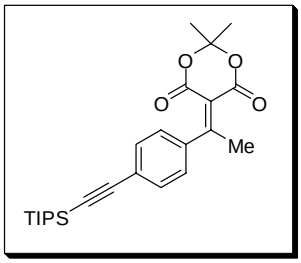
2,2-Dimethyl-5-[1-(4-phenylphenyl)ethylidene]-1,3-dioxane-4,6-dione (2.54): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 93% yield. M.p. 118-120 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.67-7.62 (m, 4H), 7.50-7.45 (m, 2H), 7.41 (d, *J* = 7.2 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 2.80 (s, 3H), 1.88 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.7, 161.1, 160.4, 142.4, 140.4, 140.0, 128.8, 127.7, 127.1, 127.0, 126.7, 116.6, 103.8, 27.3, 26.2; HRMS(EI) *m/z* calc'd for $C_{20}H_{18}O_4$ (M^+): 322.1205. Found: 322.1210.



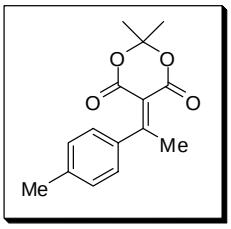
2,2-Dimethyl-5-(1-(4-vinylphenyl)ethylidene)-1,3-dioxane-4,6-dione (2.56): Prepared according to general procedure A. Recrystallization from MeOH afforded a dark beige solid in 29% yield. M.p. 108-110 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 6.70 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.78 (d, *J* = 17.6 Hz, 1H), 5.28 (d, *J* = 10.9 Hz, 1H), 2.70 (s, 3H), 1.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.7, 161.1, 160.4, 140.9, 138.8, 135.9, 126.4, 126.2, 116.5, 115.4, 103.8, 27.3, 26.0; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_4$ (M^+): 272.1049. Found: 272.1053.



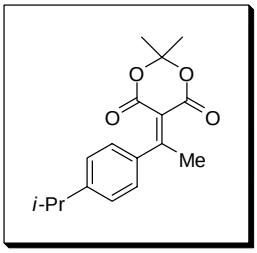
Methyl 4-(1-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)ethyl)benzoate (2.58): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 60% yield. M.p. 136-137 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.03 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 8.3 Hz, 2H), 3.87 (s, 3H), 2.66 (s, 3H), 1.78 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.8, 166.1, 160.7, 159.8, 146.1, 130.4, 129.7, 125.5, 117.2, 104.0, 52.1, 27.2, 26.0; HRMS(EI) *m/z* calc'd for $C_{15}H_{13}O_6$ (M^+-CH_3): 289.0712. Found: 289.0717.



2,2-Dimethyl-5-(1-(4-((triisopropylsilyl)ethynyl)phenyl) ethylidene)-1,3-dioxane-4,6-dione (2.60): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 62% yield. M.p. 118-119 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 2.69 (s, 3H), 1.81 (s, 6H), 1.11 (s, 21H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.3, 161.0, 160.2, 141.4, 132.1, 125.9, 124.8, 116.9, 106.2, 103.9, 92.8, 27.4, 26.1, 18.6, 11.2; HRMS(EI) *m/z* calc'd for $C_{25}H_{34}O_4Si$ (M^+): 426.2226. Found: 426.2215.

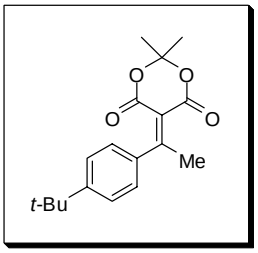


2,2-Dimethyl-5-[1-(4-methylphenyl)ethylidene]-1,3-dioxane-4,6-dione (2.62): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 47% yield. M.p. 103-104 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.20 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 2.70 (s, 3H), 2.37 (s, 3H), 1.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.3, 161.2, 160.5, 139.9, 138.7, 129.1, 126.1, 116.3, 103.7, 27.3, 26.1, 21.3; HRMS(EI) *m/z* calc'd for $C_{15}H_{16}O_4$ (M^+): 260.1049. Found: 260.1039.

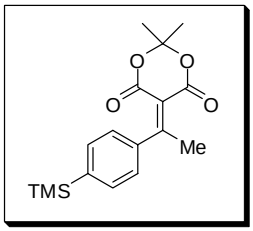


5-(1-(4-Isopropylphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.64): Prepared according to general procedure A. Recrystallization from MeOH afforded an off-white solid in 51% yield. M.p. 121-123 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ

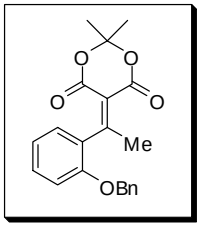
7.24 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 2.92 (septet, *J* = 6.9 Hz, 1H), 2.71 (s, 3H), 1.82 (s, 6H), 1.24 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.3, 161.3, 160.7, 150.7, 139.0, 126.6, 126.4, 116.3, 103.8, 33.9, 27.3, 26.2, 23.7; HRMS(EI) *m/z* calc'd for $C_{17}H_{20}O_4$ (M^+): 288.1362. Found: 288.1360.



5-(1-(4-*tert*-Butylphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.66): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 56% yield. M.p. 150-151 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 2.71 (s, 3H), 1.82 (s, 6H), 1.31 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.2, 161.3, 160.6, 153.0, 138.6, 126.2, 125.4, 116.4, 103.7, 34.8, 31.1, 27.3, 26.2; HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_4$ (M^+): 302.1518. Found: 302.1521.

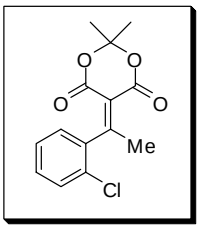


2,2-Dimethyl-5-(1-(4-(trimethylsilyl)phenyl)ethylidene)-1,3-dioxane-4,6-dione (2.68): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 38% yield. M.p. 108-111 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 2.70 (s, 3H), 1.82 (s, 6H), 0.26 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.2, 161.2, 160.4, 142.4, 141.9, 133.3, 125.1, 116.7, 103.8, 27.3, 26.2, -1.3; HRMS(EI) *m/z* calc'd for $C_{16}H_{19}O_4Si$ (M^+): 303.1053. Found: 303.1063.

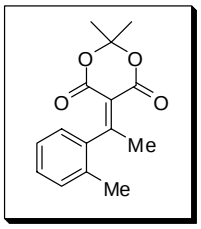


5-1-[2-(Benzyloxy)phenyl)]ethylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (2.70): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 38% yield. M.p. 125-126 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.58-7.27 (m, 6H), 7.10-7.00 (m, 2H), 6.94 (d, *J* = 8.3 Hz, 1H), 5.05 (AB d, *J* = 11.9 Hz, 1H), 5.02 (AB d, *J* = 12.0 Hz, 1H), 2.66 (s, 3H), 1.64 (s, 3H), 1.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.8, 161.4, 160.1, 152.8, 136.3, 131.1, 129.9, 128.6, 128.2, 127.6, 127.1,

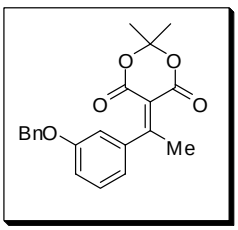
121.0, 118.1, 112.3, 103.9, 70.5, 27.3, 26.3, 26.1; HRMS(EI) *m/z* calc'd for $C_{21}H_{20}O_5$ (M^+): 352.1311. Found: 352.1305.



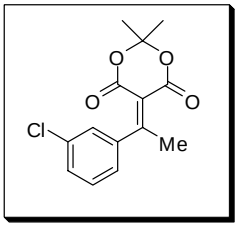
5-[1-(2-Chlorophenyl)ethylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.71): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 32% yield. M.p. 117-118 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43-7.28 (m, 3H), 7.14-7.11 (m, 1H), 2.69 (s, 3H), 1.85 (s, 3H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.7, 160.8, 159.2, 140.5, 129.6, 129.4, 128.4, 126.8, 126.7, 118.3, 104.1, 27.4, 25.7; HRMS(EI) *m/z* calc'd for $C_{13}H_{10}{}^{35}ClO_4$ (M^+-CH_3): 265.0268. Found: 265.0261.



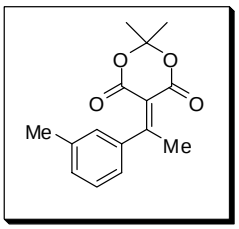
2,2-Dimethyl-5-[1-(2-methylphenyl)ethylidene]-1,3-dioxane-4,6-dione (2.72): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 41% yield. M.p. 122-123 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29-7.19 (m, 3H), 6.86 (d, *J* = 7.0 Hz, 1H), 2.67 (s, 3H), 2.24 (s, 3H), 1.81 (s, 3H), 1.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.0, 161.1, 159.2, 141.8, 132.4, 130.2, 128.1, 125.8, 123.5, 117.5, 103.8, 27.5, 27.2, 26.3, 19.3; HRMS(EI) *m/z* calc'd for $C_{15}H_{16}O_4$ (M^+): 260.1049. Found: 260.1042.



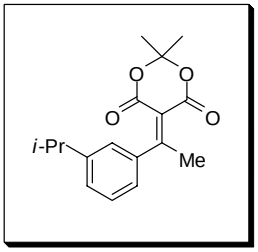
5-1-[3-(Benzyloxy)phenyl)]ethylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (2.73): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 54% yield. M.p. 72-73 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43-7.28 (m, 6H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 2H), 5.05 (s, 2H), 2.68 (s, 3H), 1.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.6, 161.1, 160.1, 158.7, 143.1, 136.5, 129.7, 128.6, 128.0, 127.5, 118.2, 117.0, 115.1, 112.8, 103.8, 70.1, 27.3, 26.1; HRMS(EI) *m/z* calc'd for $C_{21}H_{20}O_5$ (M^+): 352.1311. Found: 352.1317.



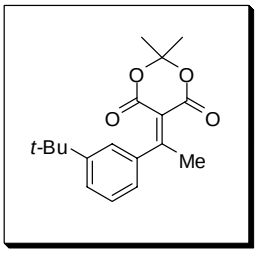
5-[1-(3-Chlorophenyl)ethylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.75): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 21% yield. M.p. 82-84 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36-7.29 (m, 2H), 7.12 (s, 1H), 7.02 (d, *J* = 6.8 Hz, 1H), 2.67 (s, 3H), 1.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.1, 160.8, 159.8, 143.3, 134.4, 129.8, 129.2, 125.6, 123.9, 117.4, 104.0, 27.4, 26.2; HRMS(EI) *m/z* calc'd for $C_{14}H_{13}{}^{35}ClO_4$ (M^+): 280.0502. Found: 280.0508.



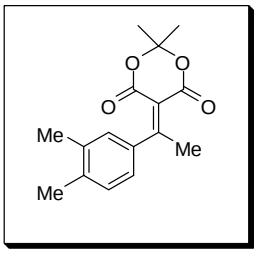
2,2-Dimethyl-5-[1-(3-methylphenyl)ethylidene]-1,3-dioxane-4,6-dione (2.77): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 68% yield. M.p. 119-120 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28 (d, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 2.69 (s, 3H), 2.36 (s, 3H), 1.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.4, 161.2, 160.3, 141.8, 138.2, 130.2, 128.3, 126.3, 122.9, 116.7, 103.8, 27.3, 26.3, 21.4; HRMS(EI) *m/z* calc'd for $C_{15}H_{16}O_4$ (M^+): 260.1049. Found: 260.1057.



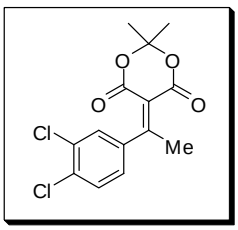
5-(1-(3-Isopropylphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.79): Prepared according to general procedure A. The crude red oil was first purified through a short column of Davisil 200-425, eluted with 10:1 petroleum ether: EtOAc. Recrystallization from MeOH (2X) afforded a pale yellow solid in 26% yield. M.p. 72-73 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33-7.27 (m, 2H), 7.02-6.98 (m, 2H), 2.91 (septet, *J* = 6.9 Hz, 1H), 2.71 (s, 3H), 1.82 (s, 6H), 1.25 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.3, 161.2, 160.2, 148.9, 141.6, 128.3, 127.6, 124.2, 123.4, 116.7, 103.7, 33.9, 27.3, 26.2, 23.7; HRMS(EI) *m/z* calc'd for $C_{17}H_{20}O_4$ (M^+): 288.1362. Found: 288.1365.



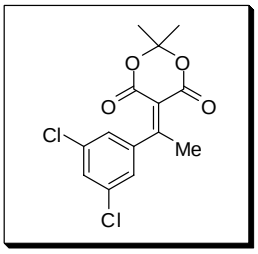
5-(1-(3-*tert*-Butylphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.81): Prepared according to general procedure A. Recrystallization from hexanes afforded a beige solid in 38% yield. M.p. 79-80 ºC (hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38 (d, *J* = 8.1 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.19 (s, 1H), 7.01 (d, *J* = 7.5 Hz, 1H), 2.72 (s, 3H), 1.83 (s, 6H), 1.31 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.6, 161.3, 160.4, 151.2, 141.3, 128.2, 126.7, 123.4, 123.2, 116.7, 103.7, 34.8, 31.2, 27.6, 27.3, 26.3; HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_4$ (M^+): 302.1518. Found: 302.1513.



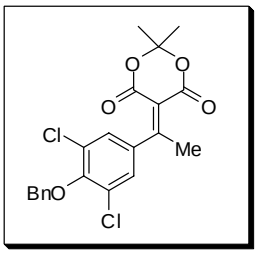
5-(1-(3,4-Dimethylphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.83): Prepared according to general procedure A. Recrystallization from MeOH afforded a yellow solid in 80% yield. M.p. 127-130 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.14 (d, *J* = 7.7 Hz, 1H), 6.97 (s, 1H) 6.93 (d, *J* = 7.7 Hz, 1H), 2.70 (s, 3H), 2.27 (s, 6H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.5, 161.3, 160.7, 139.2, 138.7, 136.8, 129.6, 127.3, 123.7, 116.1, 103.7, 27.3, 26.2, 19.9, 19.7; HRMS(EI) *m/z* calc'd for $C_{16}H_{18}O_4$ (M^+): 274.1205. Found: 274.1200.



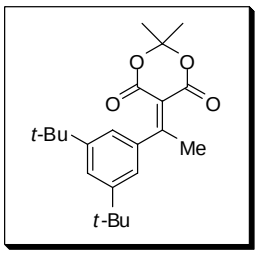
5-[1-(3,4-Dichlorophenyl)ethylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.85): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 29% yield. M.p. 119-120 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.46 (d, *J* = 8.3 Hz, 1H), 7.24 (d, J = 2.0 Hz, 1H), 6.99 (dd, *J* = 8.3, 2.0 Hz, 1H), 2.67 (s, 3H), 1.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.0, 160.7, 159.8, 141.3, 133.6, 132.9, 130.6, 127.6, 125.2, 117.6, 104.1, 27.4, 26.2; HRMS(EI) m/z calc'd for $C_{14}H_{12}{}^{35}Cl_2O_4$ (M^+): 314.0113. Found: 314.0116.



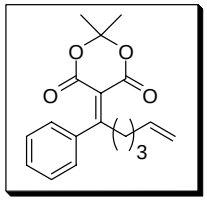
5-(1-(3,5-Dichlorophenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.87): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 40% yield. M.p. 140-142 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (s, 1H), 6.99 (d, *J* = 1.8 Hz, 2H), 2.66 (s, 3H), 1.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.5, 160.5, 159.5, 144.4, 135.3, 128.9, 123.9, 117.9, 104.2, 27.5, 26.2; HRMS(EI) *m/z* calc'd for $C_{14}H_{12}{}^{35}Cl_2O_4$ (M^+): 314.0113. Found: 314.0107.



5-(1-(4-(Benzyloxy)-3,5-dichlorophenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.89): Prepared according to general procedure A. Recrystallization from MeOH afforded an off-white solid in 50% yield. M.p. 136-137 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.54 (d, *J* = 7.4 Hz, 2H), 7.42-7.35 (m, 3H), 7.11 (s, 2H), 5.07 (s, 2H), 2.67 (s, 3H), 1.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.4, 160.6, 159.8, 151.7, 138.8, 136.0, 130.0, 128.5 (2C), 126.4, 117.7, 104.2, 75.2, 27.4, 26.2; HRMS(EI) *m/z* calc'd for $C_{18}H_{12}{}^{35}Cl_2O_4$ (M^+-acetone): 362.0113. Found: 362.0117.

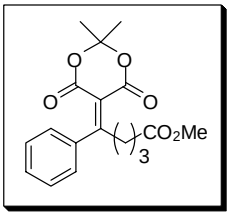


5-(1-(3,5-Di-*tert*-butylphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.91): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 46% yield. M.p. 121-123 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45 (s, 1H), 7.03 (d, *J* = 0.9 Hz, 2H), 2.72 (s, 3H), 1.83 (s, 6H), 1.31 (s, 18H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.0, 161.5, 160.5, 150.6, 140.6, 123.9, 120.8, 116.5, 103.6, 34.9, 31.3, 27.2, 26.2; HRMS(EI) *m/z* calc'd for $C_{24}H_{36}O_4$ (M^+): 358.2144. Found: 358.2131.

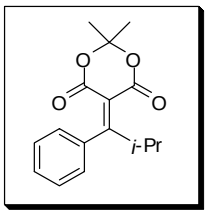


2,2-Dimethyl-5-(1-phenylhex-5-enylidene)-1,3-dioxane-4,6-dione (2.93): Prepared according to general procedure A. Purified using flash chromatography using a gradient on Davisel (100-200 mesh, 60 Å) eluting with 9:1 then 5:1 hexanes/EtOAc, afforded a white solid upon

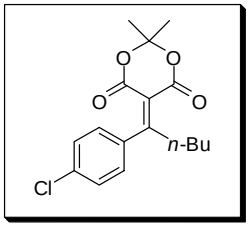
standing in 58% yield. M.p. 55-57 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40-7.38 (m, 3H), 7.16-7.13 (m, 2H), 5.69 (ddt, *J* = 16.9, 10.3, 6.6 Hz, 1H), 4.97-4.91 (m, 2H), 3.12 (t, *J* = 8.0 Hz, 2H), 2.06 (q, *J* = 7.1 Hz, 2H), 1.80 (s, 6H), 1.50 (quintet, *J* = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.5, 160.9, 160.2, 140.1, 137.3, 129.1, 128.2, 126.0, 117.2, 115.4, 103.7, 37.3, 33.6, 27.2 (2C); HRMS(EI) *m/z* calc'd for $C_{15}H_{14}O_3$ (M^+-acetone): 242.0943. Found: 242.0949.



Methyl 5-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-5-phenylpentanoate (2.95): Prepared according to general procedure A. Purified using flash chromatography using a gradient on Davisel (100-200 mesh, 60 Å) eluting with 5:1 then 3:1 hexanes/EtOAc, afforded a pasty white solid upon standing in 46% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40-7.38 (m, 3H), 7.17-7.14 (m, 2H), 3.61 (s, 3H), 3.15 (t, *J* = 7.9 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 1.80 (s, 6H), 1.75 (quintet, *J* = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.3, 173.0, 160.9, 160.2, 139.6, 129.4, 128.4, 126.2, 117.7, 103.9, 51.6, 36.8, 33.5, 27.3, 23.2; HRMS(EI) *m/z* calc'd for $C_{15}H_{14}O_5$ (M^+-acetone): 274.0841. Found: 274.0844.

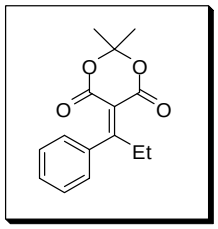


2,2-Dimethyl-5-(2-methyl-1-phenylpropylidene)-1,3-dioxane-4,6-dione (2.97): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 68% yield. M.p. 134-136 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.41-7.36 (m, 3H), 7.02-6.98 (m, 2H), 4.01 (septet, *J* = 6.8 Hz, 1H), 1.78 (s, 6H), 1.04 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.7, 160.7, 160.1, 136.7, 128.0, 127.8, 125.7, 118.0, 103.8, 32.6, 27.2, 20.5; HRMS(EI) *m/z* calc'd for $C_{16}H_{18}ClO_4$ (M^+): 259.0970. Found: 259.0962.

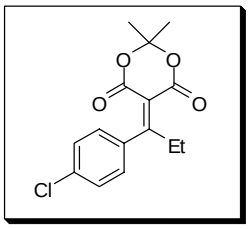


5-[1-(4-Chlorophenyl)pentylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.99): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 18% yield.

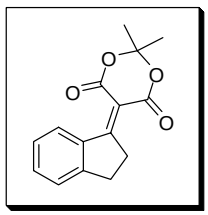
M.p. 121-122 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 3.09 (t, *J* = 7.0 Hz, 2H), 1.79 (s, 6H), 1.38-1.29 (m, 4H), 0.84 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.6, 160.8, 160.2, 138.6, 135.2, 128.7, 127.6, 117.5, 103.9, 37.7, 30.1, 27.3, 22.8, 13.6; HRMS(EI) *m/z* calc'd for $C_{17}H_{19}{}^{35}ClO_4$ (M^+): 322.0972. Found: 322.0981.



2,2-Dimethyl-5-(1-phenylpropylidene)-1,3-dioxane-4,6-dione (2.101): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 43% yield. M.p. 98-100 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40-7.38 (m, 3H), 7.15-7.13 (m, 2H), 3.12 (q, *J* = 7.4 Hz, 2H), 1.80 (s, 6H), 1.06 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.0, 160.9, 160.3, 140.0, 129.1, 128.3, 126.1, 116.8, 103.8, 31.3, 27.2, 12.3; HRMS(EI) *m/z* calc'd for $C_{15}H_{16}O_4$ (M^+): 260.1049. Found: 260.1040

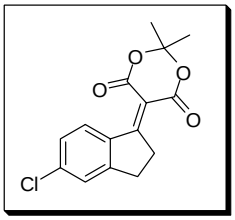


5-[1-(4-Chlorophenyl)propylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.102): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 15% yield. M.p. 120-122 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (d, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 3.07 (q, *J* =7.5 Hz, 2H), 1.78 (s, 6H), 1.05 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.6, 160.7, 160.1, 138.2, 135.2, 128.6, 127.6, 117.2, 103.9, 31.4, 27.3, 12.3; HRMS(EI) *m/z* calc'd for $C_{15}H_{15}{}^{35}ClO_4$ (M^+): 294.0659. Found: 294.0668.

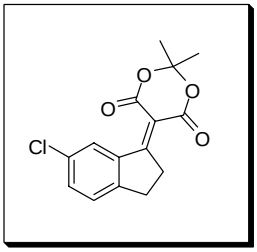


5-(2,3-Dihydro-1*H*-1-indenylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.105):[28] Prepared according to general procedure A. To avoid decomposition, the crude mixture was purified by quick flash chromatography over a short pad of Davisil 200-425; eluted with 8:1 hexanes:EtOAc to afford **2.105**. The residue was recrystallized from diethyl ether (3X) and finally from toluene to give white crystals. M.p. 107-108 ºC (toluene); ^{1}H NMR (acetone-d_6, 300 MHz) δ 8.67 (d, *J* = 8.3 Hz, 1H), 7.60-7.56 (m, 2H), 7.37 (d, *J* = 7.6 Hz,

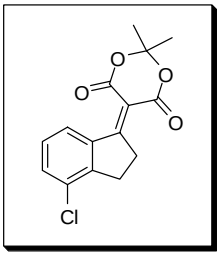
1H) 3.55 (t, *J* = 5.4 Hz, 2H), 3.17 (t, *J* = 5.3 Hz, 2H), 1.76 (s, 6H); ^{13}C NMR (acetone-d_6, 75 MHz) δ 177.5, 162.9, 161.7, 156.5, 138.0, 134.9, 130.3, 127.5, 126.6, 111.4, 104.2, 37.2, 31.0, 27.1; HRMS(EI) *m/z* calc'd for $C_{15}H_{14}O_4$ (M^+): 258.0892. Found: 258.0894.



5-(5-Chloro-2,3-dihydro-1H-1-indenylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.107): Prepared according to the described procedure for **2.105**. The purified material was filtered over kimwipes to ensure all silica particles have been separated. Final recrystallization from toluene afforded a beige solid in 6% yield. M.p. 109-110 ºC (MeOH); ^{1}H NMR (acetone-d_6, 300 MHz) δ 8.66 (d, *J* = 8.8 Hz, 1H), 7.58 (s, 1H), 7.38 (d, *J* = 8.8 Hz, 1H) 3.55 (t, *J* = 5.5 Hz, 2H), 3.17 (t, *J* = 5.3 Hz, 2H), 1.74 (s, 6H); ^{13}C NMR (acetone-d_6, 75 MHz) δ 175.8, 162.7, 161.6, 158.4, 140.4, 136.8, 131.7, 127.8, 126.4, 111.7, 104.3, 37.4, 30.8, 27.0; HRMS(EI) *m/z* calc'd for $C_{15}H_{13}{}^{35}ClO_4$ (M^+): 292.0502. Found: 292.0495.

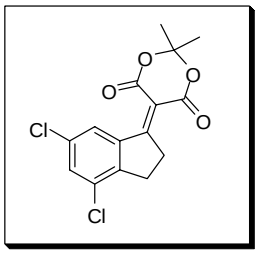


5-(6-Chloro-2,3-dihydro-*1H*-inden-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.112): Prepared according to general procedure A. Recrystallization from MeOH (2X), ether, then MeOH again afforded a dark brown solid in 10% yield. M.p. 127-130 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.67 (s, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 3.57 (t, *J* = 5.2 Hz, 2H), 3.08 (t, *J* = 5.2 Hz, 2H), 1.75 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.3, 162.3, 161.0, 153.6, 138.6, 134.3, 133.2, 129.4, 126.5, 110.8, 103.7, 37.1, 30.1, 27.2; HRMS(EI) *m/z* calc'd for $C_{15}H_{13}{}^{35}ClO_4$ (M^+): 292.0502. Found: 292.0500.

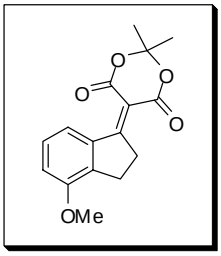


5-(4-Chloro-2,3-dihydro-*1H*-inden-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.114): Prepared according to general procedure A. Recrystallization from Et_2O (2X) afforded a light yellow solid in 15% yield. For an analytically pure sample, the product was further purified using flash column chromatography on Davisil 200-425 column eluting with 10:1 petroleum ether: EtOAc M.p. 143-144 ºC; ^{1}H NMR ($CDCl_3$,

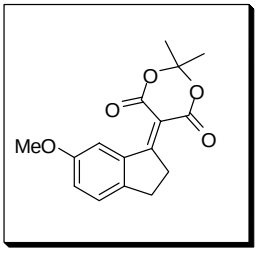
300 MHz) δ 8.58 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.26 (t, *J* = 7.9 Hz, 1H), 3.56 (t, *J* = 5.3 Hz, 2H), 3.11 (t, *J* = 5.3 Hz, 2H), 1.73 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.7, 162.2, 160.8, 152.8, 138.8, 133.6, 131.6, 128.5, 128.1, 111.0, 103.6, 36.1, 30.0, 27.1; HRMS(EI) *m/z* calc'd for $C_{15}H_{13}{}^{35}ClO_4$ (M^+): 292.0502. Found: 292.0509.



5-(4,6-Dichloro-2,3-dihydro-*1H*-inden-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.116): Prepared according to general procedure A. The crude product was first recrystallized in MeOH, the filtrate was collected, evaporated, and passed through a short Davisil 200-425 column eluted with 10:1 petroleum ether: EtOAc. Further recrystallization in MeOH and ether afforded the light pink solid in 40% yield. M.p. 138-141 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.61 (s, 1H), 7.49 (s, 1H), 3.57 (t, *J* = 5.2 Hz, 2H), 3.07 (t, *J* = 5.2 Hz, 2H), 1.74 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.0, 161.9, 160.6, 151.1, 139.5, 133.8, 133.2, 132.2, 127.8, 111.9, 103.9, 36.2, 29.6, 27.1; HRMS(EI) *m/z* calc'd for $C_{15}H_{12}{}^{35}Cl_2O_4$ (M^+): 326.0113. Found: 326.0117.

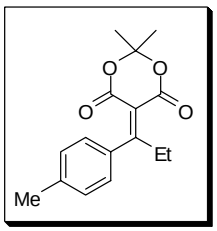


5-(4-Methoxy-2,3-dihydro-*1H*-inden-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.118): Prepared according to general procedure A. Purification using 5:1 hexanes/EtOAc on Davisel silica (100-200 mesh size) followed by recrystallization from MeOH afforded a light orange solid in 20% yield. M.p. 160-161 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.19 (d, *J* = 8.3 Hz, 1H), 7.28 (t, *J* = 8.1 Hz, 1H), 6.98 (d, *J* = 8.0 Hz, 1H), 3.87 (s, 3H), 3.56 (t, *J* = 5.0 Hz, 2H), 3.03 (t, *J* = 5.0 Hz, 2H), 1.75 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.7, 162.6, 161.3, 156.1, 144.7, 138.5, 128.4, 121.2, 114.4, 109.8, 103.5, 55.5, 36.9, 27.3, 27.1; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_5$ (M^+): 288.0998. Found: 288.1001.

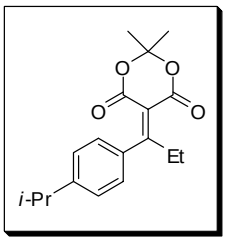


5-(6-Methoxy-2,3-dihydro-*1H*-inden-1-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.120): Prepared according to general procedure A. The crude product was dissolved in MeOH and filtrate was separated and discarded. The filtrate was collected,

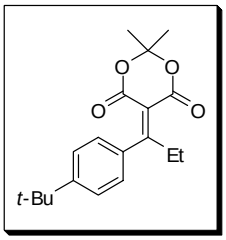
evaporated, and subjected to flash chromatography using Davisil 100-200 mesh size silica, eluting with 5:1 petroleum ether: EtOAc. The product was further crystallized from MeOH to afford an orange-yellow solid in 43% yield. M.p. 90-94 ºC (Et_2O); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.23 (d, *J* = 2.3 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.12 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.82 (s, 3H), 3.57 (t, *J* = 5.0 Hz, 2H), 3.04 (t, *J* = 5.0 Hz, 2H), 1.75 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.5, 162.6, 161.4, 158.6, 148.8, 138.1, 126.0, 123.9, 111.6, 109.4, 103.4, 55.5, 37.7, 29.8, 27.1; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_5$ (M^+): 288.0998. Found: 288.0995.



2,2-Dimethyl-5-(1-p-tolylpropylidene)-1,3-dioxane-4,6-dione (2.128): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 7% yield (unoptimized). M.p. 145-147 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.20 (d, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 7.7 Hz, 2H), 3.12 (q, *J* = 7.4 Hz, 2H), 2.37 (s, 3H), 1.80 (s, 6H), 1.05 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.4, 161.0, 160.6, 139.5, 137.1, 129.1, 126.3, 116.5, 103.7, 31.3, 27.3, 21.4, 12.5; HRMS(EI) *m/z* calc'd for $C_{16}H_{18}O_4$ (M^+): 274.1205. Found: 274.1201.

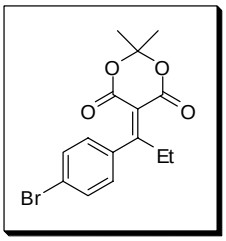


5-(1-(4-Isopropylphenyl)propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.129): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 33% yield. M.p. 106-108 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.24 (d, *J* = 7.5 Hz, 2H), 7.10 (d, *J* = 7.6 Hz, 2H), 3.11 (q, *J* = 7.3 Hz, 2H), 2.91 (sept, *J* = 6.8 Hz, 1H), 1.80 (s, 6H), 1.24 (d, *J* = 6.9 Hz, 2H), 1.05 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.2, 160.9, 160.5, 150.1, 137.2, 126.4, 126.3, 116.3, 103.6, 33.7, 31.2, 27.1, 23.6, 12.5; HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_4$ (M^+): 302.1558. Found: 302.1521.

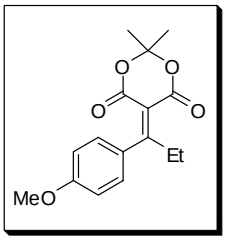


5-(1-(4-*tert*-Butylphenyl)propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.130): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 26% yield.

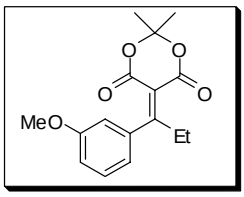
M.p. 110-112 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39 (d, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), 3.11 (q, *J* = 7.4 Hz, 2H), 1.80 (s, 6H), 1.31 (s, 9H), 1.06 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.4, 161.0, 160.7, 152.5, 137.0, 126.2, 125.2, 116.4, 103.7, 34.7, 31.3, 31.1, 27.2, 12.6; HRMS(EI) *m/z* calc'd for $C_{16}H_{18}O_5$ (M^+): 316.1675. Found: 316.1673.



5-(1-(4-Bromophenyl)propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.131): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 25% yield. M.p. 124-125 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.01 (d, *J* = 8.1 Hz, 2H), 3.06 (q, *J* = 7.4 Hz, 2H), 1.77 (s, 6H), 1.03 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.5, 160.6, 160.1, 138.7, 131.4, 127.7, 123.3, 117.0, 103.9, 31.2, 27.2, 12.2; HRMS(EI) *m/z* calc'd for $C_{15}H_{15}{}^{79}BrO_4$ (M^+): 338.0154. Found: 338.0160.

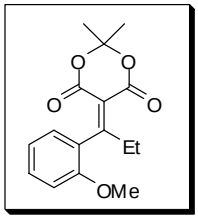


5-(1-(4-Methoxyphenyl)propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.132): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 29% yield. M.p. 113-114 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.16 (d, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 7.8 Hz, 2H), 3.82 (s, 3H), 3.13 (q, *J* = 7.3 Hz, 2H), 1.80 (s, 6H), 1.05 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.2, 161.1, 161.0, 160.9, 132.0, 128.6, 115.8, 113.8, 103.6, 55.3, 31.3, 27.3, 12.9; HRMS(EI) *m/z* calc'd for $C_{16}H_{18}O_5$ (M^+): 290.1154. Found: 290.1156.

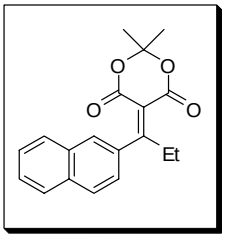


5-(1-(3-Methoxyphenyl)propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.134): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 26% yield. M.p. 72-74 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32 (t, *J* = 7.9 Hz, 1H), 6.91 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.71-6.67 (m, 2H), 3.80 (s, 3H), 3.10 (q, *J* = 7.5 Hz, 2H), 1.79 (s, 3H), 1.06 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.5,

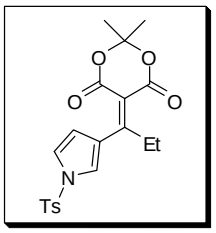
160.9, 160.2, 159.4, 141.4, 129.5, 118.4, 117.0, 113.8, 112.3, 103.8, 55.2, 31.2, 27.3, 12.3; HRMS(EI) *m/z* calc'd for $C_{16}H_{18}O_5$ (M^+): 290.1154. Found: 290.1159.



5-(1-(2-Methoxyphenyl)propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.136): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 64% yield. M.p. 105-107 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33 (dt, *J* = 7.7, 1.8 Hz, 1H), 7.08-6.99 (m, 2H), 6.88 (d, *J* = 8.3 Hz, 1H), 3.74 (s, 3H), 3.36 (dq, *J* = 12.9, 7.4 Hz, 1H), 2.85 (dq, *J* = 12.8, 7.6 Hz, 1H), 1.86 (s, 3H), 1.73 (s, 3H), 1.02 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.0, 161.2, 160.4, 154.2, 130.0, 129.0, 127.3, 120.7, 118.0, 110.8, 103.9, 55.2, 30.7, 27.6, 26.4, 11.8; HRMS(EI) *m/z* calc'd for $C_{16}H_{18}O_5$ (M^+): 290.1154. Found: 290.1163.

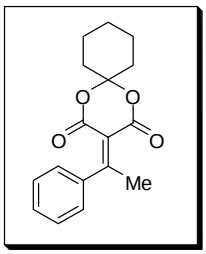


2,2-Dimethyl-5-(1-(naphthalen-2-yl)propylidene)-1,3-dioxane-4,6-dione (2.138): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 14% yield. M.p. 123-125 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.87-7.82 (m, 3H), 7.63 (s, 1H), 7.52-7.49 (m, 2H), 7.26 (d, *J* = 8.6 Hz, 1H), 3.23 (q, *J* = 7.5 Hz, 2H), 1.84 (s, 6H), 1.09 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.2, 161.0, 160.4, 137.5, 133.3, 132.7, 128.3, 128.0, 127.8, 126.9, 126.6, 125.3, 124.3, 116.9, 103.8, 31.6, 27.3, 12.5; HRMS(EI) *m/z* calc'd for $C_{19}H_{18}O_4$ (M^+): 310.1205. Found: 310.1213.

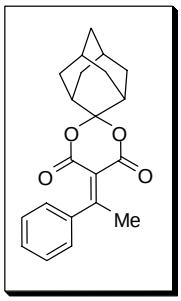


2,2-Dimethyl-5-(1-(1-tosyl-1*H*-pyrrol-3-yl)propylidene)-1,3-dioxane-4,6-dione (2.139): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 39% yield. M.p. 133-134 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.64 (s, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.11-7.09 (m, 1H), 6.39-6.37 (m, 1H), 2.99 (q, *J* = 7.4 Hz, 2H), 2.39 (s, 3H), 1.73 (s, 6H), 1.12 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.2, 161.2, 161.1, 145.8, 135.2, 130.3,

127.1, 125.6, 123.8, 120.9, 114.6, 114.0, 103.6, 30.8, 27.1, 21.7, 14.1; HRMS(EI) *m/z* calc'd for $C_{20}H_{21}NO_6S$ (M^+): 403.1090. Found: 403.1082.

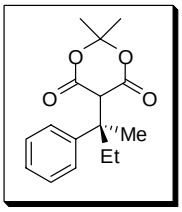


3-(1-Phenylethylidene)-1,5-dioxaspiro[5.5]undecane-2,4-dione (2.140): Prepared according to general procedure A. Recrystallization from MeOH afforded a yellow solid in 68% yield. M.p. 79-80 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39-7.37 (m, 3H), 7.17-7.14 (m, 2H), 2.69 (s, 3H), 2.05 (t, *J* = 6.0 Hz, 3H), 1.74 (quintet, *J* = 5.9 Hz, 4H), 1.52-1.47 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.3, 161.1, 160.3, 141.7, 129.3, 128.4, 125.8, 117.2, 104.6, 36.1, 26.1, 24.1, 22.1; HRMS(EI) *m/z* calc'd for $C_{17}H_{18}O_4$ (M^+): 286.1205. Found: 286.1211.

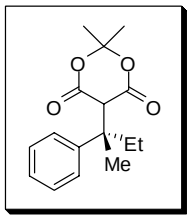


Adamantyl substituted alkylidene Meldrum's acid (2.142): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 82% yield. M.p. 163-165 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39-7.37 (m, 3H), 7.15-7.11 (m, 2H), 2.69 (s, 3H), 2.39 (bs, 2H), 2.18-2.14 (m, 4H), 1.91 (bs, 2H), 1.82-1.77 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.6, 161.1, 160.4, 141.8, 129.3, 128.5, 126.0, 117.5, 107.1, 37.2, 36.8, 33.5, 33.3, 26.1 (2C), 25.9; HRMS(EI) *m/z* calc'd for $C_{21}H_{22}O_4$ (M^+): 338.1518. Found: 338.1508.

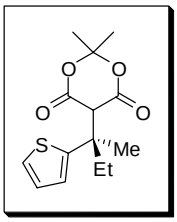
(V) Product Specific Information



(*R*)-2,2-Dimethyl-5-(1-methyl-1-phenylpropyl)-1,3-dioxane-4,6-dione (2.2): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 5:1 petroleum ether:EtOAc, afforded a white solid upon standing in 95% yield. M.p. 44-46 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36-7.21 (m, 5H), 3.64 (s, 1H), 2.22 (dq, *J* = 7.2, 7.0, Hz 1H), 2.11 (dq, *J* = 7.1, 7.0 Hz, 1H), 1.64 (s, 3H), 1.61 (s, 3H), 1.19 (s, 3H), 0.78 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.4, 163.9, 142.2, 128.2, 126.8, 126.7, 105.0, 57.0, 46.0, 32.5, 29.2, 27.0, 21.6, 8.6; An enantiomeric excess of 84% (*R*) was measured by chiral HPLC [OD, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 14.7 min (*S*), t_{R2} = 16.4 min (*R*)]. $[\alpha]^{28}_D$ = +3.3 (*c* 0.33, CH_2Cl_2). Absolute configuration was assigned by chemical transformation to chiral indanone **2.146** as shown below. HRMS(EI) *m/z* calc'd for $C_{16}H_{20}O_4$ (M^+): 276.1362. Found: 276.1367.

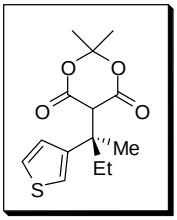


(*S*)-2,2-Dimethyl-5-(2-phenylbutan-2-yl)-1,3-dioxane-4,6-dione (ent-2.2): Prepared according to general procedure C. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 93% yield; An enantiomeric excess of 76% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 15.5 min (*S*), t_{R2} = 20.3 min (*R*)]. Absolute configuration was assigned by analogy to **2.2**.

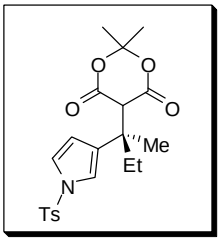


(*R*)-2,2-Dimethyl-5-(2-(thiophen-2-yl)butan-2-yl)-1,3-dioxane-4,6-dione (2.16): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 8:1 hexanes:EtOAc, afforded a beige solid in 77% yield. M.p. 90-92 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.16 (d, *J* = 5.0 Hz, 1H), 6.93 (app t, *J* = 4.3 Hz, 1H), 6.86 (d, *J* = 3.5 Hz, 1H), 3.56 (s, 1H), 2.25 (dq, *J* = 14.1, 7.2 Hz, 1H), 2.00 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.64 (s, 3H), 1.59 (s, 3H), 1.18 (s, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C

NMR ($CDCl_3$, 75 MHz) δ 164.1, 163.6, 148.1, 126.8, 125.1, 124.1, 105.2, 56.5, 45.0, 34.6, 29.2, 27.2, 24.0, 8.7; An enantiomeric excess of 92% (*R*) was measured by chiral HPLC [AD-H, 0.5% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 32.4 min (*S*), t_{R2} = 36.0 min (*R*)]. $[\alpha]^{26}_D$ = +11.3 (*c* 1.2, THF). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{14}H_{18}O_4S$ (M^+): 282.0926. Found: 282.0918.

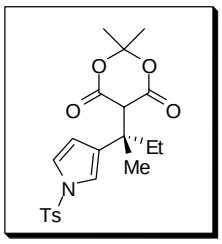


(*R*)-2,2-Dimethyl-5-(2-(thiophen-3-yl)butan-2-yl)-1,3-dioxane-4,6-dione (2.18): Prepared according to general procedure B with reaction time of 31 h. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a beige solid in 95% yield. M.p. 69-71 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25 (dd, *J* = 5.1, 2.9 Hz, 1H), 7.04-7.03 (m, 1H), 6.98 (dd, *J* = 5.1, 1.1 Hz, 1H), 3.46 (s, 1H), 2.12 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.04 (dq, *J* = 14.2, 7.2 Hz, 1H), 1.58 (s, 3H), 1.57 (s, 3H), 1.16 (s, 3H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.3, 144.1, 126.8, 125.5, 122.3, 105.4, 56.3, 44.8, 33.3, 29.8, 27.0, 23.3, 8.7; An enantiomeric excess of 96% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 19.1 min (*S*), t_{R2} = 20.4 min (*R*)]. $[\alpha]^{31}_D$ = -0.81 (*c* 1.2, THF). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{14}H_{18}O_4S$ (M^+): 282.0926. Found: 282.0926.

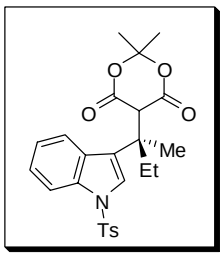


(*R*)-2,2-Dimethyl-5-(2-(1-tosyl-1*H*-pyrrol-3-yl)butan-2-yl)-1,3-dioxane-4,6-dione (2.20): Prepared according to general procedure B with reaction time of 30 h. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, afforded a light yellow oil in 99% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.05-7.03 (m, 1H), 6.96 (t, *J* = 1.9 Hz, 1H), 6.16 (dd, *J* = 3.2, 1.8 Hz, 1H), 3.37 (s, 1H), 2.37 (s, 3H), 2.01 (dq, *J* = 14.0, 7.2 Hz, 1H), 1.85 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.52 (s, 3H), 1.44 (s, 3H), 1.01 (s, 3H), 0.80 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6, 164.2, 144.9, 136.0, 131.5, 129.9, 126.8, 120.8, 118.6, 113.1, 105.2, 55.9, 42.6, 32.8, 29.7, 26.8, 22.9, 21.5, 8.6; An enantiomeric excess of 96% (*R*) was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 17.9 min (*S*), t_{R2} = 19.5 min (*R*)]. $[\alpha]^{32}_D$ = -1.9 (*c* 2.4,

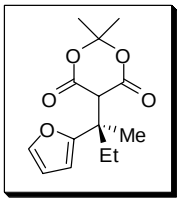
CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{21}H_{25}NO_6S$ (M^+): 419.1403. Found: 419.1401.



(*S*)-2,2-Dimethyl-5-(2-(1-tosyl-1*H*-pyrrol-3-yl)butan-2-yl)-1,3-dioxane-4,6-dione (ent-2.20): Prepared according to general procedure C. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, afforded a clear oil in 93% yield; An enantiomeric excess of 97% (*S*) was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 16.7 min (*S*), t_{R2} = 18.2 min (*R*)]. Absolute configuration was assigned by analogy to **2.2**.

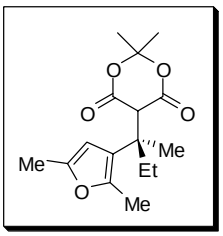


(*R*)-2,2-Dimethyl-5-(2-(1-tosyl-*1H*-indol-3-yl)butan-2-yl)-1,3-dioxane-4,6-dione (2.22): Prepared according to general procedure B with reaction time of 29 h. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 74% yield. M.p. 75-77 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.90 (d, *J* = 7.9 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.39 (s, 1H), 7.27-7.15 (m, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 3.89 (s, 1H), 2.38-2.26 (m, 1H), 2.30 (s, 3H), 2.06 (dq, *J* = 14.0, 7.2 Hz, 1H), 1.59 (s, 3H), 1.58 (s, 3H), 1.34 (s, 3H), 0.64 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6, 164.6, 144.7, 135.7, 135.0, 129.8, 128.6, 126.9, 125.8, 124.5 (2C), 123.1, 120.7, 114.1, 105.0, 55.3, 43.8, 30.8, 29.3, 27.3, 21.5, 21.2, 8.8; An enantiomeric excess of 96% (*R*) was measured by chiral HPLC [AD-H, 5% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 26.6 min (*S*), t_{R2} = 34.3 min (*R*)]. $[\alpha]^{29.5}_D$ = +10.9 (*c* 1.9, CH_2Cl_2). HRMS(EI) *m/z* calc'd for $C_{25}H_{27}NO_6S$ (M^+): 469.1559. Found: 469.1566.

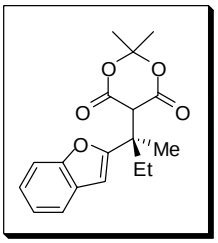


(*R*)-5-[1-(2-Furyl)-1-methylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.24): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 4:1 hexanes:EtOAc, afforded a white solid upon standing in 97% yield. M.p. 49-50 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31 (d, *J* = 1.8 Hz,1H), 6.30 (dd, *J* = 3.2, 1.8

Hz, 1H), 6.10 (d, *J* = 3.3 Hz, 1H), 3.82 (s, 1H), 2.05 (q, *J* = 7.5 Hz, 1H), 2.04 (q, *J* = 7.4 Hz, 1H), 1.70 (s, 3H), 1.50 (s, 3H), 1.49 (s, 3H), 0.77 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.8, 163.2, 157.0, 141.0, 110.2, 106.3, 104.7, 53.8, 43.0, 31.8, 28.2, 27.7, 19.8, 8.5; An enantiomeric excess of 91% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 18.2 min (*S*), t_{R2} = 20.7 min (*R*)]. $[\alpha]^{28}_D$ = -2.4 (*c* 0.93, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{14}H_{18}O_5$ (M^+): 266.1154. Found: 266.1157.

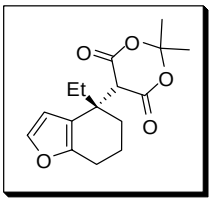


(*R*)-5-(2-(2,5-Dimethylfuran-3-yl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.26): Prepared according to general procedure B with reaction time of 29 h. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a beige solid in 92% yield. M.p. 70-72 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.73 (s, 1H), 3.30 (s, 1H), 2.24 (s, 3H), 2.14 (s, 3H), 2.05 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.88 (dq, *J* = 14.1, 7.1 Hz, 1H), 1.59 (s, 3H), 1.51 (s, 3H), 1.31 (s, 3H), 0.82 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.9, 164.5, 148.5, 146.4, 120.8, 107.5, 105.5, 56.2, 43.1, 32.7, 30.0, 27.0, 23.3, 14.4, 13.2, 8.8; An enantiomeric excess of 84% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 10.5 min (*S*), t_{R2} = 11.4 min (*R*)]. $[\alpha]^{26}_D$ = +0.33 (*c* 1.7, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{16}H_{22}O_5$ (M^+): 294.1467. Found: 294.1463.

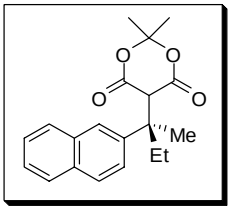


(*R*)-5-(2-(Benzofuran-2-yl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.28): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a bright yellow solid in 63% yield. M.p. 94-97 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.50 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.21-7.14 (m, 2H), 6.50 (s, 1H), 4.06 (s, 1H), 2.21 (dq, *J* = 14.0, 7.4 Hz, 1H), 2.11 (dq, *J* = 14.1, 7.4 Hz, 1H), 1.76 (s, 3H), 1.59 (s, 3H), 1.52 (s, 3H), 0.80 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.6, 163.0, 160.3, 154.3, 128.3, 123.6, 122.7, 120.8, 110.8, 104.7, 103.2, 53.5, 43.2, 31.7, 28.0, 27.8, 19.2, 8.7; An

enantiomeric excess of 77% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 14.0 min (*S*), t_{R2} = 20.1 min (*R*)]. $[\alpha]^{31}_{D}$ = -8.3 (*c* 1.1, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{18}H_{20}O_5$ (M^+): 316.1311. Found: 316.1315.

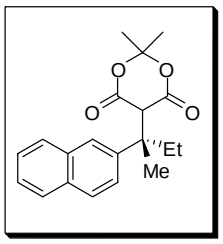


(*S*)-5-(4-Ethyl-4,5,6,7-tetrahydrobenzofuran-4-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.30): Prepared according to general procedure B with reaction time of 22 h. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 77% yield. M.p. 91-93 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.21 (d, *J* = 0.8 Hz, 1H), 6.22 (d, *J* = 1.8 Hz, 1H), 3.57 (s, 1H), 2.58-2.49 (m, 2H), 2.16 (ddd, *J* = 13.4, 6.6, 2.5 Hz, 1H), 1.92 (q, *J* = 7.3 Hz, 2H), 1.89-1.87 (m, 1H), 1.80-1.73 (m, 1H), 1.69-1.65 (m, 1H), 1.65 (s, 3H), 1.47 (s, 3H), 0.83 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.0, 164.5, 151.9, 140.2, 119.5, 109.7, 105.5, 53.5, 43.4, 32.3, 30.4, 29.4, 27.5, 22.5, 19.2, 8.7; An enantiomeric excess of 76% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 17.4 min (*R*), t_{R2} = 18.4 min (*S*)]. $[\alpha]^{24.5}_{D}$ = +0.45 (*c* 1.4, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{16}H_{20}O_5$ (M^+): 292.1311. Found: 292.1317.

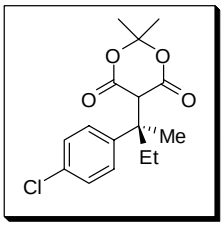


(*R*)-2,2-Dimethyl-5-[1-methyl-1-(2-naphthyl)propyl]-1,3-dioxane-4,6-dione (2.32): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 5:1 hexanes:EtOAc, afforded a white solid in 66% yield. M.p. 130-131 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.81-7.78 (m, 3H), 7.70 (s, 1H), 7.46-7.41 (m, 3H), 3.71 (s, 1H), 2.29 (dq, *J* = 14.2, 7.4 Hz, 1H), 2.17 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.72 (s, 3H), 1.59 (s, 3H), 1.14 (s, 3H), 0.75 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.7, 164.1, 139.7, 133.1, 132.1, 128.2, 127.9, 127.3, 126.1 (2C), 126.0, 124.6, 105.2, 57.2, 46.5, 32.8, 29.4, 27.2, 21.7, 8.8; An enantiomeric excess of 95% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 16.0 min (*S*), t_{R2} = 22.7 min (*R*)]. $[\alpha]^{28}_{D}$ = +4.2 (*c* 0.50, CH_2Cl_2).

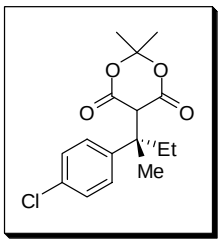
Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{20}H_{22}O_4$ (M^+): 326.1518. Found: 326.1519.



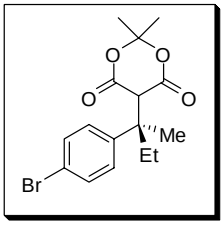
(*S*)-2,2-Dimethyl-5-[1-methyl-1-(2-naphthyl)propyl]-1,3-dioxane-4,6-dione (ent-2.32): Prepared according to general procedure D. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a beige solid in 82% yield; An enantiomeric excess of 79% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 26.0 min (*S*), t_{R2} = 39.1 min (*R*)]. Absolute configuration was assigned by analogy to **2.2**.



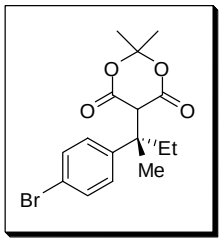
(*R*)-5-[1-(4-Chlorophenyl)-1-methylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.35): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 4:1 hexanes:EtOAc, afforded a white solid in 88% yield. M.p. 89-92 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 2H), 3.60 (s, 1H), 2.10 (q, *J* = 7.3 Hz, 2H), 1.63 (s, 3H), 1.58 (s, 3H), 1.33 (s, 3H), 0.72 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.3, 163.8, 141.2, 132.8, 128.4, 128.3, 105.1, 57.0, 45.7, 32.7, 29.1, 27.4, 21.4, 8.6; An enantiomeric excess of 95% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 13.8 min (*S*), t_{R2} = 16.3 min (*R*)]. $[\alpha]^{28}_D$ = +9.4 (*c* 0.50, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{16}H_{19}{}^{35}ClO_4$ (M^+): 310.0972. Found: 310.0975.



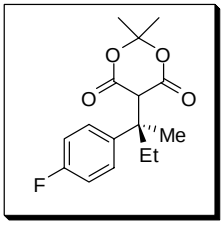
(*S*)-5-[1-(4-Chlorophenyl)-1-methylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (ent-2.35): Prepared according to general procedure C. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 68% yield; An enantiomeric excess of 90% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 20.4 min (*S*), t_{R2} = 25.6 min (*R*)]. Absolute configuration was assigned by analogy to **2.2**.



(*R*)-5-[1-(4-Bromophenyl)-1-methylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.37): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 5:1 petroleum ether:EtOAc, afforded a white solid in 84% yield. M.p. 84-85 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.44 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 3.60 (s, 1H), 2.10 (q, *J* = 7.3 Hz, 2H), 1.63 (s, 3H), 1.57 (s, 3H), 1.34 (s, 3H), 0.72 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.2, 163.8, 141.8, 131.4, 128.6, 120.9, 105.1, 56.9, 45.7, 32.7, 29.0, 27.5, 21.3, 8.6; An enantiomeric excess of 92% (*R*) was measured by chiral HPLC [OD 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 15.3 min (*S*), t_{R2} = 17.4 min (*R*)]. $[\alpha]^{28}_D$ = +8.8 (*c* 1.3, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{16}H_{19}{}^{79}BrO_4$ (M^+): 354.0467. Found: 354.0470.

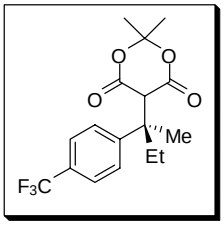


(*S*)-5-[1-(4-Bromophenyl)-1-methylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (ent-2.37): Prepared according to general procedure C. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 68% yield; An enantiomeric excess of 91% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 21.7 min (*S*), t_{R2} = 27.7 min (*R*)]. Absolute configuration was assigned by analogy to **2.2**.

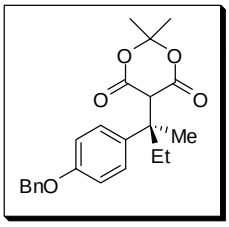


(*R*)-5-[1-(4-Fluorophenyl)-1-methylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.39): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 5:1 petroleum ether:EtOAc, afforded a white solid in 83% yield. M.p. 94-95 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30-7.26 (m, 2H), 7.03 (t, *J* = 8.6 Hz, 2H), 3.60 (s, 1H), 2.19-2.11 (m, 2H), 1.64 (s, 3H), 1.63 (s, 3H), 1.31 (s, 3H), 0.78 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.4, 164.0 161.6 (d, *J* = 245.0 Hz), 138.1 (d, *J* = 3.2 Hz), 128.6 (d, *J* = 7.9 Hz), 115. 1 (d, *J* = 20.9 Hz), 105.2, 57.2, 45.8, 32.8, 29.3, 27.3, 21.9, 8.6; An enantiomeric excess of 92% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 12.5 min

(*S*), t_{R2} = 15.1 min (*R*)]. $[\alpha]^{28}_D$ = +1.1 (*c* 0.90, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{16}H_{19}FO_4$ (M^+): 294.1267. Found: 294.1260.

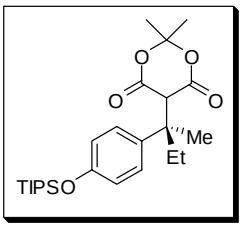


(*R*)-2,2-Dimethyl-5-1-methyl-1-[4-(trifluoromethyl)phenyl] propyl-1,3-dioxane-4,6-dione (2.41): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 5:1 petroleum ether:EtOAc, afforded a white solid in 87% yield. M.p. 94-96 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.57 (d, *J* = 8.3 Hz, 2 H), 7.39 (d, *J* = 8.3 Hz, 2H), 3.71 (s, 1H), 2.22 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.15 (dq, *J* = 14.2, 7.2 Hz, 1H), 1.66 (s, 3H), 1.63 (s, 3H), 1.38 (s, 3H), 0.70 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.9, 163.5, 147.3, 129.0 (q, *J* = 32.5 Hz), 127.1, 125.2 (q, *J* = 3.8 Hz), 124.7 (q, *J* = 270.3 Hz), 105.0, 56.7, 45.7, 32.7, 28.6, 27.6, 21.0, 8.5; An enantiomeric excess of 92% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 11.5 min (*S*), t_{R2} = 13.5 min (*R*)]. $[\alpha]^{28}_D$ = +8.9 (*c* 1.1, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{17}H_{19}F_2O_4$ (M^+-F): 325.1251. Found: 325.1248.

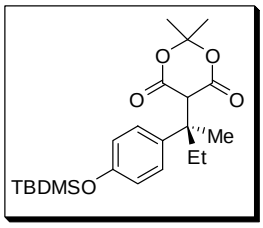


(*R*)-5-1-[4-(Benzyloxy)phenyl]-1-methylpropyl-2,2-dimethyl-1,3-dioxane-4,6-dione (2.43): Prepared according to general procedure B with a slight modification. Due to its insolubility, the substrate was added to the tube as a solid in one portion, followed by addition of DME. Purification by flash column chromatography on silica gel using 7:1 petroleum ether:EtOAc, afforded a white solid in 75% yield. M.p. 71-72 ºC (1% *i*-PrOH/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.41-7.27 (m, 5H), 7.19 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.03 (s, 2H), 3.50 (s, 1H), 2.17 (dq, *J* = 14.2, 7.0 Hz, 1H), 2.05 (dq, *J* = 14.1, 7.1 Hz, 1H), 1.58 (s, 3H), 1.56 (s, 3H), 1.10 (s, 3H), 0.78 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.8, 164.3, 157.6, 136.9, 134.2, 128.6, 128.2, 127.9, 127.4, 114.6, 105.3, 69.9, 57.3, 46.1, 32.7, 29.7, 27.0, 22.4, 8.7; $[\alpha]^{28}_D$ = -1.5 (*c* 0.33, CH_2Cl_2). An enantiomeric excess of 94% (*R*) was measured by chiral HPLC [OD, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 33.2 min (*R*), t_{R2} = 39.9 min

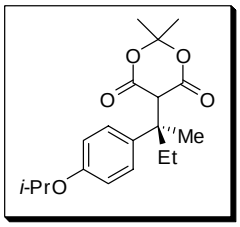
(*S*)]. Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{23}H_{26}O_5$ (M^+): 382.1780. Found: 382.1781.



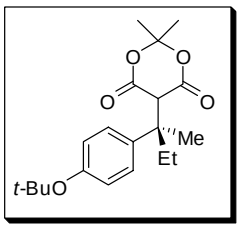
(*R*)-2,2-Dimethyl-5-(2-(4-(triisopropylsilyloxy)phenyl)butan-2-yl)-1,3-dioxane-4,6-dione (2.45): Prepared according to general procedure B with reaction time of 31 h. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 81% yield. M.p. 56-57 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.17 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 3.48 (s, 1H), 2.14 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.03 (dq, *J* = 14.1, 7.1 Hz, 1H), 1.56 (s, 3H), 1.55 (s, 3H), 1.27-1.17 (m, 3H), 1.15 (s, 3H), 1.07-1.03 (m, 18H), 0.75 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.8, 164.3, 155.0, 134.0, 128.1, 119.5, 105.3, 57.3, 46.2, 32.8, 29.8, 27.1, 22.4, 17.9, 12.6, 8.7; An enantiomeric excess of 94% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 11.2 min (*S*), t_{R2} = 12.8 min (*R*)]. $[\alpha]^{29.5}_D$ = -18.7 (*c* 2.1, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{25}H_{40}O_5Si$ (M^+): 448.2645. Found: 448.2650.



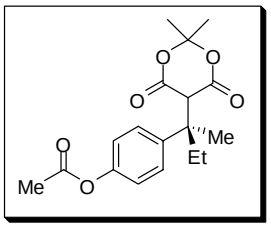
(*R*)-5-(2-(4-(*tert*-Butyldimethylsilyloxy)phenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.47): Prepared according to general procedure B with reaction time of 30 h. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 74% yield. M.p. 55-56 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.12 (d, *J* = 8.7 Hz, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 3.47 (s, 1H), 2.16 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.04 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.57 (s, 3H), 1.55 (s, 3H), 1.11 (s, 3H), 0.94 (s, 9H), 0.77 (t, *J* = 7.3 Hz, 3H), 0.14 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.8, 164.3, 154.6, 134.3, 128.2, 119.8, 105.3, 57.2, 46.1, 32.7, 29.8, 27.1, 25.6, 22.5, 18.1, 8.7, -4.5; An enantiomeric excess of 96% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 14.1 min (*S*), t_{R2} = 22.6 min (*R*)]. $[\alpha]^{30.5}_D$ = +0.63 (*c* 1.7, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{22}H_{34}O_5Si$ (M^+): 406.2176. Found: 406.2181.



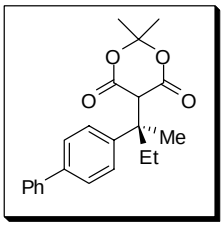
(*R*)-5-(2-(4-isopropoxyphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.49): Prepared according to general procedure B with reaction time of 27 h. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 84% yield. M.p. 45-48 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.15 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 4.49 (septet, *J* = 6.1 Hz, 1H), 3.47 (s, 1H), 2.16 (dq, *J* = 14.2, 7.1 Hz, 1H), 2.04 (dq, *J* = 14.1, 7.1 Hz, 1H), 1.57 (s, 3H), 1.55 (s, 3H), 1.28 (d, *J* = 6.1 Hz, 6H), 1.10 (s, 3H), 0.77 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.3, 156.7, 133.5, 128.1, 115.5, 105.3, 69.7, 57.2, 46.1, 32.6, 29.7, 26.9, 22.4, 21.9, 8.7; An enantiomeric excess of 95% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 17.2 min (*S*), t_{R2} = 19.2 min (*R*)]. $[\alpha]^{28.5}_{D}$ = +1.8 (*c* 1.5, THF). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{19}H_{26}O_5$ (M^+): 334.1780. Found: 334.1773.



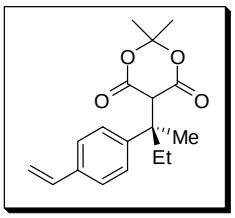
(*R*)-5-(2-(4-*tert*-Butoxyphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.51): Prepared according to general procedure B with reaction time of 24 h. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 87% yield. M.p. 88-90 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.13 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 3.47 (s, 1H), 2.14 (dq, *J* = 14.1, 7.1 Hz, 1H), 2.05 (dq, *J* = 14.1, 7.1 Hz, 1H), 1.56 (s, 3H), 1.52 (s, 3H), 1.28 (s, 9H), 1.07 (s, 3H), 0.75 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6, 164.2, 154.3, 136.4, 127.5, 123.6, 105.2, 78.3, 57.0, 46.1, 32.7, 29.7, 28.7, 27.1, 22.4, 8.7; An enantiomeric excess of 95% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 13.1 min (*S*), t_{R2} = 16.6 min (*R*)]. $[\alpha]^{31.5}_{D}$ = -5.6 (*c* 1.8, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{20}H_{28}O_5$ (M^+): 348.1937. Found: 348.1932.



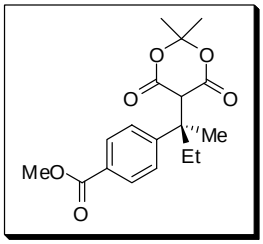
(*R*)-4-(2-(2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-yl)butan-2-yl)phenyl acetate (2.53): Prepared according to general procedure B with reaction time of 29 h. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, afforded a white, waxy solid in 87% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28 (d, *J* = 8.7 Hz, 2H), 7.03 (d, *J* = 8.7 Hz, 2H), 3.54 (s, 1H), 2.26 (s, 3H), 2.15 (dq, *J* = 15.0, 7.3 Hz, 1H), 2.10 (dq, *J* = 14.4, 7.2 Hz, 1H), 1.61 (s, 3H), 1.58 (s, 3H), 1.19 (s, 3H), 0.78 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.2, 164.5, 164.1, 149.6, 139.6, 128.0, 121.4, 105.4, 57.1, 46.0, 32.6, 29.5, 27.1, 22.2, 21.1, 8.7; An enantiomeric excess of 93% (*R*) was measured by chiral HPLC [AD-H, 5% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 13.2 min (*S*), t_{R2} = 14.1 min (*R*)]. $[\alpha]^{26.5}_{D}$ = +5.9 (*c* 1.7, THF). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_6$ (M^+): 334.1416. Found: 334.1414.



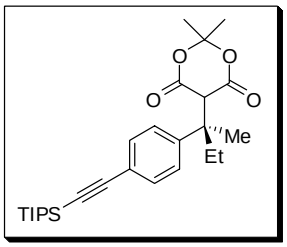
(*R*)-2,2-Dimethyl-5-[1-methyl-1-(4-phenylphenyl)propyl]-1,3-dioxane-4,6-dione (2.55): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 5:1 hexanes:EtOAc, afforded a white solid in 76% yield. M.p. 117-118 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.57-7.54 (m, 4H), 7.44-7.30 (m, 5H), 3.61 (s, 1H), 2.23 (dq, *J* = 14.3, 7.6 Hz, 1H), 2.13 (dq, *J* = 14.3, 7.6 Hz, 1H), 1.65 (s, 3H), 1.60 (s, 3H), 1.19 (s, 3H), 0.81 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.6, 164.1, 141.2, 140.4, 139.7, 128.8, 127.3 (2C), 126.9 (2C), 105.3, 57.1, 46.1, 32.7, 29.5, 27.1, 21.9, 8.8; An enantiomeric excess of 95% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 19.7 min (*S*), t_{R2} = 23.1 min (*R*)]. $[\alpha]^{28}_{D}$ = +6.3 (*c* 1.0, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{22}H_{24}O_4$ (M^+): 352.1675. Found: 352.1671.



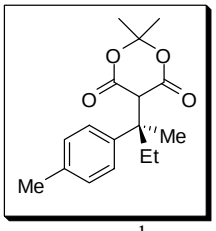
(*R*)-2,2-Dimethyl-5-(2-(4-vinylphenyl)butan-2-yl)-1,3-dioxane-4,6-dione (2.57): Prepared according to general procedure B with reaction time of 26 h. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 90% yield. M.p. 67-69 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.66 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.71 (d, *J* = 17.6 Hz, 1H), 5.21 (d, *J* = 10.9 Hz, 1H), 3.60 (s, 1H), 2.17 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.09 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.60 (s, 6H), 1.22 (s, 3H), 0.75 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.5, 164.0, 141.9, 136.2, 127.0, 126.1, 113.9, 105.2, 57.1, 46.1, 32.7, 29.3, 27.2, 21.7, 8.7; An enantiomeric excess of 94% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 17.8 min (*S*), t_{R2} = 22.2 min (*R*)]. $[\alpha]^{31.5}_{D}$ = -8.3 (*c* 1.7, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_4$ (M^+): 302.1518. Found: 302.1524.



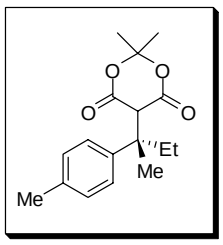
(*R*)-Methyl 4-(2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)butan-2-yl)benzoate (2.59): Prepared according to general procedure B with reaction time of 33 h. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, afforded a white solid in 99% yield. M.p. 74-76 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.98 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.5 Hz, 2H), 3.88 (s, 3H), 3.72 (s, 1H), 2.16-2.12 (m, 2H), 1.66 (s, 3H), 1.61 (s, 3H), 1.38 (s, 3H), 0.68 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.7, 164.1, 163.5, 148.5, 129.6, 128.5, 126.7, 105.0, 56.7, 52.1, 45.8, 32.8, 28.7, 27.7, 20.8, 8.6; An enantiomeric excess of 93% (*R*) was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 11.7 min (*S*), t_{R2} = 13.0 min (*R*)]. $[\alpha]^{28}_{D}$ = +23.9 (*c* 2.1, THF). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_6$ (M^+): 334.1416. Found: 334.1426.



(*R*)-2,2-Dimethyl-5-(2-(4-((triisopropylsilyl)ethynyl)phenyl) butan-2-yl)-1,3-dioxane-4,6-dione (2.61): Prepared according to general procedure B with reaction time of 30 h. Purification by flash column chromatography on silica gel, eluting with 8:1 hexanes:EtOAc, afforded a clear oil in 95% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 3.65 (s, 1H), 2.11 (q, *J* = 7.3 Hz, 2H), 1.66 (s, 3H), 1.64 (s, 3H), 1.37 (s, 3H), 1.10 (s, 21H), 0.69 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.2, 163.7, 143.1, 131.9, 126.6, 122.0, 106.7, 105.0, 90.8, 46.9, 45.8, 32.7, 28.9, 27.5, 21.1, 18.6, 11.3, 8.6; An enantiomeric excess of 97% (*R*) was measured by chiral HPLC [OD-H, 0.5% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 15.6 min (*S*), t_{R2} = 18.5 min (*R*)]. $[\alpha]^{31}_{D}$ = +11.1 (*c* 2.5, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{27}H_{40}O_4Si$ (M^+): 456.2696. Found: 456.2708.

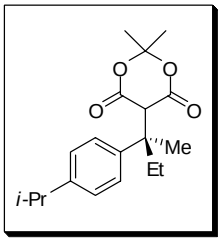


(*R*)-2,2-Dimethyl-5-[1-methyl-1-(4-methylphenyl)propyl]-1,3-dioxane-4,6-dione (2.63): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 5:1 hexanes:EtOAc, afforded a white solid in 82% yield. M.p. 80-81 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.17 (d, *J* = 13.8 Hz, 2H), 7.12 (d, *J* = 13.8 Hz, 2H), 3.55 (s, 1H), 2.29 (s, 3H), 2.17 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.06 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.58 (s, 6H), 1.17 (s, 3H), 0.75 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.2, 139.1, 136.5, 129.0, 126.8, 105.2, 57.2, 46.1, 32.7, 29.5, 27.1, 22.0, 20.8, 8.7; An enantiomeric excess of 89% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 18.9 min (*R*), t_{R2} = 21.2 min (*S*)]. $[\alpha]^{28}_{D}$ = -1.8 (*c* 0.50, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{17}H_{22}O_4$ (M^+): 290.1518. Found: 290.1515.

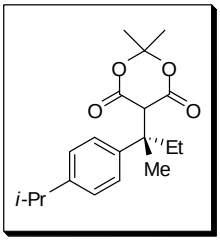


(*S*)-2,2-Dimethyl-5-[1-methyl-1-(4-methylphenyl)propyl]-1,3-dioxane-4,6-dione (ent-2.63): Prepared according to general procedure C. Purification by flash column chromatography on silica

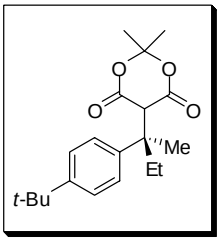
gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 85% yield; An enantiomeric excess of 83% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 15.3 min (*S*), t_{R2} = 19.1 min (*R*)]. Absolute configuration was assigned by analogy to **2.2**.



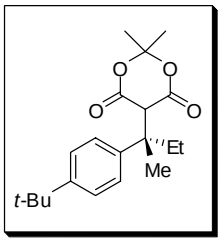
(*R*)-5-(2-(4-Isopropylphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.65): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 10:1 hexanes:EtOAc, afforded an off-white solid in 88% yield. M.p. 80-82 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.19 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 8.7 Hz, 2H), 3.50 (s, 1H), 2.85 (septet, *J* = 6.9 Hz, 1H), 2.24 (dq, *J* = 14.3, 7.2 Hz, 1H), 2.12 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.60 (s, 3H), 1.54 (s, 3H), 1.19 (d, *J* = 6.9 Hz, 6H), 0.80 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.2, 147.6, 139.0, 126.9, 126.4, 105.3, 57.1, 46.2, 33.5, 32.5, 29.7, 26.8, 23.8, 22.4, 8.8; An enantiomeric excess of 98% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 12.2 min (*S*), t_{R2} = 14.7 min (*R*)]. $[\alpha]^{32}_D$ = -9.3 (*c* 1.0, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{19}H_{26}O_4$ (M^+): 318.1831. Found: 318.1832.



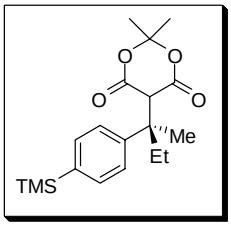
(*S*)-5-(2-(4-Isopropylphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (ent-2.65): Prepared according to general procedure D. Purification by flash column chromatography on silica gel, eluting with 9:1 hexanes:EtOAc, afforded a white solid in 99% yield; An enantiomeric excess of 94% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 11.4 min (*S*), t_{R2} = 13.6 min (*R*)]. Absolute configuration was assigned by analogy to **2.2**.



(*R*)-5-(2-(4-*tert*-Butylphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.67): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 10:1 hexanes:EtOAc, afforded a white solid in 91% yield. M.p. 94-95 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32 (d, *J* = 8.6 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 3.49 (s, 1H), 2.25 (dq, *J* = 14.1, 7.2 Hz, 1H), 2.13 (dq, *J* = 14.1, 7.1 Hz, 1H), 1.61 (s, 3H), 1.54 (s, 3H), 1.26 (s, 9H), 0.96 (s, 3H), 0.82 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.3, 150.0, 138.6, 126.7, 125.3, 105.4, 57.1, 46.2, 34.3, 32.4, 31.2, 29.8, 26.7, 22.5, 8.8; An enantiomeric excess of 99% (*S*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 7.7 min (*S*), t_{R2} = 8.1 min (*R*)]. $[\alpha]^{30}_{D}$ = +4.1 (*c* 0.7, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{20}H_{28}O_4$ (M^+): 332.1988. Found: 332.1996.

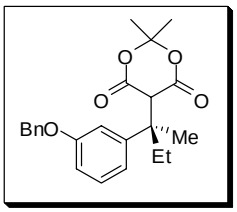


(*S*)-5-(2-(4-*tert*-Butylphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (ent-2.67): Prepared according to general procedure C. Purification by flash column chromatography on silica gel, eluting with 9:1 hexanes:EtOAc, afforded a white solid in 84% yield; An enantiomeric excess of 97% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 11.7 min (*S*), t_{R2} = 14.3 min (*R*)]. Absolute configuration was assigned by analogy to **2.2**.

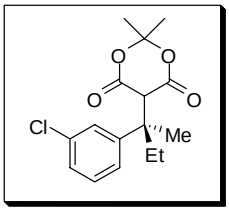


(*R*)-2,2-Dimethyl-5-(2-(4-(trimethylsilyl)phenyl)butan-2-yl)-1,3-dioxane-4,6-dione (2.69): Prepared according to general procedure B with reaction time of 25 h. Purification by flash column chromatography on silica gel, eluting with 9:1 hexanes:EtOAc, afforded a white solid in 90% yield. M.p. 85-87 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.46 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 7.5 Hz, 2H), 3.56 (s, 1H), 2.20 (dq, *J* = 14.2, 7.0 Hz, 1H), 2.09 (dq, *J* = 14.1, 7.1 Hz, 1H), 1.62 (s, 3H), 1.57 (s, 3H), 1.07 (s, 3H), 0.78 (t, *J* = 7.3 Hz, 3H), 0.22 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.5, 164.1, 142.6, 139.0, 133.4, 126.2, 105.3, 57.0, 46.3, 32.5, 29.5, 26.9, 21.9, 8.8, -1.2; An enantiomeric excess of 93% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-

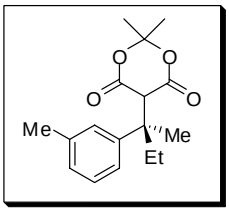
PrOH/hexanes, 1.0 mL/min, t_{R1} = 8.2 min (*S*), t_{R2} = 9.9 min (*R*)]. $[\alpha]^{24.5}_{D}$ = +1.0 (*c* 1.9, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{19}H_{28}O_4Si$ (M^+): 348.1757. Found: 348.1757.



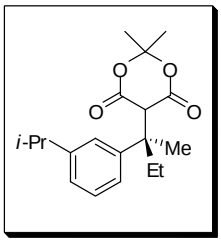
(*R*)-5-1-[3-(Benzyloxy)phenyl]-1-methylpropyl-2,2-dimethyl-1,3-dioxane-4,6-dione (2.74): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 6:1 petroleum ether:EtOAc, afforded an oil in 97% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43-7.20 (m, 6H), 6.90-6.83 (m, 3H), 5.04 (s, 2H), 3.60 (s, 1H), 2.16 (apt q, *J* = 7.1 Hz, 1H), 2.07 (apt q, *J* = 6.9 Hz, 1H), 1.60 (s, 3H), 1.59 (s, 3H), 1.23 (s, 3H), 0.73 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.4, 163.8, 158.7, 144.2, 136.9, 129.2, 128.5, 127.9, 127.5, 119.5, 114.4, 112.7, 105.1, 69.9, 56.9, 46.1, 32.7, 29.2, 27.2, 21.6, 8.6; An enantiomeric excess of 79% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 50.7 min (*R*), t_{R2} = 63.7 min (*S*)]. $[\alpha]^{30}_{D}$ = +2.7 (*c* 0.64, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{23}H_{26}O_5$ (M^+): 382.1780. Found: 382.1792.



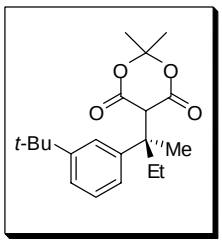
(*R*)-5-[1-(3-Chlorophenyl)-1-methylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.76): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 5:1 petroleum ether:EtOAc, afforded a white solid in 96% yield. M.p. 104-106 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28-7.14 (m, 4H), 3.63 (s, 1H), 2.15-2.06 (m, 2H), 1.64 (s, 3H), 1.58 (s, 3H), 1.36 (s, 3H), 0.72 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.2, 163.6, 145.1, 134.4, 129.5, 127.1, 127.0, 125.0, 105.1, 56.8, 45.8, 32.8, 29.0, 27.5, 21.2, 8.6; An enantiomeric excess of 74% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 14.7 min (*S*), t_{R2} = 17.7 min (*R*)]. $[\alpha]^{30}_{D}$ = +8.8 (*c* 1.1, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{16}H_{19}{}^{35}ClO_4$ (M^+): 310.0972. Found: 310.0966.



(*R*)-2,2-Dimethyl-5-[1-methyl-1-(3-methylphenyl)propyl]-1,3-dioxane-4,6-dione (2.78): Prepared according to general procedure B except that the reaction was carried out for a period of 72 h. Purification by flash column chromatography on silica gel using 6:1 hexanes:EtOAc, afforded a white solid in 93% yield. M.p. 55-56 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.21-7.16 (m, 1H), 7.07-7.01 (m, 3H), 3.56 (s, 1H), 2.31 (s, 3H), 2.18 (dq, *J* = 7.2, 7.0 Hz, 1H), 2.05 (dq, *J* = 7.1, 7.0 Hz, 1H), 1.59 (s, 3H), 1.57 (s, 3H), 1.14 (s, 3H), 0.75 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.5, 164.0, 142.0.1, 137.7, 128.1, 127.6, 127.5, 123.9, 105.1, 57.0, 46.2, 32.6, 29.4, 27.0, 21.9, 21.6, 8.7; An enantiomeric excess of 78% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 12.5 min (*S*), t_{R2} = 13.7 min (*R*)]. $[\alpha]^{30}_D$ = +1.5 (*c* 0.20, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{17}H_{22}O_4$ (M^+): 290.1518. Found: 290.1513.

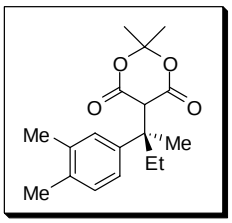


(*R*)-5-(2-(3-Isopropylphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.80): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 12:1 hexanes:EtOAc, afforded a white solid in 91% yield. M.p. 47-50 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.23 (t, *J* = 7.6 Hz 1H), 7.10-7.08 (m, 3H), 3.50 (s,1H), 2.86 (septet, *J* = 6.9 Hz, 1H), 2.24 (dq, *J* = 14.3, 7.2 Hz, 1H), 2.07 (dq, *J* = 14.3, 7.1 Hz, 1H), 1.62 (s, 3H), 1.54 (s, 3H), 1.21 (d, *J* = 6.9 Hz, 6H), 0.97 (s, 3H), 0.81 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.8, 164.3, 148.9, 141.5, 128.4, 125.5, 125.0, 124.5, 105.4, 57.2, 46.7, 34.3, 32.5, 29.8, 26.9, 24.0, 22.5, 8.8; An enantiomeric excess of 97% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 0.5 mL/min, t_{R1} = 18.9 min (*S*), t_{R2} = 19.7 min (*R*)]. $[\alpha]^{32}_D$ = -7.8 (*c* 1.0, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{19}H_{26}O_4$ (M^+): 318.1831. Found: 318.1831.

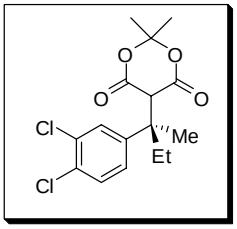


(*R*)-5-(2-(3-*tert*-Butylphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.82): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting

with 10:1 hexanes:EtOAc, afforded a white solid in 99% yield. M.p. 58-60 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (s, 1H), 7.25-7.21 (m, 2H), 7.09-7.08 (m, 1H), 3.49 (s, 1H), 2.26 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.08 (dq, *J* = 14.2, 7.2 Hz, 1H), 1.63 (s, 3H), 1.53 (s, 3H), 1.28 (s, 9H), 0.93 (s, 9H), 0.82 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.3, 151.0, 141.0, 128.0, 124.3, 124.1, 124.0, 105.4, 57.2, 46.8, 34.8, 32.5, 31.4, 31.3, 29.9, 26.9, 22.6, 8.8; An enantiomeric excess of 98% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 9.4 min (*S*), t_{R2} = 10.4 min (*R*)]. $[\alpha]^{30}_{D}$ = -0.83 (*c* 0.5, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{20}H_{28}O_4$ (M^+): 332.1988. Found: 332.1988.

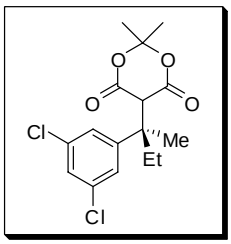


(*R*)-5-(2-(3,4-Dimethylphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.84): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 10:1 hexanes:EtOAc, afforded a white solid in 98% yield. M.p. 66-70 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.07-6.97 (m, 3H), 3.55 (s, 1H), 2.23 (s, 3H), 2.20 (s, 3H), 2.16 (dq, *J* = 14.1, 7.1 Hz, 1H), 2.07 (dq, *J* = 14.0, 7.0 Hz, 1H), 1.58 (s, 6H), 1.14 (s, 3H), 0.76 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.2, 139.4, 136.3, 135.1, 129.5, 128.1, 124.3, 105.2, 57.1, 46.1, 32.6, 29.6, 26.9, 22.1, 20.0, 19.2, 8.8; An enantiomeric excess of 91% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 15.0 min (*S*), t_{R2} = 19.4 min (*R*)]. $[\alpha]^{32}_{D}$ = -8.0 (*c* 1.1, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{18}H_{24}O_4$ (M^+): 304.1675. Found: 304.1684.

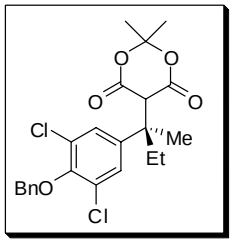


(*R*)-5-[1-(3,4-Dichlorophenyl)-1-methylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.86): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 5:1 petroleum ether:EtOAc, afforded a white solid, after trituration in hexanes, in 72% yield. M.p. 77-79 ºC (hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39-7.34 (m, 2H), 7.11 (d, *J* = 8.3 Hz, 1H), 3.64 (s, 1H), 2.15 (dq, *J* = 14.1, 7.2 Hz, 1H), 2.03 (dq, *J* = 14.2, 7.2 Hz, 1H), 1.67 (s, 3H), 1.56 (s, 3H), 1.47 (s, 3H), 0.70 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.8, 163.4, 143.7,

132.5, 130.8, 130.1, 128.9, 126.2, 105.0, 56.6, 45.3, 32.7, 28.6, 27.7, 20.8, 8.5; An enantiomeric excess of 90% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 13.4 min (*S*), t_{R2} = 15.6 min (*R*)]. $[\alpha]^{30}_{D}$ = +13.7 (*c* 0.30, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{16}H_{18}{}^{35}Cl_2O_4$ (M^+): 344.0582. Found: 344.0587.

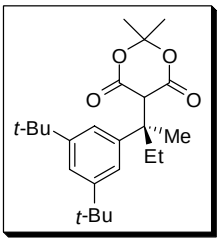


(*R*)-5-(2-(3,5-Dichlorophenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.88): Prepared according to general procedure B with different catalyst loading (copper(II) triflate used was 8 mol % and 16 mol % ligand for 3 days). Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 91% yield. M.p. 108-110 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.23 (t, *J* = 1.7 Hz, 1H), 7.14 (d, *J* = 1.7 Hz, 2H), 3.65 (s, 1H), 2.17 (dq, *J* = 14.4, 7.3 Hz, 1H), 2.00 (dq, *J* = 14.3, 7.2 Hz, 1H), 1.69 (s, 3H), 1.56 (s, 3H), 1.51 (s, 3H), 0.70 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.7, 163.2, 147.2, 135.0, 127.0, 125.5, 105.0, 56.5, 45.5, 32.8, 28.5, 27.8, 20.7, 8.5; An enantiomeric excess of 50% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 14.5 min (*S*), t_{R2} = 17.7 min (*R*)]. $[\alpha]^{32}_{D}$ = -4.5 (*c* 0.3, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{16}H_{18}{}^{35}Cl_2O_4$ (M^+): 344.0582. Found: 344.0583.

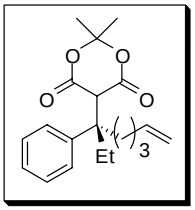


(*R*)-5-(2-(4-(Benzyloxy)-3,5-dichlorophenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.90): Prepared according to general procedure B with different catalyst loading (copper(II) triflate used was 8 mol % and 16 mol % ligand for 3 days). Purification by flash column chromatography on silica gel, eluting with 8:1 hexanes:EtOAc, afforded a white solid in 82% yield. M.p. 96-100 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53 (d, *J* = 6.7 Hz, 2H), 7.41-7.34 (m, 3H), 7.21 (s, 2H), 5.02 (s, 2H), 3.63 (s, 1H), 2.17 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.00 (dq, *J* = 14.2, 7.1 Hz, 1H), 1.69 (s, 3H), 1.56 (s, 3H), 1.49 (s, 3H), 0.72 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.8, 163.4, 149.7, 141.2, 136.3, 129.5, 128.5 (2C), 127.5 (2C), 105.1, 75.0, 56.6, 45.3, 32.8, 28.7, 27.7, 21.0, 8.6;

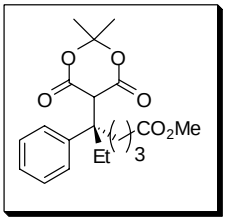
An enantiomeric excess of 59% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 13.9 min (*S*), t_{R2} = 16.9 min (*R*)]. $[\alpha]^{32}_{D}$ = -2.0 (*c* 0.7, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{20}H_{18}{}^{35}Cl_2O_4$ (M^+-acetone): 392.0582. Found: 392.0583.



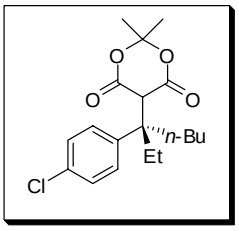
(*R*)-5-(2-(3,5-Di-*tert*-butylphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.92): Prepared according to general procedure B with different catalyst loading (copper(II) triflate used was 8 mol % and 16 mol % ligand for 3 days). Purification by flash column chromatography on silica gel, eluting with 20:1 hexanes:EtOAc, afforded a white solid in 31% yield. M.p. 112-113 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.27 (s, 1H), 7.12 (s, 2H), 3.41 (s, 1H), 2.30 (dq, *J* = 14.3, 7.2 Hz, 1H), 2.09 (dq, *J* = 14.2, 7.2 Hz, 1H), 1.65 (s, 3H), 1.48 (s, 3H), 1.28 (s, 18H), 0.88 (t, *J* = 7.3 Hz, 3H), 0.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.9, 164.5, 150.5, 139.9, 121.5, 121.0, 105.6, 57.2, 47.3, 34.9, 32.3, 31.4, 30.2, 26.6, 23.2, 8.9; An enantiomeric excess of 26% (*R*) was measured by chiral HPLC [AD-H, 0.2% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 10.4 min (*R*), t_{R2} = 12.1 min (*S*)]. Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{24}H_{36}O_4$ (M^+): 388.2614. Found: 388.2623.



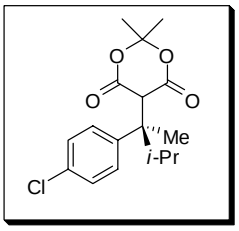
(*S*)-2,2-Dimethyl-5-(3-phenyloct-7-en-3-yl)-1,3-dioxane-4,6-dione (2.94): Prepared according to general procedure B with reaction time of 28 h. Purification by flash column chromatography on silica gel, eluting with 8:1 hexanes:EtOAc, afforded a clear oil in 60% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31-7.17 (m, 5H), 5.78 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 4.99 (d, *J* = 17.1 Hz, 1H), 4.93 (d, *J* = 10.2 Hz, 1H), 3.48 (s, 1H), 2.27-1.99 (m, 6H), 1.44 (s, 3H), 1.41-1.39 (m, 1H), 1.22-1.18 (m, 1H), 0.86 (t, *J* = 7.2 Hz, 3H), 0.72 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6 (2C), 140.6, 138.2, 128.4, 127.3, 127.2, 114.8, 105.4, 54.4, 49.5, 33.9, 32.6, 30.3, 26.3, 26.1, 22.9, 8.1; An enantiomeric excess of 89% (*S*) was measured by chiral HPLC [OJ-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 9.3 min (*R*), t_{R2} = 12.8 min (*S*)]. $[\alpha]^{31}_{D}$ = +11.8 (*c* 1.1, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{20}H_{26}O_4$ (M^+): 330.1831. Found: 330.1827.



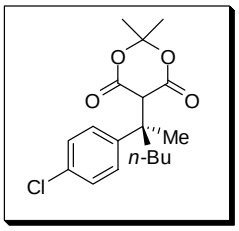
(*S*)-Methyl 5-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-5-phenylheptanoate (2.96): Prepared according to general procedure B with reaction time of 27 h. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, afforded a clear oil in 67% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31-7.17 (m, 5H), 3.61 (s, 3H), 3.47 (s, 1H), 2.39-2.05 (m, 6H), 1.66-1.62 (m, 1H), 1.45-1.43 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.6, 164.7, 164.5, 140.3, 128.5, 127.4, 127.2, 105.6, 54.2, 51.4, 49.4, 34.0, 32.6, 30.3, 26.3, 26.2, 19.0, 8.0; An enantiomeric excess of 89% (*S*) was measured by chiral HPLC [OD-H, 5% *i*-PrOH/heptane with 0.1% TFA, 1.0 mL/min, t_{R1} = 20.2 min (*R*), t_{R2} = 21.6 min (*S*)]. $[\alpha]^{31}_{D}$ = -31.9 (*c* 1.4, THF). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{20}H_{26}O_6$ (M^+): 362.1729. Found: 362.1737.



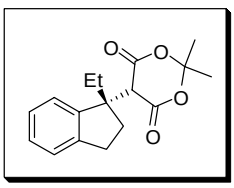
(*S*)-5-[1-(4-Chlorophenyl)-1-ethylpentyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.100): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 7:1 petroleum ether:EtOAc, afforded an oil in 78% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 9.2 Hz, 2H), 3.50 (s, 1H), 2.24 (dq, *J* = 14.7, 7.2 Hz, 1H), 2.20 (dq, *J* = 13.7, 7.1 Hz, 1H), 2.09-1.95 (m, 2H), 1.49 (s, 3H), 1.38 (dq, *J* = 15.3, 7.3 Hz, 2H), 1.33 (dq, *J* = 13.3, 6.8 Hz, 1H), 1.06 (m, 1H), 0.92-0.85 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.8 (2C), 139.6, 133.3, 128.9, 128.5, 105.5, 54.5, 49.3, 33.1, 30.4, 26.6, 26.5, 25.7, 23.1, 14.0, 8.2; An enantiomeric excess of 94% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 0.5 mL/min, t_{R1} = 17.9 min (*R*), t_{R2} = 20.3 min (*S*)]. $[\alpha]^{28}_{D}$ = +4.3 (*c* 0.70, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{19}H_{25}{}^{35}ClO_4$ (M^+): 352.1441. Found: 352.1444.



(*R*)-5-[1-(4-Chlorophenyl)-1,2-dimethylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.103): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 7:1 petroleum ether:EtOAc, afforded an oil in 99% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.27 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 1H), 2.90 (septet, *J* = 6.7 Hz, 1H), 1.58 (s, 3H), 1.54 (s, 3H), 1.10 (s, 3H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.69 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6, 164.0, 140.3, 132.9, 128.6, 128.3, 105.1, 54.3, 49.0, 32.7, 29.3, 27.1, 17.9, 17.8, 17.1; An enantiomeric excess of 65% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 0.5 mL/min, t_{R1} = 24.2 min (*R*), t_{R2} = 27.3 min (*S*)]. $[\alpha]^{30}_D$ = +6.7 (*c* 0.70, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{17}H_{21}{}^{35}ClO_4$ (M^+): 324.1128. Found: 324.1132.

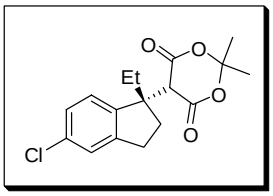


(*R*)-5-[1-(4-Chlorophenyl)-1-methylpentyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (2.104): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 10:1 petroleum ether:EtOAc, afforded a white solid in 87% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 2H), 3.60 (s, 1H), 2.03 (apt dd, *J* = 15.3, 14.0 Hz, 2H), 1.63 (s, 3H), 1.59 (s, 3H), 1.34 (s, 3H), 1.34-1.10 (m, 3H), 0.92-0.80 (m, 1H), 0.82 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.2, 163.8, 141.6, 132.7, 128.4, 128.2, 105.1, 57.3, 45.4, 39.9, 29.1, 27.5, 26.4, 23.1, 22.1, 14.0; An enantiomeric excess of 87% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 11.7 min (*S*), t_{R2} = 14.2 min (*R*)]. $[\alpha]^{30}_D$ = +2.3 (*c* 0.77, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{18}H_{23}{}^{35}ClO_4$ (M^+): 338.1285. Found: 338.1292.

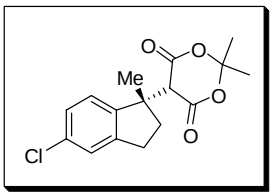


(*S*)-5-(1-Ethyl-2,3-dihydro-1*H*-1-indenyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.106): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 7:1 hexanes:EtOAc, afforded a white solid in 96% yield. M.p. 75-76 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.19-7.08 (m, 4H), 3.70 (s, 1H), 2.95-2.77

(m, 2H), 2.60 (ddd, *J* = 13.1, 8.7, 4.0 Hz, 1H), 2.29 (dq, *J* = 14.1, 7.2 Hz, 1H), 2.13 (dt, *J* = 13.5, 8.7 Hz, 1H), 1.82 (dq, *J* = 14.1, 7.4 Hz, 1H), 1.61 (s, 3H), 1.11 (s, 3H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.2, 164.0, 144.7, 144.3, 127.9, 126.3, 124.9, 124.4, 105.6, 55.8, 52.7, 34.8, 32.1, 30.6, 29.1, 27.3, 8.8; An enantiomeric excess of 96% (*S*) was measured by chiral HPLC [OD, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 8.9 min (*R*), t_{R2} = 14.5 min (*S*)]. $[\alpha]^{28}_D$ = -3.4 (*c* 0.53, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{17}H_{20}O_4$ (M^+): 288.1362. Found: 288.1368.

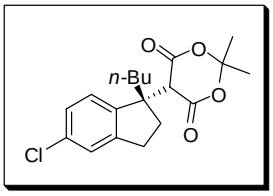


(*S*)-5-(5-Chloro-1-ethyl-2,3-dihydro-1*H*-1-indenyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.108): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 7:1 petroleum ether:EtOAc, afforded an oil in 94% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.17 (s, 1H), 7.12 (d, *J* = 8.3 Hz, 1H), 7.00 (d, *J* = 8.2 Hz, 1H), 3.72 (s, 1H), 2.98-2.77 (m, 2H), 2.51 (ddd, *J* = 13.6, 8.8, 4.1 Hz, 1H), 2.27-2.11 (m, 2H), 1.83 (dq, *J* = 14.0, 7.2 Hz, 1H), 1.66 (s, 3H), 1.32 (s, 3H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 163.6, 146.2, 143.5, 133.4, 126.4, 125.1 (2C), 105.3, 54.7, 52.9, 34.7, 31.8, 30.5, 28.5, 27.7, 8.6; An enantiomeric excess of 99% (*S*) was measured by chiral HPLC [OD, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 9.3 min (*R*), t_{R2} = 11.5 min (*S*)]. $[\alpha]^{28}_D$ = +2.7 (*c* 1.2, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{17}H_{19}{}^{35}ClO_4$ (M^+): 322.0972. Found: 322.0976.

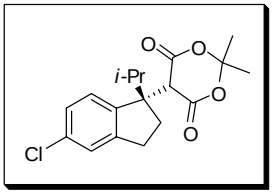


(*S*)-5-(5-Chloro-1-methyl-2,3-dihydro-1*H*-1-indenyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.109): Prepared according to general procedure B, using 5 equiv of Me_2Zn (1.0 M in heptanes) was used. Purification by flash column chromatography on silica gel using 8:1 petroleum ether:EtOAc, afforded an oil in 96% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.18 (s, 1H), 7.14 (d, *J* = 8.8 Hz, 1H), 7.10 (d, *J* = 8.2 Hz, 1H), 3.83 (s, 1H), 2.99-2.80 (m, 2H), 2.60 (ddd, *J* = 13.3, 8.2, 4.9 Hz, 1H), 2.09 (ddd, *J* = 13.4, 8.1, 8.1 Hz, 1H), 1.71 (s, 3H), 1.57 (s, 3H), 1.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.2, 163.6,

145.6, 145.2, 133.3, 126.5, 125.0, 124.9, 105.1, 54.8, 50.2, 38.0, 30.0, 28.1, 28.0, 26.8; An enantiomeric excess of 99% (*S*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 0.8 mL/min, t_{R1} = 30.5 min (*R*), t_{R2} = 38.5 min (*S*)]. $[\alpha]^{30}_{D}$ = -8.6 (*c* 0.50, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{16}H_{17}{}^{35}ClO_4$ (M^+): 308.0815. Found: 308.0811.

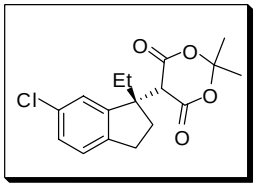


(*S*)-5-(1-Butyl-5-chloro-2,3-dihydro-1*H*-1-indenyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.110): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 10:1 petroleum ether:EtOAc, afforded a white solid in 97% yield; M.p. 88-90 ºC (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.16 (s, 1H), 7.12 (d, *J* = 8.3 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 3.72 (s, 1H), 2.98-2.84 (m, 1H), 2.81 (ddd, *J* = 12.6, 9.0, 4.2 Hz, 1H), 2.53 (ddd, *J* = 13.4, 8.7, 4.6 Hz, 1H), 2.23 (m, 2H), 1.79-1.71 (m, 1H), 1.66 (s, 3H), 1.33 (s, 3H), 1.30-1.23 (m, 3H), 1.07-1.04 (m, 1H), 0.85 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6, 163.6, 146.1, 143.9, 133.4, 126.4, 125.1 (2C), 105.3, 54.3, 53.3, 39.0, 35.2, 30.5, 28.5, 27.7, 26.4, 23.0, 14.0; An enantiomeric excess of 97% (*S*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 8.2 min (*R*), t_{R2} = 10.9 min (*S*)]. $[\alpha]^{30}_{D}$ = -2.1 (*c* 0.60, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{19}H_{23}{}^{35}ClO_4$ (M^+): 350.1285. Found: 350.1293.

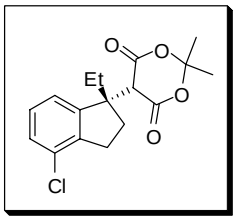


(*S*)-5-(5-Chloro-1-isopropyl-2,3-dihydro-1*H*-1-indenyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.111): Prepared according to general procedure B. Purification by flash column chromatography on silica gel using 10:1 petroleum ether:EtOAc, afforded an oil in 99% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.15 (s, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 6.99 (d, *J* = 8.2 Hz, 1H), 3.84 (s, 1H), 2.98-2.73 (m, 3H), 2.43 (ddd, *J* = 13.7, 9.4, 3.7 Hz, 1H), 2.23 (ddd, *J* = 14.0, 8.9, 8.9 Hz, 1H), 1.61 (s, 3H), 1.15 (s, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.67 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.3, 163.9, 147.1, 141.9, 133.6, 126.4, 125.8, 125.0, 105.4, 59.2, 52.9, 32.7, 30.9, 30.3, 29.1, 27.2, 17.8, 17.6; An enantiomeric excess of 57% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-

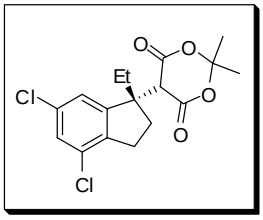
PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 13.4 min (*R*), t_{R2} = 14.2 min (*S*)]. $[\alpha]^{30}_{D}$ = +14.1 (*c* 1.1, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{18}H_{21}{}^{35}ClO_4$ (M^+): 324.1128. Found: 336.1122.



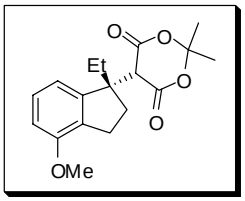
(*S*)-5-(6-Chloro-1-ethyl-2,3-dihydro-*1H*-inden-1-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.113): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 10:1 hexanes:EtOAc, afforded a clear oil in 87% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.14 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.03 (d, *J* = 1.6 Hz, 1H), 3.75 (s, 1H), 2.97-2.76 (m, 2H), 2.49 (ddd, *J* = 13.7, 8.8, 4.9 Hz, 1H), 2.30-2.15 (m, 2H), 1.82 (dq, *J* = 14.0, 7.2, 1H), 1.70 (s, 3H), 1.36 (s, 3H), 0.84 (t, *J* = 7.3 Hz, 3H);); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.5, 163.4, 147.3, 142.6, 131.9, 127.8, 125.9, 124.0, 105.3, 54.9, 53.1, 34.8, 32.0, 30.3, 28.3, 27.8, 8.6; An enantiomeric excess of >99% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 12.4 min (*R*), t_{R2} = 15.7 min (*S*)]. $[\alpha]^{32}_{D}$ = -62.8 (*c* 1.2, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{17}H_{19}{}^{35}ClO_4$ (M^+): 322.0972. Found: 322.0963.



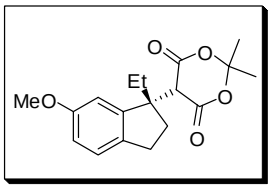
(*S*)-5-(4-Chloro-1-ethyl-2,3-dihydro-*1H*-inden-1-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.115): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 99% yield. M.p. 60-62 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.19 (d, *J* = 7.7 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.98 (d, *J* = 7.4 Hz, 1H), 3.74 (s, 1H), 3.00-2.90 (m, 2), 2.52 (ddd, *J* = 13.6, 8.3, 5.2 Hz, 1H), 2.30-2.14 (m, 2H), 1.87 (dq, *J* = 14.0, 7.2 Hz, 1H), 1.68 (s, 3H), 1.33 (s, 3H), 0.85 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6, 163.5, 147.2, 142.5, 131.0, 127.8 (2C), 122.3, 105.3, 56.1, 53.2, 34.0, 32.1, 30.2, 28.5, 27.6, 8.6; An enantiomeric excess of 79% (*S*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 12.7 min (*R*), t_{R2} = 22.6 min (*S*)]. $[\alpha]^{32}_{D}$ = -3.8 (*c* 0.3, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{14}H_{13}{}^{35}ClO_3$ (M^+-acetone): 264.0553. Found: 264.0560.



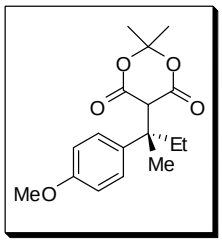
(*S*)-5-(4,6-dichloro-1-ethyl-2,3-dihydro-*1H*-inden-1-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.117): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 10:1 hexanes:EtOAc, afforded a white solid in 86% yield; M.p. 91-93 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.20 (d, *J* = 1.6 Hz, 1H), 6.93 (d, *J* = 1.5 Hz, 1H), 3.79 (s, 1H), 3.00-2.83 (m, 2H), 2.41 (ddd, *J* = 14.1, 8.8, 5.5 Hz, 1H), 2.29-2.16 (m, 2H), 1.84 (dq, *J* = 13.9, 7.1 Hz, 1H), 1.75 (s, 3H), 1.52 (s, 3H), 0.80 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.8, 163.0, 149.1, 141.0, 132.7, 131.4, 127.5, 122.2, 105.1, 55.2, 53.5, 33.9, 32.1, 30.0, 29.7, 27.6, 8.5; An enantiomeric excess of 97% (*S*) was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 10.9 min (*R*), t_{R2} = 13.6 min (*S*)]. $[\alpha]^{23.5}_{D}$ = -7.8 (*c* 0.5, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{14}H_{12}{}^{35}Cl_2O_3$ (M^+-acetone): 298.0163. Found: 298.0169.



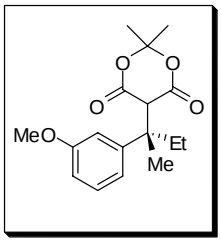
(*S*)-5-(1-Ethyl-4-methoxy-2,3-dihydro-*1H*-inden-1-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.119): Prepared according to general procedure B with minor modifications. The alkylidene was added in one portion in the Schlenk tube under argon and washed with DME, due to the poor solubility of the alkylidene in desired amount of solvent. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a white solid in 91% yield. M.p. 78-80 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.13 (t, *J* = 7.9 Hz, 1H), 6.70 (dd, *J* = 7.8, 2.7 Hz, 2H), 3.78 (s, 3H), 3.71 (s, 1H), 2.80 (t, *J* = 7.2 Hz, 2H), 2.55 (dt, *J* = 13.8, 6.5 Hz, 1H), 2.25 (dq, *J* = 14.0, 7.1 Hz, 1H), 2.13 (dt, *J* = 13.6, 8.3 Hz, 1H), 1.82 (dq, *J* = 14.0, 7.2 Hz, 1H), 1.62 (s, 3H), 1.19 (s, 3H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.9, 163.8, 155.9, 146.6, 131.8, 127.7, 116.3, 109.0, 105.3, 55.9, 55.0, 52.8, 34.6, 32.1, 28.7, 27.4, 27.3, 8.7; An enantiomeric excess of 75% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 22.6 min (*S*), t_{R2} = 24.9 min (*R*)]. $[\alpha]^{32}_{D}$ = -10.8 (*c* 0.7, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_5$ (M^+): 318.1467. Found: 318.1467.



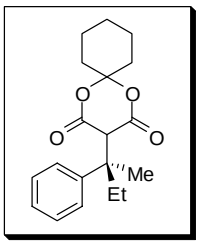
(*S*)-5-(1-Ethyl-6-methoxy-2,3-dihydro-*1H*-inden-1-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.121): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a yellow oil in 99% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.08 (d, *J* = 8.3 Hz, 1H), 6.74 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.63 (d, *J* = 2.0 Hz, 1H), 3.75 (s, 3H), 3.69 (s, 1H), 2.90-2.70 (m, 2H), 2.58 (ddd, *J* = 13.2, 8.7, 4.1 Hz, 1H), 2.27 (dq, *J* = 14.1, 7.2 Hz, 1H), 2.15 (dt, *J* = 13.5, 8.5 Hz, 1H), 1.82 (dq, *J* = 14.1, 7.1 Hz, 1H), 1.63 (s, 3H), 1.18 (s, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.0, 163.8, 158.6, 146.2, 136.2, 125.3, 113.8, 109.8, 105.4, 55.6, 55.4, 52.7, 35.4, 32.1, 29.8, 28.9, 27.4, 8.7; An enantiomeric excess of 99% (*S*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 18.2 min (*R*), t_{R2} = 23.2 min (*S*)]. $[\alpha]^{32}_{D}$ = -49.9 (*c* 1.1, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_5$ (M^+): 318.1467. Found: 318.1472.



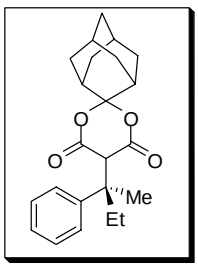
(*S*)-5-(2-(4-Methoxyphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.133): Prepared according to general procedure C. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a clear oil in 93% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.18 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 3.76 (s, 3H), 3.50 (s, 1H), 2.15 (dq, *J* = 14.2, 7.3 Hz, 1H), 2.05 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.57 (s, 3H), 1.56 (s, 3H), 1.16 (s, 3H), 0.76 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.2, 158.4, 133.9, 128.1, 113.6, 105.2, 57.3, 55.2, 46.0, 32.7, 29.6, 27.1, 22.3, 8.7; An enantiomeric excess of 85% (*S*) was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 8.0 min (*S*), t_{R2} = 8.7 min (*R*)]. $[\alpha]^{23.5}_{D}$ = +0.11 (*c* 5.5, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{17}H_{22}O_5$ (M^+): 306.1467. Found: 306.1475.



(*S*)-5-(2-(3-Methoxyphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (2.135): Prepared according to general procedure C. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a clear oil in 79% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.21 (t, *J* = 8.1 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.80 (bs, 1H), 6.74 (dd, *J* = 8.1, 2.1 Hz), 3.75 (s, 3H), 3.60 (s, 1H), 2.09 (dq, *J* = 18.5, 7.1 Hz, 2H), 1.59 (s, 3H), 1.57 (s, 3H), 1.23 (s, 3H), 0.73 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.4, 163.8, 159.5, 144.1, 129.1, 119.1, 113.4, 111.4, 105.0, 56.9, 55.1, 46.0, 32.7, 29.1, 27.2, 21.5, 8.6; An enantiomeric excess of 69% (*S*) was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 7.2 min (*S*), t_{R2} = 8.4 min (*R*)]. $[\alpha]^{25}_{D}$ = –0.38 (*c* 4.8, CH_2Cl_2). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{17}H_{22}O_5$ (M^+): 306.1467. Found: 306.1471.

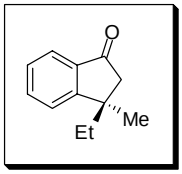


3-((*R*)-2-Phenylbutan-2-yl)-1,5-dioxaspiro[5.5]undecane-2,4-dione (2.141): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 10:1 hexanes:EtOAc, afforded a beige solid in 95% yield. M.p. 85-86 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33-7.19 (m, 5H), 3.59 (s, 1H), 2.18-2.08 (m, 2H), 1.77-1.73 (m, 2H), 1.64-1.60 (m, 5H), 1.52-1.46 (m, 2H), 1.39-1.35 (m, 2H), 1.26-1.22 (m, 2H), 0.75 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.2, 142.3, 128.3, 126.9, 105.9, 57.6, 46.3, 38.6, 35.8, 32.7, 24.0, 22.5, 21.9, 21.7, 8.7; An enantiomeric excess of 86% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 18.1 min (*S*), t_{R2} = 20.7 min (*R*)]. $[\alpha]^{32}_{D}$ = -4.3 (*c* 0.5, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{19}H_{24}O_4$ (M^+): 316.1675. Found: 316.1673.

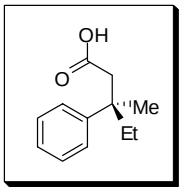


Adamantyl benzyl Meldrum's acid derivative (2.143): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 20:1 hexanes:EtOAc, afforded a white solid in 87% yield. M.p. 97-98 ºC; ^{1}H NMR ($CDCl_3$,

300 MHz) δ 7.32-7.18 (m, 5H), 3.63 (s, 1H), 2.18-2.04 (m, 7H), 1.79-1.78 (m, 2H), 1.69-1.61 (m, 7H), 1.55-1.49 (m, 2H), 1.18-1.17 (m, 1H), 0.74 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 164.1, 142.7, 128.3, 126.8, 108.2, 57.4, 46.0, 39.8, 37.0, 36.9, 33.8, 33.7, 33.1 (2C), 32.8, 26.2, 21.6, 8.7; An enantiomeric excess of 90% (*R*) was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 19.2 min (*R*), t_{R2} = 20.4 min (*S*)]. $[\alpha]^{32}_D$ = -3.5 (*c* 0.6, $CHCl_3$). Absolute configuration was assigned by analogy to **2.2**. HRMS(EI) *m/z* calc'd for $C_{23}H_{28}O_4$ (M^+): 368.1988. Found: 368.1989.



(*R*)-3-Ethyl-3-methyl-1-indanone (2.146): $Sc(OTf)_3$ (10 mol %) and **2.2** were added to a Schlenk tube in the glove box. The Schlenk tube was charged with CH_3NO_2 (0.1 M) outside the glove box.[21] The reaction mixture was then placed in a pre-heated bath at 100 ºC. After 30 minutes the crude mixture was concentrated and purified by flash column chromatography on silica gel using 14:1 petroleum ether:EtOAc to afford a light yellow oil in 60% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.67 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 1H), 2.63 (d, *J* = 18.9 Hz, 1H), 2.40 (d, *J* = 18.9 Hz, 1H), 1.73 (dq, *J* = 14.4, 7.3 Hz, 1H), 1.63 (dq, *J* = 14.0, 7.2 Hz, 1H), 1.37 (s, 3H), 0.71 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 206.0, 162.5, 136.1, 134.8, 127.3, 123.8, 123.2, 49.6, 42.3, 34.7, 27.9, 9.2; $[\alpha]^{21}_D$ = -7.5 (84% ee) (*c* 0.42, benzene), literature (*R* isomer) $[\alpha]^{22}_D$ = -10.1 (*c* 3.4, benzene).[29] HRMS(EI) *m/z* calc'd for $C_{12}H_{14}O$ (M^+): 174.1045. Found: 174.1040.



(*R*)-3-Methyl-3-phenylpentanoic acid (2.147):[29,30] A solution of Meldrum's acid **2.2** in water/DMF (3:1) and catalytic amount of H_2SO_4 was heated to 80 ºC for 2 hours. The reaction was cooled to room temperature then extracted with ether (3X) and washed with brine (1X). The combined organics were dried with $MgSO_4$, filtered and concentrated. The crude malonic acid derivative was then heated to 190 ºC neat for 1 hour. The residue was dissolved in CH_2Cl_2 and the organic layer washed with 5% HCl (3X), dried over $MgSO_4$, filtered and concentrated. Purification by flash column chromatography on silica gel

using 5:1 petroleum ether:EtOAc, afforded a light yellow oil in 89% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33-7.24 (m, 4H), 7.19-7.15 (m, 1H), 2.71 (d, *J* = 14.2 Hz, 1H), 2.59 (d, *J* = 14.2 Hz, 1H), 1.83 (dq, *J* = 13.9, 7.2 Hz, 1H), 1.71 (dq, *J* = 13.9, 7.2 Hz, 1H), 1.45 (s, 3H), 0.67 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.7, 146.0, 128.1, 126.1, 125.9, 46.4, 40.4, 35.1, 23.9, 8.6. An enantiomeric excess of 84% (*R*) was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.5 mL/min, t_{R1} = 14.3 min (*S*), t_{R2} = 15.5 min (*S*)]. $[\alpha]^{20}_{D}$ = -8.8 (*c* 0.24, $CHCl_3$), literature (*R* isomer) $[\alpha]^{22}_{D}$ = -15.2 (*c* 3.7, $CHCl_3$).[29] HRMS(EI) *m/z* calc'd for $C_{12}H_{16}O_2$ (M^+): 192.1150. Found: 192.1149.

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[24] Compound **2.150** was not isolated. It was verified by independent synthesis via the 1,4-addition of MeMgBr to 5-(2-fluorobenzylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione. Also, it is assumed that the **2.150** is racemic: see reference 11 and Chapter 3 for further discussion.

[25] For example C-C bond length in propane is 1.526 Å while C-Si in mono-, di-, and trimethyl silane is 1.867 Å, see: Lide, D. R. Jr. *Tetrahedron* **1962**, *17*, 125-134 and references cited therein.

[26] The word "exo" is used to describe the *meta* substituent facing away from the olefin while "endo" indicates positioning of *meta* substituent pointing closer to the olefin.

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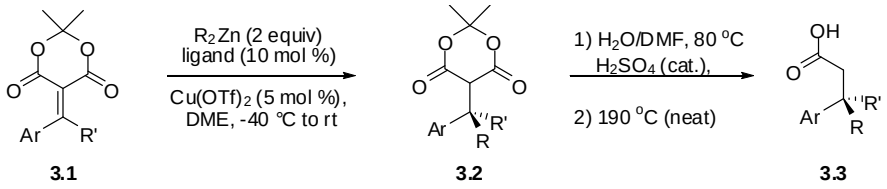
Chapter 3*

Catalytic Asymmetric 1,4-Addition to 2-Arylacetate Derivatives: A Class of Functionalized Benzylidene Meldrum's Acids

(A) Introduction

In Chapter 2 the asymmetric synthesis of benzylic quaternary stereocentres via the copper catalyzed 1,4-addition of dialkylzinc reagents to 5-(1-arylalkylidene) Meldrum's acids was described.[1] Products obtained from this reaction can be used for the preparation of carboxylic acids having an β-quaternary centre (Scheme 3.1).

Scheme 3.1: Preparation of carboxylic acids having an β-quaternary centres via a transformation of 1,4-addition products



3.1 **3.2** **3.3**

We were encouraged to broaden the scope and the synthetic versatility of this methodology and hypothesized that acyclic, tetrasubstituted 2-aryl acetate derivatized olefins might be suitable and direct precursors to carboxylic acid derivatives bearing an α-quaternary centre in the asymmetric 1,4-addition reaction (Scheme 3.2).

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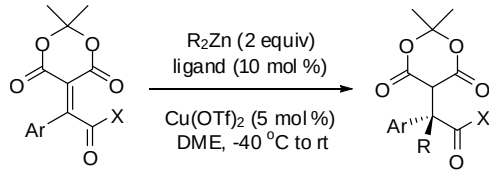
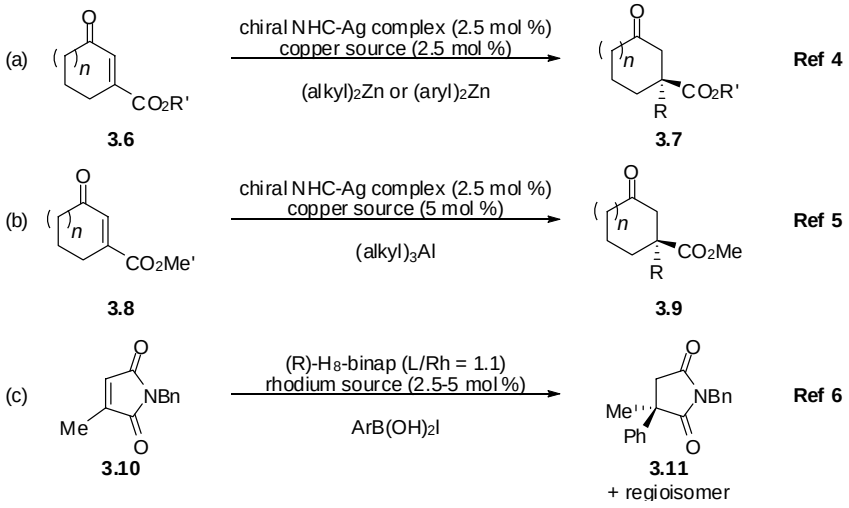
Scheme 3.2: Preparation of carboxylic acids having an α-quaternary centres via a direct 1,4-addition to 2-aryl acetate derivatives



3.4 **3.5**

Not only is the asymmetric synthesis of carboxylic acid derivatives having an α-quaternary centre a long-standing challenge in organic chemistry, with a growing number of catalytic methods that are available to access this structural motif,[2,3] there are only three reports that were reported during and subsequent to our investigations for the access of this moiety in the context of asymmetric conjugate addition. Copper-catalyzed addition of organozinc and trialkylaluminium reagents to cyclic γ-keto esters and Rh-catalyzed reaction of arylboronic acids with 3-substituted maleimides and 2-methyl-1,4-naphthoquinone were described.[4,5,6] In all these reports, excellent yields and selectivities were obtained on cyclic, trisubstituted olefins.

Scheme 3.3: Literature precedent on the preparation of carboxylic acids having an α-quaternary centres via direct 1,4-addition



In this chapter, a general approach to the asymmetric construction of carboxylic acid derivatives having an α-quaternary centre via copper-catalyzed conjugate addition of

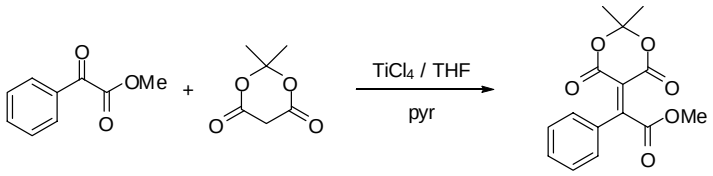
dialkylzinc reagents to 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)aryl acetates is described (Scheme 3.2).[7] The proposed general strategy relies on the highly activated nature of these Michael acceptors to induce umpolung of the position α to the non-Meldrum's acid carbonyl, and allow this centre to act as an electrophile toward organozinc reagents.

(B) Results and Discussion

(I) Substrate Preparation

In order to investigate the asymmetric 1,4-addition to 2-aryl acetate derivatives for the formation of carboxylic acids containing an α-quaternary centre, efficient access to these substrates is necessary. Conveniently, Baxter and Brown have reported the successful Knoevenagel condensation of an α-keto ester with Meldrum's acid (Scheme 3.4).[8] In addition to representing a single entry in this report, this is also the only time this compound was reported, showing that it can be made but never shown its potential use in chemical transformations.

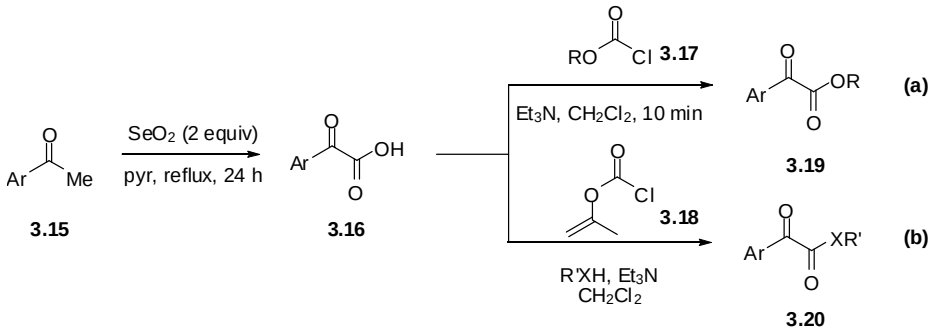
Scheme 3.4: Knoevenagel condensation of α-keto ester with Meldrum's acid



3.12 **3.13** **3.14**

On the contrary, there are numerous reports describing the synthesis of α-keto esters;[9] however, it was found that the most general and easily accessible method for their synthesis is a two-step protocol involving oxidation of acetophenones with selenium dioxide to the α-keto acids[10] and esterification of these intermediates with the appropriate chloroformates (Scheme 3.5a).[11] In the absence of the desired chloroformate, an alternative procedure involving isopropenyl chloroformate and an alcohol/thiol can be used for the esterification process (Scheme 3.5b).[12]

Scheme 3.5: Preparation of α-keto esters

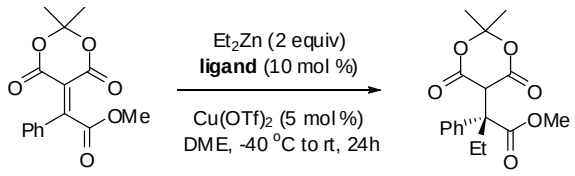


Although some of these α-keto esters are commercially available, they can be relatively expensive. Nevertheless, this three-step process for the generation of these 2-aryl acetate derivatives from acetophenones can be obtained in generally high yields. Furthermore, all intermediates are carried through without the need for purification, while the Knoevenagel compounds are purified via recrystallization/trituration.

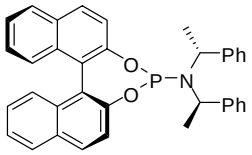
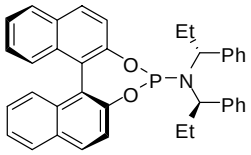
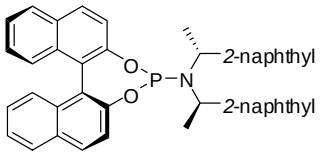
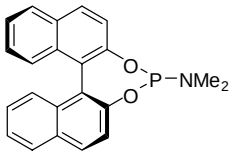
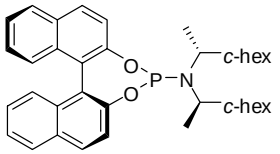
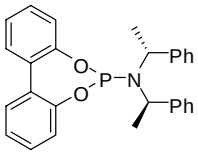
(II) Ligand Optimization

With ready access to 2-aryl acetate olefins, **3.14** was subjected to 2 equiv of Et_2Zn, 10 mol % of phosphoramidite ligand **3.22**[13] and 5 mol % of $Cu(OTf)_2$ in 1,2-dimethoxyethane (DME); **3.21** was isolated as a single regioisomer in quantitative yield and an enantiomeric excess of 88% (Table 3.1, entry 1). This result was gratifying as it represents the first example of enantioselective 1,4-addition to electrophilic sp^2-carbon centres flanked by two sp^2-hybridized carbons. In attempts to achieve higher selectivities, phosphoramidites **3.23**−**3.27** were prepared (Table 3.1).[14] It was found that the replacement of the phenyl group on **3.22** with 2-naphthyl or cyclohexyl had little effect (entries 2 and 3). Similarly, analogous ethyl-substituted ligand **3.25** furnished identical ee as **3.22** (entry 4). On the other hand, the chiral amine moiety was crucial for optimal selectivity; using **3.26**, **3.22** was obtained in a moderate 70% ee (entry 5). Furthermore, the binaphthyl moiety was necessary to achieve high enantioselectivity as the biphenol based ligand **3.27** led to a poor ee (entry 6). On the basis of these results, **3.22** was selected as the optimal ligand and used throughout this study.

Table 3.1: Survey of phosphoramidite ligands on the Et_2Zn Addition to Alkene **3.14**



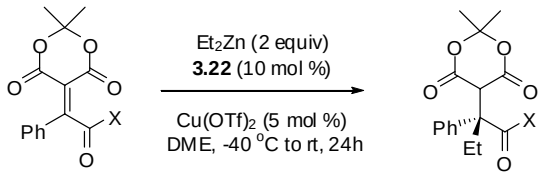
3.14 **3.21**

entry	ligand	yield (%)	ee (%)	entry	ligand	yield (%)	ee (%)
1	 **3.22**	quant	88 (*S*)	4	 **3.25**	90	88 (S)
2	 **3.23**	quant	90 (S)	5	 **3.26**	85	70 (S)
3	 **3.24**	quant	92 (S)	6	 **3.27**	86	16 (R)

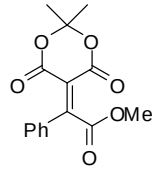
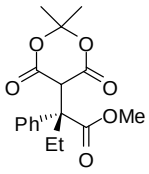
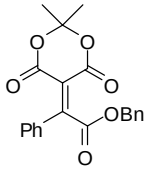
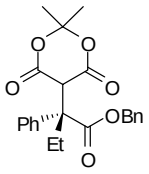
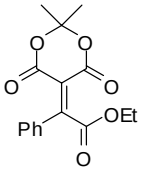
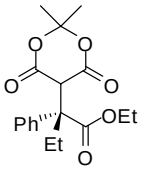
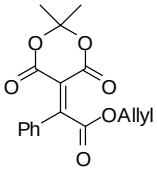
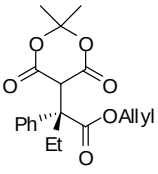
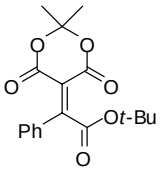
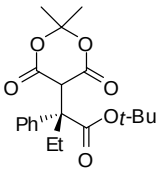
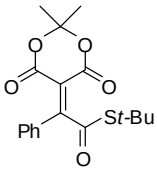
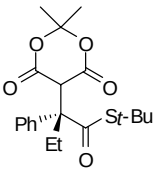
(III) Substrates – Scope for the asymmetric 1,4-addition to 2-aryl acetate derivatives

We then set out to define the scope of the methodology by modifying the ester and aromatic moieties of **3.28** (Table 3.2). It was shown that the sterics of the ester had little influence on the enantioselectivity of the reaction (entries 1-3). Esters that can be deprotected via the assistance of palladium catalysis such as benzyl and allyl esters are well tolerated (entries 4-5). Of note, thioesters are compatible with the asymmetric conjugate addition leading to good yields and enantioselectivities (entry 6).

Table 3.2: Scope of the Et_2Zn addition to modified esters on alkenes **3.28**

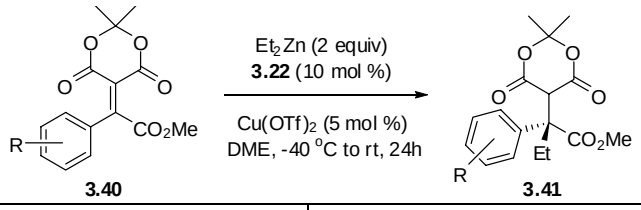


3.28 **3.29**

entry	substrate	product	yield (%)	ee (%)	entry	substrate	product	yield (%)	ee (%)
1			quant	88	4			98	88
	3.14	**3.20**				**3.34**	**3.35**		
2			94	90	5			quant	88
	3.30	**3.31**				**3.36**	**3.37**		
3			quant	86	6			90	90
	3.32	**3.33**				**3.38**	**3.39**		

Substitution at the para and meta positions of the phenyl ring was then investigated (Table 3.3). Electron-withdrawing (entries 1-2, 6), inductively donating (entries 3-4, 7) and electron-donating substituents were observed to have negligible influence on the enantioselectivity of the addition, regardless of the substituent steric demand, with ee being the highest in the *para*-substituted examples (entries 1-5 vs. 6-8). Furyl and naphthyl substrates **3.58** and **3.60** provided products **3.59** and **3.61**, respectively, in good yields and selectivities (entries 9 and 10).

Table 3.3: Scope of the Et_2Zn addition to para/*meta*-substituted phenyl ring and aryl variations on alkenes **3.40**

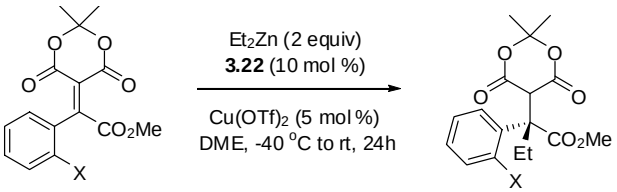


3.40 **3.41**

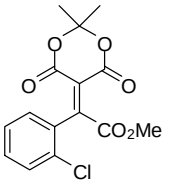
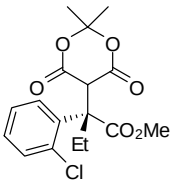
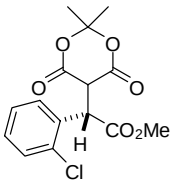
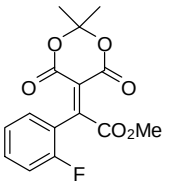
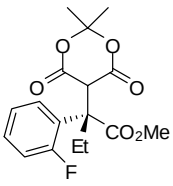
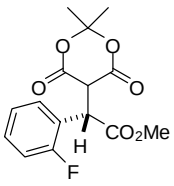
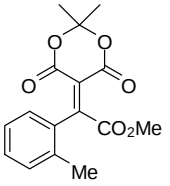
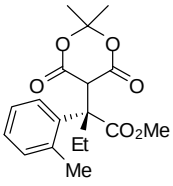
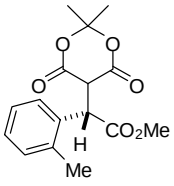
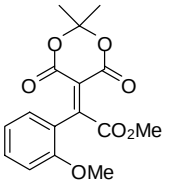
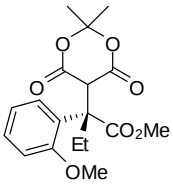
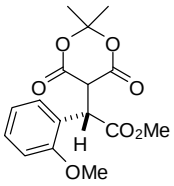
entry	substrate	product	yield (%)	ee (%)	entry	substrate	product	yield (%)	ee (%)
1	**3.42**	**3.43**	91	94	6	**3.52**	**3.53**	92	83
2	**3.44**	**3.45**	97	92	7	**3.54**	**3.55**	quant	84
3	**3.46**	**3.47**	98	90	8	**3.56**	**3.57**	87	82
4	**3.48**	**3.49**	82	92	9	**3.58**	**3.59**	97	88
5	**3.50**	**3.51**	quant	92	10	**3.60**	**3.61**	88	92

In contrast to para and meta substitution, ortho substituents led to inconsistent results, as competing, racemic conjugate reduction occurred and ee fluctuated with the nature of the substituent (Table 3.4).

Table 3.4: Scope of the Et_2Zn addition to *ortho*-substituted phenyl ring on alkenes **3.62**



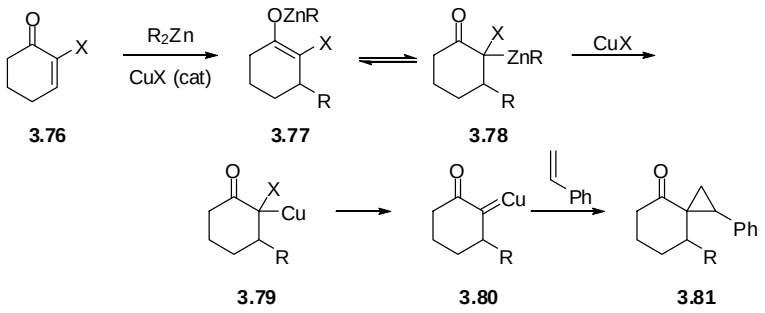
3.62 **3.63**

entry	substrate	1,4-Addition product	yield (%)	ee (%)	Reduced product	yield (%)	ee (%)
1			41	80		53	<5
	3.64	**3.65**			**3.66**		
2			62	32		12	<5
	3.67	**3.68**			**3.69**		
3			quant[a]	58		quant[a]	<5
	3.70	**3.71**			**3.72**		
3			79	42		21	<5
	3.73	**3.74**			**3.75**		

[a]isolated as a 84:16 mixture of **3.71** and reduced product **3.72**

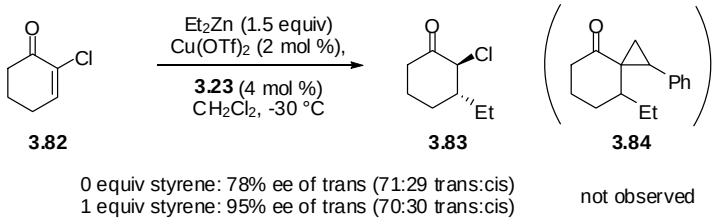
In efforts to minimize the formation of reduced products when substituents are placed at the ortho position relative to the electrophilic centre and possibly obtain 1,4-addition products in higher yields and enantioselectivities, we focused our attention on a recent report by Li and Alexakis.[15] The hypothesized tandem 1,4-addition of Et_2Zn to α-halo enones followed by cyclopropanation utilizing styrene did not give any of the expected cyclopropanated product (Scheme 3.6).

Scheme 3.6: Hypothesized pathway for tandem 1,4-addition/ cyclopropanation



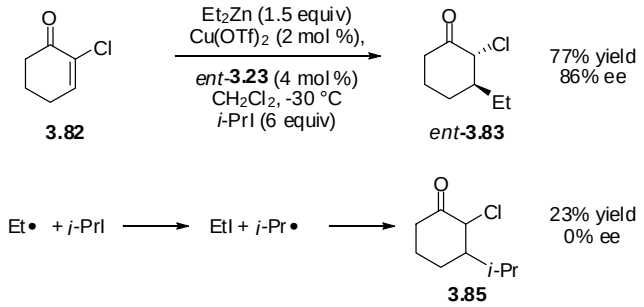
Instead, they observed an enhancement of enantioselectivity for the 1,4-addition product (Scheme 3.7).

Scheme 3.7: Use of styrene enhances the enantioselectivity for the asymmetric 1,4-conjugate addition to α-haloenones



The authors postulated that an ethyl radical generated in the reaction is responsible for lower ee while the styrene acts as a radical scavenger. Evidently, the addition of *i*-PrI to the reaction gave enhanced ee for the 1,4-product and also observation of an i-Pr 1,4-addition product in racemic fashion (Scheme 3.8).

Scheme 3.8: Evidence for radical generation in the asymmetric 1,4-conjugate of Et_2Zn to α-haloenones



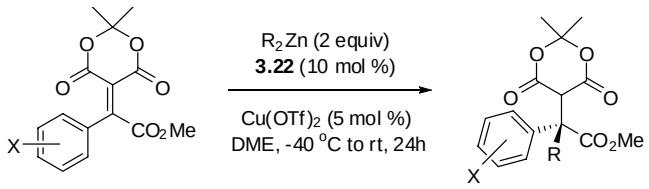
Encouraged by their findings, and in hopes to obtain higher enantioselectivities for the 1,4-addition and diminish the formation of reduced products, we subjected *ortho*-substituted 2-aryl acetate derivatives **3.64**, **3.67**, **3.70** and **3.73** to optimized conjugate addition conditions with the addition of 10 equiv of styrene. Unfortunately, similar outcomes were obtained for both enantioselectivities and ratios of 1,4-addition products and reduced products. The observation of these reduced products can be rationalized via the β-hydride addition of the alkyl nucleophile to alkylidene Meldrum's acid acceptors. Nevertheless, the complete conversion for the addition of dialkylzinc reagents to *ortho*-substituted 2-aryl acetates **3.62** is a significant improvement in comparison to unreactive *ortho*-substituted alkylidene Meldrum's acids discussed in the previous chapter.

(IV) Dialkylzinc reagents – Scope for the asymmetric 1,4-addition to 2-aryl acetate derivatives

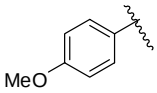
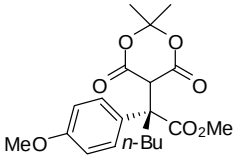
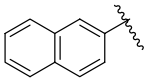
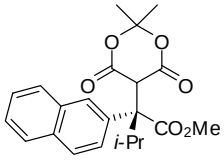
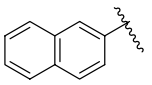
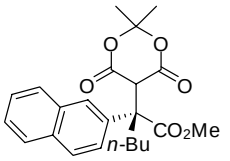
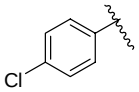
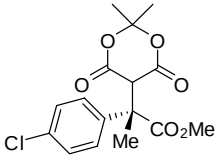
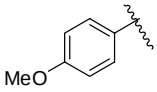
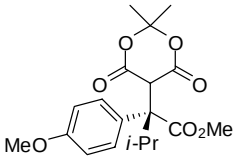
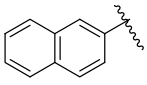
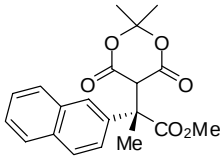
To complete the investigation on the scope of the asymmetric 1,4-addition to 2-aryl acetate derivatives, organozinc reagents other than Et_2Zn were considered. The addition of *n*-Bu_2Zn, *i*-Pr_2Zn, and Me_2Zn to benzylidenes **3.50**, **3.60**, and **3.42** led to Meldrum's acids **3.87-3.92** in ee's up to 92% (Table 3.5). *n*-Bu_2Zn and *i*-Pr_2Zn gave results comparable to Et_2Zn, but Me_2Zn furnished lower enantioselectivity.

In Chapter 2, the asymmetric copper-catalyzed 1,4-addition of Me_2Zn to alkylidene Meldrum's acids was successful upon optimization of conditions initially performed with Et_2Zn as the nucleophile.[16] In light of such optimizations, we set to improve the yields and enantioselectivities of the Me_2Zn addition to 2-aryl acetate derivatives by varying the chiral phosphoramidite ligand, the copper source, and the solvent.

Table 3.5: Scope of the R_2Zn addition to 2-aryl acetate derivatives

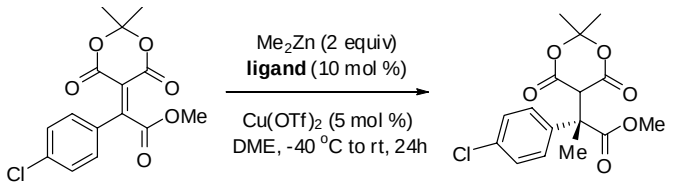


3.40 **3.86**

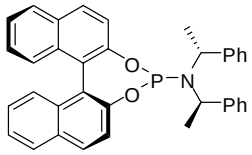
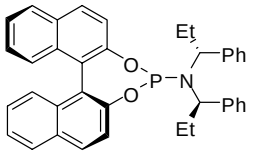
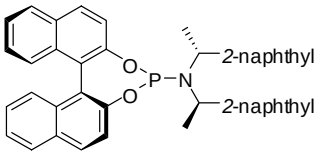
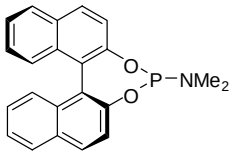
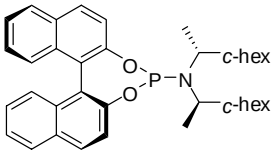
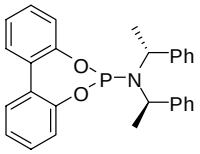
entry	substrate	product	yield (%)	ee (%)	entry	substrate	product	yield (%)	ee (%)
1	 **3.50**	 **3.87**	91	90	4	 **3.60**	 **3.90**	79	88
2	 **3.60**	 **3.88**	88	92	5	 **3.42**	 **3.91**	quant	60
3	 **3.50**	 **3.89**	86	84	6	 **3.60**	 **3.92**	90	62

Chiral phosphoramidite ligands **3.23-3.27** were initially investigated for optimal enantioselectivity and yield (Table 3.6). Despite changing the aryl substituent on the phosphoramidite to 2-naphthyl or cyclohexyl, the enantioselectivity was only modest in comparison to **3.22** (entries 2-3 versus 1). Switching the alkyl moiety of the phosphoramidite ligand from a methyl to an ethyl led to lower enantioselectivity and yield (entry 4). Ligands **3.26** and **3.27** illustrate the importance of the chiral BINOL moiety of the phosphoramidite ligand for the asymmetric 1,4-addition to 2-aryl acetate derivative **3.42**. With these results at hand **3.22** was chosen as the ligand of choice for optimization of the copper source and solvent.

Table 3.6: Survey of phosphoramidite ligands for the Me_2Zn addition to alkene **3.42**

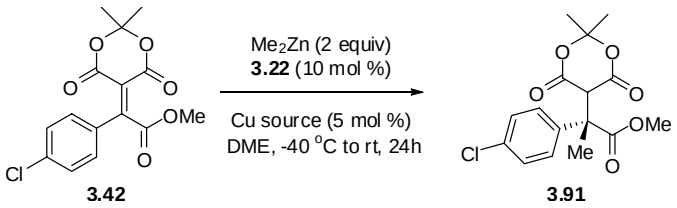


3.42 **3.91**

entry	ligand	yield (%)	ee (%)	entry	ligand	yield (%)	ee (%)
1	 **3.22**	quant	60	4	 **3.25**	90	35
2	 **3.23**	quant	32	5	 **3.26**	85	37
3	 **3.24**	quant	49	6	 **3.27**	85	< 5

A survey of copper catalysts was used in the optimization of Me_2Zn addition to 2-aryl acetate derivative **3.42**. Most copper catalysts investigated effectively catalyzed the conjugate addition reaction with various success, however $Cu(OTf)_2$ remains the optimal copper catalyst of choice. The analogous copper(I) triflate also catalyzes the reaction efficiently in high yield and similar enantioselectivity.

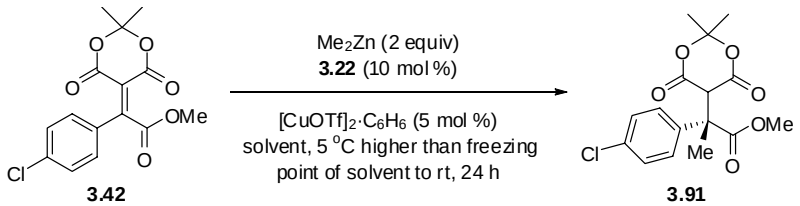
Table 3.7: Survey of copper sources for the Me_2Zn addition to alkene **3.42**



Entry	Cu Source	Yield (%)	ee (%)
1	*$Cu(OTf)_2$*	*quant*	*60*
2	$Cu(O_2CCF_3)\cdot H_2O$	86	47
3	$Cu(acac)_2$	83	47
4	$CuBr_2$	n/a	7
5	$CuCl_2\cdot H_2O$	76	27
6	CuTC	81	43
7	CuF_2	96	36
8	$(CH_3CN)_4CuPF_6$	79	41
9	CuSPh	85	38
10	$[Cu(OTf)]_2\cdot C_6H_6$	quant	50

Although copper(II) triflate led to slightly higher ee in comparison to copper(I) triflate, the latter was chosen in the optimization of solvents in the Me_2Zn addition to **3.42** (Table 3.8). Since the catalytic metal is copper(I), problems associated with reducing copper(II) to copper(I) in situ for certain solvents may be avoided. The use of ethereal solvents such as THF or diethyl ether was less effective for both yields and enantioselectivities (entries 2-3). A polar solvent such as nitromethane was detrimental to the observed selectivity (entry 4). Aromatic based solvents were similarly effective in the asymmetric conjugate addition in comparison to DME (entries 5-6). Although chlorinated solvents led to slower rate in the conjugate addition, a modest improvement of enantioselectivity was observed for chloroform in comparison to DME (entries 7-9). The use of styrene in combination with a chlorinated solvent did not increase the ee (entry 10).[15] Of note, the use of acetonitrile as solvent led to observation of trace amounts of **3.91**. With only a modest increase of ee in chloroform while the reaction rate decreased considerably, the initial condition employing 1,2-dimethoxyethane was set as the optimal conditions in the asymmetric 1,4-addition of Me_2Zn to 2-aryl acetate derivatives.

Table 3.8: Survey of solvents for the Me_2Zn addition to alkene **3.42**



3.42 **3.91**

Entry	Solvent	Yield (%)	ee (%)
1	*DME*	*quant*	*60*
2	THF	50	44
3	Et_2O	71	44
4	CH_3NO_2	86	racemic
5	PhMe	79	54
6	PhCl	98	58
7	CH_2Cl_2	31	48
8	$(CH_2)_2Cl_2$	83	54
9	$CHCl_3$	90	66[a]
10	$CHCl_3$	44	62[b]
11	MeCN	trace	n/a

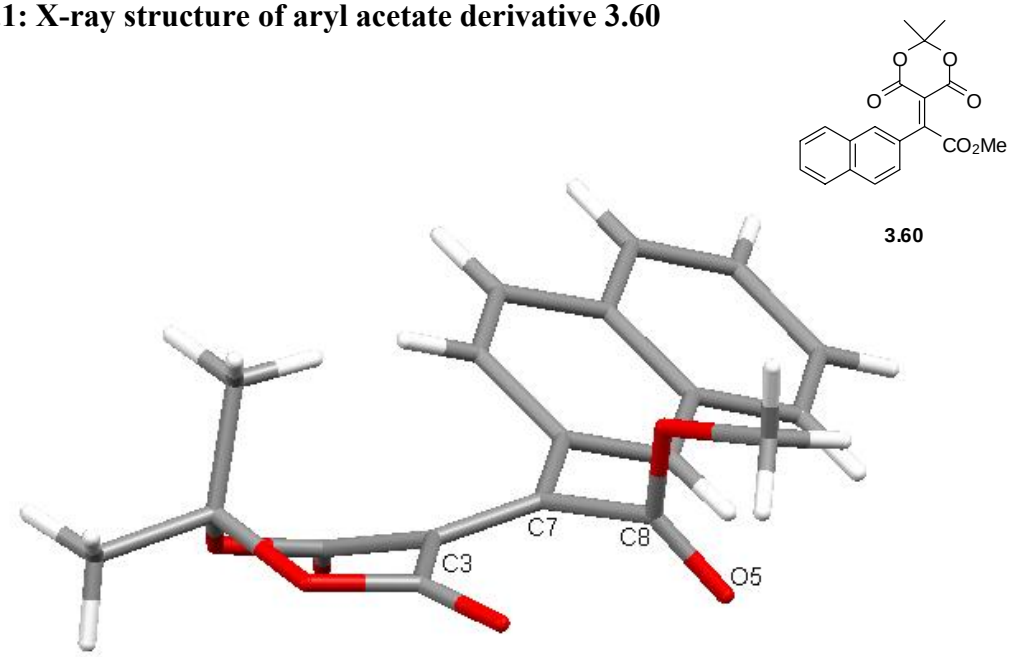
[a]72 h [b]10 equiv styrene, 45% conversion

(V) Insights into factors determining the enantioselectivity observed for the asymmetric 1,4-addition to 2-aryl acetate derivatives

For the successful formation of carboxylic acids with an α-all carbon benzylic quaternary stereocentres via the asymmetric 1,4-addition to 2-aryl acetate derivatives, differentiation between two sp^2-carbons must be evident. We set to investigate some possible factors influencing the observed enantioselectivity for this reaction.

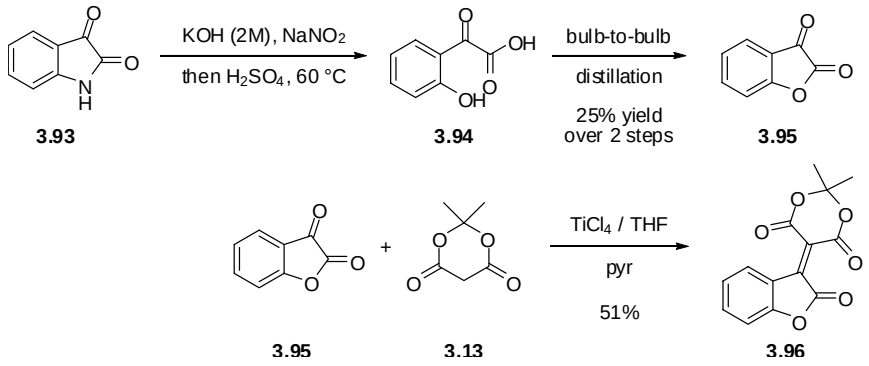
Although conjugation would favour the planarity of the benzylidene Meldrum's acids, the x-ray structure of **3.60** clearly shows otherwise. Figure 3.1 shows that the carbonyl group of the ester is nearly perpendicular to the alkene (dihedral angle C3−C7−C8−O5 = 101.5°), which suggests that the nonplanar environment around the electrophilic carbon centre created by the ester group's orientation might be key in the enantiodifferentiating step.

Figure 3.1: X-ray structure of aryl acetate derivative 3.60



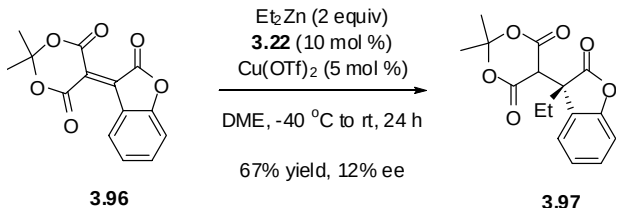
To support this hypothesis, conformationally locked and planar benzylidene **3.96** was synthesized in three steps (Scheme 3.9). Interestingly, a number of methods to synthesize α-keto lactones were attempted, and an older literature procedure starting from commercially available isatin (**3.93**) prevailed.[17]

Scheme 3.9: Synthesis of conformationally locked and planar benzylidene **3.96**



As shown in Scheme 3.10, the addition of Et_2Zn to benzylidene **3.96** furnished nearly racemic **3.97**, which contrasts with the selectivity obtained with nonplanar ortho substituted substrates **3.64**, **3.67**, **3.70**, and **3.73** (Table 3.4).

Scheme 3.10: Addition of Et_2Zn to conformationally locked and planar benzylidene **3.96**



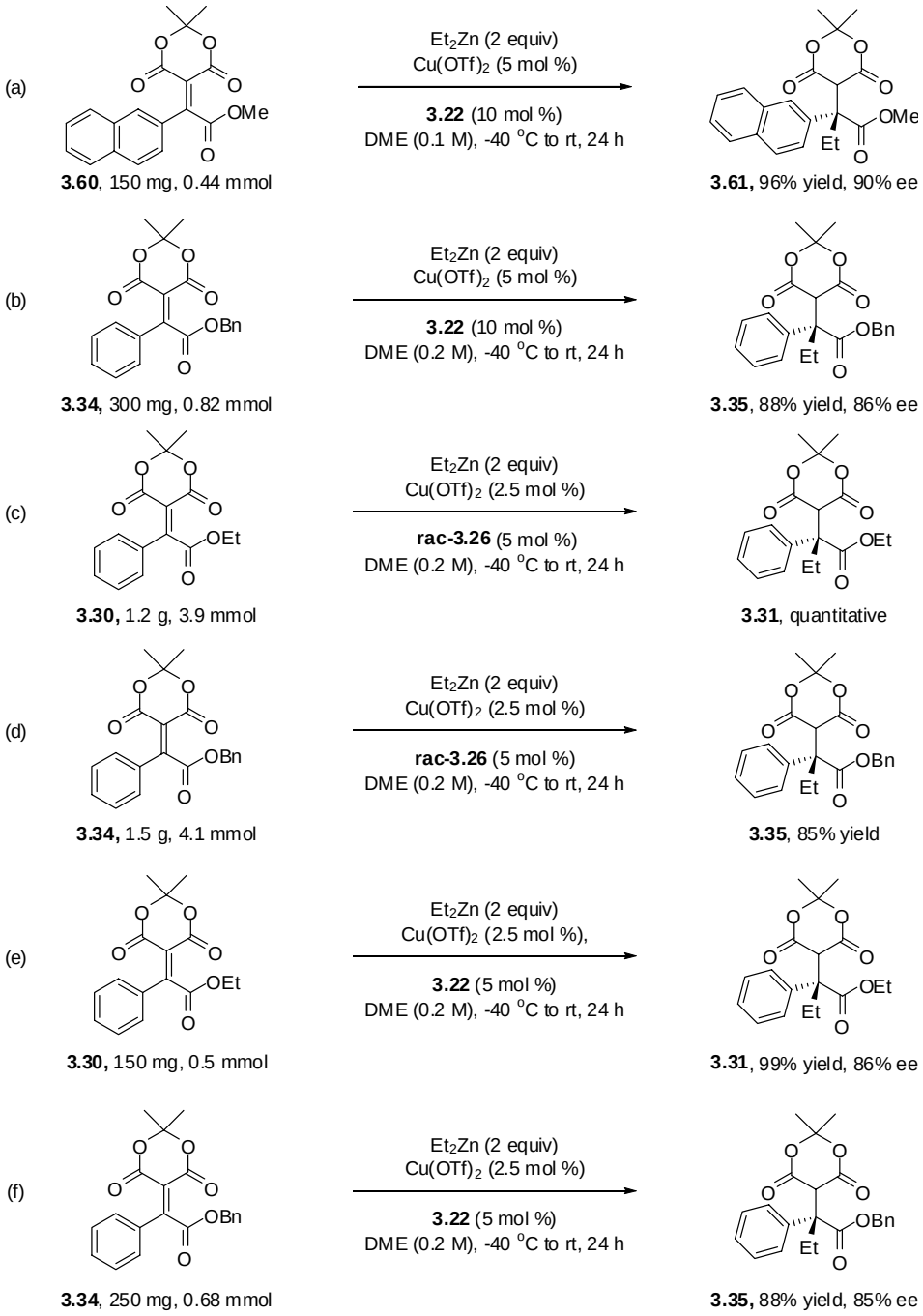
3.96 **3.97**

(VI) Applications

The significance of preparing highly functionalized quaternary centres lies in the variety of subsequent transformations and diversity of chiral structures accessible through these intermediates. Since the conjugate addition products were performed on a 0.1 mmol scale, a larger preparative scale was necessary to investigate the transformation of the generated quaternary stereocentres in reactions.

Standard conditions employing aryl acetate derivative **3.60** at a 0.4 mmol scale led to 1,4-addition product **3.61** in 96% yield and 90% ee, which is a higher yield and a similar ee to that of the typical 0.1 mmol scale (Scheme 3.11a versus Table 3.3, entry 10). It was observed that increasing the concentration of the benzylidene Meldrum's acid **3.34** (0.8 mmol scale) in DME from 0.1 M to 0.2 M led to **3.35** in 88% yield and 86% ee, respectively, having little effect on the enantioselectivity and yield (Scheme 3.11b versus Table 3.3, entry 4). Furthermore, the use of lower $Cu(OTf)_2$ loading (2.5 mol %) and 5 mol % of *rac*-**3.26** with benzylidene Meldrum's acid **3.30** and **3.34** (concentration of 0.2 M in DME), was also effective for the preparation of *rac*-**3.31** (4 mmol, quantitative yield) and *rac*-**3.35** (4 mmol, 85% yield) (Scheme 3.11c,d). Asymmetric 1,4-addition using **3.22** as the chiral ligand and 2-aryl acetate derivatives **3.30** or **3.34** with low catalyst loading and concentrated solvent conditions, was effective in the preparation of **3.31** (0.5 mmol, 99% yield, 86% ee) and **3.35** (0.7 mmol, 88% yield, 85% ee) (Scheme 3.11e,f).

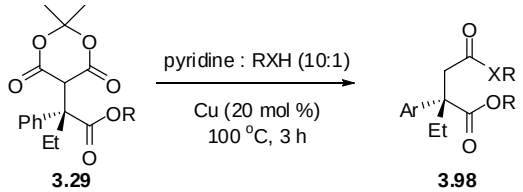
Scheme 3.11: Preparative scale



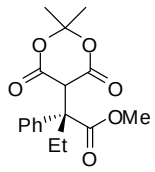
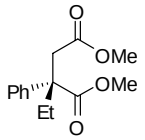
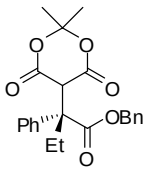
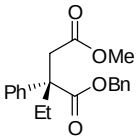
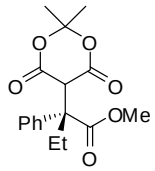
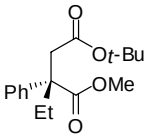
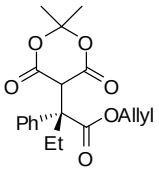
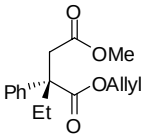
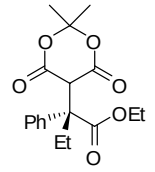
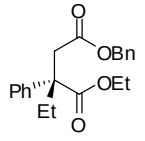
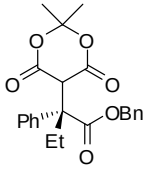
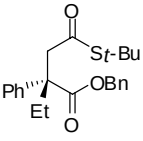
In summary, carboxylic acid derivatives with α-quaternary stereocentres can be obtained in high yields and enantioselectivities for up to at least 4 mmol scale under lower catalyst loading and more concentrated solvent conditions.

With readely access to highly functionalized quaternary stereocentres, we first set to investigate chemical transformations that would chemoselectively transform either the Meldrum's acid or ester moieties. Subjecting 1,4-addition products to alcohols in the presence of pyridine and powdered copper at 100 °C promotes the ring opening of Meldrum's acids and decarboxylation to afford diesters in good yields (Table 3.9).[18] The reaction is tolerant to various nucleophiles such as MeOH (entries 1, 4-5), *t*-BuOH (entry 2), BnOH (entry 3), and even *t*-BuSH (entry 6). Also, various esters in **3.29** are compatible including methyl (entries 1-2), ethyl (entry 3), benzyl (entries 4 and 6), and allyl (entry 5) esters without any transesterification.

Table 3.9: Chemoselective ring opening of Meldrum's acid moiety

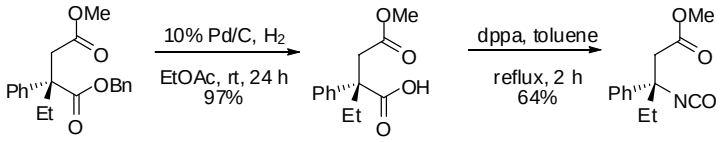


3.29 **3.98**

entry	substrate	product	yield (%)	entry	substrate	product	yield (%)
1			82	4			88
	rac-**3.20**	*rac*-**3.99**			*rac*-**3.35**	*rac*-**3.102**	
2			91	5			95
	rac-**3.20**	*rac*-**3.100**			*rac*-**3.37**	*rac*-**3.103**	
3			85	6			86
	rac-**3.31**	*rac*-**3.101**			*rac*-**3.35**	*rac*-**3.104**	

To illustrate the potential use of these diesters in reactions, isocyanate **3.104** was readily prepared through the deprotection of **3.102**, followed by Curtius rearrangement of carboxylic acid **3.103** (Scheme 3.12).

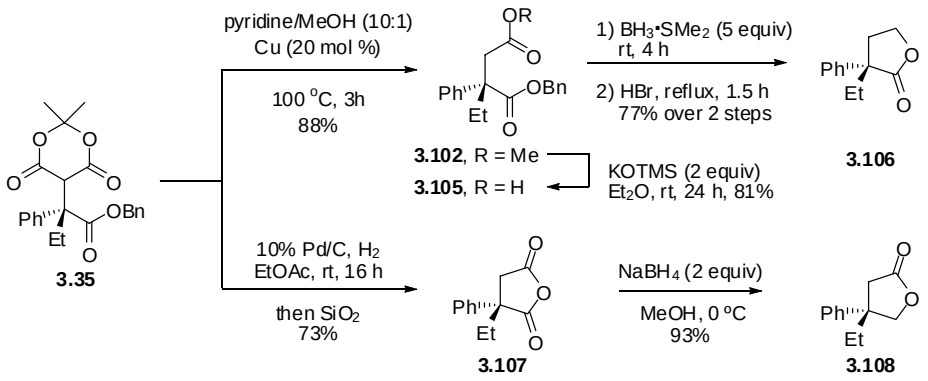
Scheme 3.12: Isocyanate formation via chemical manipulation of diester **3.102**



3.102 **3.103** **3.104**

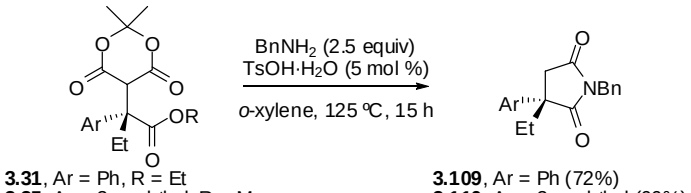
From compound **3.35**, 3,3- and 4,4-disubstituted γ-butyrolactones **3.106** and **3.108** were readily accessed (Scheme 3.13). The more reactive Meldrum's acid moiety found in **3.35** could be transformed chemoselectively to provide **3.102**, as shown above. From diester **3.102**, α,α-disubstituted γ-butyrolactone **3.106** was synthesized in three high-yielding steps by selective hydrolysis of the methyl ester,[19] borane reduction of the carboxylic acid, and acid-promoted lactonization. β,β-Disubstituted γ-butyrolactone **3.108** was obtained in only two steps by hydrogenolysis of **3.35** to cyclic anhydride **3.107**, which was selectively reduced with $NaBH_4$ to give **3.108**/**3.106** in an excellent 18:1 ratio. The regioselective reduction of cyclic anhydrides has been reported first using $LiAlH_4$[20] in 1967 and extended to the use of $NaBH_4$[21] in 1970. Interestingly, both reducing reagents regioselectively reduce unsymmetrical cyclic anhydrides, the hydride attack takes place principally at the carbonyl group adjacent to the more highly substituted carbon.[22] The use of K-Selectride was reported to offer a reversal of regioselectivity in the reduction of *gem*-disubstituted cyclic anhydrides.[23]

Scheme 3.13: Synthesis of γ-butyrolactones



Lastly, chiral succinimides **3.109** and **3.110** were prepared in one step by treating **3.31** and **3.35**, respectively, with $BnNH_2$ (Scheme 3.14). The two amidation, and one decarboxylation reactions occur all in a one-pot sequence allowing the establishment of the absolute stereochemistry for conjugate addition product **3.31** by comparison of known succinimides **3.109** and **3.110**.[6] Interestingly, it was shown that the debenzylated succinimide derivative of **3.109** has anticonvulsant properties.[24]

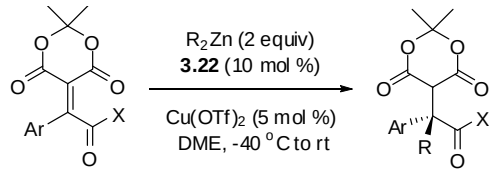
Scheme 3.14: Synthesis of succinimides



(C) Summary

In summary, a highly enantioselective asymmetric synthesis of carboxylic acid derivatives **3.5** having an α-quaternary centre through Cu-catalyzed 1,4-addition of dialkylzinc reagents to aryl acetate derivatives **3.4** has been described (Scheme 3.15). This method employs commercially available ligand **3.22** and readily accessible Meldrum's acids **3.4**. Brief insights into the factors affecting the observed selectivities are also discussed.

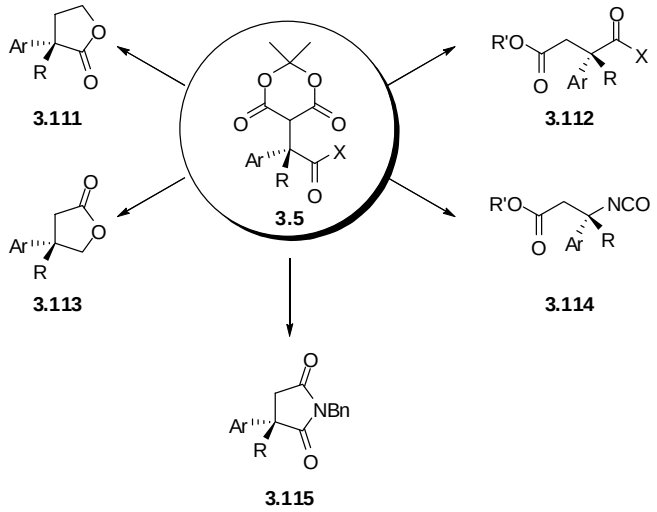
Scheme 3.15: Asymmetric synthesis of carboxylic acid derivatives having an α-quaternary centre through 1,4-addition of R_2Zn to aryl acetate derivatives



3.4 **3.5**

The significance of this method was established by the expedient preparation of diesters, succinimides, γ-butyrolactones, and isocyanates from Meldrum's acids **3.5**.

Figure 3.2: Preparation of γ-butyrolactones (**3.111-3.112)**, diesters (**3.112**), isocyanates (**3.114)**, and succinimides (3.115) from highly functionalized 1,4-conjugate addition products **3.5**



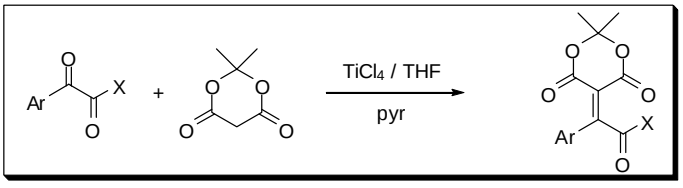
3.111 **3.112** **3.5** **3.113** **3.114** **3.115**

(D) Experimental Section

(I) General Methods

All reactions were carried out in flame-dried glassware under a dry argon atmosphere. 1,2-Dimethoxyethane was distilled from sodium-benzophenone ketyl under nitrogen and degassed via freeze-pump-thaw method. $Cu(OTf)_2$ was obtained from commercial sources and used without further purification. Dialkylzinc reagents namely, Et_2Zn (1.0 M in hexanes), *n*-Bu_2Zn (1.0 M in heptanes), Me_2Zn (1.0 M in heptanes), and *i*-Pr_2Zn (1.0 M in toluene), were also obtained from commercial sources and used without further purification. Chiral phosphoramidite ligands were prepared following literature procedures.[14] ^1H NMR spectra were referenced to residual ^1H shift in $CDCl_3$ (7.24 ppm). $CDCl_3$ (77.0 ppm) was used as the internal reference for ^{13}C NMR spectra. Flash chromatography was performed using 230-400 mesh silica gel. Melting points are uncorrected. Optical rotations were recorded in cells with 1 dm path length. Chiral HPLC analyses were performed using a Chiralcel OD-H or AD-H column. All columns are 250 x 4.6 mm. High resolution mass spectra were run by Dr. R. Smith at the University of Waterloo with a source temperature of 200 °C, mass resolution of 9000, and electron energy of 70 eV. Dr. Alan Lough, University of Toronto, is gratefully acknowledged for X-ray structure determination.

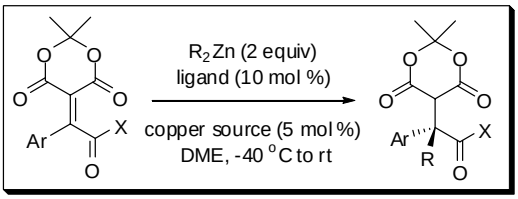
(II) General Procedure A: Preparation of 2-Aryl Acetate Derivatives



Alkylidene Meldrum's acids were prepared by the Knoevenagel condensation of Meldrum's acid with ketones using Brown and coworkers' method.[8] In a typical reaction, a solution of $TiCl_4$ (2.1 equiv) in CH_2Cl_2 (3 M) was added dropwise under nitrogen to dry THF (0.3 M), which was cooled at 0 ºC, resulting in a yellow suspension. A solution containing the ketone (1.0 equiv) and Meldrum's acid (1.0 equiv) in dry THF (0.7 M) was added dropwise via a syringe to the $TiCl_4$•THF complex. The flask containing the

solution of ketone and Meldrum's acid was rinsed with THF (2X) and added to the reaction mixture. Subsequently, pyridine (5.0 equiv) was added to the reaction mixture dropwise at 0 ºC. The reaction was allowed to warm up slowly to room temperature and stirred until completion of reaction or for 24 h. The reaction was quenched by the addition of water and diluted with either Et_2O or EtOAc. After the solid was dissolved, the layers were partitioned. The aqueous layer was extracted was Et_2O, or EtOAc (2X), and the combined organic layers were washed with $NaHCO_3$ saturated solution (2X), brine (1X), dried over $MgSO_4$, filtered and concentrated. Purification by either crystallization or flash chromatography provided the alkylidene Meldrum's acids.

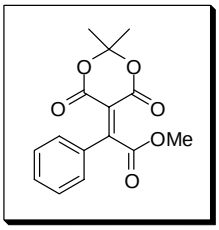
(III) General Procedure B: 1,4-Addition of $(alkyl)_2Zn$ to 2-Aryl Acetate Derivatives



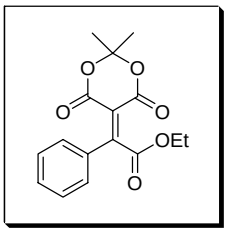
Although most reactions were typically carried out using 0.12 mmol of substrate, in a number of instances the reaction was performed on a preparative scale as described above. In a glove box, $Cu(OTf)_2$ (5 mol %) and phosphoramidite chiral ligand (10 mol %) were charged in a flame-dried resealable Schlenk tube. DME (0.5 mL) was then added to the Schlenk tube to wash down any residual solids to the bottom. The reaction mixture was allowed to stir at ambient temperature for 30 minutes, outside the glove box, and then cooled to -40 ºC. In the dry box, the $(alkyl)_2Zn$ solution (2.0 equiv) was transferred to a round-bottom flask equipped with a septum. This solution was added to the Schlenk tube dropwise via a syringe and the resulting solution stirred for 5 min. A solution of alkylidene Meldrum's acid (1.0 equiv) in DME (0.5 mL) was then added dropwise via a syringe. Finally, DME (0.2 mL) was added to wash down the remaining solid on the sides of the Schlenk tube. The reaction mixture was allowed to warm up slowly to room temperature. After stirring for 24 h, 5% HCl and Et_2O were added to the reaction mixture. The layers were partitioned and the aqueous layer was extracted with Et_2O (3X). The combined organic layers were washed with water, dried over anhydrous $MgSO_4$, filtered and concentrated. The crude residue was purified by flash column chromatography on

silica gel using hexanes in EtOAc to yield the desired product. HPLC using a chiral column OD-H or AD-H was used to measure the enantiomeric ratio of the products. The conjugate addition product racemates were prepared using a racemic phosphoramidite (*rac*-**3.26)** with the above procedure. The conjugate reduction product racemates were prepared using $NaBH_4$ in ethanol.

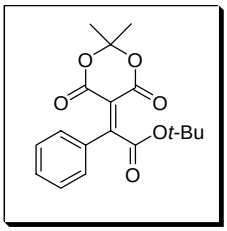
(IV) Substrate Specific Information



Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-phenylacetate (3.14)[8]: Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in quantitative yield. M.p. 142-144 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48-7.41 (m, 5H), 3.86 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.3, 160.4, 160.0, 158.6, 131.7, 131.3, 128.6, 127.9, 116.3, 105.1, 53.5, 27.6; HRMS(EI) *m/z* calc'd for $C_{14}H_{14}O_6$ (M^+-CH_3): 275.0556. Found: 275.0551.

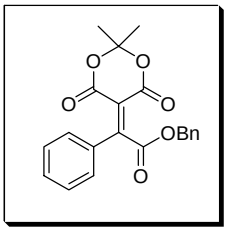


Ethyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-phenylacetate (3.30): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 73% yield. M.p. 93-94 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49-7.41 (m, 5H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.83 (s, 6H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.8, 160.3 (2C), 158.7, 131.8, 131.2, 128.5, 127.9, 116.1, 105.0, 62.8, 27.6, 13.7; HRMS(EI) *m/z* calc'd for $C_{15}H_{13}O_6$ (M^+-CH_3): 289.0712. Found: 289.0717.

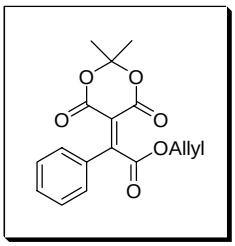


***tert*-Butyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-phenylacetate (3.32):** Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 26% yield. M.p. 122-123 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47-7.41 (m, 5H), 1.82 (s, 6H), 1.51 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ

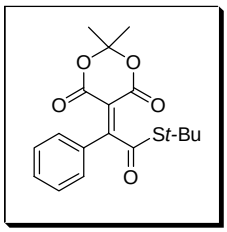
164.6, 160.7, 160.4, 159.1, 132.2, 131.0, 128.4, 127.9, 115.5, 104.9, 85.0, 27.8, 27.5; HRMS(EI) *m/z* calc'd for $C_{15}H_{14}O_5$ (M^+-acetone): 274.0841. Found: 274.0841.



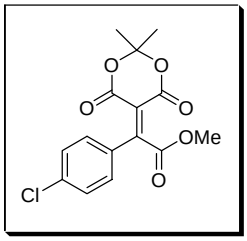
Benzyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-phenylacetate (3.34): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 75% yield. M.p. 129-130 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47-7.40 (m, 5H), 7.32 (s, 5H), 5.30 s, 2H), 1.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.7, 160.4, 158.6, 134.4, 131.6, 131.3, 128.6 (3C), 128.5, 128.0, 116.3, 105.1, 68.6, 27.6; HRMS(EI) *m/z* calc'd for $C_{18}H_{12}O_5$ (M^+-acetone): 308.0685. Found: 308.0693.



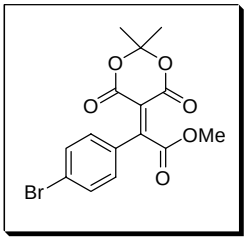
Allyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-phenylacetate (3.36): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 69% yield. M.p. 93-95 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49-7.39 (m, 4H), 5.99-5.86 (m, 1H), 5.29 (d, *J* = 17.8 Hz, 1H), 5.25 (d, *J* = 10.5 Hz, 1H), 4.76 (d, *J* = 5.8 Hz, 2H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.5, 160.3, 160.0, 158.6, 131.7, 131.3, 130.8, 128.5, 127.9, 119.6, 116.3, 105.1, 67.3, 27.6; HRMS(EI) *m/z* calc'd for $C_{14}H_{10}O_5$ (M^+-acetone): 258.0528. Found: 258.0533.



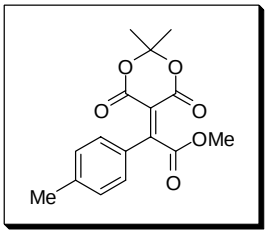
S-*tert*-butyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-phenylethanethioate (3.38): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 39% yield. M.p. 132-134 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.44-7.42 (m, 5H), 1.84 (s, 6H), 1.50 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 192.0, 164.3, 159.7, 159.0, 131.9, 131.0, 128.5, 127.8, 116.6, 105.0, 51.2, 29.7, 27.6; HRMS(EI) *m/z* calc'd for $C_{15}H_{14}O_4S$ (M^+-acetone): 290.0613. Found: 290.0611.



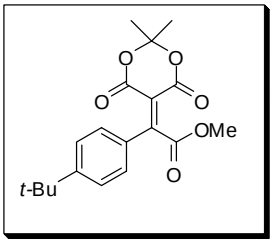
Methyl 2-(4-chlorophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)acetate (3.42): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 66% yield. M.p. 147-148 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42 (d, *J* = 9.0 Hz, 2H), 7.38 (d, *J* = 9.0 Hz, 2H), 3.86 (s, 3H), 1.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.1, 160.2, 158.7, 158.5, 137.8, 129.9, 129.4, 128.9, 116.5, 105.2, 53.6, 27.6; HRMS(EI) *m/z* calc'd for $C_{14}H_{10}{}^{35}ClO_6$ (M^+-CH_3): 309.0166. Found: 309.0169.



Methyl 2-(4-bromophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)acetate (3.44): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 59% yield. M.p. 133-135 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 3.87 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.0, 160.2, 158.8, 158.5, 131.9, 130.4, 129.5, 126.2, 116.5, 105.3, 53.6, 27.6; HRMS(EI) *m/z* calc'd for $C_{12}H_7{}^{79}BrO_5$ (M^+-acetone): 309.9477. Found: 309.9466.

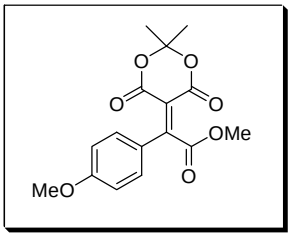


Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-*p*-tolylacetate (3.46): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 53% yield. M.p. 136-137 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 3.84 (s, 3H), 2.36 (s, 3H), 1.81 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.3, 160.4, 160.0, 158.7, 142.3, 129.2, 128.5, 128.2, 115.2, 104.8, 53.2, 27.4, 21.4; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_6$ (M^+): 304.0947. Found: 304.0950.

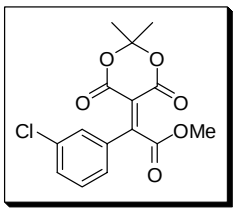


Methyl 2-(4-*tert*-butylphenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)acetate (3.48): Prepared according to general procedure A. Recrystallization from MeOH afforded a

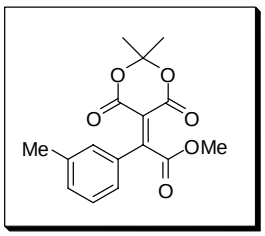
beige solid in 69% yield. M.p. 142-143 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45 (d, *J* = 9.1 Hz, 2H), 7.42 (d, *J* = 9.1 Hz, 2H), 3.87 (s, 3H), 1.83 (s, 6H), 1.31 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.5, 160.7, 160.2, 159.0, 155.5, 128.5, 128.4, 125.6, 115.3, 105.0, 53.4, 35.0, 31.0, 27.6; HRMS(EI) *m/z* calc'd for $C_{19}H_{18}O_6$ (M^+-CH_3): 331.1182. Found: 331.1180.



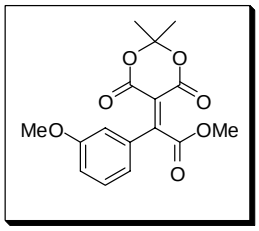
Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-(4-methoxyphenyl)acetate (3.50): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 82% yield. M.p. 137-138 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 3.88 (s, 3H), 3.84 (s, 2H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.8, 163.0, 160.9, 160.2, 159.4, 131.4, 123.5, 114.1, 113.6, 104.8, 55.5, 53.4, 27.6; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_7$ (M^+): 320.0896. Found: 320.0890.



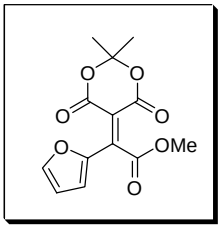
Methyl 2-(3-chlorophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)acetate (3.52): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 55% yield. M.p. 120-121 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42-7.33 (m, 4H), 3.87 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.9, 160.0, 158.3, 158.2, 134.7, 133.3, 131.1, 129.9, 127.4, 126.0, 117.2, 105.4, 53.7, 27.7; HRMS(EI) *m/z* calc'd for $C_{14}H_{10}{}^{35}ClO_6$ (M^+-CH_3): 309.0166. Found: 309.0174.



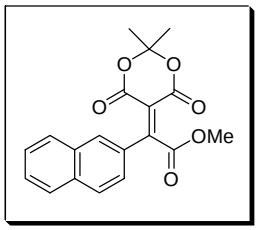
Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-*m*-tolylacetate (3.54): Prepared according to general procedure A. Recrystallization from MeOH afforded a pink solid in 54% yield. M.p. 111-112 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31-7.27 (m, 4H), 3.86 (s, 3H), 2.36 (s, 3H), 1.84 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.4, 160.5, 160.4, 158.7, 138.5, 132.2, 131.6, 128.5, 128.2, 125.1, 116.1, 105.1, 53.5, 27.6, 21.4; HRMS(EI) *m/z* calc'd for $C_{15}H_{13}O_6$ (M^+-CH_3): 289.0712. Found: 289.0721.



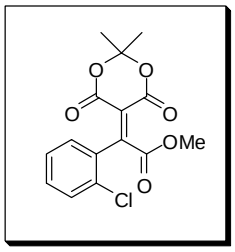
Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-(3-methoxyphenyl)acetate (3.56): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 55% yield. M.p. 134-135 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32 (t, *J* = 7.8 Hz, 1H), 7.00 (d, *J* = 7.9 Hz, 2H), 7.00 (s, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.2, 160.4, 159.7, 159.5, 158.5, 132.8, 129.7, 120.1, 116.8, 116.5, 113.4, 105.1, 55.3, 53.5, 27.6; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_7$ (M^+): 320.0896. Found: 320.0898.



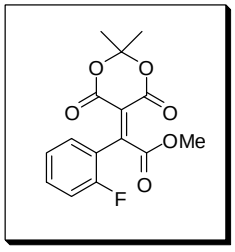
Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-(furan-2-yl)acetate (3.58): Prepared according to general procedure A. Recrystallization from MeOH afforded a light brown solid in 29% yield. M.p. 108-109 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.26 (d, *J* = 3.9 Hz, 1H), 7.75 (d, *J* = 1.4 Hz, 1H), 6.69-6.67 (m, 1H), 3.96 (s, 3H), 1.76 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.0, 161.4, 159.5, 149.8, 146.7, 145.0, 127.9, 114.6, 108.0, 104.6, 53.6, 27.2; HRMS(EI) *m/z* calc'd for $C_{13}H_{12}O_7$ (M^+): 280.0583. Found: 280.0585.



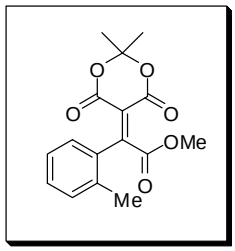
Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-(naphthalen-2-yl)acetate (3.60): Prepared according to general procedure A. Recrystallization from MeOH afforded a bright yellow solid in 76% yield. M.p. 164-165 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.07 (s, 1H), 7.89-7.82 (m, 3H), 7.56-7.51 (m, 2H), 7.47-7.24 (m, 1H), 3.89 (s, 3H), 1.87 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.4, 160.5, 160.4, 158.9, 134.4, 132.5, 129.1, 129.0, 128.8, 128.3 (2C), 127.9, 127.0, 124.8, 115.9, 105.2, 53.6, 27.7; HRMS(EI) *m/z* calc'd for $C_{19}H_{16}O_6$ (M^+): 340.0947. Found: 340.0946.



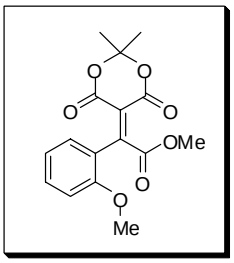
Methyl 2-(2-chlorophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)acetate (3.64): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 33% yield. M.p. 123-125 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52-7.49 (m, 1H), 7.42-7.34 (m, 3H), 3.85 (s, 3H), 1.83 (bs, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.5, 159.7, 158.1, 155.8, 131.2, 131.0, 130.7, 129.8, 128.6, 127.1, 119.4, 105.6, 53.6, 27.7; HRMS(EI) *m/z* calc'd for $C_{14}H_{10}{}^{35}ClO_6$ (M^+-CH_3): 309.0166. Found: 309.0169.



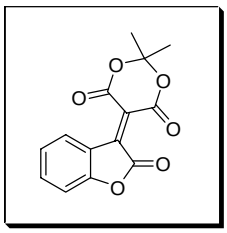
Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-(2-fluorophenyl)acetate (3.67): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 38% yield. M.p. 137.5-138.5 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.62 (dt, *J* = 7.5, 1.6 Hz, 1H), 7.48-7.41 (m, 1H), 7.23 (app t, *J* = 7.6 Hz, 1H), 7.10 (dd, *J* = 10.2, 8.6 Hz, 1H), 3.87 (s, 3H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.6, 159.9, 158.9, 158.6 (d, *J* = 249.4 Hz), 151.1, 133.0 (d, *J* = 8.9 Hz), 128.9 (d, *J* = 1.3 Hz), 124.7 (d, *J* = 3.5 Hz), 120.0 (d, *J* = 14.0 Hz), 118.7, 116.0 (d, *J* = 22.1 Hz), 105.5, 53.6, 27.4; HRMS(EI) *m/z* calc'd for $C_{14}H_{10}FO_6$ (M^+-CH_3): 293.0461. Found: 293.0470.



Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-*o*-tolylacetate (3.70): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 16% yield. M.p. 136-137 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34-7.23 (m, 4H), 3.87 (s, 3H), 2.39 (s, 3H), 1.84 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.2, 161.0, 160.0, 157.8, 135.1, 132.2, 130.3, 129.5, 125.8, 125.4, 118.0, 105.1, 53.3, 27.6, 19.7; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_6$ (M^+): 304.0947. Found: 304.0951.

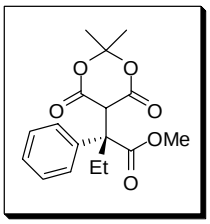


Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)-2-(2-methoxyphenyl)acetate (3.73): Prepared according to general procedure A. Recrystallization from MeOH afforded a dark yellow solid in 45% yield. M.p. 151-152 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.39 (dt, *J* = 7.9, 1.6 Hz, 1H), 7.01 (app t, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 1.84 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.3, 160.4, 159.2, 155.8, 153.3, 132.6, 128.7, 120.9, 120.8, 117.9, 111.4, 105.0, 55.3, 53.3, 27.2; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_7$ (M^+): 320.0896. Found: 320.0895.



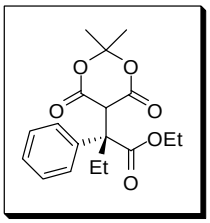
2,2-Dimethyl-5-(2-oxobenzofuran-3(2H)-ylidene)-1,3-dioxane-4,6-dione (3.96): Prepared according to general procedure A. Recrystallization from MeOH afforded an orange solid in 51% yield. M.p. 180-182 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.83 (d, *J* = 8.1 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.24 (app t, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 1.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.6, 159.7, 157.4, 157.3, 137.8, 137.4, 130.5, 125.2, 122.5, 120.4, 111.5, 105.8, 27.4; HRMS(EI) *m/z* calc'd for $C_{14}H_{10}O_6$ (M^+): 274.0477. Found: 274.0477.

(V) Product Specific Information

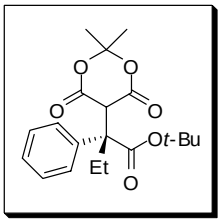


(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylbutanoate (3.20): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a white solid upon standing in quantitative yield. M.p. 80-82 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.46 (d, *J* = 7.5 Hz, 2H), 7.32-7.21 (m, 3H), 4.57 (s, 1H), 3.76 (s, 3H), 2.94 (dq, *J* = 14.6, 7.3 Hz, 1H), 2.37 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.76 (s, 3H), 1.45 (s, 3H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.8, 163.6, 162.8, 136.4, 128.7, 127.9, 127.4, 104.7, 55.8, 53.2, 52.5, 28.9, 28.2, 26.8, 9.7; An enantiomeric excess of 88% (*S*) was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 8.4 min

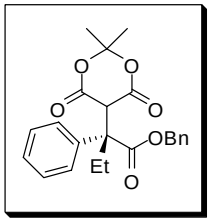
(*S*), t_{R2} = 9.6 min (*R*)]. $[\alpha]^{26.5}_D$ = +17.3 (*c* 1.3, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{17}H_{20}O_6$ (M^+): 320.1260. Found: 320.1257.



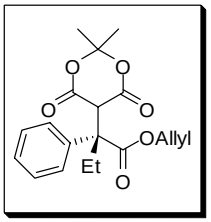
(*S*)-Ethyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylbutanoate (3.31): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a white solid upon standing in 94% yield. M.p. 48-50 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47 (d, *J* = 7.3 Hz, 2H), 7.32-7.21 (m, 3H), 4.57 (s, 1H), 4.25 (app q, *J* = 7.1 Hz, 2H), 2.91 (dq, *J* = 14.5, 7.3 Hz, 1H), 2.40 (dq, *J* = 14.6, 7.4 Hz, 1H), 1.77 (s, 3H), 1.45 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.3, 163.6, 162.9, 136.6, 128.8, 127.9, 127.4, 104.6, 61.6, 55.8, 53.2, 28.9, 28.2, 26.8, 13.9, 9.7; An enantiomeric excess of 90% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 7.4 min (*S*), t_{R2} = 8.6 min (*R*)]. $[\alpha]^{25}_D$ = +27.8 (*c* 1.6, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_6$ (M^+): 334.1416. Found: 334.1425.



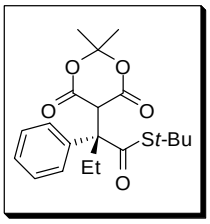
(*S*)-*tert*-Butyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylbutanoate (3.33): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear oil in quantitative yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45 (d, *J* = 7.8 Hz, 2H), 7.31-7.19 (m, 3H), 4.51 (s, 1H), 2.81 (dq, *J* = 14.6, 7.4 Hz, 1H), 2.39 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.76 (s, 3H), 1.46 (s, 12H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.0, 163.6, 163.0, 137.2, 128.7, 127.8, 127.1, 104.4, 82.2, 56.2, 53.2, 29.1, 28.3, 27.7, 26.7, 9.6; An enantiomeric excess of 86% was measured by chiral HPLC [AD, 5% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 8.8 min (*S*), t_{R2} = 10.4 min (*R*)]. $[\alpha]^{27.5}_D$ = -6.1 (*c* 1.6, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. LRMS(EI) *m/z* calc'd for $C_{20}H_{26}O_6$ (M^+-acetone): 304.1311.



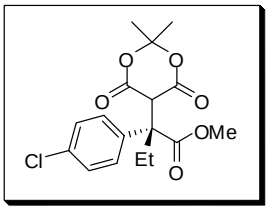
(*S*)-Benzyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylbutanoate (3.35): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a light yellow oil in 98% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47 (d, *J* = 7.5 Hz, 2H), 7.30-7.17 (m, 7H), 5.23 (AB d, *J* = 12.5 Hz, 1H), 5.17 (AB d, *J* = 12.6 Hz, 1H), 4.57 (s, 1H), 2.94 (dq, *J* = 14.5, 7.4 Hz, 1H), 2.39 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.82 (s, 3H), 1.42 (s, 3H), 0.84 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.0, 163.6, 162.8, 136.4, 135.4, 128.7, 128.4, 128.2 (2C), 128.0, 127.5, 104.7, 67.4, 55.8, 53.1, 28.7, 28.2, 26.8, 9.7; An enantiomeric excess of 88% was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 10.9 min (*S*), t_{R2} = 13.1 min (*R*)]. $[\alpha]^{22}_{D}$ = -112.5 (*c* 0.5, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{20}H_{18}O_5$ (M^+-acetone): 338.1154. Found: 338.1160.



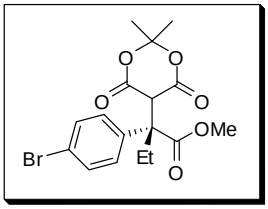
(*S*)-Allyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylbutanoate (3.37): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear oil in quantitative yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47 (d, *J* = 7.4 Hz, 2H), 7.32-7.21 (m, 3H), 5.97-5.84 (m, 1H), 5.29-5.18 (m, 2H), 4.72-4.62 (m, 2H), 4.58 (s, 1H), 2.94 (dq, *J* = 14.6, 7.3 Hz, 1H), 2.41 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.76 (s, 3H), 1.45 (s, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.9, 163.5, 162.8, 136.4, 131.7, 128.6, 127.8, 127.3, 118.4, 104.6, 66.1, 55.8, 53.1, 28.7, 28.1, 26.7, 9.7; An enantiomeric excess of 88% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 8.03 min (*S*), t_{R2} = 9.6 min (*R*)]. $[\alpha]^{28}_{D}$ = -0.8 (*c* 1.4, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{19}H_{22}O_6$ (M^+): 346.1416. Found: 346.1419.



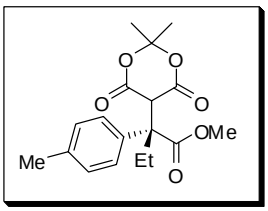
(*S*)-S-*tert*-Butyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylbutanethioate (3.39): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear oil in 90% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53-7.50 (m, 2H), 7.34-7.26 (m, 3H), 4.84 (s, 1H), 2.66 (q, *J* = 7.5 Hz, 2H), 1.82 (s, 3H), 1.59 (s, 3H), 1.41 (s, 9H), 1.01 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.8, 163.2, 162.8, 137.1, 128.7, 128.0, 127.7, 104.4, 61.6, 51.9, 48.3, 29.5, 28.4, 28.2, 26.3, 9.8; An enantiomeric excess of 90% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 0.5 mL/min, t_{R1} = 15.7 min (*S*), t_{R2} = 17.6 min (*R*)]. $[\alpha]^{24}_{D}$ = +34.0 (*c* 1.9, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(ESI) *m/z* calc'd for $C_{20}H_{26}O_5S$ $(M+Li)^+$: 385.1661. Found: 385.1668.



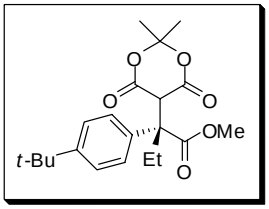
(*S*)-Methyl 2-(4-chlorophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)butanoate (3.43): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear oil in 91% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45 (d, *J* = 8.8 Hz, 2H), 7.26 (d, *J* = 8.9 Hz, 2H), 4.51 (s, 1H), 3.77 (s, 3H), 2.98 (dq, *J* = 14.6, 7.4 Hz, 1H), 2.31 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.78 (s, 3H), 1.77 (s, 3H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.7, 163.5, 162.6, 134.4, 133.6, 130.9, 128.0, 104.8, 55.4, 53.6, 52.7, 29.2, 28.3, 26.7, 9.6; An enantiomeric excess of 94% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 0.5 mL/min, t_{R1} = 25.3 min (*S*), t_{R2} = 26.7 min (*R*)]. $[\alpha]^{24}_{D}$ = -22.6 (*c* 2.0, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{17}H_{19}{}^{35}ClO_6$ (M^+): 354.0870. Found: 354.0882.



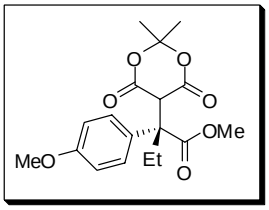
(*S*)-Methyl 2-(4-bromophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)butanoate (3.45): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear oil in 97% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42 (d, *J* = 9.1 Hz, 2H), 7.37 (d, *J* = 9.2 Hz, 2H), 4.51 (s, 1H), 3.77 (s, 3H), 2.97 (dq, *J* = 14.6, 7.4 Hz, 1H), 2.30 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.78 (s, 3H), 1.55 (s, 3H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.6, 163.4, 162.5, 135.0, 131.2, 131.0, 121.9, 104.8, 55.5, 53.6, 52.7, 29.1, 28.3, 26.7, 9.6; An enantiomeric excess of 92% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 0.5 mL/min, t_{R1} = 18.5 min (*S*), t_{R2} = 19.6 min (*R*)]. $[\alpha]^{29}_{D}$ = +10.1 (*c* 2.1, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{17}H_{19}{}^{79}BrO_6$ (M^+): 398.0365. Found: 398.0361.



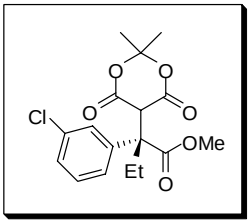
(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-*p*-tolylbutanoate (3.47): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a waxy beige solid in 98% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 2H), 4.56 (s, 1H), 3.75 (s, 3H), 2.93 (dq, *J* = 14.7, 7.3 Hz, 1H), 2.35 (dq, *J* = 14.7, 7.3 Hz, 1H), 2.29 (s, 3H), 1.76 (s, 3H), 1.47 (s, 3H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.1, 163.6, 162.9, 137.2, 133.4, 128.7 (2C), 104.6, 55.5, 53.3, 52.5, 28.9, 28.2, 26.9, 20.9, 9.8; An enantiomeric excess of 90% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 7.5 min (*S*), t_{R2} = 8.5 min (*R*)]. $[\alpha]^{26}_{D}$ = -1.0 (*c* 1.7, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_6$ (M^+): 334.1416. Found: 334.1420.



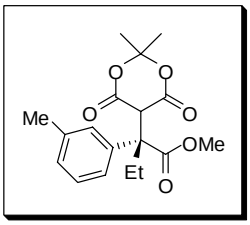
(*S*)-Methyl 2-(4-*tert*-butylphenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)butanoate (3.49): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a white solid upon standing in 82% yield. M.p. 46-48 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 2H), 4.55 (s, 1H), 3.77 (s, 3H), 2.93 (dq, *J* = 14.6, 7.4 Hz, 1H), 2.35 (dq, *J* = 14.5, 7.4 Hz, 1H), 1.74 (s, 3H), 1.35 (s, 3H), 1.26 (s, 9H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.9, 163.8, 163.0, 150.2, 133.2, 128.4, 125.0, 104.8, 55.7, 53.3, 52.5, 34.3, 31.2, 28.9, 28.2, 27.1, 9.8; An enantiomeric excess of 92% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 6.2 min (*S*), t_{R2} = 7.2 min (*R*)]. $[\alpha]^{30}_{D}$ = +30.9 (*c* 1.6, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{21}H_{28}O_6$ (M^+): 376.1886. Found: 376.1878.



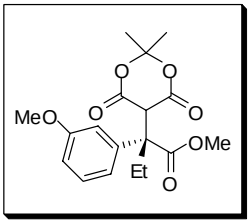
(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(4-methoxyphenyl)butanoate (3.51): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear oil in quantitative yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40 (d, *J* = 6.9 Hz, 2H), 6.82 (d, *J* = 6.9 Hz, 2H), 4.51 (s, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 2.97 (dq, *J* = 14.5, 7.4 Hz, 1H), 2.31 (dq, *J* = 14.5, 7.3 Hz, 1H), 1.76 (s, 3H), 1.46 (s, 3H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.1, 163.8, 162.9, 158.7, 130.5, 127.9, 113.3, 104.7, 55.4, 55.1, 53.8, 52.6, 29.1, 28.3, 27.0, 9.7; An enantiomeric excess of 92% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 11.9 min (*S*), t_{R2} = 14.6 min (*R*)]. $[\alpha]^{29}_{D}$ = +14.0 (*c* 1.8, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_7$ (M^+): 350.1366. Found: 350.1375.



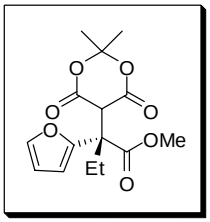
(*S*)-Methyl 2-(3-chlorophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)butanoate (3.53): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear, colorless oil in 92% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49 (bs, 1H), 7.38-7.34 (m, 1H), 7.24-7.22 (m, 2H), 4.53 (s, 1H), 3.77 (s, 3H), 2.92 (dq, *J* = 14.6, 7.3 Hz, 1H), 2.34 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.80 (s, 3H), 1.56 (s, 3H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.5, 163.3, 162.6, 138.4, 138.9, 129.4, 129.0, 127.8, 127.3, 104.8, 55.5, 53.3, 52.8, 29.0, 28.3, 26.7, 9.7; An enantiomeric excess of 83% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 8.5 min (*S*), t_{R2} = 9.9 min (*R*)]. $[\alpha]^{29}_{D}$ = -23.6 (*c* 1.9, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{17}H_{19}{}^{35}ClO_6$ (M^+): 354.0870. Found: 354.0867.



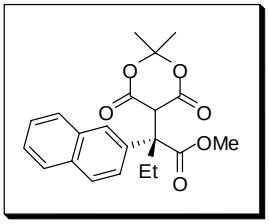
(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-*m*-tolylbutanoate (3.55): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear, colorless oil in quantitative yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25-7.15 (m, 3H), 7.05 (d, *J* = 7.1 Hz, 1H), 4.57 (s, 1H), 3.75 (s, 3H), 2.90 (dq, *J* = 14.7, 7.3 Hz, 1H), 2.37 (dq, *J* = 14.7, 7.2 Hz, 1H), 2.31 (s, 3H), 1.76 (s, 3H), 1.45 (s, 3H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.9, 163.5, 162.9, 137.5, 136.6, 129.3, 128.3, 127.8, 125.6, 104.7, 55.7, 53.1, 52.5, 28.8, 28.2, 26.9, 21.7, 9.9; An enantiomeric excess of 84% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 6.6 min (*S*), t_{R2} = 7.3 min (*R*)]. $[\alpha]^{25}_{D}$ = +6.8 (*c* 2.1, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_6$ (M^+): 334.1416. Found: 334.1420.



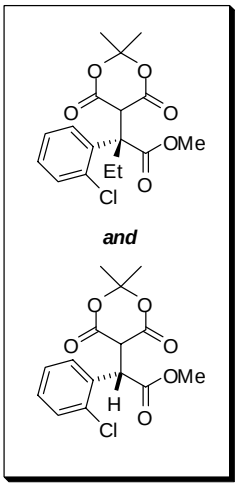
(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(3-methoxyphenyl)butanoate (3.57): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear, colorless oil in 87% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.23 (app t, *J* = 8.1 Hz, 1H), 7.03 (s, 1H), 7.02 (d, *J* = 8.3 Hz, 1H), 6.80-6.76 (m, 1H), 4.56 (s, 1H), 3.75 (s, 6H), 2.88 (dq, *J* = 14.7, 7.3 Hz, 1H), 2.36 (dq, *J* = 14.7, 7.3 Hz, 1H), 1.76 (s, 3H), 1.48 (s, 3H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.7, 163.5, 162.8, 159.1, 138.2, 128.8, 120.8, 115.3, 112.4, 104.7, 55.7, 55.1, 53.1, 52.6, 28.9, 28.2, 26.8, 9.8; An enantiomeric excess of 82% was measured by chiral HPLC [AD-H, 5% *i*-PrOH/hexanes, 0.5 mL/min, t_{R1} = 30.6 min (*S*), t_{R2} = 32.2 min (*R*)]. $[\alpha]^{24}_{D}$ = -5.8 (*c* 1.8, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. LRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_7$ (M^+): 350.1366.



(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(furan-2-yl)butanoate (3.59): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a bright yellow solid upon standing in 97% yield. M.p. 98-100 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28 (d, *J* = 1.1 Hz, 1H), 6.38 (d, *J* = 3.3 Hz, 1H), 6.34-6.32 (m, 1H), 4.52 (s, 1H), 3.76 (s, 3H), 2.65 (dq, *J* = 14.2, 7.3 Hz, 1H), 2.33 (dq, *J* = 14.2, 7.3 Hz, 1H), 1.82 (s, 3H), 1.69 (s, 3H), 0.95 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.5, 163.5, 162.8, 151.4, 141.2, 110.8, 108.6, 104.7, 53.0, 52.9, 50.8, 29.5, 28.3, 26.8, 9.7; An enantiomeric excess of 88% was measured by chiral HPLC [AD, 5% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 15.8 min (*R*), t_{R2} = 20.1 min (*S*)]. $[\alpha]^{25}_{D}$ = +16.1 (*c* 1.3, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{15}H_{18}O_7$ (M^+): 310.1053. Found: 310.1059.

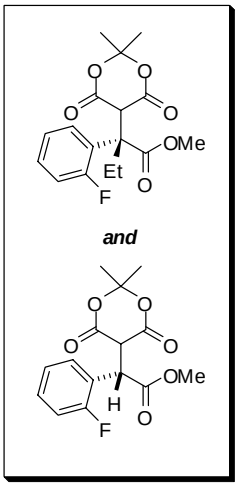


(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(naphthalene-2-yl)butanoate (3.61): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a white solid upon standing in 88% yield. M.p. 66-68 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.94 (s, 1H), 7.83-7.76 (m, 3H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.46-7.43 (m, 2H), 4.67 (s, 1H), 3.79 (s, 3H), 3.09 (dq, *J* = 14.5, 7.3 Hz, 1H), 2.49 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.78 (s, 3H), 1.46 (s, 3H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.0, 163.6, 162.9, 133.9, 132.8, 132.4, 128.5, 128.4, 127.3, 127.2, 126.7, 126.3, 125.9, 104.7, 56.0, 53.4, 52.7, 29.0, 28.2, 26.8, 9.9; An enantiomeric excess of 92% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 12.5 min (*S*), t_{R2} = 15.6 min (*R*)]. $[\alpha]^{27}_{D}$ = -9.0 (*c* 2.1, CH_2Cl_2). Absolute configuration was assigned by chemical transformation to **3.110** (see below). HRMS(EI) *m/z* calc'd for $C_{21}H_{22}O_6$ (M^+): 370.1416. Found: 370.1406.



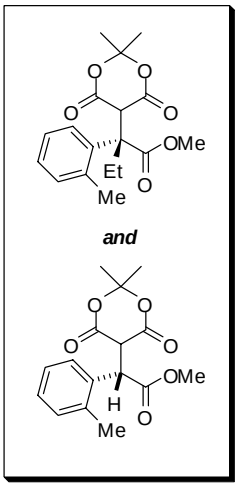
(*S*)-Methyl 2-(2-chlorophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)butanoate (3.65) *and* methyl 2-(2-chlorophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)acetate (3.66): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded conjugate addition product first followed by conjugate reduction product. ***Conjugate addition product:*** white solid upon standing in 41% yield. M.p. 135-138 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32-7.29 (m, 1H), 7.23-7.20 (m, 2H), 7.02-6.98 (m, 1H), 5.17 (s, 1H), 3.79 (s, 3H), 2.90 (dq, *J* = 14.5, 7.2 Hz, 1H), 2.35 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.83 (s, 3H), 1.73 (s, 3H), 0.77 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.3, 164.0, 162.0, 136.2, 131.5, 130.9, 130.8, 128.4, 127.0, 104.1, 57.4, 53.4, 52.6, 28.9, 28.7, 25.9, 10.4; An enantiomeric excess of 80% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 7.7 min (*S*), t_{R2} = 8.6 min (*R*)]. $[\alpha]^{28.5}_{D}$ = -8.2 (*c* 0.8, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{17}H_{19}O_6$ (M^+-Cl): 319.1181.

Found: 319.1184. ***Conjugate reduction product:*** white solid in 53% yield. M.p. 136-137 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56-7.53 (m, 1H), 7.39-7.36 (m, 1H), 7.27-7.24 (m, 2H), 5.34 (d, *J* = 2.9 Hz, 1H), 3.89 (d, *J* = 2.9 Hz, 1H), 3.74 (s, 3H), 1.79 (s, 3H), 1.74 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.7, 164.3, 163.8, 133.8, 133.2, 132.5, 129.2, 129.1, 126.6, 105.1, 52.9, 47.6, 46.6, 28.2, 26.9; A racemic mixture was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 9.6 min, t_{R2} = 17.8 min. HRMS(EI) *m/z* calc'd for $C_{15}H_{15}{}^{35}ClO_6$ (M^+): 326.0557. Found: 326.0560.

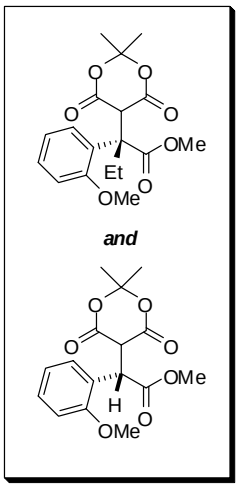


(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(2-fluorophenyl)butanoate (3.68) ***and*** **methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(2-fluorophenyl)acetate (3.69):** Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded conjugate addition product first followed by conjugate reduction product. ***Conjugate addition product:*** beige waxy solid in 62% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.27-7.18 (m, 2H), 7.11 (app t, *J* = 7.0 Hz, 1H), 6.97 (dd, *J* = 13.5, 8.2 Hz, 1H), 4.68 (d, *J* = 2.7 Hz, 1H), 3.74 (s, 3H), 2.68 (dq, *J* = 14.7, 7.3 Hz, 1H), 2.31 (dq, *J* = 14.3, 7.6 Hz, 1H), 1.84 (s, 3H), 1.73 (s, 3H), 0.85 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.5, 163.9, 162.6, 160.3 (d, *J* = 241.7 Hz), 129.4 (d, *J* = 4.7 Hz), 128.9 (d, *J* = 9.5 Hz), 126.1 (d, *J* = 11.0 Hz), 124.3 (d, *J* = 2.9 Hz), 115.8 (d, *J* = 25.2 Hz), 104.4, 54.4 (d, *J* = 3.5 Hz), 52.7, 51.7 (d, *J* = 7.8 Hz), 30.4, 28.6, 26.0, 9.9; An enantiomeric excess of 32% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 7.4 min (*S*), t_{R2} = 8.0 min (*R*)]. $[\alpha]^{28}{}_D$ = +25.7 (*c* 0.011 g/mL, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{17}H_{19}FO_6$ (M^+): 338.1166. Found: 338.1165. ***Conjugate reduction product:*** white solid in 12% yield. M.p. 116-118 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.32-7.27 (m, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.04 (t, *J* = 9.4 Hz, 1H), 5.12 (d, *J* = 3.5 Hz, 1H), 3.94 (d, *J* = 3.6 Hz, 1H), 3.73 (s, 3H), 1.76 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.7, 164.2, 163.8, 160.5 (d, *J* = 245.0 Hz), 131.5 (d,

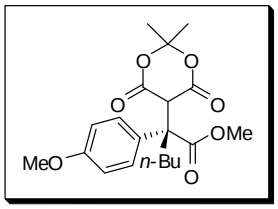
J = 2.8 Hz), 129.6 (d, J = 8.5 Hz), 124.0 (d, J = 3.5 Hz), 122.7 (d, J = 13.2 Hz), 115.2 (d, J = 22.1 Hz), 105.2, 52.9, 48.4, 42.2 (d, J = 2.9 Hz), 28.2, 26.8; A racemic mixture was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 11.5 min, t_{R2} = 17.1 min). HRMS(EI) *m/z* calc'd for $C_{15}H_{15}FO_6$ (M^+): 310.0853. Found: 310.0858.



(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-*o*-tolylbutanoate (3.71) *and* methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-*o*-tolylacetate (3.72): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded inseparable mixture of 84:16 conjugate reduction to conjugate addition product in quantitative yield. ***Conjugate addition product:*** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.17-7.09 (m, 3H), 7.00-6.97 (m, 1H), 4.44 (s, 1H), 3.75 (s, 3H), 2.90 (dq, J = 14.7, 7.3 Hz, 1H), 2.37 (s, 3H), 2.19 (dq, J = 14.8, 7.4 Hz, 1H), 1.79 (s, 3H), 1.65 (s, 3H), 0.83 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.8, 163.9, 162.2, 137.0, 135.4, 132.7, 128.4, 127.1, 126.2, 104.2, 57.3, 53.5, 52.5, 29.9, 28.5, 26.7, 22.3, 10.5; An enantiomeric excess of 58% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 9.3 min (*S*), t_{R2} = 10.2 min (*R*)]. Absolute configuration was assigned by analogy to **3.61**. ***Conjugate reduction product:*** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47-7.44 (m, 1H), 7.19-7.18 (m, 3H), 4.95 (d, J = 4.7 Hz, 1H), 4.00 (d, J = 4.7 Hz, 1H), 3.70 (s, 3H), 2.40 (s, 3H), 1.78 (s, 3H), 1.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.7, 164.1, 164.0, 136.6, 133.9, 130.4, 128.9, 127.8, 126.1, 105.2, 52.7, 49.2, 45.0, 28.4, 26.7, 19.8; A racemic mixture was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 10.8 min, t_{R2} = 15.9 min). HRMS(EI) *m/z* calc'd for $C_{16}H_{18}O_6$ (M^+): 306.1103. Found: 306.1114.

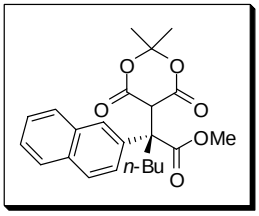


(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(2-methoxyphenyl)butanoate (3.74) ***and*** **methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(2-methoxyphenyl)acetate (3.75):** Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded conjugate addition product first followed by conjugate reduction product. ***Conjugate addition product:*** white solid upon standing in 79% yield. M.p. 132-134 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.24 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.11 (d, *J* = 7.4 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 8.1 Hz, 1H), 4.98 (s, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 2.69 (dq, *J* = 14.4, 7.1 Hz, 1H), 2.22 (dq, *J* = 14.5, 7.2 Hz, 1H), 1.82 (s, 3H), 1.69 (s, 3H), 0.82 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.5, 164.5, 162.7, 156.3, 129.4, 128.3, 127.0, 121.0, 111.1, 103.9, 55.3, 55.0, 52.4 (2C), 30.5, 28.6, 26.1, 10.3; An enantiomeric excess of 42% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 10.3 min (*S*), t_{R2} = 13.2 min (*R*)]. $[\alpha]^{27}_D$ = -3.6 (*c* 1.6, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_7$ (M^+): 350.1366. Found: 350.1362. ***Conjugate reduction product:*** white solid in 21% yield. M.p. 156-157 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.29 (dt, *J* = 7.9, 1.5 Hz, 1H), 6.96 (app t, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 5.26 (d, *J* = 3.0 Hz, 1H), 3.90 (d, *J* = 3.1 Hz, 1H), 3.85 (s, 3H), 3.73 (s, 3H), 1.77 (s, 3H), 1.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.8, 165.0, 164.0, 156.3, 131.5, 129.0, 123.7, 120.4, 110.2, 104.8, 55.6, 52.6, 47.4, 43.5, 28.3, 27.0; A racemic mixture was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.2 mL/min, t_{R1} = 11.0 min, t_{R2} = 25.2 min. HRMS(EI) *m/z* calc'd for $C_{16}H_{18}O_7$ (M^+): 322.1053. Found: 322.1060.

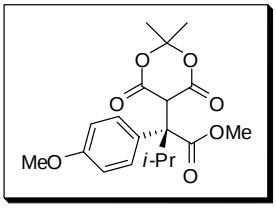


(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(4-methoxyphenyl)hexanoate (3.87): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc,

followed by 1:1 hexanes:EtOAc, afforded a light yellow solid upon standing in 91% yield. M.p. 90-92 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40 (d, *J* = 9.0 Hz, 2H), 6.81 (d, *J* = 9.0 Hz, 2H), 4.53 (s, 1H), 3.76 (s, 6H), 2.89 (dt, *J* = 13.4, 3.0 Hz, 1H), 2.29-2.18 (m, 1H), 1.75 (s, 3H), 1.46 (s, 3H), 1.46-1.16 (m, 3H), 1.11-1.00 (m, 1H), 0.87 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.3, 163.7, 162.9, 158.7, 130.3, 128.2, 113.2, 104.7, 55.1, 54.9, 54.0, 52.6, 35.8, 28.2, 27.2, 26.9, 23.0, 13.8; An enantiomeric excess of 90% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 10.6 min (*S*), t_{R2} = 26.7 min (*R*)]. $[\alpha]^{30}_D$ = -10.7 (*c* 1.9, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{20}H_{26}O_7$ (M^+): 378.1679. Found: 378.1686.

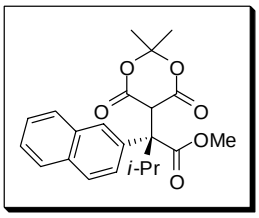


(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(napthalen-2-yl)hexanoate (3.88): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a white solid upon standing in 88% yield. M.p. 56-58 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.93 (s, 1H), 7.83-7.25 (m, 3H), 7.62 (dd, *J* = 8.8, 1.7 Hz, 1H), 7.46-7.42 (m, 2H), 4.68 (s, 1H), 3.78 (s, 3H), 3.00 (dt, *J* = 13.4, 3.1 Hz, 1H), 2.46-2.35 (m, 1H), 1.79 (s, 3H), 1.46 (s, 3H), 1.43-1.14 (m, 4H), 0.90 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.2, 163.5, 162.8, 134.2, 132.8, 132.4, 128.5, 128.3, 127.3, 127.2, 126.5, 126.3, 125.9, 104.7, 55.4, 53.6, 52.7, 35.7, 28.2, 27.3, 26.8, 23.1, 13.9; An enantiomeric excess of of 92% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 13.9 min (*S*), t_{R2} = 33.4 min (*R*)]. $[\alpha]^{30}_D$ = -6.9 (*c* 2.0, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{23}H_{26}O_6$ (M^+): 398.1729. Found: 398.1728.

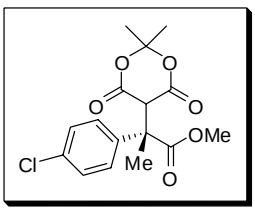


(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(4-methoxyphenyl)-3-methylbutanoate (3.89): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a light yellow oil in 80% yield; ^{1}H NMR

($CDCl_3$, 300 MHz) δ 7.52 (d, *J* = 9.1 Hz, 2H), 6.77 (d, *J* = 9.1 Hz, 2H), 4.68 (s, 1H), 3.79 (s, 3H), 3.74 (s, 3H), 3.71 (septet, *J* = 6.8 Hz, 1H), 1.69 (s, 3H), 1.31 (s, 3H), 1.14 (d, *J* = 6.6 Hz, 3H), 0.77 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 164.4, 162.8, 158.5, 131.4, 128.3, 112.8, 104.4, 59.1, 55.0, 52.5, 51.8, 31.3, 28.1, 27.1, 18.6, 18.3; An enantiomeric excess of 84% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 9.0 min (*S*), t_{R2} = 10.2 min (*R*)]. $[\alpha]^{28.5}_D$ = -0.3 (*c* 1.4, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{19}H_{24}O_7$ (M^+): 364.1522. Found: 334.1519.

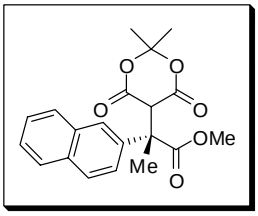


(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-3-methyl-2-(naphthalene-2-yl)butanoate (3.90): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a clear oil in 79% yield; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.12 (s, 1H), 7.83-7.80 (m, 1H), 7.77-7.74 (m, 3H), 7.46-7.42 (m, 2H), 4.79 (s, 1H), 3.95 (septet, *J* = 6.8 Hz, 1H), 3.86 (s, 3H), 1.71 (s, 3H), 1.25 (s, 3H), 1.20 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 164.3, 162.8, 133.9, 132.7, 132.4, 130.0, 128.8, 128.5, 127.9, 127.0, 126.8, 126.3, 125.7, 104.5, 59.8, 52.4, 52.0, 31.5, 28.0, 27.0, 18.8, 18.4; An enantiomeric excess of 88% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 10.3 min (*S*), t_{R2} = 12.8 min (*R*)]. $[\alpha]^{29.5}_D$ = -5.0 (*c* 1.4, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{22}H_{24}O_6$ (M^+): 384.1573. Found: 384.1580.

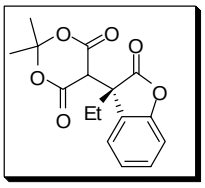


(*S*)-Methyl 2-(4-chlorophenyl)-2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)propanoate (3.91): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a white solid in quantitative yield. M.p. 127-129 ºC; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.43 (d, *J* = 8.8 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 4.84 (s, 1H), 3.67 (s, 3H), 1.89 (s, 3H), 1.84 (s, 3H), 1.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.5,

163.2, 161.6, 137.7, 133.6, 128.6, 127.7, 104.9, 54.3, 53.2, 49.3, 28.6, 26.0, 16.7; An enantiomeric excess of 60% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 8.6 min (*S*), t_{R2} = 10.3 min (*R*)]. $[\alpha]^{27.5}_{D}$ = -22.4 (*c* 1.2, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{16}H_{17}{}^{35}ClO_6$ (M^+): 340.0714. Found: 340.0717.



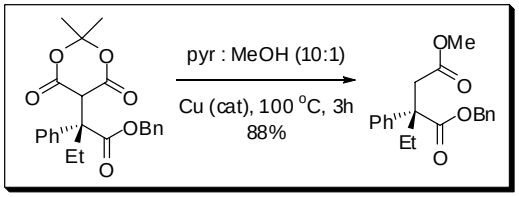
(*S*)-Methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(naphthalene-2-yl)propanoate (3.92): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a beige solid upon standing in 90% yield. M.p. 65-67 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.96 (d, *J* = 1.4 Hz, 1H), 7.84-7.80 (m, 3H), 7.64 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.49-7.43 (m, 2H), 5.07 (s, 1H), 3.67 (s, 3H), 2.00 (s, 3H), 1.92 (s, 3H), 1.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.7, 163.5, 161.6, 136.4, 133.1, 132.4, 128.3, 128.1, 127.4, 126.3, 126.2, 125.7, 123.7, 104.8, 54.4, 53.1, 49.8, 28.7, 26.0, 16.8; An enantiomeric excess of 62% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 12.9 min (*S*), t_{R2} = 15.5 min (*R*)]. $[\alpha]^{27}_{D}$ = +9.6 (*c* 1.8, CH_2Cl_2). Absolute configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{20}H_{20}O_6$ (M^+): 356.1260. Found: 356.1260.



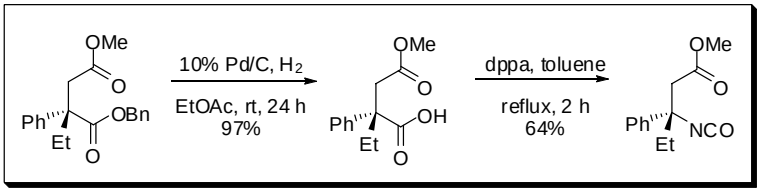
(*S*)-5-(3-Ethyl-2-oxo-2,3-dihydrobenzofuran-3-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (3.97): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc, afforded a white solid upon standing in 67% yield. M.p. 147-150 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.15-7.07 (m, 2H), 4.30 (s, 1H), 2.79 (dq, *J* = 13.7, 7.2 Hz, 1H), 2.11 (dq, *J* = 13.7, 6.9 Hz, 1H), 1.87 (s, 3H), 1.56 (s, 3H), 0.71 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.7, 162.2, 154.4, 129.7, 126.5, 124.9, 124.6, 110.8, 105.7, 52.8, 51.5, 30.4, 28.4, 26.1, 8.1; An enantiomeric excess of 12% was measured by chiral HPLC [AD-H, 10% *i*-PrOH/hexanes, 0.5 mL/min, t_{R1} = 16.2 min (*R*), t_{R2} = 17.7 min (*R*)]. Absolute

configuration was assigned by analogy to **3.61**. HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_6$ (M^+): 304.0947. Found: 304.0954.

(III) Chemical Transformations of Various Conjugate Addition Products



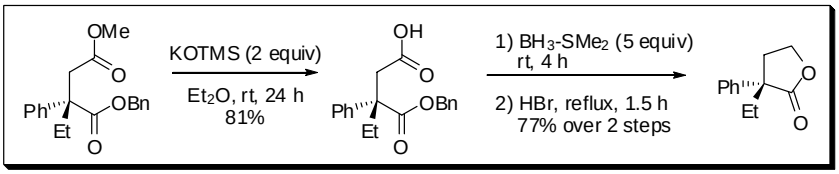
(*S*)-1-Benzyl 4-methyl 2-ethyl-2-phenylsuccinate (3.102): A mixture of (*S*)-benzyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylbutanoate (1 equiv) and copper (0.2 equiv) was dissolved in a 10:1 pyridine/methanol (0.1 M) solution.[18] The mixture was heated to 100 °C for 3 hours. Concentration of the crude reaction and immediate loading onto flash column chromatography using silica gel while eluting with 10:1 hexanes:EtOAc, afforded a light yellow oil in 88% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34-7.19 (m, 10H), 5.16 (AB d, *J* = 12.6 Hz, 1H), 5.11 (AB d, *J* = 12.7 Hz, 1H), 3.55 (s, 3H), 3.27 (d, *J* = 15.9 Hz, 1H), 3.06 (d, *J* = 15.9 Hz, 1H), 2.35 (dq, *J* = 14.4, 7.3 Hz, 1H), 2.20 (dq, *J* = 14.3, 7.2 Hz, 1H), 0.73 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.3, 171.2, 140.6, 135.8, 128.3, 128.2, 127.9 (2C), 126.9, 126.2, 66.6, 52.2, 51.4, 38.3, 28.0, 8.4; HRMS(EI) *m/z* calc'd for $C_{20}H_{22}O_4$ (M^+): 326.1518. Found: 326.1525.



(*S*)-Methyl 3-isocyanato-3-phenylpentanoate (3.104): (*S*)-1-Benzyl 4-methyl 2-ethyl-2-phenylsuccinate and 10% Pd/C (1.5 mol % Pd) were suspended in degassed EtOAc under H_2 (1 atm). After 24 h, the reaction was filtered over a pad of celite, eluting with CH_2Cl_2. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc and EtOAc, afforded the acid as a white solid 97% yield. M.p. 69-71 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35-7.22 (m, 5H), 3.59 (s, 3H), 3.22 (d, *J* = 16.0 Hz, 1H), 3.02 (d, *J* = 16.0 Hz, 1H), 2.27 (dq, *J* = 14.5, 7.3 Hz,

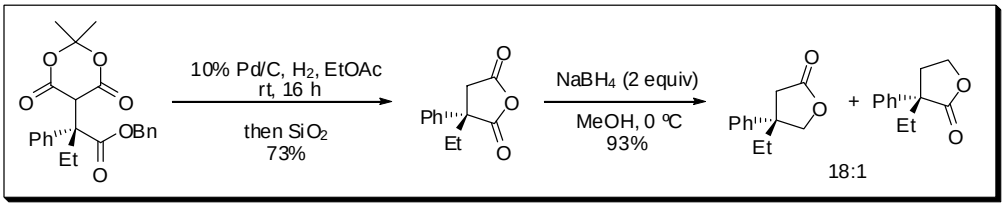
1H), 2.15 (dq, *J* = 14.4, 7.2 Hz, 1H), 0.73 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 180.5, 171.4, 140.1, 128.5, 127.2, 126.3, 52.1, 51.6, 38.3, 27.9, 8.4; HRMS(EI) *m/z* calc'd for $C_{12}H_{16}O_2$ (M^+-CO_2): 192.1150. Found: 192.1149.

To a solution of the acid (1 equiv) in toluene (0.1 M) was added Et_3N (1.5 equiv) and diphenyl phosphoryl azide (1.5 equiv) at room temperature. The mixture was then refluxed for 2 hours then cooled to room temperature. Evaporation of solvent under vacuum and purification by flash column chromatography on silica gel, eluting with 1:1 hexanes:CH_2Cl_2 afforded the isocyanate as a clear colourless liquid in 64% yield. An enantiomeric excess of 86% was measured by chiral HPLC [AD-H, 5% *i*-PrOH/hexanes, 0.5 mL/min, t_{R1} = 15.2 min (*S*), t_{R2} = 16.2 min (*R*)]. $[\alpha]^{22}_D$ = +32.3 (*c* 0.026 , CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35-7.29 (m, 4H), 7.27-7.24 (m, 1H), 3.59 (s, 3H), 2.92 (s, 2H), 2.08 (dq, *J* = 14.1, 7.2 Hz, 1H), 1.98 (dq, *J* = 14.1, 7.2 Hz, 1H), 0.78 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.8, 141.6, 128.4, 125.1, 123.1, 65.3, 51.7, 47.4, 36.2, 8.3; HRMS(EI) *m/z* calc'd for $C_{13}H_{15}NO_3$ (M^+): 233.1052. Found: 233.1056.



(*S*)-3-Ethyl-3-phenyl-dihydrofuran-2(*3H*)-one (3.106): Potassium trimethylsilanolate[19] (2 equiv) was added to a solution of (*S*)-1-benzyl 4-methyl 2-ethyl-2-phenylsuccinate (1 equiv) in ether (0.1 M). After stirring for 24 h of room temperature, the reaction was quenched with 5% HCl and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by flash column chromatography on silica gel, eluting with 3:1 hexanes:EtOAc, followed by 1:1 hexanes:EtOAc and EtOAc, afforded the acid as a white solid upon standing in 81% yield. M.p. 69-71 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32-7.20 (m, 8H), 7.19-7.14 (m, 2H), 5.10 (s, 2H), 3.29 (d, *J* = 16.3 Hz, 1H), 3.06 (d, *J* = 16.3 Hz, 1H), 2.31 (dq, *J* = 14.4, 7.3 Hz, 1H), 2.19 (dq, *J* = 14.4, 7.3 Hz, 1H), 0.71 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (CDCl3, 75 MHz) δ 176.1, 174.5, 140.4, 135.7, 128.5, 128.4, 128.0 (2C), 127.2, 126.2, 66.9, 52.2, 38.3, 28.1, 8.6. HRMS(EI) m/z calc'd for $C_{19}H_{20}O_4$ (M^+): 312.1362. Found: 312.1364.

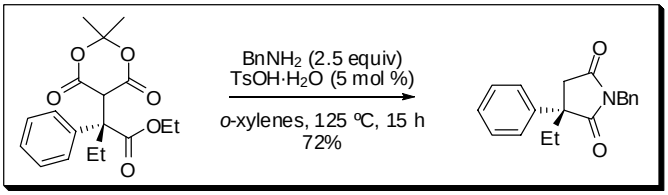
To a solution of (*S*)-3-(benzyloxycarbonyl)-3-phenylpentanoic acid (1 equiv) in THF (0.2 M) was added $BH_3 \cdot SMe_2$ dropwise at room temperature. After 3 h, the reaction was cooled to 0 °C and quenched by dropwise addition of MeOH. The reaction mixture was then diluted with water and extracted with CH_2Cl_2 (3X). The organic layer was dried over $MgSO_4$, filtered and concentrated. The crude alcohol was diluted with HBr (48%, 0.05 M) and refluxed for 1.5 h. After cooling, the reaction was diluted with water and extracted with CH_2Cl_2 (3X). The organic layer was dried over $MgSO_4$, filtered and concentrated. Purification by column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded the lactone as a clear colourless liquid in 77% yield over two steps. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43 (d, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 6.9 Hz, 1H), 4.31 (dt, *J* = 8.5, 3.3 Hz, 1H), 4.10 (dt, *J* = 9.1, 6.5 Hz, 1H), 2.67 (ddd, *J* = 13.0, 6.4. 3.3 Hz, 1H), 2.45 (m,1H), 2.02 (dq, *J* = 14.2, 7.3, 1H), 1.90 (dq, *J* = 14.2, 7.3 Hz, 1H), 0.83 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.1, 138.8, 128.7, 127.4, 126.4, 65.1, 51.4, 33.7, 32.0, 9.1; An enantiomeric excess of 90% was measured by chiral HPLC [AD-H, 5% i-PrOH/hexanes, 0.5 mL/min, t_{R1} = 24.3 min (*R*), t_{R2} = 25.3 min (*S*)]. $[\alpha]^{25}_D$ = -51.6 (*c* 0.042 , CH_2Cl_2). HRMS(EI) *m/z* calc'd for $C_{12}H_{14}O_2$ (M^+): 190.0994. Found: 190.0997.



(*S*)-4-Ethyl-4-phenyl-dihydrofuran-2(*3H*)-one (3.108): A mixture of (*S*)-benzyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylbutanoate (1 equiv) and 10% Pd/C (5 mol % Pd) was dissolved in degassed EtOAc (0.5 M) solution. The mixture was stirred at room temperature under a hydrogen balloon for 16 h. Filtration of the reaction mixture over a pad of silica, eluting with EtOAc, affords the crude anhydride. Purification by flash column chromatography using silica gel while eluting with 5:1 hexanes:EtOAc, afforded a clear oil in 73% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42-7.31 (m, 5H), 3.35 (d, *J* = 18.5 Hz, 1H), 3.14 (d, *J* = 18.5 Hz, 1H), 2.12 (q, *J* = 7.4 Hz, 2H), 0.92 (t, *J* = 7.4

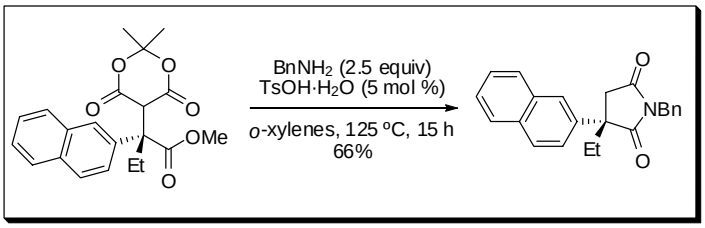
Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.8, 169.0, 138.1, 129.1, 128.2, 125.8, 54.4, 40.3, 33.4, 9.0. HRMS(EI) *m/z* calc'd for $C_{12}H_{12}O_3$ (M^+): 204.0786. Found: 204.0788.

A solution of the anhydride (1 equiv) dissolved in MeOH (0.1 M) was cooled to 0 °C. $NaBH_4$[21] (2 equiv) was then added, and the reaction was allowed to stir for 2 h. The reaction was then quenched with 5% HCl, diluted and extracted with CH_2Cl_2 (3X). The organic layer was dried over $MgSO_4$, filtered and concentrated. ^{1}H NMR of the crude reaction mixture shows a mixture of inseparable lactones in a 18:1 ratio. Purification by flash column chromatography on silica gel, eluting with 5:1 hexanes:EtOAc, afforded a clear colourless liquid in 93% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34-7.29 (m, 2H), 7.25-7.20 (m, 1H), 7.05 (d, *J* = 7.3 Hz, 2H), 4.46 (d, *J* = 8.8 Hz, 1H), 4.36 (d, *J* = 8.8Hz, 1H), 2.82 (d, *J* = 16.9 Hz, 1H), 2.71 (d, *J* = 16.9 Hz, 1H), 1.78 (q, *J* = 7.4 Hz, 2H), 0.70 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.0, 142.5, 128.5, 126.8, 125.7, 76.4, 47.9, 39.1, 33.1, 8.6; An enantiomeric excess of 88% was measured by chiral HPLC [AD-H, 10% i-PrOH/hexanes, 1.0 mL/min, t_{R1} = 13.4 min (*S*), t_{R2} = 17.7 min (*R*)]. $[\alpha]^{23.5}_D$ = -3.3 (*c* 0.037, CH_2Cl_2). HRMS(EI) *m/z* calc'd for $C_{12}H_{14}O_2$ (M^+): 190.0994. Found: 190.0992.



(*S*)-1-Benzyl-3-ethyl-3phenylpyrrolidine-2,5-dione (3.109)[6]: Benzylamine (2.5 equiv) was added to a solution of (*S*)-ethyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylbutanoate in *o*-xylene (0.1 M) at room temperature. *p*-toluenesulfonic acid monohydrate (5 mol %) was then added in one portion and the reaction mixture was heated to 125 ºC for 15 h and then cooled to room temperature upon which 5% HCl was added. The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3X). The organic layer was dried over $MgSO_4$**,** filtered, and concentrated. Purification of the crude mixture by flash column chromatography on silica gel, eluting with 9:1 hexanes:EtOAc, afforded a light yellow oil in 72% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.22 (m, 10H), 4.71 (AB d, *J* = 14.4 Hz, 1H), 4.66 (AB d, *J* = 14.4 Hz, 1H), 3.07 (d, *J* = 18.2 Hz,

1H), 2.89 (d, *J* = 18.2 Hz, 1H), 2.04 (app q, *J* = 7.3 Hz, 2H), 0.79 (t, *J* = 7.4 Hz, 3H) ; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.8, 175.3, 140.7, 135.7, 128.8, 128.6, 127.9, 127.4, 126.1, 52.1, 42.5, 41.2, 32.5, 8.9; An enantiomeric excess of 88% was measured by chiral HPLC [OD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 16.3 min (*R*), t_{R2} = 17.1 min (*S*)]. $[\alpha]^{23}_D$ = -10.3 (*c* 2.9, CH_2Cl_2). HRMS(EI) *m/z* calc'd for $C_{19}H_{19}NO_2$ (M^+): 293.1416. Found: 293.1414.



(*S*)-1-Benzyl-3-ethyl-3-(naphthalen-2-yl)pyrrolidine-2,5-dione (3.110)[6]: Benzylamine (2.5 equiv) was added to a solution of (*S*)-methyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(naphthalene-2-yl)butanoate in *o*-xylene (0.1 M) at room temperature. *p*-toluenesulfonic acid monohydrate (5 mol %) was then added in one portion and the reaction mixture was heated to 125 ºC for 15 h and then cooled to room temperature upon which 5% HCl was added. The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3X). The organic layer was dried over $MgSO_4$**,** filtered, and concentrated. Purification of the crude mixture by flash column chromatography on silica gel, eluting with 10:1 hexanes:EtOAc, afforded a beige solid upon standing in 66% yield. M.p. 86-87 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.83-7.74 (m, 4H), 7.48-7.45 (m, 3H), 7.39-7.37 (m, 2H), 7.31-7.27 (m, 3H), 4.73 (s, 2H), 3.18 (d, *J* = 18.2, 1H), 2.97 (d, *J* = 18.2 Hz, 1H), 2.15 (q, *J* = 7.4 Hz, 3H), 0.84 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.8, 137.9, 135.7, 133.0, 132.3, 128.7, 128.6 (2C), 128.1, 127.9, 127.4, 126.4, 126.3, 124.9, 124.1, 52.3, 42.6, 41.2, 32.3, 8.9; An enantiomeric excess of 90% was measured by chiral HPLC [OD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, t_{R1} = 17.5 min (*R*), t_{R2} = 27.4 min (*S*)]. $[\alpha]^{25}_D$ = -6.0 (*c* 1.5, CH_2Cl_2). Absolute configuration was compared to the HPLC chromatogram reported by Hayashi and coworkers.[6] *All conjugate addition products were assigned the same absolute stereochemistry as* ***3.110***. HRMS(EI) *m/z* calc'd for $C_{23}H_{21}NO_2$ (M^+): 343.1572. Found: 343.1573.

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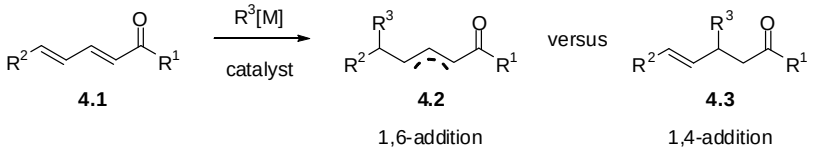
Chapter 4*

Catalytic Asymmetric 1,6-Addition to 5-(3-Aryl-2-Propenylidene) Meldrum's Acid Derivatives

(A) Introduction

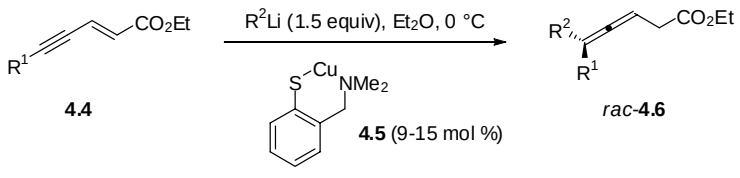
Conjugate addition of carbon nucleophiles to α,β-unsaturated carbonyls is a powerful carbon-carbon bond forming process, and catalytic asymmetric versions have become useful synthetic tools for the generation of tertiary[1] and quaternary[2] carbon stereocentres. Despite a large body of literature on 1,4-additions, analogous 1,6-addition methods are underdeveloped (Scheme 4.1).[3]

Scheme 4.1: 1,6-Addition versus 1,4-addition in unsaturated carbonyl compounds



The presence of two electrophilic sites and difficulties in controlling the regioselectivity has limited the investigations on this reaction. Thus, much work on 1,6-additions has been conducted on enynones where the 1,6-acceptor carbon is sp-hybridized while the 1,4-carbon acceptor is sp^2-hybidized (Scheme 4.2).[4]

Scheme 4.2: An illustrative example of 1,6-acceptor carbon that is sp-hybridized



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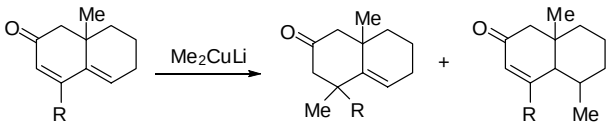
Another approach for the control of regioselectivity is to add a bulky substituent at the 1,4-carbon acceptor to bias the system towards 1,6-addition (Scheme 4.3).[5]

Scheme 4.3: Introduction of sterics for regioselective control of 1,6- versus 1,4-addition

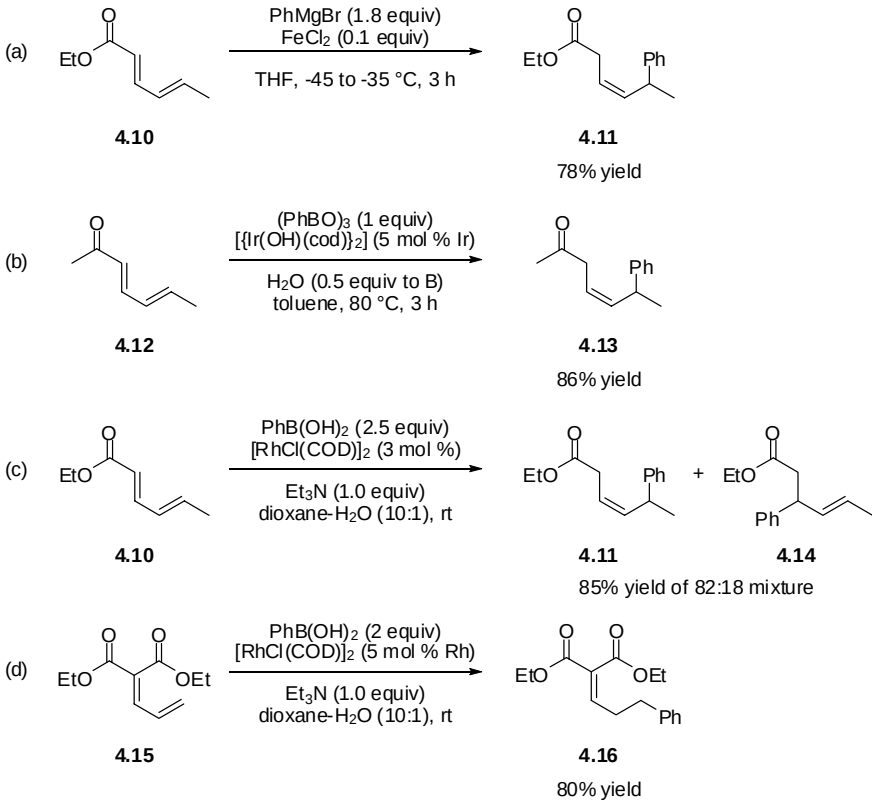


4.7 **4.8** **4.9**

R = H; 84% yield; 60:40
R = Me; 82% yield; 20:80

More recently, a few reports have moved away from traditional copper catalysis to other metals for high regioselectivities. The iron-catalyzed 1,6-addition of Grignard reagents to 2,4-dienoates and 2,4-dienamides has been reported by Urabe's group (Scheme 4.4a).[6]

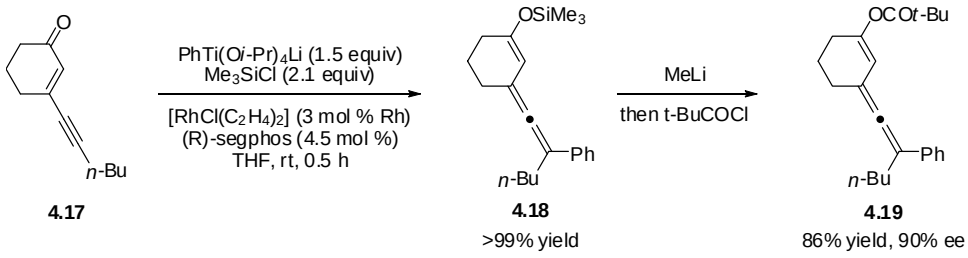
Scheme 4.4: Non-copper catalyzed 1,6-addition reactions



Hayashi and coworkers have reported the 1,6-addition of arylboronic acids to α,β,γ,δ-unsaturated carbonyl compounds in the presence of catalytic amounts of iridium complexes (Scheme 4.4b).[7] The reaction of aryl- and alkenylboronic acids with 2,4-dienoate esters, catalyzed by rhodium, has also been investigated by Csákÿ's group (Scheme 4.4c).[8] This work was recently extended to the 1,6-addition to 2-allylidenemalonates (Scheme 4.4d).[9]

Despite the importance of such methodology, the asymmetric 1,6-addition for the formation of either tertiary or quaternary stereocentres remains underdeveloped. Prior to our investigations in this area there have been only two examples of asymmetric 1,6-addition reactions. Hayashi and coworkers reported the Rh-catalyzed asymmetric 1,6-addition of aryltitanates to alkyne acceptors to afford chiral allenes (Scheme 4.5).[10] Enantioselectivities of up to 93% ee were obtained with good isolated yields.

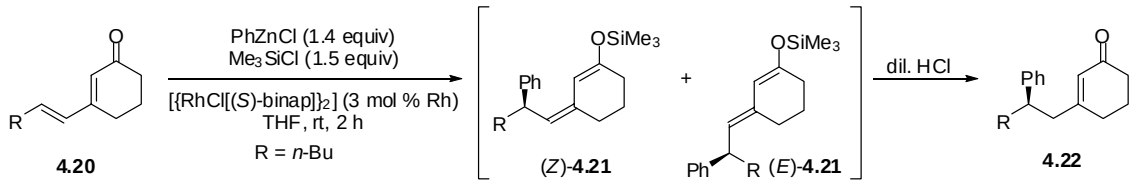
Scheme 4.5: Rh-catalyzed asymmetric 1,6-addition of aryltitanates to enynones



4.17 → **4.18** >99% yield → **4.19** 86% yield, 90% ee

The same group subsequently described the Rh-catalyzed asymmetric 1,6-addition of arylzinc reagents to dienones (Scheme 4.6).[11]

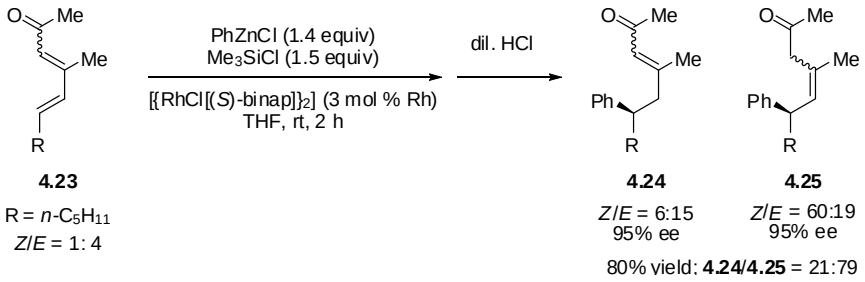
Scheme 4.6: Rh-catalyzed asymmetric 1,6-addition of arylzinc reagents to dienones



4.20 → (*Z*)-**4.21** + (*E*)-**4.21** >99% yield, *Z*/*E* = 4:1 → **4.22** 99% yield, 96% ee

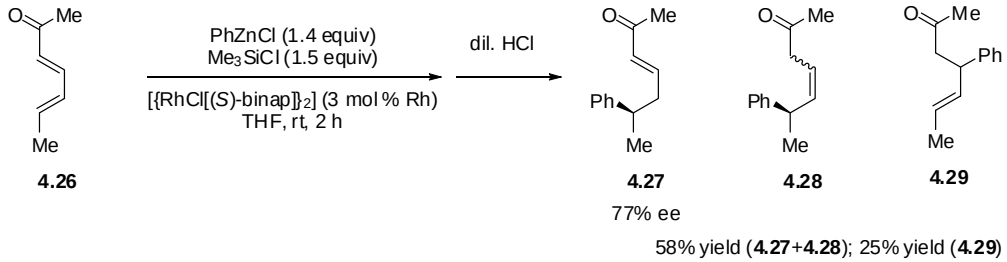
Although 1,6-addition to cyclic dienones lead to single products after an acidic workup, a mixture of 1,6-products were obtained when linear dienone **4.32** was used (Scheme 4.7).

Scheme 4.7: Rh-catalyzed asymmetric 1,6-addition of arylzinc reagents to dienone **4.23**



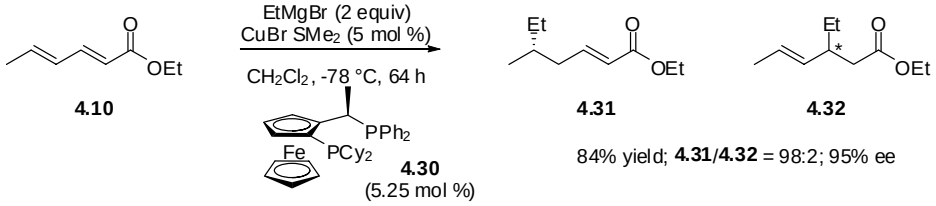
Interestingly, when the β and γ positions had similar pattern substitution, the regioselectivity as well as the enantioselectivity decreases significantly, as illustrated by removal of the β-methyl substituent from **4.23** to give linear dienone **4.26** (Scheme 4.8).

Scheme 4.8: Rh-catalyzed asymmetric 1,6-addition of arylzinc reagents to dienone **4.26**



Subsequent to our investigations, Feringa reported the copper-catalyzed enantioselective 1,6-addition of Grignard reagents to linear dienoates (Scheme 4.9).[12] Excellent regioselectivities and enantioselectivities were obtained for the formation of tertiary stereocentres.

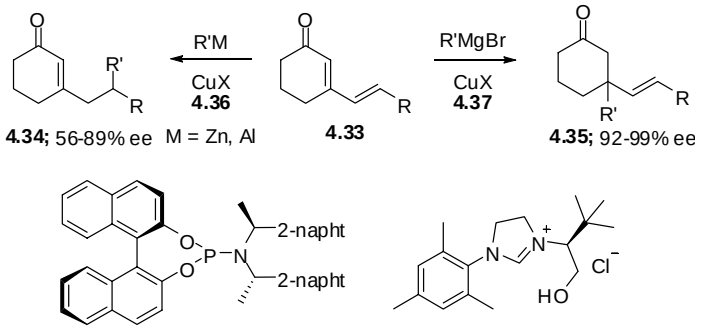
Scheme 4.9: Cu-catalyzed asymmetric 1,6-addition of Grignard reagents to dienoates



A regiodivergent 1,4 versus 1,6 asymmetric copper-catalyzed conjugate addition was reported by Alexakis and coworkers (Scheme 4.10).[13] Changing the metal nucleophile

and the chiral ligand allowed for reversal in regioselectivity for the same electrophile. Of note, the hydroxyl group in **4.37** was necessary for the formation of the 1,4-product since other NHC ligands and Grignard reagents gave exclusively the 1,6-adduct.

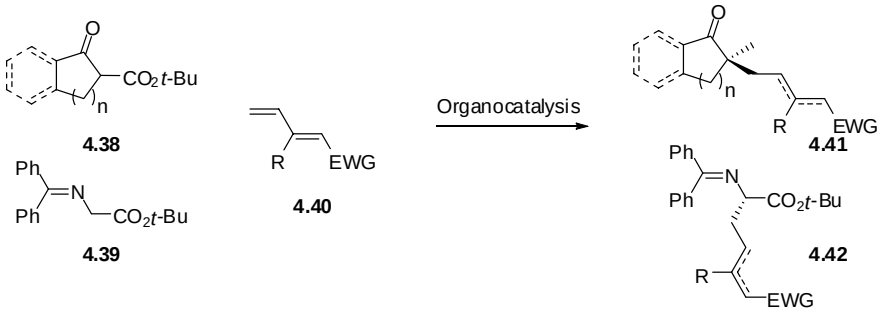
Scheme 4.10: Regiodivergent 1,4 versus 1,6 asymmetric Cu-catalyzed conjugate addition



4.36 **4.37**

Although the focus of this thesis is on the asymmetric conjugate addition reactions involving metal carbon nucleophilies with metal catalysis, Jorgensen's group offers an alternative for the asymmetric 1,6-addition that complements the recent work in this area. The organocatalytic asymmetric 1,6-additions of β-ketoesters and glycine imine onto various α,β,γ,δ-unsaturated carbonyls and sulfones were reported with generally excellent yields and enantioselectivities (Scheme 4.11).[14]

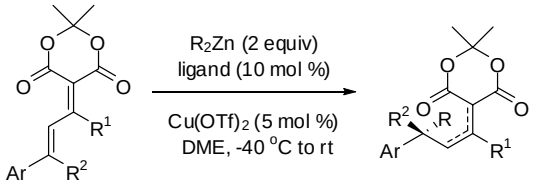
Scheme 4.11: Organocatalytic asymmetric 1,6-additions of β-ketoesters and glycine imine



As seen with the relatively few reports, the addition of carbon nucleophiles in a 1,6-conjugate fashion remains a challenging topic of great synthetic interest. In this chapter, the first catalytic asymmetric 1,6-addition of dialkylzinc reagents to 5-(3-aryl-2-

propenylidene) Meldrum's acids to afford tertiary and quaternary stereogenic centres is presented (Scheme 4.12).

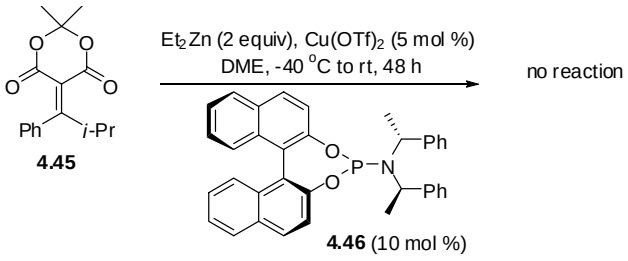
Scheme 4.12: Cu-catalyzed asymmetric 1,6-addition to propenylidene Meldrum's acids



(B) Results and Discussion

The enantioselective formation of benzylic quaternary stereocentres via the 1,4-addition of dialkylzinc reagents to 5-(1-arylethylidene) Meldrum's acid was discussed in Chapter 2. In the course of our studies, it was observed that increased substitution around the electrophilic carbon of the alkylidene inhibited the conjugate addition. As illustrated in Scheme 4.13, 5-(1-phenyl-2-methylpropylidene) Meldrum's acid **4.45** was inert under our optimal reaction conditions, and starting material was quantitatively recovered. This observation indicated that the 1,4-addition pathway could be blocked effectively, and was an incentive to explore 1,6-addition to dienyl Meldrum's acids.

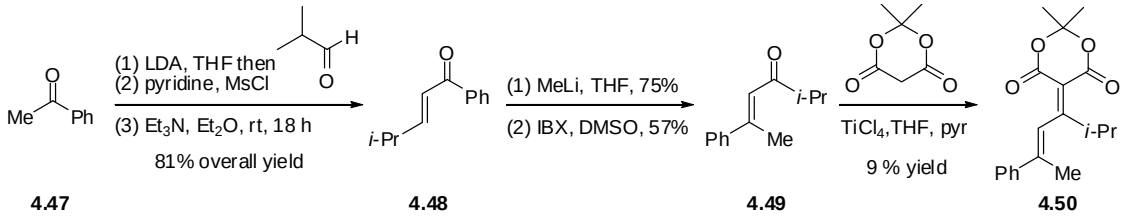
Scheme 4.13: Increased substitution around the electrophilic centre in the Cu-catalyzed asymmetric 1,4-addition to alkylidene Meldrum's acids



Next, it remained to establish that 1,6-addition would proceed on 5-(3-aryl-2-propenylidene) Meldrum's acid derivatives. Along the line of our previous investigations, the formation of benzylic quaternary stereocentres was initially attempted. Propenylidene Meldrum's acid **4.50** was synthesized in a number steps beginning with commercially available acetophenone (Scheme 4.14). Aldol condensation of acetophenone **4.47** and

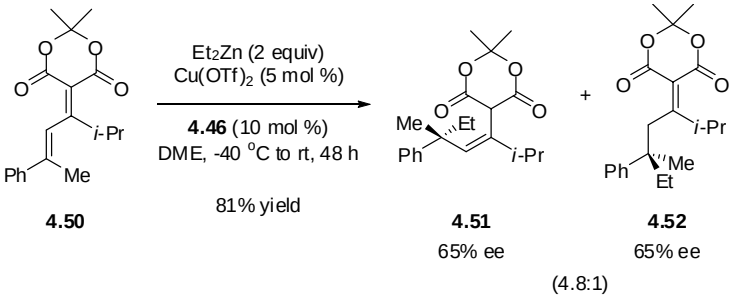
isobutyraldehyde gave ketone **4.48** in 81% overall yield.[15] Ketone **4.48** was reacted with MeLi to give a tertiary alcohol that was subjected to an oxidative rearrangement with IBX[16] in DMSO.[17] The resulting ketone (**4.49**) was subjected to Knoevenagel condensation with Meldrum's acid[18] to provide propenylidene Meldrum's acid **4.50** in 9% yield.

Scheme 4.14: Synthesis of propenylidene Meldrum's acid **4.50**



With Meldrum's acid **4.50** in hand, it was subjected to Et_2Zn in the presence of $Cu(OTf)_2$ (5 mol %), and phosphoramidite ligand **4.46** (10 mol %) to afford exclusively 1,6-adducts **4.51** and **4.52** in a 4.8:1 ratio and an 81% combined isolated yield, and in 65% enantiomeric excess (Scheme 4.15). The β,γ-unsaturated compound **4.51** was the major component of the mixture, and alkylidene Meldrum's acid **4.52** was minor. It is noteworthy that Z-olefin **4.51** was obtained as a single isomer and the stereochemistry of the trisubstituted alkene was determined by nOe experiments.

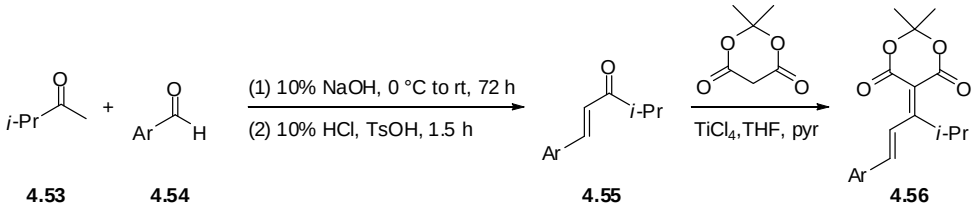
Scheme 4.15: Formation of quaternary stereocentres via 1,6-addition to propenylidene Meldrum's acid **4.50**



Our attention then turned to the formation of tertiary stereocentres.[19] The propenylidene Meldrum's acids were readily prepared in two steps, aldol condensation of 3-methylbutan-2-one with benzaldehydes to afford the desired ketones, followed by

condensation with Meldrum's acid to generate propenylidene Meldrum's acids (Scheme 4.16).

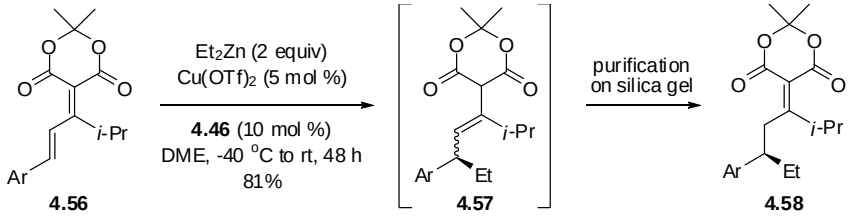
Scheme 4.16: Synthesis of propenylidene Meldrum's acids **4.56**

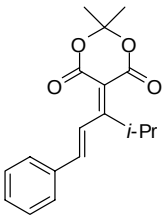
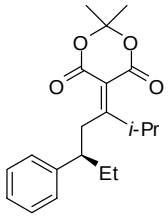
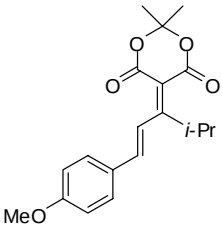
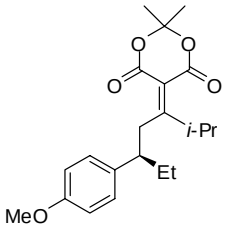
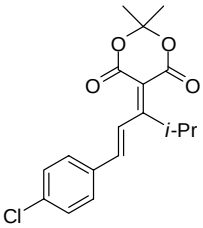
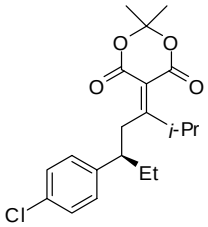
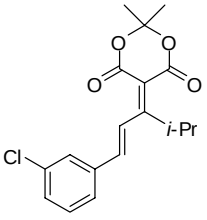
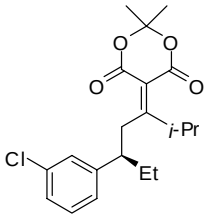
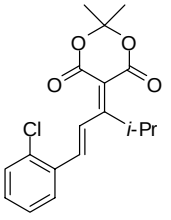
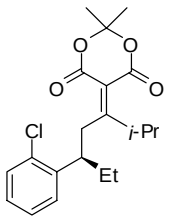


4.53 **4.54** **4.55** **4.56**

When Meldrum's acid **4.59** was reacted with Et_2Zn, **4.60** was isolated in 70% ee and 65% yield after 24 h (Table 4.1, entry 1). The β,γ-unsaturated product was formed initially as determined by analysis of the crude ^1H NMR, but readily isomerized to the corresponding alkylidene Meldrum's acid upon purification on silica gel. The alkene isomerization limited the yield in some cases as the alkylidenes decomposed during flash chromatography and upon standing.

Table 4.1: Scope of the aryl substitution for the asymmetric 1,6-addition of Et_2Zn to propenylidene Meldrum's acids **4.56** for the formation of tertiary stereocentres

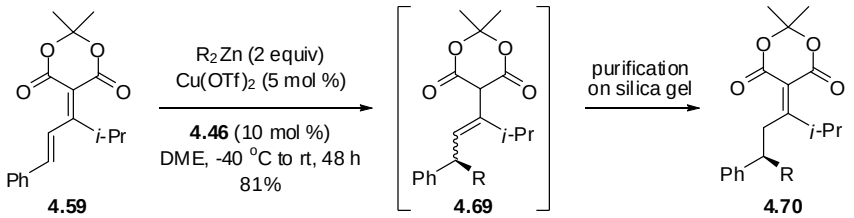


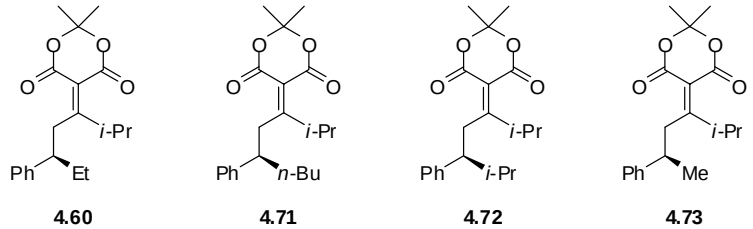
entry	substrate	product	yield (%)	ee (%)
1	 **4.59**	 **4.60**	65	70
2	 **4.61**	 **4.62**	19	74
3	 **4.63**	 **4.64**	26	84
4	 **4.65**	 **4.66**	50	60
5	 **4.67**	 **4.68**	29	84

The effect of substituting the aromatic moiety on the enantioselectivity of the conjugate process was then investigated. Introduction of an electron-donating group at the 4-position furnished Meldrum's acid **4.62** in 74% ee, while an electron withdrawing group at the same position gave 84% ee (Table 4.1, entries 2 and 3). Furthermore, substitution variations around the ring showed that meta substitution decreased the enantioselectivity, while there was no change between the *ortho*- and *para*- positions (Table 4.1, entries 3-5).

Additionally, various dialkylzinc reagents reacted with **4.59** resulting in good enantioselectivities (Table 4.2). Dibutylzinc afforded the 1,6-adduct in an 82% ee, while sterically demanding diisopropylzinc afforded the product in a 75% ee. Dimethylzinc also added smoothly to give the 1,6-product in a 83% ee.

Table 4.2: Scope of the dialkylzinc addition for the asymmetric 1,6-addition to propenylidene Meldrum's acid **4.59** for the formation of tertiary stereocentres





4.60	**4.71**	**4.72**	**4.73**
65% yield 70% ee	44% yield 82% ee	56% yield 75% ee	19% yield 83% ee

(C) Summary

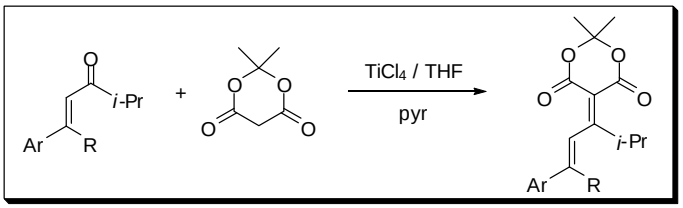
In summary, an enantioselective asymmetric synthesis of benzylic tertiary and quaternary stereogenic centres via 1,6-addition of dialkylzinc reagents to Meldrum's acid acceptors has been achieved. This work represents one of the early examples of asymmetric 1,6-addition reactions.

(D) Experimental Section

(I) General Methods

All reactions were carried out in flame-dried glassware under a dry argon atmosphere. 1,2-Dimethoxyethane was distilled from sodium-benzophenone ketyl under nitrogen and degassed via a freeze-pump-thaw method. $Cu(OTf)_2$ was obtained from commercial sources and used without further purification. Dialkylzinc reagents namely, Et_2Zn (1.0 M in hexanes), *n*-Bu_2Zn (1.0 M in heptanes), Me_2Zn (1.0 M in heptanes), and *i*-Pr_2Zn (1.0 M in toluene), were also obtained from commercial sources and used without further purification. Chiral phosphoramidite ligand **4.46** was prepared following a literature procedure.[20] ^1H NMR spectra were referenced to residual ^1H shift in $CDCl_3$ (7.24 ppm). $CDCl_3$ (77.0 ppm) was used as the internal reference for ^{13}C NMR spectra. Flash chromatography was performed using 230-400 mesh silica gel. Melting points are uncorrected. Optical rotations were recorded in cells with 1 dm path length. Chiral HPLC analyses were performed using a Chiralcel OD-H or AD-H column. All columns are 250 x 4.6 mm. High resolution mass spectra were run by Dr. R. Smith at the University of Waterloo with a source temperature of 200 °C, mass resolution of 9000, and electron energy of 70 eV.

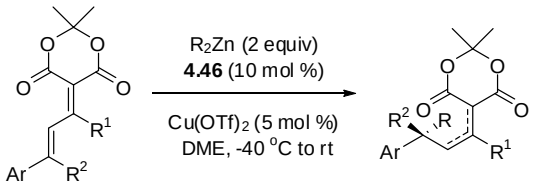
(II) General Procedure A: Preparation of Propenylidene Meldrum's Acids



Alkylidene Meldrum's acids were prepared by the Knoevenagel condensation of Meldrum's acid with ketones.[18] In a typical reaction, a solution of $TiCl_4$ (2.1 equiv) in CH_2Cl_2 (3 M) was added dropwise under nitrogen to dry THF (0.3 M), which was cooled at 0 ºC, resulting in a yellow suspension. A solution containing the ketone (1.0 equiv) and Meldrum's acid (1.0 equiv) in dry THF (0.7 M) was added dropwise via a syringe to the $TiCl_4$•THF complex. The flask containing the solution of ketone and Meldrum's acid was rinsed with THF (2X) and added to the reaction mixture. Subsequently, pyridine (5.0

equiv) was added to the reaction mixture dropwise at 0 ºC. The reaction was allowed to warm up slowly to room temperature and stirred until completion of reaction or for 24 h. The reaction was quenched by the addition of water and diluted with either Et_2O or EtOAc. After the solid was dissolved, the layers were partitioned. The aqueous layer was extracted was Et_2O, or EtOAc (2X), and the combined organic layers were washed with $NaHCO_3$ saturated solution (2X), brine (1X), dried over $MgSO_4$, filtered and concentrated. Purification by either crystallization or flash chromatography provided the alkylidene Meldrum's acids.

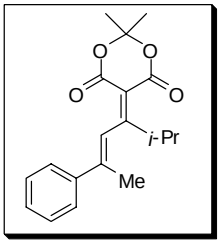
(III) General Procedure B: 1,6-Addition of $(alkyl)_2Zn$ to Propenylidene Meldrum's Acids



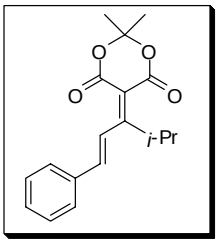
In a glove box, a flame-dried resealable Schlenk tube was charged with $Cu(OTf)_2$ (5 mol %) and **4.46** (10 mol %). Dry DME (1 mL) was then added to the Schlenk tube to wash down any residual solids to the bottom. The resulting solution was allowed to stir at rt for 15 min, outside the glove box, and then cooled to -40 ºC using an acetone/dry-ice bath. In a dry box, the commercially available solution of R_2Zn (2.0 equiv) was transferred to a capped round-bottom flask. This solution was added to the Schlenk tube dropwise via a syringe and the resulting reaction mixture stirred for 5 min at -40 °C. A solution of freshly purified 5-(3-aryl-2-propenylidene) Meldrum's acid (1.0 equiv) in DME (0.5 mL) was then added dropwise using a syringe, and additional DME (0.2 mL) was added to rinse the sides of the Schlenk tube. This mixture was allowed to warm up slowly to ambient temperature, and stirred for 24-48 h. The reaction was quenched by the addition of a 5% HCl solution and diluted with Et_2O. The layers were partitioned and the aqueous layer extracted with Et_2O (3X). The combined organic layers were washed with water (2X), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by flash column chromatography on silica gel using a combination of EtOAc and hexanes or petroleum ether (35-60 ºC) as eluent to yield the desired product. HPLC equipped with a

chiral column (OD-H or AD-H) was used to measure the enantiomeric excess of the products. The racemates were prepared using the corresponding Grignard reagent (2.5 equiv) in THF at -40 °C.

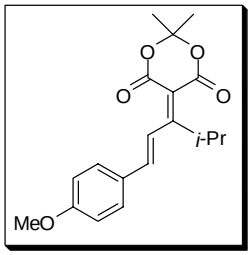
(IV) Substrate Specific Information



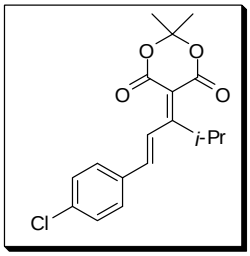
(*E*)-2,2-Dimethyl-5-(2-methyl-5-phenylhex-4-en-3-ylidene)-1,3-dioxane-4,6-dione (4.50): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 9% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47-7.45 (m, 2H), 7.37-7.25 (m, 3H), 6.38 (s, 1H), 4.00 (sept, *J* = 6.8 Hz, 1H), 3.19 (s, 3H), 1.76 (s, 6H), 1.17 (d, *J* = 6.7 Hz, 6H).



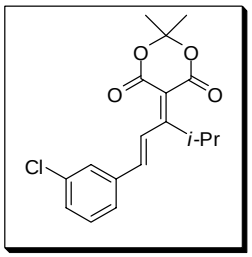
(*E*)-2,2-Dimethyl-5-(4-methyl-1-phenylpent-1-en-3-ylidene)-1,3-dioxane-4,6-dione (4.59): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid in 43% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.55-7.49 (m, 3H), 7.39-7.32 (m, 3H), 7.19 (d, *J* = 16.6 Hz, 1H), 4.00 (sept, *J* = 7.1 Hz, 1H), 1.75 (s, 6H), 1.35 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.4, 161.5, 161.2, 139.7, 135.7, 129.6, 128.8, 127.6, 124.5, 115.6, 103.5, 31.9, 26.9, 21.7; HRMS(EI) *m/z* calc'd for $C_{18}H_{20}O_4$ (M^+): 300.1362. Found: 300.1354.



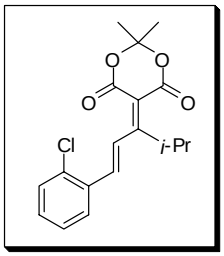
(*E*)-5-(1-(4-Methoxyphenyl)-4-methylpent-1-en-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.61): Prepared according to general procedure A. Purification of crude mixture with 10:1 hexanes:EtOAc, afforded a yellow pasty solid in 21% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53 (d, *J* = 16.5 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.26 (d, *J* = 16.5 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 2H), 4.00 (sept, *J* = 7.0 Hz, 1H), 3.77 (s, 3H), 1.71 (s, 6H), 1.34 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.3, 161.7, 161.4, 140.8, 129.3, 128.3, 122.2, 114.2, 103.2, 67.7, 55.2, 31.6, 26.8, 21.8; HRMS(EI) *m/z* calc'd for $C_{19}H_{22}O_5$ (M^+): 330.1467. Found: 330.1464.



(*E*)-5-(1-(4-Chlorophenyl)-4-methylpent-1-en-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.63): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49-7.42 (m, 3H), 7.34-7.31 (m, 2H), 7.10 (d, *J* = 16.6 Hz, 1H), 3.99 (sept, *J* = 7.1 Hz, 1H), 1.78 (s, 6H), 1.34 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.2, 161.5, 161.1, 138.0, 134.3, 129.8, 129.1, 128.8, 125.1, 115.9, 103.7, 31.9, 27.0, 21.7; HRMS(EI) *m/z* calc'd for $C_{18}H_{19}{}^{35}ClO_4$ (M^+): 334.0972. Found: 334.0969.

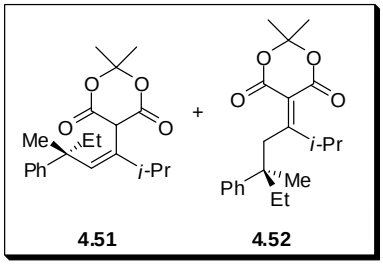


(*E*)-5-(1-(3-Chlorophenyl)-4-methylpent-1-en-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.65): Prepared according to general procedure A. Recrystallization from MeOH afforded a beige solid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.46-7.43 (m, 1H), 7.37-7.36 (m, 2H), 7.29-7.24 (m, 2H), 7.01 (d, *J* = 16.6 Hz, 1H), 3.99 (sept, *J* = 7.0 Hz, 1H), 1.75 (s, 6H), 1.32 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.2, 161.3, 161.0, 137.6, 137.2, 134.8, 130.0, 129.3, 127.4, 125.8, 125.6, 116.3, 103.7, 32.0, 27.0, 21.6; HRMS(EI) *m/z* calc'd for $C_{18}H_{19}{}^{35}ClO_4$ (M^+): 334.0972. Found: 334.0965.

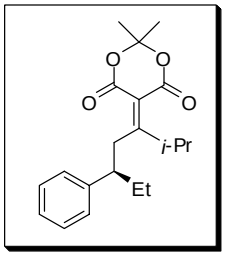


(*E*)-5-(1-(2-Chlorophenyl)-4-methylpent-1-en-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.65): Prepared according to general procedure A. Recrystallization from MeOH afforded a light yellow solid in 46% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70-7.67 (m, 1H), 7.53 (d, *J* = 16.6 Hz, 1H), 7.41-7.35 (m, 2H), 7.28-7.24 (m, 2H), 4.04 (sept, *J* = 7.1 Hz, 1H), 1.75 (s, 6H), 1.36 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.7, 161.5, 161.0, 134.7, 134.3, 134.1, 130.3, 129.7, 127.4, 127.2, 126.9, 116.3, 103.8, 31.9, 27.0, 21.8; HRMS(EI) *m/z* calc'd for $C_{18}H_{19}{}^{35}ClO_4$ (M^+): 334.0972. Found: 334.0981.

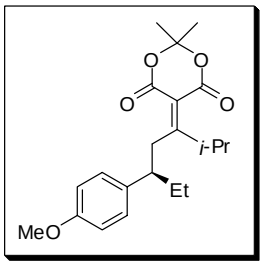
(V) Product Specific Information



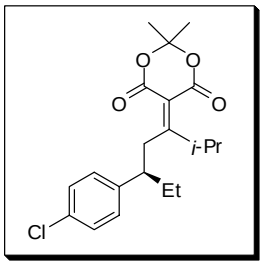
(*R*,*Z*)-5-(2,5-Dimethyl-5-phenylhept-3-en-3-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.51) and (*R*)-5-(2,5-dimethyl-5-phenylheptan-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.52): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 12:1 hexanes:EtOAc, afforded an inseparable mixture of **4.51** and **4.52** as an oil in 81% yield; An enantiomeric excess of 65% was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 5.1 min, t_{R2} = 5.7 min for **4.52** and t_{R3} = 9.0 min, t_{R4} = 10.3 min for the 4.51).



(*R*)-2,2-Dimethyl-5-(2-methyl-5-phenylheptan-3-ylidene)-1,3-dioxane-4,6-dione (4.60): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 10:1 hexanes:EtOAc, afforded an oil in 65% yield; An enantiomeric excess of 70% was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 13.8 min, t_{R2} = 17.9 min).

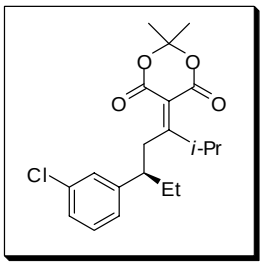


(*R*)-5-(5-(4-Methoxyphenyl)-2-methylheptan-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.62): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 12:1 hexanes:EtOAc, afforded an oil in 19% yield; An enantiomeric excess of 74% was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA added, 1.0 mL/min, t_{R1} = 16.9 min, t_{R2} = 23.0 min).

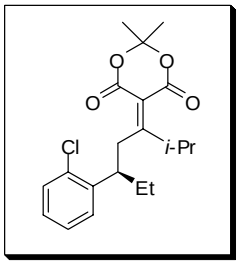


(*R*)-5-(5-(4-Chlorophenyl)-2-methylheptan-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.64): Prepared according to general procedure B. Purification by flash column

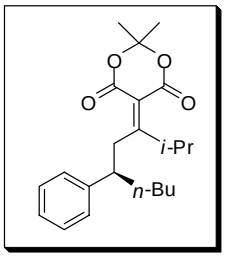
chromatography on silica gel, eluting with 12:1 hexanes:EtOAc, afforded an oil in 26% yield; An enantiomeric excess of 84% was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA added, 1.0 mL/min, t_{R1} = 12.4 min, t_{R2} = 16.5 min).



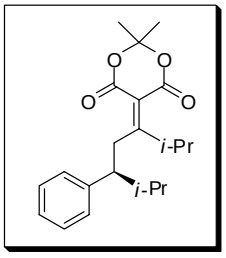
(*R*)-5-(5-(3-Chlorophenyl)-2-methylheptan-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.66): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 12:1 hexanes:EtOAc, afforded an oil in 50% yield; An enantiomeric excess of 60% was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA added, 1.0 mL/min, t_{R1} = 8.3 min, t_{R2} = 9.4 min).



(*R*)-5-(5-(2-Chlorophenyl)-2-methylheptan-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.68): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 12:1 hexanes:EtOAc, afforded an oil in 29% yield; An enantiomeric excess of 84% was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA added, 1.0 mL/min, t_{R1} = 9.9 min, t_{R2} = 10.8 min).

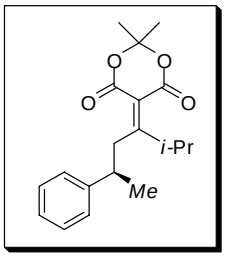


(*R*)-2,2-Dimethyl-5-(2-methyl-5-phenylnonan-3-ylidene)-1,3-dioxane-4,6-dione (4.71): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 12:1 hexanes:EtOAc, afforded an oil in 44% yield; An enantiomeric excess of 82% was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 10.2 min, t_{R2} = 13.5 min).



(*S*)-5-(2,6-Dimethyl-5-phenylheptan-3-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4.72): Prepared according to general procedure B. Purification by flash column chromatography on silica

gel, eluting with 12:1 hexanes:EtOAc, afforded an oil in 56% yield; An enantiomeric excess of 75% was measured by chiral HPLC [AD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 9.6 min, t_{R2} = 12.3 min).



(*R*)-2,2-Dimethyl-5-(2-methyl-5-phenylhexan-3-ylidene)-1,3-dioxane-4,6-dione (4.73): Prepared according to general procedure B. Purification by flash column chromatography on silica gel, eluting with 12:1 hexanes:EtOAc, afforded an oil in 19% yield; An enantiomeric excess of 83% was measured by chiral HPLC [OD-H, 1% *i*-PrOH/hexanes with 0.1% TFA, 1.0 mL/min, t_{R1} = 10.4 min, t_{R2} = 13.3 min).

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Chapter 5*

Probing Persistent Intramolecular C–H•••X (X = O, S, Br, Cl, and F) Bonding in Solution using Benzyl Meldrum's Acid Derivatives

(A) Introduction

Non-classical C–H•••X (where X = O and N) hydrogen bonds are prominent and well documented in the solid state.[1] However, limited experimental evidence supports persistent C–H•••X hydrogen bonds in solution, which have been postulated to be of particular importance in a wide array of biological phenomenon, as well as in supramolecular chemistry. Infrared and proton magnetic resonance spectroscopy have been utilized to survey the propensities of haloforms and related compounds to act as proton donors in intermolecular hydrogen bond with DMSO, pyridine, acetone, and Et_3N.[2,3] Other reports, using ^1H NMR spectroscopy, concern intramolecular *o*-carboranyl C–H•••N and C–H•••O interactions.[4] Further evidence of C–H•••X bonding in this system has been extended to acceptors such as Br, Cl and F.[5] The common feature of the haloforms and the *o*-carboranes is the relatively high acidity of the hydrogen involved. Consequently, the formation of persistent C–H•••X bonds in solution should be promoted by enhancing the acidity of the C–H donor and thus its ability to hydrogen bond.[6,7]

Meldrum's acid (**5.1**) and derivatives are valuable reagents in organic synthesis (Figure 5.1), serving as powerful acylating agents in C–C,[8] C–O, and C–N bond forming reactions[9] and as building blocks in the synthesis of numerous natural products.[10] Considerable attention has also been paid to the exceptionally high C–H acidity of **5.1**.[11] The hydrogens located α to the two carbonyl groups (5-position), with a remarkable pK_a of 4.83-4.93[12] (7.3 in DMSO)[13], confer unique chemical properties to Meldrum's acid (**5.1**), one of them being the ability to participate in hydrogen bonding. X-Ray structural determination of this atypical carbon-based Brønsted acid revealed the presence of non-

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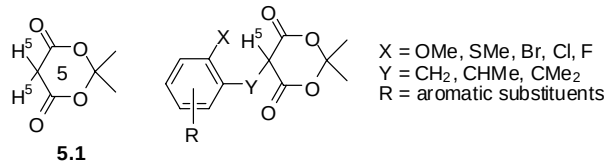
classical intermolecular C–H•••O bond (2.43 Å) between the oxygen atom of the carbonyl group and the pseudo axial hydrogen H(5) at the 5-position.[14,15]

Figure 5.1: Meldrum's acid (**5.1**) and 5-benzyl derivatives



5.1

Toward an understanding of the interactions between acidic C–H hydrogens and a variety of acceptors (X), we set out to probe persistent hydrogen bonding in solution using Meldrum's acid derivatives. To bring about formation of unprecedented intramolecular hydrogen bond, *ortho*-substituted benzyl Meldrum's acids were designed, for which hydrogen bonding would occur through a six-membered ring. As illustrated in Figure 5.1, introduction of substituents (R) on the aromatic moiety and in the tether (Y) would allow variation of electronic and steric factors.

In this chapter benzyl Meldrum's acid derivatives are presented as a class of compounds newly identified as displaying persistent intramolecular C–H•••X bonds (X = O, S, Br, Cl, and F) (Figure 5.1) in solution, as evidenced by ^{1}H NMR experiments and correlation with solid-state X-ray analysis.

(B) Results and Discussion

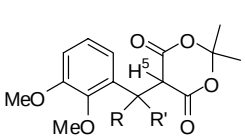
(I) Characterization of Persistent Intramolecular C−H•••X (X = O, S, Br, Cl, and F) Bonds in Solution Using ^{1}H NMR Spectroscopy.

(1) Identification of Anomalous Chemical Shift Differences in Benzyl Meldrum's Acid Derivatives.

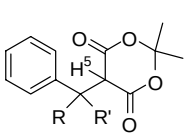
In the course of our studies using Meldrum's acids as acylating agents in the catalytic intramolecular Friedel-Crafts reaction, 5-(2,3-dimethoxybenzyl) Meldrum's acids **5.2**-**5.4** were prepared, in which the degree of substitution at the benzylic position was varied (Table 5.1).[8e] It was noted that the ^{1}H NMR chemical shift difference for H(5) spanned 1.25 ppm; as substitution increased at the benzylic position, so did deshielding of H(5) (entries 1-3). To determine if the origin of this unexpected chemical shift variation was

attributable to the *gem*-dimethyl group, unsubstituted counterparts **5.5-5.7** were synthesized. The latter showed an insignificant variation of 0.16 ppm (entries 4-6). A direct comparison of compounds **5.2-5.4** with **5.5-5.7** (Δ ppm in Table 5.1) revealed that the largest ^{1}H NMR chemical shift difference, 1.80 ppm, was observed for *gem*-dimethyl substituted Meldrum's acid **5.4** versus **5.7**. Obviously, the presence of the *gem*-dimethyl group had a large influence on the chemical shift of H(5) in **5.2-5.4**. However, since increasing substitution at the benzylic position of Meldrum's acids **5.5-5.7** had a slight shielding effect on H(5), an additional factor had to be involved. It was hypothesized that the methoxy group present at the ortho position of the aromatic moiety was key in deshielding H(5). Indeed, ^{1}H NMR chemical shifts of 3,4-, 3,5-dimethoxybenzyl and 4-methoxybenzyl Meldrum's acids (**5.8**), (**5.9**) and (**5.10**) revealed no significant difference when related to **5.7** (entries 7-9). The influence of the ortho methoxy group on the chemical shift of H(5) was further confirmed with Meldrum's acids **5.11-5.13**. The introduction (entries 10-11) or absence (entry 12) of an additional electron-donating methoxy group at various positions of the aromatic ring had little influence on the chemical shift of H(5), which remained unusually deshielded for a C–H bond of this type, with a Δ ppm between 1.47 and 1.71 when compared with **5.7**.

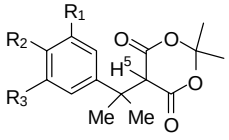
Table 5.1: ^{1}H NMR Chemical shifts of benzyl Meldrum's acid



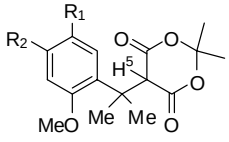
5.2, R = R' = H
5.3, R = H; R' = Me
5.4, R = R' = Me



5.5, R = R' = H
5.6, R = H; R' = Me
5.7, R = R' = Me



5.8, $R_1 = R_2 = MeO$; $R_3 = H$
5.9, $R_1 = R_3 = MeO$; $R_2 = H$
5.10, $R_1 = R_3 = H$; $R_2 = MeO$



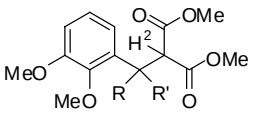
5.11, $R_1 = H$; $R_2 = MeO$
5.12, $R_1 = MeO$; $R_2 = H$
5.13, $R_1 = R_2 = H$

entry	compound	H(5) chemical shift[a,b,c] (ppm)[a,b]	Δ ppm[e]
1	**5.2**	4.13 (4.63) (t)	0.39 (-0.14) (**5.2-5.5**)
2	**5.3**	4.29 (4.45) (d)	0.62 (-0.27) (**5.3-5.6**)
3	**5.4**	5.38 (5.18) (s)	1.80 (0.62) (**5.4-5.7**)
4	**5.5**	3.74 (4.77) (t)	—
5	**5.6**	3.67 (4.72) (d)	—
6	**5.7**	3.58 (4.56) (s)	—
7	**5.8**	3.47 (s)	-0.11 (**5.8-5.7**)
8	**5.9**	3.59 (s)	0.01 (**5.9-5.7**)
9	**5.10**	3.50 (s)	-0.08 (**5.10-5.7**)
10	**5.11**	5.29 (s)	1.71 (**5.11-5.7**)
11	**5.12**	5.05 (s)	1.47 (**5.12-5.7**)
12	**5.13**	5.21 (5.04) (s)	1.63 (0.48) (**5.13-5.7**)

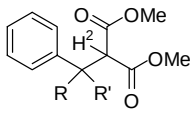
[a] ^{1}H NMR chemical shifts in $CDCl_3$. [b] H(5) multiplicity is in parentheses. [c] ^{1}H NMR chemical shifts in DMSO-d_6 are in parentheses.

These observations were unique to 5-benzyl Meldrum's acids. As shown in Table 5.2, the chemical shift variations of H(2) for malonate analogues **5.14-5.16**, and their corresponding derivatives **5.17-5.19** lacking the methoxy substituents, revealed a similar dependence of benzylic substitution, with a maximum Δ ppm of 0.78 for **5.16**. However, this effect was much lower than that observed with 5-benzyl Meldrum's acids. Therefore, the greater C–H acidity of Meldrum's acids in comparison to malonates likely plays a role in deshielding H(5) when the ortho position of the aromatic moiety is substituted with a methoxy group.

Table 5.2: ^{1}H NMR Chemical shifts of benzyl malonate derivatives



5.14, R = R' = H
5.15, R = H; R' = Me
5.16, R = R' = Me



5.17, R = R' = H
5.18, R = H; R' = Me
5.19, R = R' = Me

entry	compound	H(2) chemical shift[a,b] (ppm)[a,b]	Δ ppm
1	**5.14**	3.75 (t)	0.09 (**5.14-5.17**)
2	**5.15**	3.83 (d)	0.21(**5.15-5.18**)
3	**5.16**	4.60 (s)	0.78 (**5.16-5.19**)
4	**5.17**	3.66 (t)	—
5	**5.18**	3.62 (d)	—
6	**5.19**	3.82 (s)	—

[a] ^{1}H NMR chemical shifts in $CDCl_3$. [b] H(2) multiplicity is in parentheses.

From these results, the polarization of the C–H bond and the ensuing deshielding of H(5) in Meldrum's acids bearing a methoxy group at the ortho position of the aromatic moiety suggested persistent intramolecular C–H•••O bond in solution. The ability of Meldrum's acid to engage in non-classical C–H•••O hydrogen bonds as a result of its superior acidity, in combination with steric factors, deserved thorough investigation.

(2) Distinguishing Between van der Waals Interactions and Hydrogen Bonding as Causes of H(5) Chemical Shift Changes.

From these premises, we set out to probe persistent intramolecular hydrogen bonding in solution by studying the insensitivity of proton chemical shift to concentration and temperature changes on benzyl Meldrum's acid derivatives **5.2**, **5.3**, **5.4**, and **5.13**. As shown in Table 5.3, varying the concentration of **5.13** from 0.044 to 1.38 M had no impact on the ^{1}H chemical shift of H(5), which remained deshielded.

Table 5.3: Concentration data for Meldrum's acid **5.13** in $CDCl_3$

entry	concentration (M)	^{1}H NMR chemical shift of H(5) (ppm)
1	0.044	5.22
2	0.16	5.22
3	0.35	5.23
4	0.70	5.24
5	1.38	5.26

For acids **5.2**-**5.4**, the effect of temperature on H(5) chemical shift was minimal as judged by the slight variation over a range of 105 °C (Table 5.4).

Table 5.4: Temperature effect on Meldrum's acids **5.2**-**5.4** in $CDCl_3$

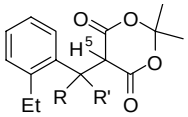
entry	Meldrum's acid	H(5) chemical shift at –50 °C (ppm)	H(5) chemical shift at 55 °C (ppm)	Δ ppm (–50—55 °C)
1	**5.2**	4.31	4.07	0.24
2	**5.3**	4.49	4.18	0.31
3	**5.4**	5.59	5.25	0.34

While the above results suggested the formation of persistent intramolecular C–H•••O bonds in Meldrum's acids **5.2**-**5.4**, compounds **5.2** and **5.3** showed non-substantial deshielding of H(5) compared to **5.4**, with Δ ppm's of 0.39 and 0.62 respectively versus 1.80 ppm (Table 1, entries 1 and 2 versus 3). It was then determined if the H(5) chemical shift variations observed for acids **5.2** and **5.3** in $CDCl_3$ was the result of van der Waals contacts rather than persistent intramolecular hydrogen bonding. The influence on the chemical shift of H(5) by a non-hydrogen bond acceptor group located at the ortho position of the aromatic was estimated by preparing compounds **5.20**-**5.22** (Table 5.5). While slightly larger, the ethyl group was rationally selected to mimic the hydrogen bond acceptor methoxy group.

A substantial effect was only observed for **5.22**, which bears a benzylic *gem*-dimethyl group (Table 5, entry 3). In $CDCl_3$, the ethyl group deshielded H(5) in **5.22** when compared with **5.7** by 0.55 ppm. Once again, the *gem*-dimethyl compound displayed a unique behavior, which likely indicates that the presence of the benzylic substituents forces the group at the ortho position of the aromatic to be in close proximity with H(5). Indeed, in $CDCl_3$, a nOe between the methylene of the ethyl groups and H(5) was observed.

The fact that H(5) in Meldrum's acids **5.20** and **5.21** relative to **5.5** and **5.6** is slightly shielded, while **5.2** and **5.3** relative to **5.5** and **5.6** is deshielded, suggests that van der Waals interactions do not account for the increased chemical shift of H(5) in **5.2** and **5.3**. Considering that the only difference between **5.2** and **5.20**, and **5.3** and **5.21**, respectively, is the presence of an oxygen atom versus a methylene group, it is logical to conclude that this deviation in chemical shift is caused by hydrogen bonding. In the same vein, while H(5) of **5.22** is deshielded by 0.55 ppm relative to **5.7**, the much larger difference between H(5) of **5.4** compared to **5.7** (1.80 ppm) must be caused by a significant intramolecular C–H•••O bond in solution.

Table 5.5: van der Waals contacts contribution of ortho substituent to Δ ppm in $CDCl_3$ and DMSO-d_6



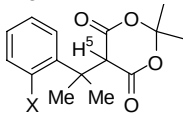
entry	R	R'	H(5) chemical shift in $CDCl_3$ (ppm)	H(5) chemical shift in DMSO (ppm)	Δ ppm in $CDCl_3$	Δ ppm in DMSO
1	H	H (**5.20**)	3.69	4.66	-0.05[a]	-0.11
2	Me	H (**5.21**)	3.63	4.47	-0.04[b]	-0.25
3	Me	Me (**5.22**)	4.13	4.45	0.55[c]	-0.11

[a] Compared with **5.5**. [b] Compared with **5.6**. [c] Compared with **5.7**.

In solution, it was then concluded that the chemical shift variations of H(5) in **5.2**-**5.4**, in comparison to their unsubstituted analogues **5.5**-**5.7**, were due to hydrogen bonding between the ortho methoxy group and H(5), in accordance with the temperature studies. These data undoubtedly established that Meldrum's acids **5.2**-**5.4** form persistent C–H•••O bonds in solution, the strength of this interaction being enhanced by increasing substitution at the benzylic position.

van der Waals interactions as the sole cause of the H(5) chemical shift changes were further ruled out by studying the effect of other potential H-bond acceptors. Thus, electronic factors controlling the formation of persistent C–H•••X (X = S, Br, Cl, and F) through a six-membered ring were then explored in detail. As the chemical shift difference was most pronounced between **5.4** and **5.7**, this effect was studied using *gem*-dimethyl benzyl substituted Meldrum's acid derivatives **5.22**-**5.27**. As depicted in Table 5.6, the chemical shift values of H(5) were determined and compared with reference compound 5-benzyl Meldrum's acid **5.7**. As for the ethyl substituted 5-benzyl Meldrum's acid **5.22** discussed previously, and the methyl derivative **5.23**, which lack the ability to hydrogen bond but are also more sterically demanding than **5.7**, slightly affected the chemical shift of H(5) (entries 3 and 4).[16] Halogens, also considered strong hydrogen-bond acceptors, interacted effectively with H(5) (entries 5-7); bromide and chloride leading to substantial deshielding of H(5). Thiomethoxy substituted Meldrum's acid **5.27** induced the strongest effects on H(5) chemical shift (entry 8).[17]

Table 5.6: ^{1}H NMR Spectroscopic data for 5-(2-substituted benzyl) Meldrum's acids in $CDCl_3$ and DMSO-d_6



entry	X	H(5) chemical shift[a] (ppm)	Δ ppm[b,c]
1	H (**5.7**)	3.58 (4.56)	–
2	OMe (**5.13**)	5.21 (5.04)	1.63 (0.48)
3	Et (**5.22**)	4.13 (4.45)	0.55 (-0.11)
4	Me (**5.23**)	4.18	0.60
5	F (**5.24**)	4.56 (4.57)[b]	0.98 (0.01)
6	Cl (**5.25**)	5.50	1.92
7	Br (**5.26**)	5.73	2.15
8	SMe (**5.27**)	6.50 (6.27)[b]	2.92 (1.71)

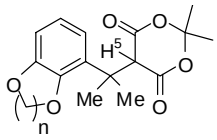
[a] ^{1}H NMR chemical shifts in DMSO-d_6 are in parentheses. [b] All the compounds were compared with **5.7**. [c] Δ ppm in DMSO-d_6 are in parentheses.

5-(2-Alkyl benzyl) Meldrum's acids **5.22** and **5.23** showed a Δ ppm between 0.55-0.60 compared to control model **5.7**. On the other hand, Meldrum's acids **5.24**-**5.27**, which contain potential hydrogen bond acceptors, show greater chemical shift differences, ranging from 0.98 to 2.92 ppm. Were this difference caused solely by van der Waals interactions, the chemical shift should increase with the van der Waals radius of the

involved atom. However, comparing **5.22** and **5.23** to **5.24**, in which a smaller fluoride atom (1.47 Å)[18] causes a greater chemical shift difference than a larger carbon atom (1.70 Å), suggests that hydrogen bonding accounts for the deshielding of H(5). The same is true of **5.26** versus **5.27**, in which smaller sulfur (1.80 Å) deshields more strongly than larger Br (1.85 Å). The fact that Δ ppm does not correlate with the van der Waals radius of the involved atom is further proof of intramolecular hydrogen bonding in 5-(2-substituted benzyl) Meldrum's acids.

Aside from the presence of a hydrogen bond accepting atom as a requirement for their formation, hydrogen bonds have been shown to depend on the directionality of the involved lone pair.[19] Conformationally constrained system **5.28** and **5.29** displayed a smaller ^{1}H NMR chemical shift difference, compared with dimethoxy substrate **5.4**, likely a result of a non-optimal orientation of the oxygen lone pairs in the C–H•••O interaction (Table 5.7). This further rules out van der Waals contacts as the cause of the increased chemical shift of H(5), as these should be relatively unaffected by such a change in orientation of lone pairs.

Table 5.7: Spectroscopic data for **5.28** and **5.29** in $CDCl_3$



entry	*n*	H(5) chemical shift (ppm)	Δ ppm[a]
1	1 (**5.28**)	4.69	1.11
2	2 (**5.29**)	5.06	1.48

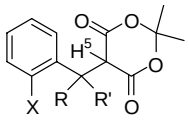
[a] The compounds were compared with **5.7**.

(3) Contribution of Geminal Benzylic Substituents to the Presence of C–H•••X (X = O, S, F) Bonding.

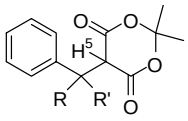
The effect of the nature of the geminal benzylic substituents on hydrogen bond formation was then examined (Table 5.8). Sterically congested diethylester and diallyl derivatives **5.30** and **5.31** displayed deshielded H(5) when compared with analogous compounds **5.39** and **5.40**, respectively (entries 1 and 2 versus entries 10 and 11). Similar observations were made for cyclopentene, cyclopentane, and cyclohexane derivatives

5.32, **5.33**, and **5.34** (entries 3-5), and dimethoxy cyclohexane substrate **5.45** (entry 16). In all these models, the chemical shift differences (Δ ppm) in $CDCl_3$ were not as sizable as that observed for the dimethyl counterpart **5.13**, indicating that the greater steric hindrance afforded by the *gem*-diester, *gem*-diallyl groups and geminal cyclic substituents had a direct impact on the ability of the ortho substituent to interact with H(5) in solution. Nonetheless, the Δ ppm's in $CDCl_3$ were indicative of persistent intramolecular C–H•••O bonding in solution for **5.30**-**5.34**, and **5.45**, but to a lesser extent than in *gem*-dimethyl systems **5.4** and **5.13**. This hypothesis was corroborated by studying the effect of an ethyl group located at the ortho position of the aromatic on the chemical shift of H(5), in the cyclohexyl series, with Meldrum's acid **5.35** (entry 6). The Δ ppm of 0.20 in $CDCl_3$ for **5.35** was almost three-fold lower than the one observed for **5.22** (0.55), despite detecting a nOe between the methylene of the ethyl groups and H(5), and was inferior to the Δ ppm's for all Meldrum's acids **5.30**-**5.34**, and **5.45**. Therefore, van der Waals contacts arguments did not account for the observed chemical shift variations for **5.30**-**5.34** and **5.45** in $CDCl_3$; it was concluded that intramolecular hydrogen bonding was key in the deshielding of H(5). The smaller Δ ppm's for this series of compounds seems to indicate that adverse steric effects were introduced, which counterbalanced the formation of persistent C–H•••O bond in solution. As a result, for compounds **5.30**-**5.34**, and **5.45**, an equilibrium of intramolecular hydrogen bonded versus non-bonded benzyl Meldrum's acid species was formed to variable degree, similar to **5.2** and **5.3**, thus furnishing less deshielded H(5) chemical shifts. In contrast, compounds **5.4** and **5.13** which have larger Δ ppm's in $CDCl_3$ suggest that either a greater percentage of the molecules were present in the hydrogen bonded form or relatively stronger intramolecular hydrogen bonds.[20,21]

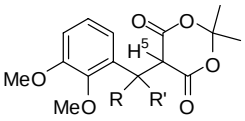
Table 5.8: Effect of benzylic substituents on the ^{1}H NMR chemical shifts of benzyl Meldrum's acids



5.30, R = R' = CO_2Et; X = OMe
5.31, R = R' = $CH_2CH{=}CH_2$; X = OMe
5.32, R–R' = $CH_2CH{=}CHCH_2$; X = OMe
5.33, R–R' = $(CH_2)_4$; X = OMe
5.34, R–R' = $(CH_2)_5$; X = OMe
5.35, R–R' = $(CH_2)_5$; X = Et
5.36, R–R' = $(CH_2)_5$; X = F
5.37, R–R' = $(CH_2)_5$; X = SMe
5.38, R–R' = $CH{=}(CH_2)_3$; X = OMe



5.39, R = R' = CO_2Et
5.40, R = R' = $CH_2CH{=}CH_2$
5.41, R–R' = $CH_2CH{=}CHCH_2$
5.42, R–R' = $(CH_2)_4$
5.43, R–R' = $(CH_2)_5$
5.44, R–R' = $CH{=}CH(CH_2)_3$



5.45, R–R' = $(CH_2)_5$

entry	Meldrum's acid	H(5) chemical shift (ppm)[a,b]	Δ ppm[c]
1	**5.30**	5.31	0.46 (**5.30-5.39**)
2	**5.31**	4.76 (4.93)	1.07 (0.69) (**5.31-5.40**)
3	**5.32**	4.16	0.49 (**5.32-5.41**)
4	**5.33**	4.19 (4.28)	0.79 (0.15) (**5.33-5.42**)
5	**5.34**	3.89 (4.04)	0.45 (0.25) (**5.34-5.43**)
6	**5.35**	3.64 (3.85)	0.20 (0.06) (**5.35-5.43**)
7	**5.36**	3.61 (3.79)	0.17 (0.00) (**5.36-5.43**)
8	**5.37**	5.63 (5.31)	2.19 (1.52) (**5.37-5.43**)
9	**5.38**	5.09 (5.06)	1.39 (0.46) (**5.38-5.44**)
10	**5.39**	4.85	—
11	**5.40**	3.69 (4.24)	—
12	**5.41**	3.67	—
13	**5.42**	3.40 (4.13)	—
14	**5.43**	3.44 (3.79)	—
15	**5.44**	3.70 (4.60)	—
16	**5.45**	4.08	0.64 (**5.45-5.43**)

[a] Chemical shifts in $CDCl_3$. [b] ^{1}H NMR chemical shifts in DMSO-d_6 are in parentheses. [c] The compared compounds are in parentheses.

The effect of other potential H-bond acceptors was investigated. A negligible Δ ppm of 0.17, comparable to ethyl derivative **5.35** (Δ ppm = 0.20), was observed for fluoro Meldrum's acid derivative **5.36** and suggested the absence of persistent C–H•••F bond in solution.[22] On the other hand, by increasing the polarizability of the acceptor, the additional steric hindrance imposed by cyclic benzylic substituents was successfully overcome and C–H•••X bond formation favored. As depicted in Table 5.8, thiomethoxy cyclohexyl substrate **5.37** led to the largest chemical shift difference in this series of Meldrum's acids, with a Δ ppm of 2.19 (Entry 8), supporting an intramolecular C–H•••S interaction in solution.

In addition, subtle variation in the structure of the *geminal* disubstituent had a profound impact on the Δ ppm as shown with cyclohexane and cyclohexene derivatives **5.34** and **5.38** (entries 5 and 9). When one of the sp^3-hybridized methylene substituent on the benzylic carbon centre was replaced with a less sterically demanding sp^2-hybridized methine group (Table 5.8, entry 9), the chemical shift of H(5) substantially increased; Meldrum's acid **5.38** revealed a H(5) chemical shift of 5.09, in comparison to 3.89 for **5.34**. The large Δ ppm of 1.39 clearly showed that the deshielding of H(5) was due to C–H•••O hydrogen bonding, and not an artifact caused by the electronics of the alkene functional group.

(4) Relative Intramolecular C–H•••X (X = O, S, F) Bond Strength in $CDCl_3$ versus DMSO-d_6.

At this stage, persistent intramolecular C–H•••X (X = O, S, F) bonds in solution had been demonstrated for a variety of benzyl Meldrum's acids. In $CDCl_3$, the chemical shifts of H(5) and related Δ ppm's likely correlate with the relative strengths of the intramolecular hydrogen bonds.

It was envisaged that further information on the relative strength of the intramolecular C–H•••X (X = O, S, F) hydrogen bonding would be revealed through solvent effects, which were initially probed using Meldrum's acid **5.13** (Table 5.9). In all solvents examined, including strong hydrogen bond acceptors, H(5) of Meldrum's acid **5.13** exhibited a similar downfield chemical shift, with a small difference of 0.36 ppm between the highest and lowest values. On the contrary, the chemical shift of H(5) for Meldrum's acid **5.7**, which does not possess the ability to form an intramolecular hydrogen bond, spanned 1.31 ppm. In DMSO-d_6, the smallest difference (0.48 ppm) of the chemical shift values of H(5) between **5.7** and **5.13** was obtained. These results suggest that **5.13** formed a persistent intramolecular hydrogen bond in solution that was not disrupted by the nature of the medium, except in DMSO-d_6, in which an equilibrium between intramolecular and intermolecular hydrogen-bonded species was likely observed, resulting in a decrease of the chemical shift.

Table 5.9: Solvent Data for Meldrum's acids **5.7** and **5.13**

entry	solvent	H(5) chemical shift for **5.13** (ppm)	H(5) chemical shift for **5.7** (ppm)	Δ ppm (**5.13** –**5.7**)
1	C_6D_6	5.20	3.25	1.95
2	$CDCl_3$	5.21	3.58	1.63
3	CD_3NO_2	5.40	4.06	1.34
4	CD_3CN	5.28	4.05	1.23
5	Acetone-d_6	5.37	4.31	1.06
6	DMSO-d_6	5.04	4.56	0.48
	Δ ppm (high – low)	0.36	1.31	—

The relative strength of the C–H•••O bond for Meldrum's acids **5.2**-**5.4** was also evaluated. The ^{1}H chemical shifts of H(5) for **5.2** (4.63 ppm), **5.3** (4.45 ppm) and **5.4** (5.18 ppm) in DMSO-d_6 were measured and spanned 0.73 ppm, whereas the ^{1}H chemical shifts of H(5) for **5.2** (4.13 ppm), **5.3** (4.29 ppm) and **5.4** (5.38 ppm) in $CDCl_3$ spanned 1.25 ppm (Table 1, entries 1-3). In DMSO-d_6, comparing **5.2**-**5.4** with analogues **5.5**-**5.7** and **5.20**-**5.22** revealed negligible and negative Δ ppm's for **5.2** (Δ ppm **5.2** vs. **5.5** = -0.14 and Δ ppm **5.2** vs. **5.20** = -0.03) and **5.3** (Δ ppm **5.3** vs. **5.6** = -0.27 and Δ ppm **5.3** vs. **5.21** = -0.02), but significant and positive Δ ppm's for **5.4** (Δ ppm **5.4** vs. **5.7** = 0.62 and Δ ppm **5.4** vs. **5.22** = 0.73). That data suggests that in DMSO-d_6, an equilibrium of intramolecular and intermolecular hydrogen-bonded species was established for **5.4**, thus lowering the chemical shift of H(5). For compounds **5.2**-**5.3**, this equilibrium was entirely displaced toward the intermolecular hydrogen bonded species, providing consistent increases in H(5) chemical shifts (Table 5.1, entries 1-2), equivalent to the chemical shift values observed for **5.20** and **5.21** (Table 5.6, entries 1 and 2). The H(5) chemical shift increases for **5.2**-**5.3** in DMSO-d_6 versus $CDCl_3$ indicated that the intramolecular C–H•••O interactions were weaker than the intermolecular C–H•••OS$(CH_3)_2$, and accordingly, weaker than the intramolecular hydrogen bond found in Meldrum's acid **5.4**. A parallel was made with mono-methoxy Meldrum's acid **5.13** and **5.38**, for which the intramolecular C–H•••O interactions were of comparable strength as the one observed for **5.4**, with Δ ppm's in $CDCl_3$ of 1.63 and 1.39 and DMSO-d_6 of 0.48 and 0.46 respectively (Table 5.1, entry 12, and Table 5.9, entry 9). Of note, Meldrum's acid **5.22** did not show a deshielded H(5) in DMSO-d_6, with relatively similar chemical shifts for **5.20**-**5.22** (Table 5.5). This observation may suggest an alternative conformation for **5.22** in DMSO-d_6

compared to that in $CDCl_3$, a consequence of intermolecular C–H•••O hydrogen bonding of **5.22** with DMSO-d_6.

Similar solvent effects were observed with other hydrogen bond acceptors. The acquisition of the ^{1}H NMR spectra of **5.27** and **5.37** in strong hydrogen bond acceptor solvent DMSO-d_6 further substantiated intramolecular C–H•••S bonding in these compounds (Table 5.6, entry 8 and Table 5.8, entry 8); the H(5) chemical shifts were insensitive to solvent polarity and remained practically unchanged at a distinctly downfield position compared to **5.7** and **5.43**.

In comparison to $CDCl_3$, the chemical shift of H(5) for Meldrum's acid **5.24** was unaffected in DMSO-d_6 at 4.57 ppm, the same shift as **5.7** (Table 5.6, entries 1 and 5), suggesting that intramolecular C–H•••F bond in **5.24** is of equal strength to the intermolecular bond C–H•••OS$(CH_3)_2$. The chemical shift of H(5) for Meldrum's acid **5.36** was equal in DMSO-d_6 to the chemical shift of H(5) for acid **5.43,** with a Δ ppm of zero, which further supported the absence of C–H•••F in **5.36** (Table 5.8, entries 7 and 14). These data suggested that **5.36**, like **5.43**, exclusively formed intermolecular C–H•••O S$(CH_3)_2$ bond in DMSO-d_6.

Solvent effect studies were also carried out with **5.34** and **5.43**. As shown in Table 5.10, the chemical shift of H(5) for Meldrum's acid **5.43**, which does not possess the ability to form an intramolecular hydrogen bond, spanned 0.60 ppm, and a smaller range of 0.31 ppm was observed for **5.34**. It is noteworthy that the chemical shift of H(5) for **5.43** was affected to a lesser extent by the nature of the solvent then Meldrum's acid **5.7**. Consequently, a smaller range of 0.60 ppm for **5.43** versus 1.31 ppm for **5.7** was observed. In DMSO-d_6, the smallest difference (0.25 ppm) in the chemical shift values of H(5) between **5.34** and **5.43** was measured. The Δ ppm's discussed above are indicative of a persistent intramolecular hydrogen bond in solution for Meldrum's acid **5.34**, which overall parallel the observations reported in Table 5.9 using *gem*-dimethyl substrates **5.7** and **5.13**. The trend was similar than the one observed with **5.7** and **5.13** (Table 5.9), the smallest Δ ppm's were in DMSO-d_6 and the largest in C_6D_6 (Table 5.10, entries 6 and 1). Again, these results suggested that DMSO-d_6 displaced the equilibrium of intramolecular hydrogen bonded versus intermolecular hydrogen bonded benzyl Meldrum's acid species towards the latter. The fact that the chemical shift of H(5) increases in DMSO-d_6

compared to $CDCl_3$, despite the disruption of the C–H···O bond, suggests a substantial conformational change, which places H(5) in an entirely different chemical environment.[1c] As discussed previously, a Δ ppm of 0.45 in $CDCl_3$ for **5.34** was indicative of a weak C–H•••O bond and the results obtained in DMSO-d_6 corroborated this deduction.

That trend was also noted for compounds **5.31** and **5.33** for which the chemical shifts of H(5) in DMSO-d_6 were slightly larger than in $CDCl_3$ (Table 5.8, entries 2 and 4). Moreover, while the H(5) chemical shifts of **5.31** in $CDCl_3$ were slightly lower than **5.13**, compound **5.31** provided Δ ppm's in DMSO-d_6 superior to the one observed for the *gem*-dimethyl analogue **5.13** (0.69 versus 0.48 ppm) (Table 5.8, entry 1). Therefore, the correlation observed for the *gem*-dimethyl compounds regarding the relative intramolecular C–H•••O bond strength in $CDCl_3$ versus DMSO-d_6, illustrated by the chemical shifts of H(5) and Δ ppm's in both solvents, does not seem to hold for benzyl Meldrum's acids displaying greater steric hindrance at the benzylic position. Therefore, in DMSO-d_6, the chemical shift of H(5) does not correlate exclusively with the strength of the intramolecular C–H•••O bond, but also to conformational changes.

Table 5.10: Solvent Data for Meldrum's acids **5.34** and **5.43**

entry	solvent	H(5) chemical shift for **5.34** (ppm)	H(5) chemical shift for **5.43** (ppm)	Δ ppm (**5.34** – **5.43**)
1	C_6D_6	3.85	3.19	0.66
2	CD_3NO_2	4.16	3.58	0.58
3	CD_3CN	4.08	3.57	0.51
4	Acetone-d_6	4.12	3.67	0.45
5	$CDCl_3$	3.89	3.44	0.45
6	DMSO-d_6	4.04	3.79	0.25
	Δ ppm (high – low)	0.31	0.60	—

In the above sections, we delineated through a series of experiments that 5-benzyl Meldrum's acid derivatives bearing an acceptor group at the ortho position of the arene moiety form persistent intramolecular C–H•••X (X = O, S, Br, Cl, and F) bonds in solution as characterized by ^{1}H NMR spectroscopy. It was also established that the presence of a *gem*-dimethyl group at the benzylic position is an essential structural requirement in promoting hydrogen bonding, while larger cyclic substituent weakened the intramolecular interaction in $CDCl_3$. Next, intramolecular C–H•••X (X = O, S, F)

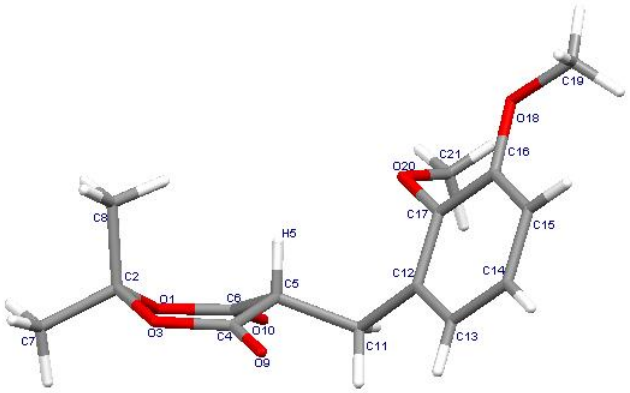
bonds in solid state will be characterized and correlated with the results obtained in solution.

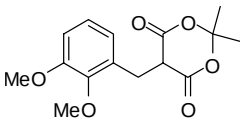
(II) Characterization of Intramolecular C–H•••X (X = O, S, F) Bonds in Solid State by X-Ray Crystallography.

Further information on intramolecular hydrogen bonding C–H•••X (X = O, S, F) bond in Meldrum's acid derivatives was revealed through X-ray analysis of **5.2**, **5.3**, **5.4**, **5.10**, **5.22**, **5.24**, **5.27**, **5.35**, **5.36**, **5.38**, **5.43**, **5.45**, and **5.46**. Two criteria are typically used to judge the presence of C–H•••X hydrogen bond in the solid state, namely bond length and directionality.[1] First, a H•••X (X = O, S, F) distance equal to or shorter than the sum of the van der Waals radii of H and X is required. Second, the directionality is characterized by the C–H•••X (X = O, S, F) bond angle (θ), a linear bond angle being ideal, and 110° being the minimum requirement.

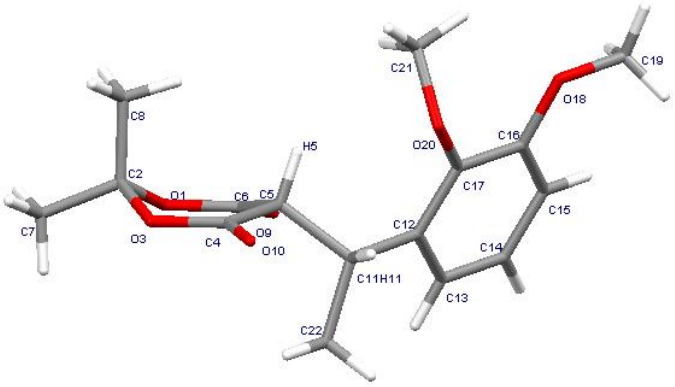
The X-ray structures of Meldrum's acids **5.2**, **5.3** and **5.4** were examined to detect the presence of an intramolecular C–H•••O bond between H(5) of Meldrum's acid with the oxygen of the *ortho* methyl ether of the aromatic moiety (Figure 5.2). In Meldrum's acid **5.4**, an obvious H(5)•••O(20) contraction was observed (by about 0.4 Å) when compared with analogous compounds **5.2** and **5.3** (Table 5.11). The H•••O distance was considerably shorter (2.13 to 2.16 Å) than 2.72 Å, the sum of the van der Waals radii for oxygen (1.52 Å) and hydrogen atoms (1.20 Å), which substantiates an intramolecular C–H•••O bond. Since the interatomic distance H(5)•••O(20) in the solid-state structures of **5.4** arises through attractive forces, this correlates with the NMR data in solution—the downfield shift of the acidic proton. Chemical shift variations were much less pronounced for compounds **5.2** and **5.3**, (Table 5.1), and accordingly, the interatomic distance H(5)•••O(20) in the solid state was significantly longer. A correlation between the C–H•••O distance and the tendency of the triad C(5)–H(5)•••O(20) to assume a linear configuration [angle (θ)] was also observed. The bond angle (θ) C(5)–H(5)•••O(20) (130.6°) found in **5.4** was larger than the one found in **5.2** and **5.3** (Table 5.11). Despite these structural differences in the solid state, compounds **5.2** and **5.3** met the criteria for C–H•••O bond, which parallels the results obtained in solution.[1,23]

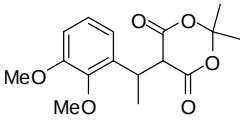
Figure 5.2: X-ray structures of Meldrum's acids **5.2**, **5.3**, and **5.4**.



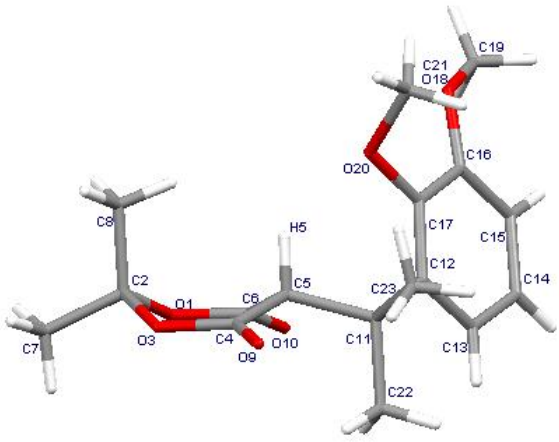


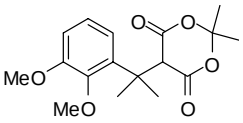
5.2





5.3





5.4

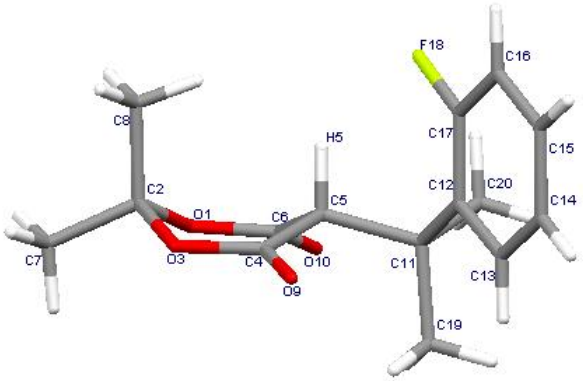
Table 5.11: Solid Phase Structures

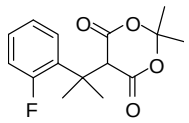
Meldrum acid	temperature (K)	bond length (Å) C(5)–H(5)•••X	Δ (sum of the van der Waals radii – observed X-ray distance) (Å)	bond angle (θ) C(5)–H(5)•••X
5.2	180	2.55 (X = O)	0.17	115.9°
5.3	180	2.57 (X = O)	0.15	119.7°
5.4	297[a]	2.15 (X = O)	0.57	130.6°
5.4	180[a]	2.16 (X = O)	0.56	128.2°
		(2.13)[b] (X = O)	(0.59)	(128.0°)[b]
5.10	180	—	—	—
5.22	180	2.42 (X = C)	0.48	—
5.24	180	2.13 (X = F)	0.54	132.1°
5.27	180	2.43 (X = S)	0.57	138.2°
5.35	150[c]	—	—	—
5.36	150	—	—	—
5.38	150	2.11 (X = O)	0.61	125.5°
5.43	150[d]	—	—	—
5.45	180	2.12 (X = O)	0.60	134.7°
5.46	180	—	—	—

[a] crystal phase change was observed at 291 K so data is reported for both phases. [b] The unit cell contains two molecules, thus two sets of data. [c] The unit cell contains four molecules, thus four sets of data. [d] The unit cell contains eight molecules, thus eight sets of data.

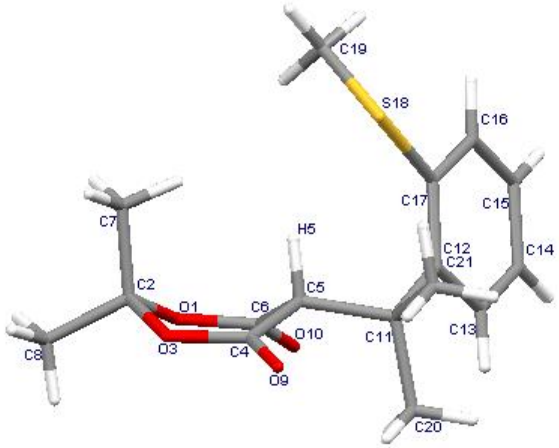
In solution, ^{1}H NMR studies supported the presence of a persistent C–H•••F bond in Meldrum's acid **5.24** (Figure 5.3). In the solid-state, bond length and directionality criteria were met (Table 5.11), with a H•••F distance of 2.13 Å, which is much shorter than the sum (2.67 Å) of the van der Waals radii for H (1.20 Å) and F (1.47 Å) atoms.[24] Similarly, Meldrum's acid **5.27** containing a thiomethoxy acceptor revealed a C–H•••S bond, with a H•••S distance of 2.43 Å, which is substantially shorter than the sum (3.60 Å) of the van der Waals radii for H (1.20 Å) and S (1.80 Å) atoms (Figure 5.3). The conformation observed in the solid state is in relation with the results obtained in solution, for which Meldrum's acid **5.27** displayed a large chemical shift variation for H(5), likely a result of the superior polarizability of the sulfur atom. Of note, regardless of the acceptor atom in C–H•••X (X = O, S, F), the difference between the sum of the van der Waals radii and the observed H•••X distance in the solid state was constant for Meldrum's acids **5.4**, **5.24**, and **5.27**, between 0.54 and 0.57 Å.

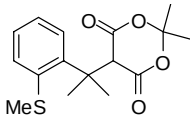
Figure 5.3: X-ray structures of Meldrum's acids **5.24**, and **5.27**.





5.24



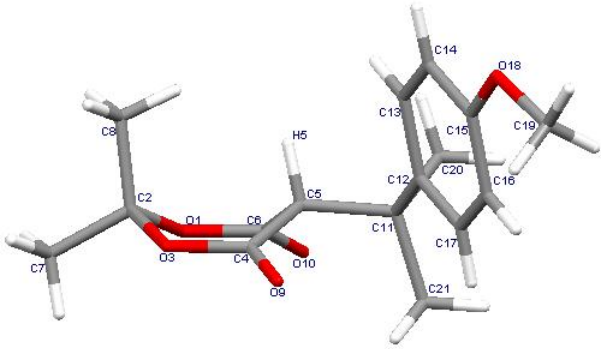


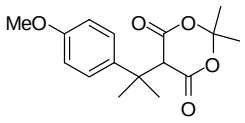
5.27

The assessment of the X-ray structure of compounds **5.2**-**5.4**, **5.24**, and **5.27** ascertained a number of conformational similarities. First, in all the structures the Meldrum's acid moiety was in a boat conformation in which the acidic H(5) hydrogen occupied the pseudo axial position and the benzylic group the pseudo equatorial one. Second, the substituents on the benzylic carbon and C(5) Meldrum's acid's carbon were staggered. This feature places one of the substituent on the benzylic carbon almost perfectly antiperiplanar to the C(5)–H(5) bond of the Meldrum's acid moiety, and the aryl group gauche to H(5) and one of the carbonyl groups. Third, the conformation adopted by the aromatic group minimizes $A^{1,3}$-allylic strain; the hydrogen at the unsubstituted ortho position (6-position) of the aromatic eclipses the benzylic substituent which is antiperiplanar to the C(5)–H(5) bond.

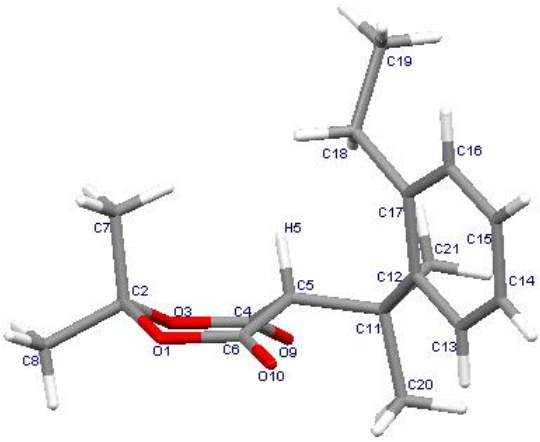
The strong tendency of benzyl Meldrum's acid to adopt that conformation was confirmed by analyzing the X-ray structure of 4-methoxy derivative **5.10** (Figure 5.4). The features observed for compounds **5.2**, **5.3**, **5.4**, **5.24** and **5.27** were found in **5.10**, even in the absence of intramolecular hydrogen bond.[25] The presence of the benzylic *gem*-dimethyl group then seems to reinforce the positioning of the ortho substituent of the aromatic ring in close proximity to H(5).

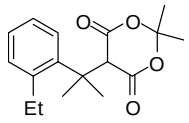
Figure 5.4: X-ray structures of Meldrum's acids **5.10**, and **5.22**.





5.10





5.22

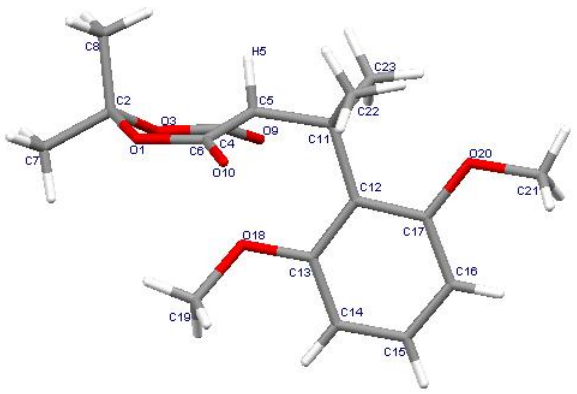
This was further established by examining the X-ray structure of **5.22** (Figure 5.4). The conformation of **5.22** in the solid state was comparable to structures **5.2**, **5.3**, **5.4**, **5.10**, **5.24**, and **5.27**. In solution, nOe studies suggested that the ethyl group was in the vicinity of H(5). In addition, the deshielding of H(5) observed by ^{1}H NMR in solution indicated that van der Waals contacts played a role (Table 5.5, entry 3). Indeed, in the solid state, the C(5)–H(5)•••C(18) distance of 2.42 Å was shorter than 2.90 Å, the sum of the van der

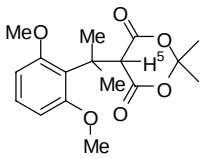
Waals radii for the carbon atom (CH_2 group) in the ethyl group (1.70 Å) and hydrogen atoms (1.20 Å).[26] These data enabled us to draw a parallel between the conformations of **5.22** in solution and in the solid state, and seemed to be matching. The difference of 0.48 Å between the sum of the van der Waals radii and the observed H(5)•••C(18) distance in **5.22** was less important than the ones determined for C–H•••X (X = O, S, F), a consequence of the attractive nature of hydrogen bonding interaction.

The results obtained with **5.2-5.4**, **5.10**, **5.22**, **5.24**, and **5.27** suggested that 5-[1-aryl-1-methylethyl] Meldrum's acids have a well-defined three-dimensional structure in solution and in the solid state. In solution, this preferred conformation is constrained and has a very limited degree of freedom as demonstrated by the absence of temperature effect on Meldrum's acids **5.2-5.4** (Table 5.4). Even when repulsive van der Waals contacts with H(5) are present, as in **5.22**, the conformation is preserved. $A^{1,3}$-Allylic strain is a major contributor to the conformation adopted by 5-[1-aryl-1-methylethyl] Meldrum's acids, and when an acceptor (X) group is introduced at the ortho position of the aromatic ring, the formation of persistent intramolecular C–H•••X bond in solution is promoted.[27] The importance of $A^{1,3}$-allylic strain was confirmed with Meldrum's acid **5.46** (Figure 5.5). Presence of two ortho methoxy substituents substantially increased $A^{1,3}$-allylic strain at the expense of hydrogen bonding. As a result, compound **5.46** adopted a different conformation, in which all eclipsing interactions were minimized (Figure 5.5). Such conformation clearly explains the chemical shift observed for H(5) in $CDCl_3$ at 3.76 ppm, resulting in a low Δ ppm of 0.18 when compared with **5.7**.

These data established that the conformational properties of benzyl Meldrum's acid in solution correlate to the conformation in the solid-state. The parallel between solution and solid-state three-dimensional structure was further studied with cyclohexyl derivatives **5.35**, **5.36**, **5.38**, **5.43**, and **5.45**.

Figure 5.5: Meldrum's acids **5.46** and its x-ray structure





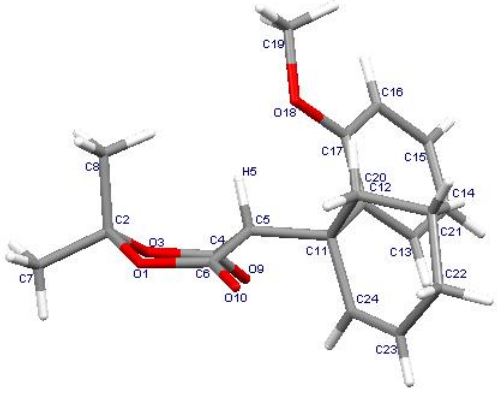
H(5) chemical shift = 3.76 ppm in $CDCl_3$

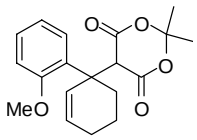
X-ray structure of Meldrum's acid **5.45** (Figure 5.6) displayed a short C–H•••O of 2.12 Å, and a large (θ) angle C(5)–H(5)–O(20) (Table 5.11). These observations are consistent with our analysis of the presence of intramolecular hydrogen bonding in solution. Similarly, the X-ray structure of Meldrum's acid **5.38** (Figure 5.6) revealed a short C–H•••O distance of 2.11 Å (Table 5.11). In solution, no nOe signal could be perceived between the hydrogen's of the alkene and H(5), suggesting an antiperiplanar orientation of these group as observed in the solid state. For **5.38** and **5.45**, the difference between the sum of the van der Waals radii and the observed H•••O distance in the solid state was constant, at 0.61 and 0.60 Å respectively, and paralleled the differences observed for the dimethyl substrates (Table 5.11).

The conformation of Meldrum's acid **5.36** in the solid state, for which no experimental evidence clearly supported persistent C–H•••F bond in solution, was similar to the one observed for compound **5.46** and revealed the absence of C–H•••F bond (Figure 5.7 vs. Figure 5.5). Exceptionally, the Meldrum's acid moiety was in a chair conformation, placing H(5) at the pseudo equatorial position, and the large alkyl group at the pseudo axial position, respectively. The Meldrum's acid moiety was positioned at the equatorial position of the cyclohexane.[28] The conformation of Meldrum's acids **5.35** and **5.43** in the solid state was closely related to **5.36** (Figure 5.7). It was rationalized that the conformation of **5.35** in solution was likely similar to the one in the solid state, as the chemical shift of H(5) was slightly affected by the presence of the ethyl group (Table 5.8, entry 6). On the other hand, a substantial chemical shift variation for H(5) in $CDCl_3$ was

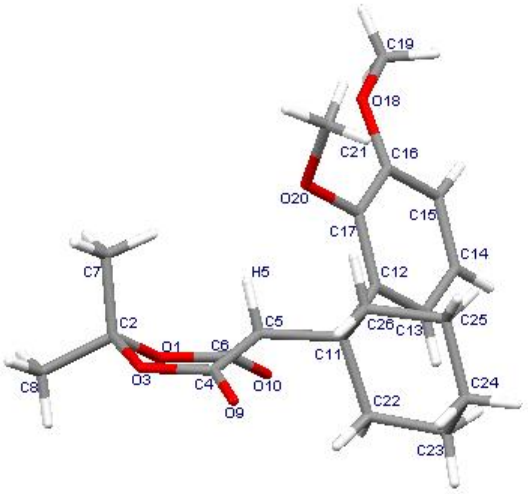
observed for Meldrum's acid **5.22**, strongly supporting that the ethyl group was in the close proximity of H(5) in solution (Table 5.5, entry 3). Indeed, a different conformation was observed for dimethyl analogue **5.22** in the solid state.

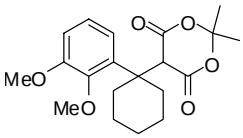
Figure 5.6: X-ray structures of Meldrum's acids **5.38**, and **5.45**.





5.38

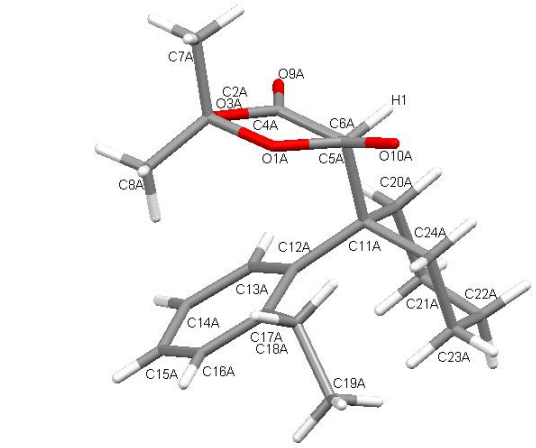


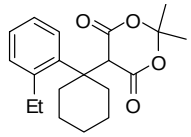


5.45

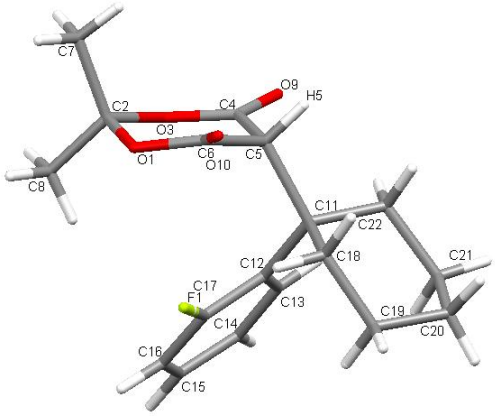
In this chapter, sound evidence of the ability of the acidic C–H bond to drive the conformational properties of benzyl Meldrum's acids in the solid state through the formation of intramolecular C–H•••X (X = O, S, F) bonds were presented. The data obtained by X-ray crystallography were consistent with the ^{1}H NMR studies in solution. However, due to possible packing effects, no direct correlations were found between C–H•••X (X = O, S, F) bond distances in the solid state and the chemical shifts and/or the Δ ppm's in solution.

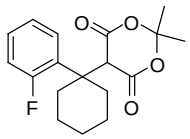
Figure 5.7: X-ray structures of Meldrum's acids **5.35**, **5.36**, and **5.43**.



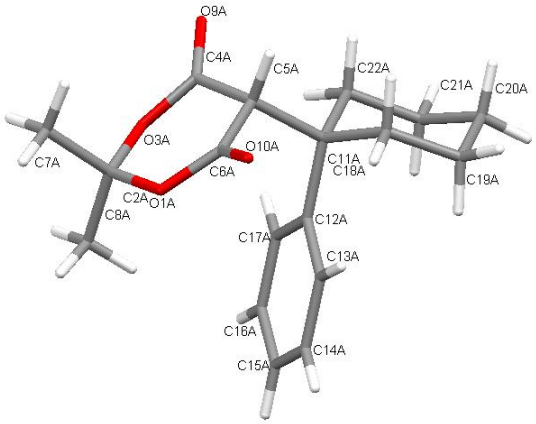


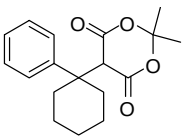
5.35





5.36



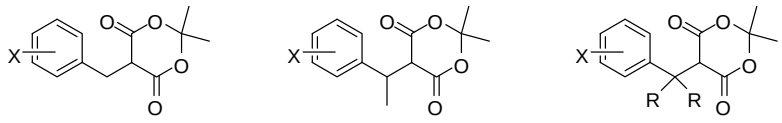


5.43

(III) Synthesis of Benzyl Meldrum's Acids Involved in the Study of Intramolecular C–H•••X Hydrogen Bonding

In order to understand the intramolecular C–H•••X hydrogen bond involving Meldrum's acid, a large number of derivatives were synthesized to complete this study. However, the synthesis of these models was not the focus this study and yields presented can be further optimized. A brief overview of the synthetic routes to the three types of models that were required in this study, differing at the benzylic position, is presented in this section (Figure 5.8).

Figure 5.8: Summary of Benzyl Meldrum's Acids Required for Complete Study

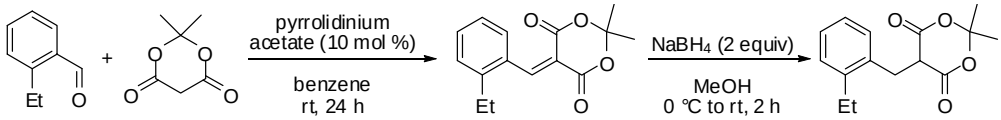


5.47 **5.48** **5.49**

(1) Synthesis of Benzyl Meldrum's Acids 5.47

Benzyl Meldrum's acids **5.47** were prepared via the condensation of benzaldehydes and Meldrum's acid involving a procedure developed in our group.[29] The isolated benzylidenes were subjected to reduction conditions involving $NaBH_4$. An illustrative example for the synthesis of **5.20** is shown below (Scheme 5.1)

Scheme 5.1: Access to benzyl Meldrum's acids **5.20** via Knoevenagel condensation of benzaldehyde **5.50** and Meldrum's acid, and reduction of the benzylidene **5.51**

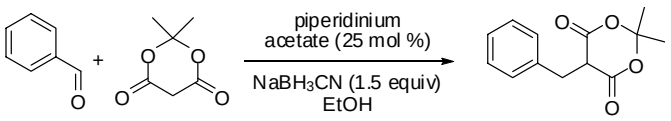


5.50 **5.1** **5.51** **5.20**

36% yield 27% yield

Alternatively, a one-pot reductive alkylation to access benzyl Meldrum's acids **5.47** is possible using $NaBH_3CN$.[8f] An illustrative example of this procedure for the synthesis of **5.5** is illustrated (Scheme 5.2).

Scheme 5.2: Access to benzyl Meldrum's acids **5.5** via one-pot reductive alkylation

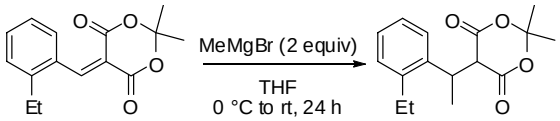


5.52 **5.1** **5.5**
47% yield

(2) Synthesis of Benzyl Meldrum's Acids 5.48

Benzyl Meldrum's acids **5.48** were prepared via the condensation of benzaldehydes and Meldrum's acid and reaction of the resulting benzylidenes with MeMgBr. An illustrative example for the synthesis of **5.21** is shown below (Scheme 5.3)

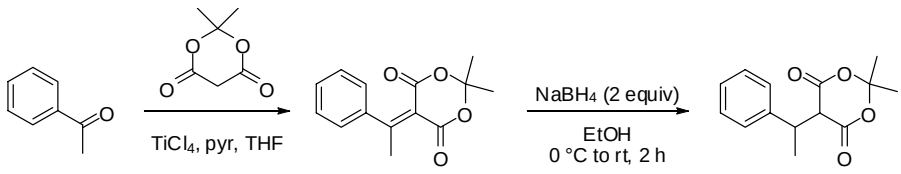
Scheme 5.3: Access to benzyl Meldrum's acid **5.21** via the reaction of benzylidene **5.51** with MeMgBr



5.51 **5.21**
27% yield

Alternatively, a Knoevenagel condensation with acetophenones and Meldrum's acid,[30] followed by reduction of the generated alkylidene Meldrum's acid with $NaBH_4$ gives access to benzyl Meldrum's acids **5.48**. An illustrative example of this procedure for the synthesis of **5.8** is shown (Scheme 5.4).

Scheme 5.4: Access to benzyl Meldrum's acid **5.8** via Knoevenagel condensation of ketone **5.53** and Meldrum's acid, and reaction of alkylidene **5.54** with $NaBH_4$

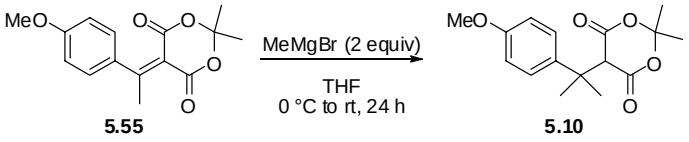


5.53 **5.54** **5.8**
49% yield 99% yield

(3) Synthesis of Benzyl Meldrum's Acids 5.49

Benzyl Meldrum's acids **5.49** were typically prepared via the 1,4-addition of MeMgBr to alkylidene Meldrum's acids. An illustrative example for the synthesis of **5.10** is shown below (Scheme 5.5)

Scheme 5.5: Access to benzyl Meldrum's acid **5.28** via the 1,4-addition of MeMgBr to alkylidene **5.59**

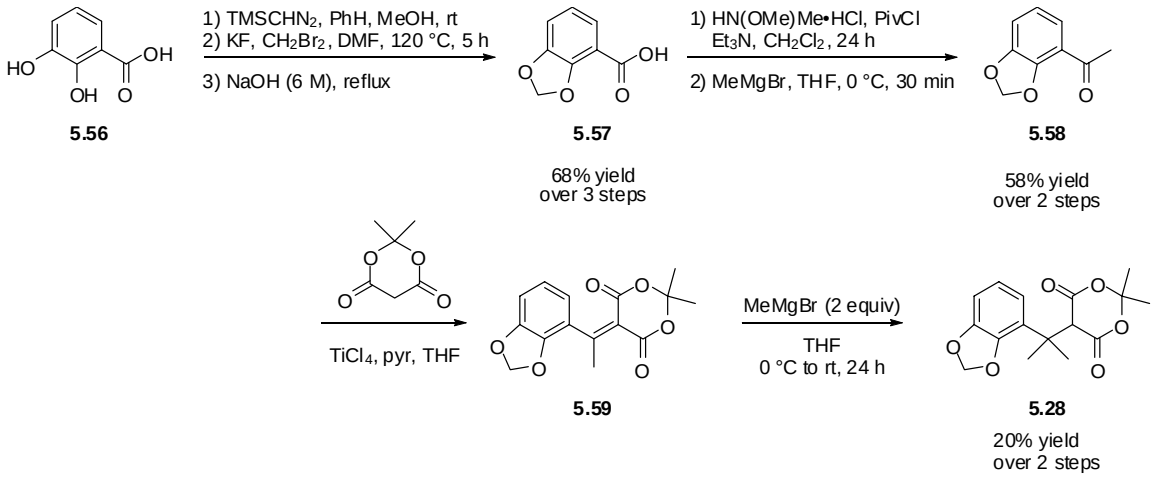


5.55 **5.10**

62% yield

Although most acetophenones were commercially available for the Knoevenagel condensation, others were prepared. Benzyl Meldrum's acid **5.28** was synthesized in a number of steps beginning with commercially available 2,3-dihydroxybenzoic acid **5.56** (Scheme 6).

Scheme 5.6: Access to benzyl Meldrum's acid **5.10** via the 1,4-addition of MeMgBr to alkylidene **5.55**



5.56 **5.57** **5.58**

68% yield over 3 steps

58% yield over 2 steps

5.59 **5.28**

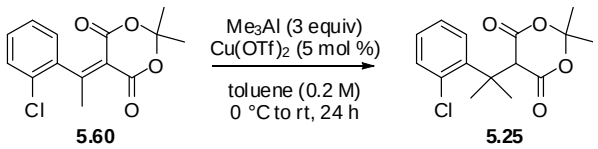
20% yield over 2 steps

The synthesis began with esterification of carboxylic acid **5.56** with $TMSCHN_2$ at room temperature. Alkylation of the *ortho*-substituted hydroxyl groups with dibromomethane followed by hydrolysis of the ester gives carboxylic acid **5.57** after

precipitation from aqueous media without further purification. Conversion of the carboxylic acid to the Weinreb amide and subsequently to methyl ketone **5.58** by Grignard addition affords product in 58% yield in two steps without purification. Knoevenagel condensation of ketone **5.58** with Meldrum's acid followed by 1,4-addition of MeMgBr gives **5.28** in 20% yield over 2 steps after recrystallization.

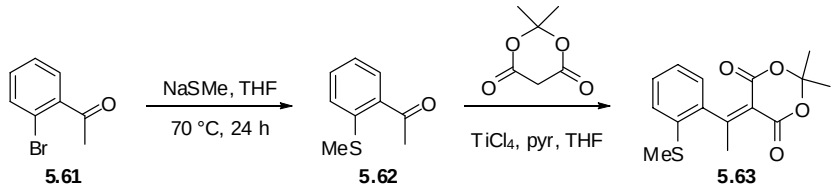
The addition of MeMgBr to alkylidene Meldrum's acids leads to a number of benzyl Meldrum's acids **5.49**. However, the addition of MeMgBr to some alkylidene Meldrum's acids did not provide the desired Meldrum's acid derivatives. One alternative to the low reactivity of MeMgBr towards alkylidene Meldrum's acids was to use more Lewis acidic aluminum reagents as illustrated for benzyl Meldrum's acids **5.49** which are *ortho*-substituted with halogens (Scheme 5.7).

Scheme 5.7: 1,4-Addition using Me_3Al as a substitute to MeMgBr for the addition to alkylidene Meldrum's acid **5.60**



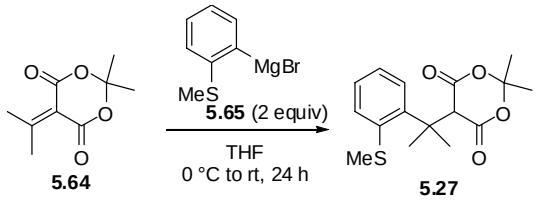
With the successful preparation of *ortho*-substituted benzyl Meldrum's acid **5.49** by either 1,4-addition of MeMgBr or Me_3Al to alkylidene Meldrum's acids, 2,2-dimethyl-5-1-methyl-1-[2-(methylsulfanyl)phenyl]ethyl- 1,3-dioxane-4,6-dione (**5.27**) was thought to be synthesized in a similar manner. Alkylidene Meldrum's acid **5.63** was synthesized in two steps via the nucleophilic aromatic substitution of sodium thiomethoxide and 2′-bromo acetophenone **5.61**, and condensation of the generated ketone **5.62** with Meldrum's acid (Scheme 5.8).

Scheme 5.8: Preparation of alkylidene Meldrum's acid **5.63**



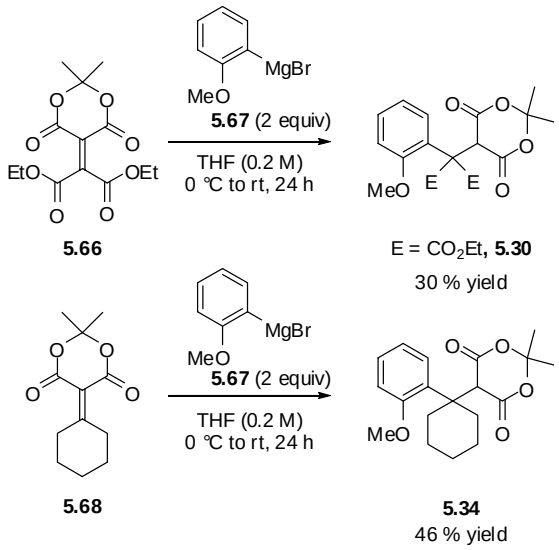
Unfortunately, attempts to add MeMgBr or Me_3Al in a 1,4-addition fashion were unsuccessful. As a result an alternative route to benzyl Meldrum's acid **5.27** was considered. Addition of freshly prepared (2-(methylthio)phenyl)magnesium bromide **5.65** to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione **5.64**[31] provided benzyl Meldrum's acid **5.27** in 40% yield (Scheme 5.9). In fact, this method offers the best alternative for the synthesis of benzyl Meldrum's acid **5.49** in general and especially for *ortho*-substituted cases.

Scheme 5.9: 1,4-Addition of (2-(methylthio)phenyl)magnesium bromide to alkylidene **5.27** to afford benzyl Meldrum's acid **5.27**



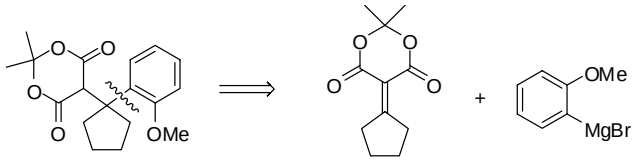
The aryl addition route was also successful for the synthesis of benzyl Meldrum's acids **5.30** and **5.34** which would be difficult to access via 1,4-addition of alkyl nucleophiles (Scheme 10). Of note, numerous routes were investigated for the synthesis of diethyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)malonate **5.66**, and the successful Knoevenagel condensation developed for aldehydes was the optimal route albeit elevated temperature were required.[29]

Scheme 5.10: Synthesis of benzyl Meldrum's acids **5.30** and **5.34**



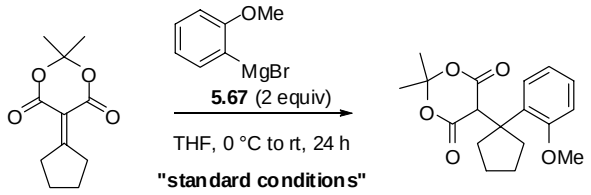
We thought that the most feasible disconnection for the retrosynthesis of benzyl Meldrum's acid **5.33** would be similar to benzyl Meldrum's acid **5.34** by which a Grignard **5.67** can add to an alkylidene Meldrum's acid **5.69** (Scheme 5.11).

Scheme 5.11: Retrosynthetic route 1 for benzyl Meldrum's acid **5.33**



Although alkylidene Meldrum's acid **5.69**[32] was obtained via the condensation of Meldrum's acid and cyclopentanone in 40% yield, all attempts to promote the 1,4-addition of Grignard **5.67** to **5.69** were unsuccessful (Table 5.12).

Table 5.12: 1,4-Addition of Grignard **5.67** to alkylidene Meldrum's acid **5.69**

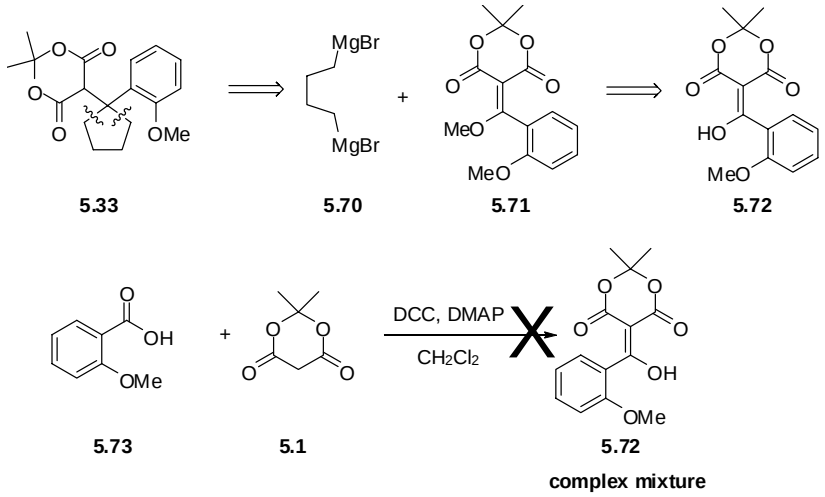


5.69 **5.33**

Entry	Deviations from "standard conditions"	% Yield
1	none	0
2	CuCN (5 mol %)	0
3	Et_2O instead of THF	0
4	TMSOTf (2 equiv), Et_2O instead of THF	0
5	**5.67** (5 equiv), $MnCl_2$ (5 equiv)	0

Alternatively, installing the cyclopentyl ring via sequential intermolecular Grignard **5.70**[33] addition and elimination, followed by intramolecular Grignard **5.70** addition to Meldrum's acid derivative **5.71** would give benzyl Meldrum's acid **5.33** (Scheme 5.12). Meldrum's acid **5.71** was thought to be accessible through an exchange of Meldrum's acid **5.71** and methanol. Unfortunately, attempts to synthesize **5.72** from benzoic acid **5.73** and Meldrum's acid were unsuccessful. Although this is a well documented literature procedure with *para* and *meta*-substituted benzoic acids, to the best of our knowledge, there is not a single example involving an ortho substituted benzoic acids.[34]

Scheme 5.12: Retrosynthetic route 2 for benzyl Meldrum's acid **5.33**

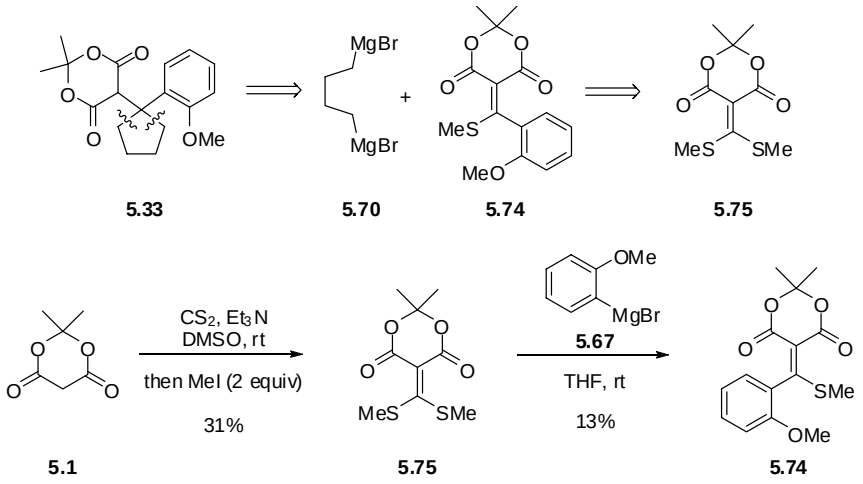


5.33 **5.70** **5.71** **5.72**

5.73 **5.1** **5.72**
complex mixture

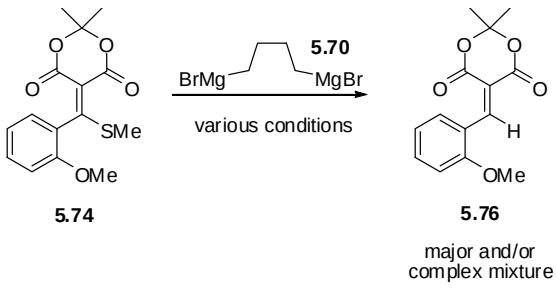
While keeping the same disconnection as previously, Meldrum's acid **5.71** was replaced with Meldrum's acid **5.74** (Scheme 5.13). The known Meldrum's acid **5.75**[35] enabled us to investigate the sequential intermolecular 1,4-Grignard addition/elimination, and intramolecular addition. First, addition of Meldrum's acid **5.1** to carbon disulfide followed by methylation produced desired Meldrum's acid derivative **5.75** in 31% yield. 1,4-Addition of Grignard **5.67** to **5.75** afforded Meldrum's acid **5.74** via a single addition/elimination reaction.[36]

Scheme 5.13: Retrosynthetic route 3 for benzyl Meldrum's acid **5.33**



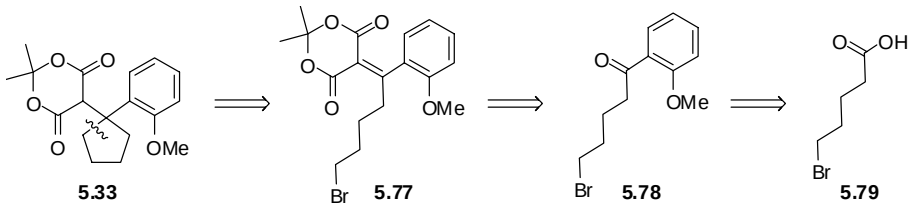
The addition of Grignard **5.70** to **5.74** did not produce any of the desired benzyl Meldrum's acid product **5.33**. In fact in most cases alkylidene Meldrum's acid **5.76** was observed despite varying the equivalence of Grignard **5.70**, temperature, and order of addition (Scheme 5.14).

Scheme 5.14: Grignard addition to Meldrum's acid derivative **5.73**



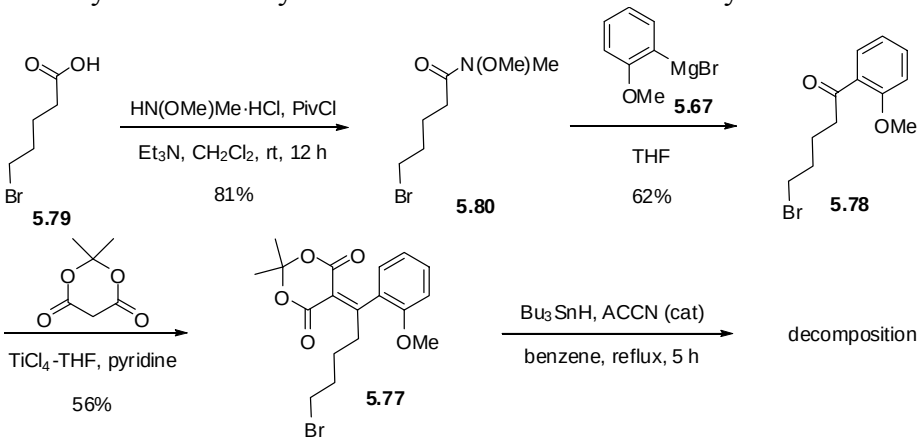
As a result of the hydride delivery, we decided to reexamine the retrosynthetic disconnection for the formation of **5.33**. Intramolecular cyclization of alkylidene Meldrum's acid **5.77**, which can be obtained in a few steps from commercially available 5-bromopentanoic acid **5.79**, would give the desired Meldrum's acid **5.33** (Scheme 5.15).

Scheme 5.15: Retrosynthetic route 4 for benzyl Meldrum's acid **5.33**



The synthesis of alkylidene Meldrum's acid **5.77** first began with the conversion of carboxylic acid **5.79** to Weinreb amide **5.80** (Scheme 5.16). Grignard addition of **5.67** to Weinreb amide **5.80** afforded ketone **5.78** in 62% yield. Knoevenagel condensation of ketone **5.78** with Meldrum's acid afforded alkylidene Meldrum's acid **5.77** in 56% yield. Attempts to promote the intramolecular cyclization using Bu_3SnH in the presence of 1,1'-azobis(cyclohexanecarbonitrile) [ACCN], were unsuccessful.

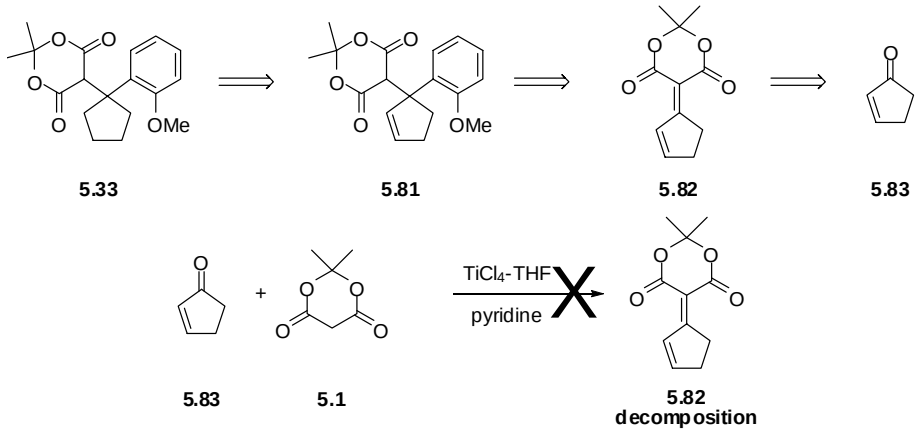
Scheme 5.16: Synthesis of alkylidene Meldrum's acid **5.76** and cyclization to **5.33**



Reconsidering the retrosynthetic disconnection, we envisioned access to benzyl Meldrum's acid **5.33** through the hydrogenation of cyclopentene ring **5.81**, which can be accessed via the Knoevenagel condensation of cyclopent-2-enone **5.83** and Meldrum's acid (Scheme 5.17). Although the condensation of cyclohex-2-enone with Meldrum's

acid is feasible, attempts to condense cyclopent-2-enone **5.83** with Meldrum's acid failed and lead to the decomposition of the starting enone.

Scheme 5.17: Retrosynthetic route 5 for benzyl Meldrum's acid **5.33**

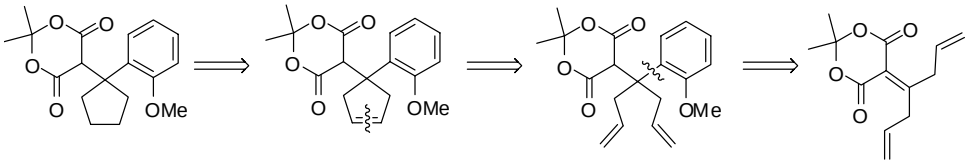


5.33 **5.81** **5.82** **5.83**

5.83 **5.1** **5.82 decomposition**

While optimistic that we can access the desired benzyl Meldrum's acid **5.33** via hydrogenation of a cyclopentene Meldrum's acid derivative, we changed the position of the double for the retrosynthetic analysis (Scheme 5.18). Access to benzyl Meldrum's acid **5.32** was envisioned from the ring closing metathesis of Meldrum's acid derivative **5.31** which can be obtained from alkylidene Meldrum's acid **5.84**.

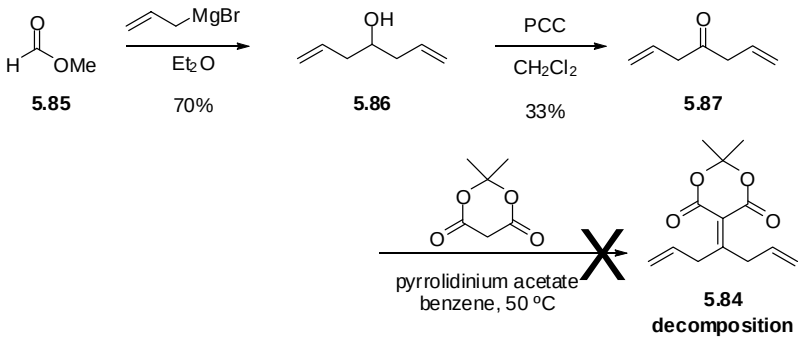
Scheme 5.18: Retrosynthetic route 6 for benzyl Meldrum's acid **5.33**



5.33 **5.32** **5.31** **5.84**

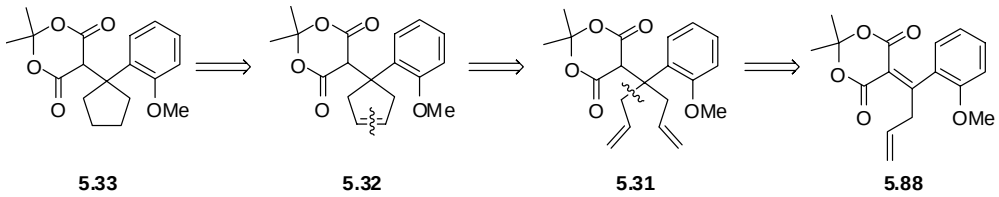
The synthesis of alkylidene Meldrum's acid **5.84** began by the nucleophilic addition of allylmagnesium bromide to methyl formate **5.85** (Scheme 5.19). Oxidation of the secondary alcohol afforded light sensitive ketone **5.87** in 33% yield. Knoevenagel condensation with Meldrum's acid and ketone **5.87** afforded decomposition of the ketone.

Scheme 5.19: Synthesis of alkylidene Meldrum's acid **5.83**



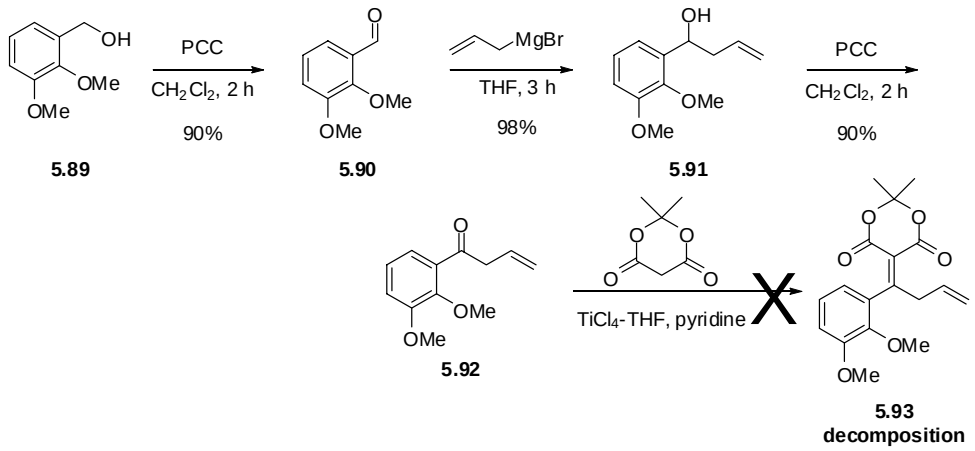
Consequently, the retrosythetic route was slightly altered upon which a different alkylidene **5.88** was envisioned as a precursor to the ring-closing metathesis (Scheme 5.20).

Scheme 5.20: Retrosynthetic route 7 for benzyl Meldrum's acid **5.33**



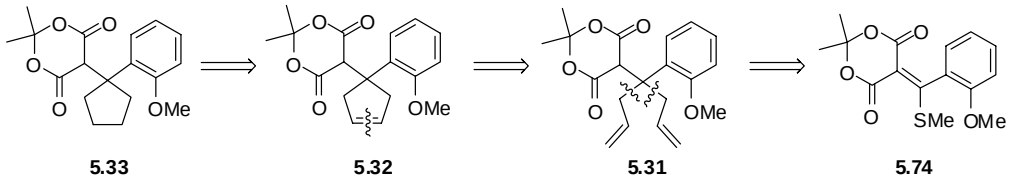
The synthesis began with the oxidation of benzyl alcohol **5.89** with PCC in dry dichloromethane affording aldehyde **5.90** in 90% yield (Scheme 5.21). Grignard addition to the aldehyde followed by oxidation afforded ketone **5.92** in excellent yields. Unfortunately condensation of ketone **5.92** with Meldrum's acid led to decomposition of the starting ketone without any trace of the desired alkylidene Meldrum's acid **5.93**.

Scheme 5.21: Retrosynthetic route 7 for benzyl Meldrum's acid **5.33**



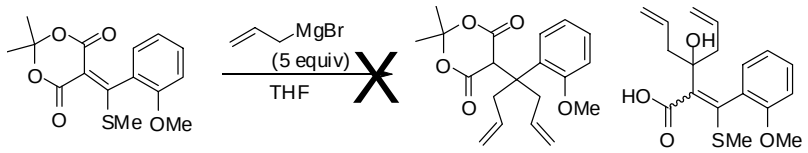
While the unsuccessful synthesis of alkylidene Meldrum's acid **5.93** was disappointing indeed, the prospect to use Meldrum's acid derivative **5.74** as an alternative for the formation of **5.31** was investigated. Thus the retrosynthesis was revised, envisioning **5.74** as a precursor to benzyl Meldrum's acid **5.33** (Scheme 5.22).

Scheme 5.22: Retrosynthetic route 8 for benzyl Meldrum's acid **5.33**



Conjugate addition of allylmagnesium bromide to **5.74** afforded no trace of desired product **5.31** but rather yielded the 1,2-addition product **5.94** (Scheme 5.23). Although allyl metal nucleophiles typically add in a 1,2- rather than 1,4-fashion, it was shown that 1,4-addition is easily promoted for the addition of allyltin nucleophiles to benzylidene Meldrum's acids after this work was completed.[37]

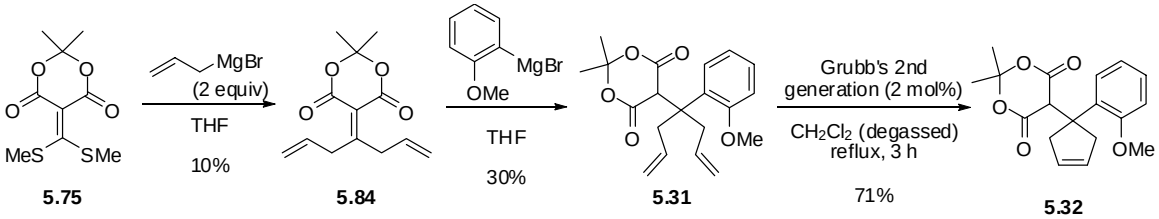
Scheme 5.23: Conjugate addition of allylmagnesium bromide to **5.74**



5.74 **5.31** not observed **5.94** major

To test this hypothesis, allylmagnesium bromide was added to Meldrum's acid derivative **5.75** and to our delight, the 1,4-addition alkylidene Meldrum's acid **5.84** was obtained (Scheme 5.24). Although the alkylidene was unstable, purification by flash chromatography was quickly performed and then resulting alkylidene Meldrum's acid **5.84** was subjected to Grignard addition to obtain benzyl Meldrum's acid **5.31**. Ring closing metathesis afforded cyclopentene **5.32** in 71% yield.

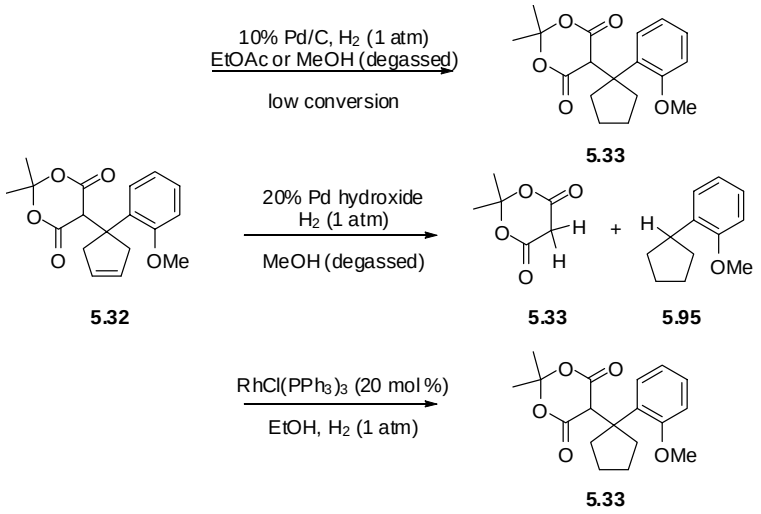
Scheme 5.24: Synthesis of benzyl Meldrum's acid **5.32**



5.75 **5.84** unstable **5.31** **5.32**

Finally, the hydrogenation of alkene **5.84** was carried out to afford desired benzyl Meldrum's acid **5.33**. The use of Pd/C in ethyl acetate or methanol under 1 atm of hydrogen afforded **5.33** in low conversion (Scheme 5.25). Alternatively, palladium hydroxide under similar conditions led to the hydrogenolysis of Meldrum's acid, an unprecedented transformation. Fortunately, the use Wilkinson's catalyst afforded the desired product quantitatively as observed by the ^{1}H NMR spectrum of the crude reaction mixture.

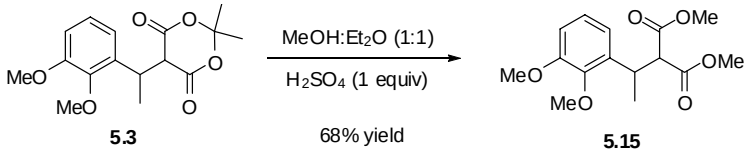
Scheme 5.25: Synthesis of benzyl Meldrum's acid **5.33**



(4) Synthesis of Benzyl Malonates

Synthesis of benzyl malonates was achieved from Meldrum's acid derivatives in one step in the presence of methanol and sulfuric acid. This was a quick access to benzyl malonates since Meldrum's acid derivatives were prepared earlier for this study. An illustrative example is shown below (Scheme 5.26).

Scheme 5.26: Synthesis of benzyl malonates



The synthesis of some of these models used for the study of the intramolecular hydrogen bonding was indeed not the focus of this study, yet the challenges that arose in synthesis gave rise to exploration of various chemistries.

(C) Summary

In summary, the occurrence and persistence of C–H•••X (O, S, Br, Cl, and F) bond in solution using ^{1}H NMR spectroscopy was established for a large number of benzyl Meldrum's acids. The latter are novel and reliable probes for the evaluation of this type of non-classical interactions in solution. The persistence of the C–H•••X bond in solution

was demonstrated to be dependent upon structural features present on the aromatic moiety and the benzylic position of the benzyl Meldrum's acid derivatives. The observations presented in this chapter highlight the large potential of Meldrum's acid in developing an understanding of the function and nature of C–H•••X interactions.

(D) Experimental Section

(I) General Methods

All reactions were carried out in flame-dried glassware under a dry nitrogen atmosphere. ^{1}H NMR spectra were referenced to residual ^{1}H shift in $CDCl_3$ (7.24 ppm). $CDCl_3$ (77.0 ppm) was used as the internal reference for ^{13}C NMR spectra. Melting points are uncorrected. High resolution mass spectra were run with a source temperature of 200 °C, mass resolution of 9000, and electron energy of 70 eV. Flash chromatography was performed using 230-400 mesh silica gel unless stated otherwise. The late Dr. Nicholas J. Taylor (Meldrum's acids **5.2**, **5.3**, **5.4**, **5.10**, and **5.46**), University of Waterloo, Dr. Jalil Assoud (Meldrum's acids **5.22**, **5.24**, **5.27**, and **5.45**), University of Waterloo, and Dr. Alan Lough (Meldrum's acid **5.35**, **5.36**, **5.38**, and **5.43**), University of Toronto, are gratefully acknowledged for X-ray structure determination.

(II) General Procedure A: Preparation of Mono-Benzylic Meldrum's Acids via a One-Pot Reductive Alkylation

Meldrum's acid (1 equiv) and the appropriate benzaldehyde (0.98 equiv) were dissolved in absolute EtOH (0.5-1.0 M), followed by the addition of a catalytic amount of piperidinium acetate (0.1 equiv). The resulting solution was stirred vigorously for 30 minutes, and then cooled to 0 °C. $NaBH_3CN$ (1.5 equiv) was added portionwise over 1 h, and the reaction allowed to warm to room temperature. The reaction was monitored by TLC and upon completion was carefully quenched with 10% HCl (*extreme caution should be exercised due to the evolution of HCN gas*). Vigorous stirring was maintained until gas evolution had ceased, after which time the reaction was concentrated *in vacuo* to remove EtOH. The residue was re-suspended in 10% HCl and extracted four times with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated.

The resulting product was generally found to be of good purity by ^{1}H NMR, but was recrystallized from MeOH or purified by flash chromatography on silica gel.

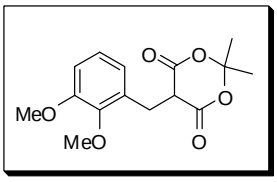
(III) General Procedure B: Conjugate Addition of Grignard Reagents to Meldrum's Alkylidenes

Meldrum's alkylidene (1 equiv) was suspended in dry THF (0.1 M) and cooled to 0 °C with stirring under inert atmosphere. A solution of the appropriate Grignard reagent (2-3 equiv) in THF (or Et_2O) (0.5 to 3 M) was added dropwise, and then the reaction was allowed to warm to room temperature and monitored by TLC. Upon completion, the reaction was quenched with 5% HCl and extracted three times with EtOAc. The combined organic layers were washed with H_2O, brine, then dried over $MgSO_4$ and filtered. Concentration of the organic layers provided the crude product which was then purified by either recrystallization or by flash chromatography on silica gel.

(IV) General Procedure C: Preparation of Malonates via Acid Catalyzed Ring Opening of Meldrum's Acid Derivatives

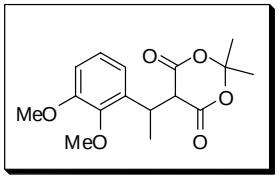
In a typical reaction, Meldrum's acid derivative (1 equiv) was dissolved in a 1:1 mixture of Et_2O:MeOH (0.2 M) and concentrated sulfuric acid (1-2 equiv). The reaction mixture was heated to 50 °C for 24 h. After cooling to room temperature, the reaction mixture was diluted with Et_2O, washed with $NaHCO_3$ (aq), brine, then dried over $MgSO_4$ and filtered. Concentration of the organic layer provided the crude product that was purified by flash chromatography on silica gel.

(IV) Compound Specific Information

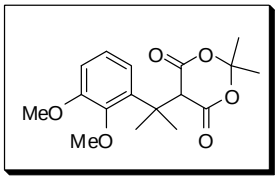


5-(2,3-Dimethoxybenzyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (5.2): Prepared by the reductive alkylation of Meldrum's acid with 2,3-dimethoxybenzaldehyde according to Procedure A. Recrystallization from MeOH provided white crystals in 44% yield. M.p. 120-121 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.00-6.95 (m, 2H), 6.80

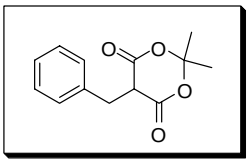
(dd, *J* = 7.5, 2.1 Hz, 1H), 4.11 (t, *J* = 5.6 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.34 (d, *J* = 5.6 Hz, 2H), 1.75 (s, 3H), 1.71 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.2, 152.4, 146.9, 131.8, 123.9,123.4, 111.2, 104.9, 60.4, 55.6, 47.1, 29.6, 27.4, 26.2; Anal. Calc'd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.26; H, 6.17; HRMS(EI) *m/z* calc'd for $C_{15}H_{18}O_6$ (M^+): 294.1103. Found: 294.1109.



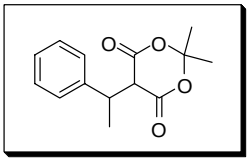
5-[1-(2,3-Dimethoxyphenyl)ethyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (5.3): Conjugate addition of Me_2AlCl to 2,3-dimethoxyphenyl Meldrum's alkylidene (prepared by condensing 2,3-dimethoxybenzaldehyde with Meldrum's acid)[38] afforded a white powder in 51% yield after flash chromatography (3:1 hexanes:EtOAc) and recrystallization from MeOH. M.p. 123-123.5 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.08−7.03 (m, 2H), 6.86-6.82 (m, 1H), 4.29 (d, *J* = 2.9 Hz, 1H), 4.12 (dq, *J* = 7.1, 2.9 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 1.69 (s, 3H), 1.67 (s, 3H),1.43 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.5, 163.5, 152.1, 146.3, 135.6, 123.7, 120.9, 110.9, 104.6, 60.6, 55.6, 50.8, 31.6, 28.3, 26.7, 13.9; HRMS(EI) *m/z* calc'd for $C_{16}H_{20}O_6$ (M^+): 308.1260. Found: 308.1251.



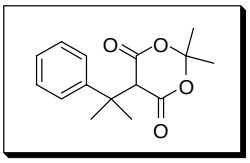
5-[1-(2,3-Dimethoxyphenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (5.4): Conjugate addition of 2,3-dimethoxyphenylmagnesium bromide to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione[31] according to Procedure B provided a 25% yield of white solid after flash chromatography (6:1 hexanes:EtOAc). M.p. 118-119 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.02-6.94 (m, 2H), 6.81 (dd, *J* = 7.2, 2.3 Hz, 1H), 5.38 (s, 1H), 3.89 (s, 3H), 3.80 (s, 3H), 1.77 (s, 3H), 1.65 (s, 3H), 1.63 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.6, 152.3, 146.4, 140.2, 123.1, 118.7, 110.7, 103.6, 60.4, 55.3, 53.5, 39.5, 28.4, 25.9, 25.5; HRMS(EI) *m/z* calc'd for $C_{17}H_{22}O_6$ (M^+): 322.1416. Found: 322.1419.



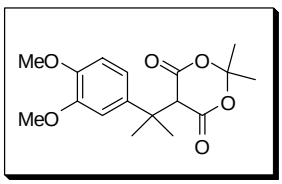
5-Benzyl-2,2-dimethyl-1,3-dioxane-4,6-dione (5.5):[39] Prepared by the reductive alkylation of Meldrum's acid with benzaldehyde according to Procedure A. Flash chromatography (4:1 hexanes:EtOAc) of the crude reaction mixture provided a white solid in 47% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31-7.20 (m, 5H), 3.74 (t, *J* = 4.8 Hz, 1H), 3.46 (d, *J* = 4.5 Hz, 2H), 1.70 (s, 3H), 1.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.3, 137.2, 129.7, 128.6, 127.2, 105.2, 48.1, 32.1, 28.4, 27.2.



2,2-Dimethyl-5-(1-phenylethyl)-1,3-dioxane-4,6-dione (5.6):[39] Conjugate addition of methylmagnesium bromide to 5-benzylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and benzaldehyde)[29] according to Procedure B provided a 99% yield of a white solid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43-7.19 (m, 5H), 3.97 (dq, *J* = 7.3, 3.1 Hz, 1H), 3.67 (d, *J* = 3.1 Hz, 1H), 1.64 (d, *J* = 3.0 Hz, 3H), 1.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.0, 164.7, 141.1, 128.5, 128.3, 127.4, 105.2, 52.5, 39.6, 28.1, 28.0, 17.7.

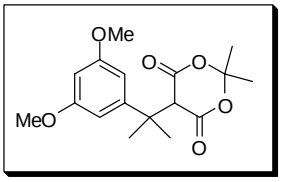


2,2-Dimethyl-5-(1-methyl-1-phenylethyl)-1,3-dioxane-4,6-dione (5.7):[40] Conjugate addition of phenylmagnesium bromide to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione according to Procedure B. Recrystallization from MeOH provided white crystals in 21% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33-7.31 (m, 4H), 7.24-7.22 (m, 1H), 3.58 (s, 1H), 1.66 (s, 6H), 1.61 (s, 3H), 1.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 1645.2, 144.67, 128.4, 127.0, 156.2 ,105.1, 57.6, 42.6, 29.2, 27.7, 27.3.

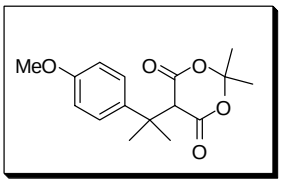


5-[1-(3,4-Dimethoxyphenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (5.8): Conjugate addition of 3,4-dimethoxyphenylmagnesium bromide to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione[31] according to Procedure B provided a white solid in 49% yield after recrystallization from EtOH. M.p. 137-138 °C (EtOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.86-6.75 (m, 3H), 3.83 (s, 3H), 3.81

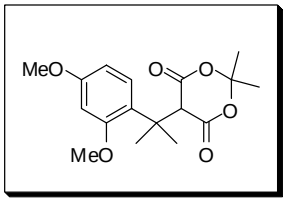
(s, 3H), 3.46 (s, 1H), 1.63 (s, 6H), 1.56 (s, 3H), 1.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.4, 148.5, 148.0, 136.5, 118.7, 110.7, 110.1, 105.2, 57.7, 55.9, 55.8, 42.7, 29.5, 28.2, 27.2; Anal. Calc'd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.69; H, 6.93.



5-[1-(3,5-Dimethoxyphenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (5.9): Prepared by conjugate addition of 3,5-dimethoxyphenylmagnesium chloride to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione[31] using Procedure B to provide a 76% yield of white solid after recrystallization from MeOH. M.p. 121-122°C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.46-6.45 (m, 2H), 6.33-6.31 (m, 1H), 3.75 (s, 6H), 3.59 (s,1H), 1.63 (s, 3H), 1.61 (s, 6H), 1.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.0, 160.6, 147.4, 105.0, 104.8, 98.1, 57.1, 55.2, 42.5, 28.9, 27.6, 27.5; Anal. Calc'd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.22; H, 7.06.

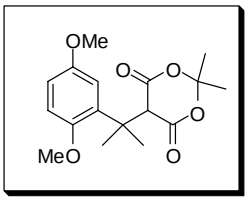


5-[1-(4-Methoxyphenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.10): Conjugate addition of methylmagnesium bromide to 5-(1-(4-methoxyphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and 4'-methoxyacetophenone)[30] according to Procedure B provided a 62% yield of a white solid after recrystallization from MeOH. M.p. 76-77 ºC °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.23 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 1H), 3.76 (s, 3H), 3.50 (s, 1H), 1.63 (s, 6H), 1.54 (s, 3H), 1.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.3, 158.3, 136.3, 127.4, 113.5, 105.1, 57.6, 55.1, 42.2, 29.3, 28.0, 27.2; HRMS(EI) *m/z* calc'd for $C_{16}H_{20}O_5$ (M^+): 292.1311. Found: 292.1308.

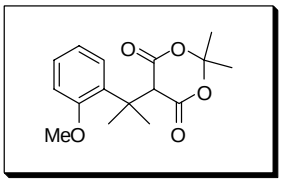


5-[1-(2,4-Dimethoxyphenyl)-1-methylethyl]-2,2-dimethyl- 1,3-dioxane-4,6-dione (5.11): Conjugate addition of methylmagnesium bromide to 5-(1-(2,4-dimethoxyphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and 2',4'-dimethoxyacetophenone)[30] according to Procedure B provided a 42% yield of a light yellow solid after flash

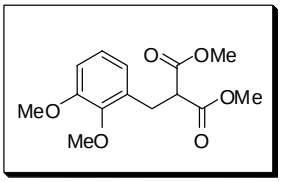
chromatography (5:1 hexanes:EtOAc). M.p. 134-135 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 6.91 (d, *J* = 2.9 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.69 (dd, *J* = 8.8, 2.9 Hz, 1H), 5.29 (s, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 1.76 (s, 3H), 1.67 (s, 3H), 1.61 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 163.8, 153.6, 150.7, 136.5, 114.4, 111.9, 110.6, 103.6, 55.6, 55.4, 52.9, 40.1, 28.5, 26.2, 25.1; HRMS(EI) *m/z* calc'd for $C_{17}H_{22}O_6$ (M^+): 322.1416. Found: 322.1429.



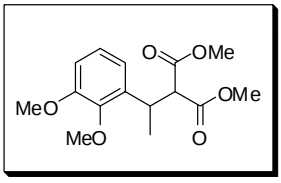
5-[1-(2,5-Dimethoxyphenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.12): Conjugate addition of methylmagnesium bromide to 5-(1-(2,5-dimethoxyphenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and 2',5'-dimethoxyacetophenone)[30] according to Procedure B provided a 50% yield of a light yellow solid after recrystallization from MeOH. M.p. 117-118 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.21 (d, *J* = 8.5 Hz, 1H), 6.49-6.44 (m, 2H), 5.05 (s, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 1.74 (s, 3H), 1.67 (s, 3H), 1.61 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.1, 159.2, 157.4, 127.6, 127.3, 104.1, 103.7, 99.3, 55.1, 55.0, 53.0, 40.0, 28.4, 26.8, 25.5; HRMS(EI) *m/z* calc'd for $C_{17}H_{22}O_6$ (M^+): 322.1416. Found: 322.1423.



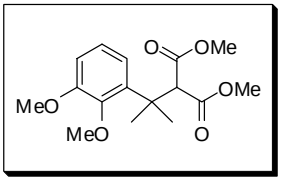
5-[1-(2-Methoxyphenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.13): Prepared by conjugate addition of 2-methoxyphenylmagnesium bromide to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione[31] using Procedure B to provide a 99% yield of white solid after recrystallization from MeOH. M.p. 117-118 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.33 (d, *J* = 3.9 Hz, 1H), 7.19 (d, *J* = 7.0 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 1H), 5.21 (s, 1H), 3.84 (s, 3H), 1.76 (s, 3H), 1.68 (s, 3H), 1.64 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.1, 156.5, 135.0, 127.6, 127.1, 121.1, 111.3, 103.7, 55.1, 53.0, 40.3, 28.5, 26.6, 25.3; HRMS(EI) *m/z* calc'd for $C_{16}H_{20}O_5$ (M^+): 292.1311. Found: 292.1310.



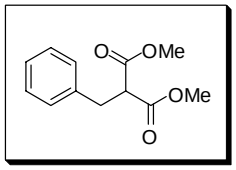
Dimethyl 2-(2,3-dimethoxybenzyl)malonate (5.14): Prepared by ring opening of 5-(2,3-dimethoxybenzyl)-2,2-dimethyl-1,3-dioxane-4,6-dione **(5.2)** using Procedure C to provide a 73% yield of a clear oil after purification using flash chromatography (9:1 hexanes:EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.91 (t, *J* = 7.9 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.78 (t, *J* = 7.8 Hz, 1H), 3.66 (s, 6H), 3.19 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.4, 152.5, 147.3, 131.3, 123.7, 122.3, 111.4, 60.4, 55.6, 52.4, 52.0, 29.8; HRMS(EI) *m/z* calc'd for $C_{14}H_{18}O_6$ (M^+): 282.1103. Found: 282.1100.



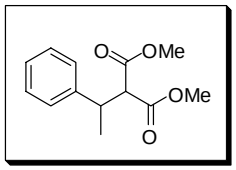
Dimethyl 2-[1-(2,3-dimethoxyphenyl)ethyl]malonate (5.15): Prepared by ring opening of 5-(1-(2,3-dimethoxyphenyl)ethyl)-2,2-dimethyl-1,3-dioxane-4,6-dione **(5.3)** using Procedure C to provide a 68% yield of a light yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.93 (t, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 3.90 (s, 3H), 3.90-3.83 (m, 1H), 3.80 (s, 3H), 3.71 (s, 3H), 3.48 (s, 3H), 1.23 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.9, 168.4, 152.7, 146.7, 136.6, 123.7, 119.2, 110.8, 60.5, 57.1, 55.5, 52.3, 52.1, 34.1, 19.4; HRMS(EI) *m/z* calc'd for $C_{15}H_{20}O_6$ (M^+): 296.1250. Found: 296.1260.



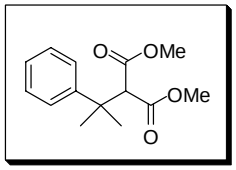
Dimethyl 2-[1-(2,3-dimethoxyphenyl)-1-methylethyl]malonate (5.16): Prepared by ring opening of 5-(2-(2,3-dimethoxyphenyl)propan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione **(5.4)** using Procedure C to provide a 65% yield of a white solid. M.p. 57-59 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.94-6.89 (m, 2H), 6.82-6.79 (m, 1H), 4.60 (s, 1H), 3.90 (s, 3H), 3.82 (s, 3H), 3.54 (s, 6H), 1.56 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.9, 152.8, 139.1, 122.8, 119.7, 111.5, 60.4, 57.9, 55.7, 51.7, 40.1, 25.9; HRMS(EI) *m/z* calc'd for $C_{16}H_{22}O_6$ (M^+): 310.1416. Found: 310.1410.



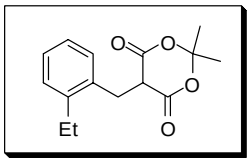
Dimethyl 2-benzylmalonate (5.17):[41] Prepared by ring opening of 5-benzyl-2,2-dimethyl-1,3-dioxane-4,6-dione **(5.5)** using Procedure C to provide a 74% yield of a clear liquid after purification using flash chromatography (5:1 hexanes:EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.29-7.16 (m, 5H), 3.66 (s, 6H), 3.66 (t, *J* = 7.8 Hz, 1H), 3.21 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) 169.1, 137.6, 128.6, 128.4, 126.7, 53.5, 52.4, 34.6.



Dimethyl 2-(1-phenylethyl)malonate (5.18):[42] Prepared by ring opening of 2,2-dimethyl-5-(1-phenylethyl)-1,3-dioxane-4,6-dione **(5.6)** using Procedure C to provide a 74% yield of a clear liquid after purification using flash chromatography (5:1 hexanes:EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.28-7.15 (m, 5H), 3.74 (s, 3H), 3.62 (d, *J* = 10.6 Hz, 1H), 3.56-3.48 (m, 1H), 3.43 (s, 3H), 1.30 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 168.6, 168.1, 142.8, 128.3, 127.1, 126.7, 58.9, 52.3, 52.0, 39.9, 19.8.

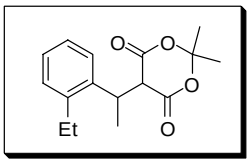


Dimethyl 2-(2-phenylpropan-2-yl)malonate (5.19):[43] Prepared by ring opening of 2,2-dimethyl-5-(2-phenylpropan-2-yl)-1,3-dioxane-4,6-dione **(5.7)** using Procedure C to provide a 29% yield of a clear liquid after purification using flash chromatography (5:1 hexanes:EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.37-7.34 (m, 2H), 7.30-7.26 (m, 2H), 7.20-7.17 (m, 1H), 3.82 (s, 1H), 3.55 (s, 6H), 1.56 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 168.2, 146.6, 128.0, 126.3, 125.8, 61.6, 51.9, 40.0, 26.1.

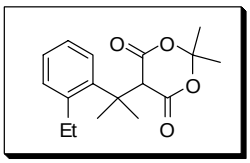


5-(2-Ethylbenzyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (5.20): To a solution of 5-(2-ethylbenzylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (1 equiv, prepared by condensation of Meldrum's acid and 2-ethylbenzaldehyde)[29] in MeOH (0.2 M) was added $NaBH_4$ (2 equiv) at 0 ºC. The reaction was followed by TLC until disappearance of starting material. The reaction was then quenched slowly with 5% HCl and the reaction mixture was concentrated using a rotary evaporator. The reaction mixture was extracted with EtOAc and washed with 5% HCl and brine. Recrystallization of the crude mixture from

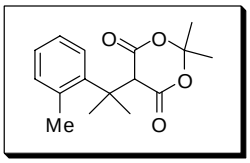
MeOH afforded a white solid in 52% yield. M.p. 128-129 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.30 (d, *J* = 7.0 Hz, 1H), 7.20-7.11 (m, 3H), 3.68 (t, *J* = 5.2 Hz, 1H), 3.49 (d, *J* = 5.2 Hz, 2H), 2.72 (q, *J* = 7.5 Hz, 2H), 1.76 (s, 3H), 1.68 (s, 3H), 1.23 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 165.2, 142.3, 135.7, 129.5, 128.7, 127.2, 126.0, 105.1, 48.0, 28.6, 27.9, 26.6, 25.5, 15.1; HRMS(EI) *m/z* calc'd for $C_{15}H_{18}O_4$ (M^+): 262.1205. Found: 262.1205.



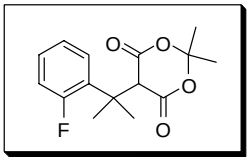
5-(1-(2-Ethylphenyl)ethyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (5.21): Prepared by conjugate addition of methylmagnesium bromide to 5-(2-ethylbenzylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and 2-ethylbenzaldehyde)[29] using Procedure B to provide a 27% yield of a white solid after purification by flash chromatography (5:1 hexanes:EtOAc). M.p. 68-70 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.54-7.49 (m, 1H), 7.21-7.17 (m, 3H), 4.24 (dq, *J* = 7.2, 3.1 Hz, 1H), 7.25 (d, *J* = 3.12, 1H), 2.79 (dq, *J* = 14.6, 7.4 Hz, 1H), 2.58 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.65 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H), 1.46 (s, 3H), 1.22 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 165.3, 164.3, 141.5, 139.3, 128.7, 128.2, 127.3, 126.1, 105.1, 51.7, 34.1, 28.1, 27.8, 25.3, 17.5, 15.6; HRMS(EI) *m/z* calc'd for $C_{16}H_{20}O_4$ (M^+): 276.1362. Found: 276.1370.



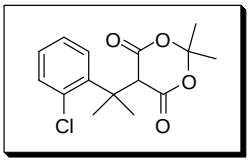
5-[1-(2-Ethylphenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (5.22): Prepared by conjugate addition of 2-ethylphenylmagnesium bromide to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione[31] using Procedure B to provide a 30% yield of white solid after recrystallization from MeOH. M.p. 106-108 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.29-7.21 (m, 3H), 7.16-7.13 (m, 1H), 4.13 (s, 1H), 2.89 (q, *J* = 7.4 Hz, 2H), 1.70 (s, 3H), 1.69 (s, 3H), 1.64 (s, 6H), 1.29 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.3, 142.7, 141.2, 131.3, 127.1, 126.8, 125.7, 104.8, 54.6, 42.9, 29.0, 27.9, 27.8, 27.1, 16.6; HRMS(EI) *m/z* calc'd for $C_{17}H_{22}O_4$ (M^+): 290.1518. Found: 290.1510.



2,2-Dimethyl-5-[1-methyl-1-(2-methylphenyl)ethyl]-1,3-dioxane- 4,6-dione (5.23): Prepared by conjugate addition of 2-methylphenylmagnesium bromide to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione[31] using Procedure B to provide an analytically pure sample of a white solid after purification by flash chromatography (3:1 hexanes:EtOAc). M.p. 70-72 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.31-7.28 (m, 1H), 7.17-7.14 (m, 3H), 4.18 (s, 1H), 2.57 (s, 3H), 1.69 (s, 3H), 1.66 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.3, 143.5, 134.7, 133.1, 126.9, 126.1, 104.8, 54.0, 43.1, 28.9, 27.9, 27.3, 23.4; HRMS(EI) *m/z* calc'd for $C_{16}H_{20}O_4$ (M^+): 276.1362. Found: 261.1354.

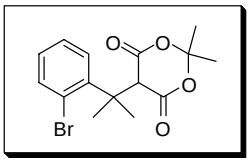


5-[1-(2-Fluorophenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.24): Conjugate addition of methylmagnesium bromide to 5-(1-(2-fluorophenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and 2′-fluoroacetophenone)[30] according to Procedure B provided a 7% yield of white solid after flash chromatography (5:1 hexanes:EtOAc). M.p. 77-78 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.37 (t, *J* = 8.1 Hz, 1H), 7.21-7.12 (m, 2H), 6.98 (dd, *J* = 13.5, 8.0 Hz, 1H), 4.56 (d, *J* = 7.5 Hz, 1H), 1.77 (s, 3H), 1.68 (s, 3H), 1.65 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 163.3, 160.6 (d, *J* = 241.4 Hz), 134.0 (d, *J* = 10.0 Hz), 128.2 (d, *J* = 9.4 Hz), 127.7 (d, *J* = 5.3 Hz), 124.3 (d, *J* = 2.9 Hz), 116.0 (d, *J* = 24.5 Hz), 104.2, 53.6 (d, *J* = 7.9 Hz), 39.6 (d, *J* = 3 Hz), 28.4, 26.5, 25.0; HRMS(EI) *m/z* calc'd for $C_{15}H_{17}O_4F$ (M^+): 280.1111. Found: 280.1105.

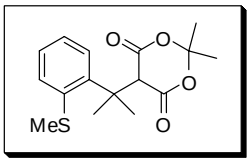


5-[1-(2-Chlorophenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.25): Prepared by the conjugate addition of Me_3Al to 5-(1-(2-chlorophenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and 2'-chloroacetophenone).[30] To a reaction mixture containing $Cu(OTf)_2$ and toluene (0.2 M), was added Me_3Al (2 M solution, 3 equiv) at 0 ºC. After 5 minutes, the alkylidene (1 equiv) was added and the reaction was allowed to warm up to room temperature. After 24 h, the reaction was quenched with NH_4Cl (sat), extracted with ethyl

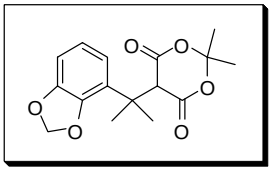
acetate (3X). The combined organic layers were washed with brine, and dried over $MgSO_4$, filtered and concentrated to provide a 9% yield of white solid after recrystallization from MeOH. M.p. 115-116 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.54 (d, *J* = 8.1 Hz, 1H), 7.52-7.25 (m, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), 5.50 (s, 1H), 1.82 (s, 3H), 1.74 (s, 6H), 1.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 163.3, 143.8, 131.6, 131.2, 128.9, 127.9, 127.2, 104.0, 52.1, 40.8, 28.6, 26.3, 24.7; HRMS(EI) *m/z* calc'd for $C_{15}H_{17}{}^{35}ClO_4$ (M^+-Cl): 261.1127. Found: 261.1125.



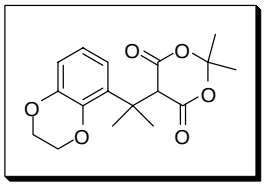
5-[1-(2-Bromophenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.26): Prepared according to outlined procedure for **5.25,** by the conjugate addition of Me_3Al to 5-(1-(2-bromophenyl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and 2'-bromoacetophenone).[30] An analytically pure white solid was obtained after purification by flash chromatography (10:1 hexanes:EtOAc) and recrystallization from MeOH. M.p. 127-129 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.54 (t, *J* = 9.3 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 5.73 (s, 1H), 1.85 (s, 3H), 1.77 (s, 6H), 1.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 163.2, 145.1, 135.3, 129.3, 128.1, 127.7, 120.4, 104.0, 52.0, 41.1, 28.7, 26.3, 24.8; HRMS(EI) *m/z* calc'd for $C_{15}H_{17}O_4$ (M^+-Br): 261.1127. Found: 261.1126.



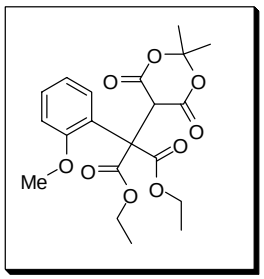
2,2-Dimethyl-5-1-methyl-1-[2-(methylthio)phenyl]ethyl- 1,3-dioxane-4,6-dione (5.27): Prepared by conjugate addition of 2-methylthiophenylmagnesium bromide to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione[31] using Procedure B to provide a 40% yield of white solid after recrystallization from MeOH. M.p. 87-88 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.51-7.47 (m, 1H), 7.37-7.34 (m, 1H), 7.22-7.20 (m, 2H), 6.50 (s, 1H), 2.49 (s, 3H), 1.84 (s, 3H), 1.71 (s, 6H), 1.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 163.6, 146.9, 133.6, 131.4, 127.5, 127.1, 126.6, 103.7, 51.9, 41.1, 28.7, 26.1, 25.6, 19.6; HRMS(EI) *m/z* calc'd for $C_{16}H_{20}O_4S$ (M^+): 308.1082. Found: 308.1086.



5-[1-(1,3-Benzodioxol-4-yl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.28): Conjugate addition of methylmagnesium bromide to 5-(1-(benzo[d][1,3]dioxol-4-yl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and 1-(benzo[d][1,3]dioxol-4-yl)ethanone)[30] according to Procedure B provided a 20% yield of a white solid after recrystallization from MeOH. M.p. 131-132 ºC °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 6.85-6.84 (m, 2H), 6.75-6.72 (m, 1H), 5.89 (s, 2H), 4.69 (s, 1H), 1.79 (s, 3H), 1.68 (s, 3H), 1.62 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 163.4, 147.0, 143.1, 130.4, 122.0, 119.1, 107.3, 104.1, 100.1, 53.5, 39.3, 28.6, 26.4, 24.6; HRMS(EI) *m/z* calc'd for $C_{16}H_{18}O_6$ (M^+): 306.1103. Found: 306.1105.

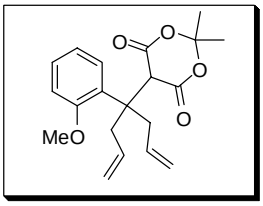


5-[1-(2,3-Dihydro-1,4-benzodioxin-5-yl)-1-methylethyl]-2,2-dimethyl- 1,3-dioxane-4,6-dione (5.29): Conjugate addition of methylmagnesium bromide to 5-(1-(2,3-dihydrobenzo[b][1,4]dioxin-5-yl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and 1-(2,3-dihydrobenzo[b][1,4]dioxin-5-yl)ethanone)[30] according to Procedure B provided a 52% yield of a white solid after recrystallization from MeOH. M.p. 152-153 ºC °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 6.87 (t, J = 7.6 Hz, 1H), 6.82-6.75 (m, 2H), 5.06 (s, 1H), 4.24 (s, 4H), 1.75 (s, 3H), 1.69 (s, 3H), 1.62 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.0, 143.6, 140.9, 135.5, 121.2, 119.2, 116.2, 103.9, 63.9, 63.7, 53.0, 40.6, 28.5, 26.9, 25.4; HRMS(EI) *m/z* calc'd for $C_{17}H_{20}O_6$ (M^+): 320.1260. Found: 320.1262.

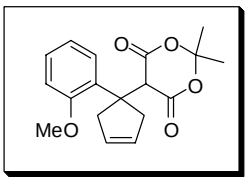


Diethyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-(2-methoxyphenyl) malonate (5.30): Conjugate addition of 2-methoxyphenylmagnesium bromide to diethyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)malonate (prepared by condensation of Meldrum's acid and diethyl 2-oxomalonate at 80 °C)[29] according to Procedure B provided a 52% yield of a beige solid after purification by flash chromatography (3:1 hexanes:EtOAc then 1:1). M.p. 106-

108 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.29 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 5.31 (s, 1H), 4.23 (q, *J* = 7.1 Hz, 1H), 3.72 (s, 3H), 1.86 (s, 3H), 1.73 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 168.1, 162.9, 156.5, 129.5, 129.3, 124.6, 121.1, 111.0, 104.3, 62.4, 61.6, 55.4, 50.9, 28.8, 26.0, 13.7; HRMS(EI) *m/z* calc'd for $C_{20}H_{24}O_9$ (M^+): 408.1420. Found: 408.1415.

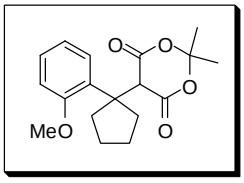


5-(4-(2-Methoxyphenyl)hepta-1,6-dien-4-yl)-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.31): Conjugate addition of 2-methoxyphenylmagnesium bromide to 5-(hepta-1,6-dien-4-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione [prepared by allylMgBr addition to 5-(bis(methylthio)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione][35] according to Procedure B provided a 30% yield of a beige solid after purification by flash chromatography (8:1 hexanes:EtOAc, 6:1 then 4:1) and crystallization from MeOH. M.p. 117-118 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.30 (d, *J* = 7.8 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.2 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 5.72-5.55 (m, 2H), 5.06 (d, *J* = 17.8 Hz, 2H), 5.00 (d, *J* = 10.2 Hz, 2H), 4.76 (s, 1H), 3.78 (s, 1H), 3.04 (d, *J* = 7.2 Hz, 4H), 1.70 (s, 3H), 1.60 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.4, 156.5, 135.0, 131.4, 128.4, 127.8, 120.9, 118.5, 111.0, 103.4, 54.7, 50.6, 47.4, 39.8, 28.3, 27.0; HRMS(EI) *m/z* calc'd for $C_{20}H_{24}O_5$ (M^+): 344.1624. Found: 344.1630.

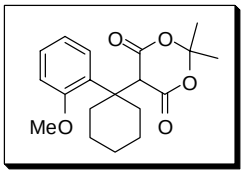


5-[1-(2-Methoxyphenyl)-3-cyclopentenyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.32): To a Schlenk tube charged with **5.31** (1 equiv), and degassed CH_2Cl_2 (0.06 M), was added Grubb's second generation catalyst (0.02 equiv) in a dry box. The reaction mixture was heated to 50 ºC for 2.5 h. Concentration of the reaction mixture and purification by flash chromatography (5:1 hexanes:EtOAc) afforded a clear oil in 71% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) 7.27 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.17-7.14 (m, 1H), 6.93-6.88 (m, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 5.80 (s, 2H), 4.16 (s, 1H), 3.74 (s, 3H), 3.30 (d, *J* = 15.9 Hz, 2H), 2.89 (d, *J* = 15.8 Hz, 2H), 1.70 (s, 3H), 1.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz)

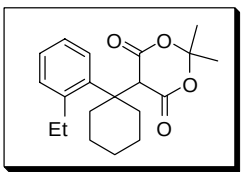
164.8, 155.8, 133.3, 129.3, 128.7, 128.0, 121.2, 111.4, 104.2, 54.7, 54.0, 51.1, 46.5, 28.1, 27.8; HRMS(EI) *m/z* calc'd for $C_{18}H_{20}O_5$ (M^+): 316.1311. Found: 316.1321.



5-[1-(2-Methoxyphenyl)cyclopentyl]-2,2-dimethyl-1,3-dioxane-4,6- dione (5.33): A mixture of **5.32** (1 equiv), $RhCl(PPh_3)_3$ (0.2 equiv) in degassed EtOH was stirred for 24 h under 1 atm of hydrogen gas. The solvent was evaporated and the residue of **5.33** was subjected to flash chromatography (4:1 hexanes:EtOAc) to afford an analytically pure sample as a white solid. M.p. 99-101 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.26-7.17 (m, 2H), 6.93 (m, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 4.19 (s, 1H), 3.76 (s, 3H), 2.60-2.54 (m, 2H), 2.15-2.09 (m, 2H), 1.84-1.79 (m, 2H), 1.71-1.62 (m, 2H), 1.59 (s, 3H), 1.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 165.0, 157.1, 132.0, 129.0, 128.2, 120.6, 111.1, 104.4, 54.6, 53.4, 52.3, 36.7, 28.5, 27.7, 23.3; HRMS(EI) *m/z* calc'd for $C_{18}H_{22}O_5$ (M^+): 318.1467. Found: 318.1464.

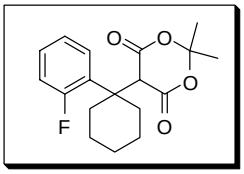


5-[1-(2-Methoxyphenyl)cyclohexyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (5.34): Prepared by conjugate addition of 2-methoxyphenylmagnesium bromide to 5-cyclohexylidene-2,2-dimethyl-1,3-dioxane-4,6-dione[32] using Procedure B to provide a 46% yield of white solid after purification by flash chromatography (8:1 hexanes:EtOAc). M.p. 146-148°C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.28-7.19 (m, 2H), 6.92 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 3.89 (s, 1H), 3.75 (s, 3H), 2.71 (d, *J* = 10.5 Hz, 2H), 1.99 (t, *J* = 10.3 Hz, 2H), 1.61-1.60 (m, 2H), 1.57 (s, 3H), 1.43-1.36 (m, 3H), 1.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.7, 158.4, 131.0, 128.4, 128.2, 120.5, 111.6, 104.6, 55.2, 54.5, 47.7, 34.7, 29.4, 27.3, 26.0, 22.9; HRMS(EI) *m/z* calc'd for $C_{19}H_{24}O_5$ (M^+): 332.1624. Found: 332.1629.

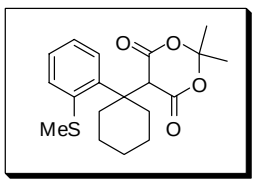


5-(1-(2-Ethylphenyl)cyclohexyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (5.35): Prepared by conjugate addition of 2-ethylphenylmagnesium bromide to 5-cyclohexylidene-2,2-dimethyl-1,3-dioxane-4,6-dione[32] using Procedure B to provide a

32% yield of white solid after purification by flash chromatography (5:1 hexanes:EtOAc). M.p. 88-90 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.24-7.17 (m, 3H), 7.15-7.09 (m, 1H), 3.64 (s, 1H), 2.80 (q, *J* = 7.4 Hz, 2H), 2.70 (d, *J* = 13.8 Hz, 2H), 1.78 (t, *J* = 12.8 Hz, 2H), 1.66-1.63 (m, 2H), 1.55 (s, 4H), 1.43-1.39 (m, 1H), 1.35 (s, 5H), 1.24 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.8, 143.2, 136.9, 131.9, 130.6, 127.4, 125.5, 105.6, 57.3, 49.7, 36.2, 30.5, 27.9, 27.0, 26.0, 23.0, 15.7; HRMS(EI) *m/z* calc'd for $C_{17}H_{20}O_3$ (M^+-acetone): 272.1412. Found: 272.1404.

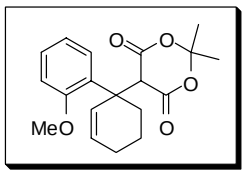


5-(1-(2-Fluorophenyl)cyclohexyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (5.36): A procedure reported by Knochel and coworkers was applied.[44] To a Schlenk tube charged with Mg metal (3 equiv) was added LiCl (0.5 M in THF, 1.75 equiv), and DIBAL-H (0.014 equiv). After 5 minutes, the mixture was cooled to -20 ºC and 2-bromofluorobenzene (1.4 equiv) was added. After 1 hr, 5-cyclohexylidene-2,2-dimethyl-1,3-dioxane-4,6-dione[32] in THF (1 equiv, 0.5 M) was added. The reaction mixture was slowly warmed up to room temperature. After 12 h, the reaction was quenched with 5% HCl, extracted with EtOAc (3X). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. After purification by flash chromatography (5:1 hexanes:EtOAc), the beige solid was obtained in 72% yield. M.p. 110-113 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.29-7.18 (m, 3H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.98 (dd, *J* = 13.5 Hz, 10.8 Hz, 1H), 2.62 (bd, *J* = 13.0 Hz, 2H), 1.93 (bt, *J* = 11.5 Hz, 2H), 1.69-1.63 (m, 3H), 1.54 (s, 3H), 1.32-1.27 (m, 3H), 1.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.1, 161.9 (d, *J* = 5.0 Hz,), 129.2 (d, *J* = 9.3 Hz), 126.8 (d, *J* = 10.0 Hz), 124.0 (d, *J* = 3.2 Hz), 116.8 (d, *J* = 25.4 Hz), 105.1, 56.4, 47.0 (d, *J* = 3.5 Hz), 34.5 (d, *J* = 9.5 Hz), 29.5, 26.9, 25.6, 22.6; HRMS(EI) *m/z* calc'd for $C_{18}H_{21}FO_4$ (M^+): 320.1424. Found: 320.1417.

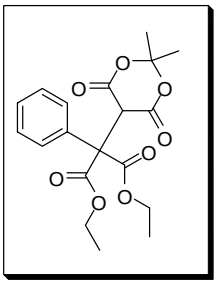


2,2-Dimethyl-5-(1-(2-(methylthio)phenyl)cyclohexyl)-1,3-dioxane-4,6-dione (5.37): Prepared by conjugate addition of 2-methylthiophenylmagnesium bromide to 5-cyclohexylidene-2,2-dimethyl-1,3-dioxane-4,6-dione[32] using Procedure B to provide a 25% yield of a beige solid after purification by flash chromatography (5:1

hexanes:EtOAc). M.p. 96-97 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.47 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.34 (d, *J* = 7.3 Hz, 1H), 7.22-7.13 (m, 2H), 5.63 (s, 1H), 2.73 (d, *J* = 13.5 Hz, 2H), 2.46 (s, 3H), 2.12 (bs, 2H), 1.72 (s, 3H), 1.66 (s, 3H), 1.55 (bs, 3H), 1.30 (bs, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 163.8, 140.4, 135.6, 132.2, 130.4, 127.2, 124.9, 104.1, 52.9, 47.2, 32.3, 28.2, 27.5, 25.7, 22.4, 19.2. HRMS(EI) *m/z* calc'd for $C_{19}H_{24}O_4S$ (M^+): 348.1395. Found: 348.1397.

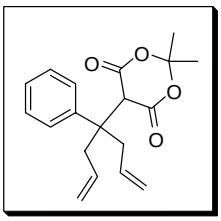


5-(1-(2-Methoxyphenyl)cyclohex-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (5.38): Conjugate addition of 2-methoxyphenylmagnesium bromide to 5-(cyclohex-2-enylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and cyclohex-2-enone)[30] according to Procedure B provided a 21% yield of a white solid after flash chromatography (5:1 hexanes:EtOAc, 3:1 then 1:1) and recrystallization from MeOH. M.p. 122-123 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.35 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.19 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.93 (t, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 8.1 Hz, 1H), 6.07-6.03 (m, 1H), 5.94 (d, *J* = 10.3 Hz, 1H), 5.09 (s, 1H), 2.54 (dt, *J* = 12.9, 2.9 Hz, 1H), 2.20-1.96 (m, 4H), 2.01(s, 3H), 1.68 (s, 3H), 1.56-1.47 (m, 1H), 1.39-1.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.1, 163.5, 155.9, 132.6, 131.1, 130.8, 129.6, 127.7, 120.5, 111.2, 103.8, 54.9, 53.1, 45.7, 30.8, 28.6, 26.8, 24.9, 18.8; HRMS(EI) *m/z* calc'd for $C_{19}H_{22}O_5$ (M^+): 330.1467. Found: 330.1461.

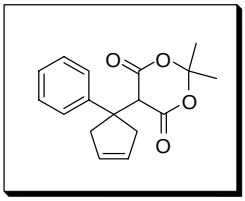


Diethyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-2-phenylmalonate (5.39): Conjugate addition of phenylmagnesium bromide to diethyl 2-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)malonate (prepared by condensation of Meldrum's acid and diethyl 2-oxomalonate at 80 °C)[29] according to procedure outlined for **5.30**. A 28% yield of a white solid was obtained after purification by flash chromatography (3:1 hexanes:EtOAc then 1:1). M.p. 105-106 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.54-7.52 (m, 2H), 7.33-7.27 (m, 2H), 4.85 (s, 1H), 4.32-4.20 (m, 4H), 1.85 (s, 3H), 1.73 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz)

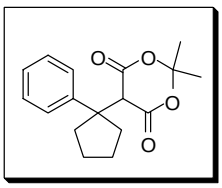
167.6, 162.9, 134.1, 128.4, 128.0, 127.8, 104.8, 62.7, 52.8, 28.4, 26.3, 13.6; HRMS(EI) *m/z* calc'd for $C_{19}H_{22}O_8$ (M^+): 378.1315. Found: 378.1313.



2,2-Dimethyl-5-(4-phenylhepta-1,6-dien-4-yl)-1,3-dioxane-4,6-dione (5.40): Conjugate addition of phenylmagnesium bromide to 5-(hepta-1,6-dien-4-ylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione [prepared by allylMgBr double addition to 5-(bis(methylthio)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione][35] according to Procedure B provided an analytically pure light yellow oil after purification by flash chromatography (5:1 hexanes:EtOAc, 2X). ^{1}H NMR ($CDCl_3$, 300 MHz) 7.34-7.24 (m, 5H), 5.77-5.63 (m, 2H), 5.25 (d, *J* = 17.1 Hz, 2H), 5.15 (d, *J* = 10.2 Hz, 2H), 3.69 (s, 1H), 3.02 (dd, *J* = 14.4, 8.3 Hz, 2H), 2.89 (dd, *J* = 14.5, 5.8 Hz, 2H), 1.54 (s, 3H), 0.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.5, 140.7, 133.4, 128.5, 127.4, 127.3, 119.8, 105.3, 53.3, 48.7, 38.7, 29.6, 26.9; HRMS(EI) *m/z* calc'd for $C_{16}H_{16}O_3$ (M^+-acetone): 256.1099. Found: 256.1102.

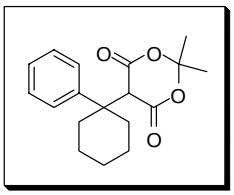


2,2-Dimethyl-5-(1-phenyl-3-cyclopentenyl)-1,3-dioxane-4,6-dione (5.41): To a Schlenk tube charged with **5.40** (1 equiv), and degassed CH_2Cl_2 (0.06 M), was added Grubb's second generation catalyst (2 mol %) in a dry box. The reaction mixture was heated to 50 ºC for 2.5 h. Concentration of the reaction mixture and purification by flash chromatography (5:1 hexanes:EtOAc), afforded a white solid in 28% yield (unoptimized). M.p. 117-119 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.28-7.20 (m, 5H), 5.86 (s, 2H), 3.67 (s, 1H), 3.42 (d, *J* = 16.1 Hz, 2H), 2.89 (d, *J* = 15.3 Hz, 2H), 1.57 (s, 3H), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.9, 143.3, 129.6, 128.4, 127.4, 127.2, 105.3, 55.7, 53.8, 43.9, 29.3, 27.1; HRMS(ESI) *m/z* calc'd for $C_{17}H_{18}O_4Li$ (M^++Li): 293.1365. Found: 293.1358.

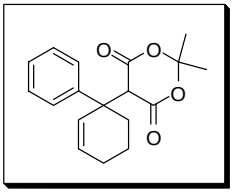


2,2-Dimethyl-5-(1-phenylcyclopentyl)-1,3-dioxane-4,6-dione (5.42): A mixture of **5.41** (1 equiv), $RhCl(PPh_3)_3$ (20 mol %) in degassed EtOH was stirred for 24 h under 1 atm of hydrogen gas.

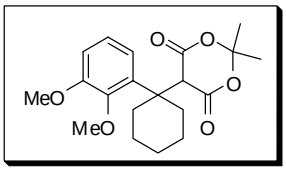
The solvent was evaporated and subjected to flash chromatography (4:1 hexanes:EtOAc) and recrystallization to afford a beige solid in 91% yield. M.p. 112-114 ºC (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.31-7.20 (m, 5H), 3.40 (s, 1H), 2.42-2.37 (m, 4H), 1.80-1.75 (m, 2H), 1.60-1.55 (m, 2H), 1.50 (s, 3H), 0.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 165.1, 141.0, 128.6, 127.7, 127.5, 105.6, 55.9, 54.8, 37.8, 30.1, 26.8, 21.7; HRMS(EI) *m/z* calc'd for $C_{17}H_{20}O_4$ (M^+): 288.1362. Found: 288.1368.



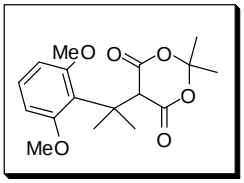
2,2-Dimethyl-5-(1-phenylcyclohexyl)-1,3-dioxane-4,6-dione (5.43): Conjugate addition of phenylmagnesium bromide to 5-cyclohexylidene-2,2-dimethyl-1,3-dioxane-4,6-dione[32] according to Procedure C provided a 66% yield of product following recrystallization from hexanes. M.p. 106-107 °C (hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.35-7.22 (m, 5H), 3.44 (s, 1H), 2.50-2.45 (m, 2H), 2.05-1.97 (m, 2H), 1.66-1.61 (m, 2H), 1.45 (s, 3H), 1.45-1.32 (m, 4H), 0.71 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.4, 139.6, 128.7, 127.7, 127.3, 105.7, 57.2, 47.2, 35.5, 30.6, 26.2, 25.7, 22.3. Anal. Calc'd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C,71.40; H, 7.32.



2,2-Dimethyl-5-(1-phenylcyclohex-2-enyl)-1,3-dioxane-4,6-dione (5.44): Conjugate addition of phenylmagnesium bromide to 5-(cyclohex-2-enylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (prepared by condensation of Meldrum's acid and cyclohex-2-enone)[30] according to Procedure B provided an analytical pure sample of a clear, colorless oil after flash chromatography (9:1 hexanes:EtOAc, 5:1 twice); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.31-7.27 (m, 5H), 6.38 (d, J = 10.4 Hz, 1H), 5.98 (dt, J = 10.3, 3.6 Hz, 1H), 3.70 (s, 1H), 2.38-2.32 (m, 2H), 2.07-1.99 (m, 2H), 1.76-1.71 (m, 1H), 1.61 (s, 3H), 1.48-1.35 (m, 1H), 1.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.1, 163.8, 143.3, 130.1, 129.9, 128.3, 127.3, 126.9, 105.2, 56.8, 46.5, 33.6, 29.3, 27.4, 24.5, 18.7; HRMS(EI) *m/z* calc'd for $C_{18}H_{20}O_4$ (M^+): 300.1362. Found: 300.1360.



5-[1-(2,3-Dimethoxyphenyl)cyclohexyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.45): Prepared by conjugate addition of 2,3-dimethoxyphenylmagnesium bromide to 5-cyclohexylidene-2,2-dimethyl-1,3-dioxane-4,6-dione[32] using Procedure B to provide a 24% yield of a white solid after purification by flash chromatography (6:1 hexanes:EtOAc) and recrystallization from MeOH. M.p. 106-107 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.00-6.90 (m, 2H), 6.83 (d, *J* = 7.6 Hz, 1H), 4.08 (s, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 2.58 (d, *J* = 13.4 Hz, 2H), 2.01 (t, *J* = 11.1 Hz, 2H), 1.60 (bs, 5H), 1.53 (bs, 1H), 1.40 (bs, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.3, 153.2, 148.4, 133.5, 122.8, 122.7, 111.7, 104.7, 60.0, 55.6, 55.5, 47.3, 34.1, 29.0, 27.5, 26.0, 23.0; HRMS(EI) *m/z* calc'd for $C_{20}H_{26}O_6$ (M^+): 362.1729. Found: 362.1736.



5-[1-(2,6-Dimethoxyphenyl)-1-methylethyl]-2,2-dimethyl-1,3-dioxane- 4,6-dione (5.46): Prepared by conjugate addition of 2,6-dimethoxyphenylmagnesium bromide to 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione[31] using Procedure B to provide a 44% yield of a white solid after recrystallization from MeOH. M.p. 148-149 °C (MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.10 (t, *J* = 8.3 Hz, 1H), 6.54 (d, *J* = 8.3 Hz, 2H), 3.76 (s, 1H), 3.74 (s, 6H), 1.86 (s, 6H), 1.80 (s, 3H), 1.75 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 164.1, 158.0, 127.3, 121.7, 106.3, 103.1, 59.1, 55.5, 40.7, 29.8, 29.0, 26.6; HRMS(EI) *m/z* calc'd for $C_{17}H_{22}O_6$ (M^+): 322.1416. Found: 322.1414.

(E) References

[1] For reviews on C—H•••O bond in the solid state, see: (a) Castellano, R. K. *Curr. Org. Chem.* **2004**, *8*, 845-865. (b) Steiner, T. *Angew. Chem. Int. Ed.* **2002**, *41*, 48-76. (c) Desiraju, G. R; Steiner, T. *The Weak Hydrogen Bond in Structural Chemistry and Biology*; Oxford University Press: Oxford, 1999.

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[16] Similarly to the observations made with **5.22**, strong nOe between the methyl group located on the aromatic moiety and H(5) was measured for **5.23**.

[17] For intramolecular C—H•••X (X = O, S) interactions in *N*-acyl-4-isopropyl-1,3-thiazolidine-2-thiones and related 1,3-oxazolidin-2-ones, see: Cosp, A.; Larrosa, I.; Anglada, J. M.; Bofill, J. M.; Romea, P.; Urpí, F. *Org. Lett.* **2003**, *5*, 2809-2812.

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[22] These two types of interaction involve different physicochemical factors and the small Δ ppm for **5.36** may have resulted from a combination of several effects unlike the C—H•••C contact in **5.35**.

[23] Compounds **5.2** revealed, through analysis of the crystal packing diagram, intermolecular C(5)—H(5)•••O(10) bond (2.24 Å). Close contacts C(5)—H(5)•••O(9) (2.90 Å) and C(5)—H(5)•••O(10) (3.25 Å) were observed for Meldrum's acid **5.3**.

[24] Analysis of the crystal packing diagram showed the formation of intermolecular C(5)—H(5)•••O(10) bond (3.13 Å).

[25] An intermolecular C(5)—H(5)•••O(9) bond (2.58 Å) was revealed by analysis of the crystal packing diagram.

[26] Analysis of the crystal packing diagram showed an intermolecular C(5)—H(5)•••O(9) bond (2.84 Å).

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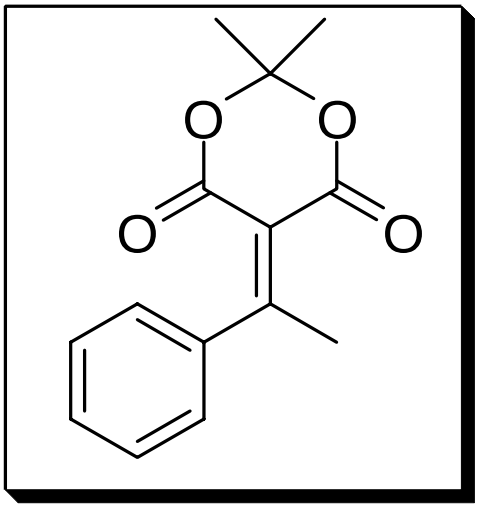
Appendix

Crystallographic data for 2.1



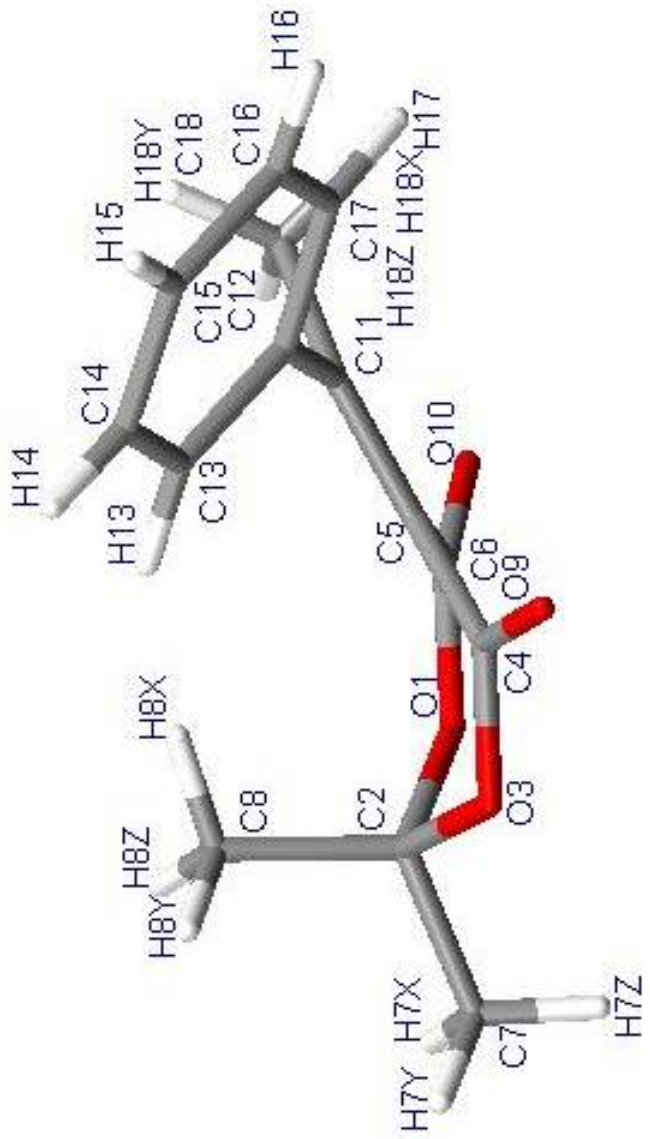

H16
H18Y
C18
C16
H17
H15
C17
H18X
H18Z
C15
C12
C11
C14
O10
H14
C13
C5
C6
O9
H13
O1
C4
H8X
O3
C8
C2
H8Z
H8Y
H7X
C7
H7Z
H7Y

Table 1 Crystal data and structure refinement for $C_{14}H_{14}O_4$

Empirical formula	$C_{15}H_{18}O_6$
Formula weight	296.25
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 5.5770(3) Å alpha = 90º
	b = 16.9946(10) Å beta = 92.842(1)º
	c = 13.0891(8) Å gamma = 90º
Volume	1239.04(12) $Å^3$
Z, Calculated density	4, 1.320 mg/m^3
Absorption coefficient	0.097 mm^{-1}
F(000)	520
Crystal size	0.46 x 0.12 x 0.12 mm
Theta range for data collection	1.97 to 28.28º
Limiting indices	-7<=h<=7, -22<=k<=12, -17<=l<=17
Reflections collected / unique	7081 / 3071 [R_{int} = 0.0278]
Completeness to theta = 27.88	99.5%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3071 / 0 / 167
Goodness-of-fit on F^2	1.932
Final R indices [I>2sigma(I)]	R1 = 0.0492, wR2 = 0.0863
R indices (all data)	R1 = 0.0593, wR2 = 0.0878
Extinction coefficient	0.024(2)
Largest diff. peak and hole	0.363 and -0.218 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	1773(2)	5035(1)	2480(1)	34(1)
C(2)	3416(2)	5144(1)	3352(1)	32(1)
O(3)	2533(2)	4711(1)	4205(1)	32(1)
C(4)	1891(2)	3952(1)	4058(1)	29(1)
C(5)	1749(2)	3679(1)	2977(1)	29(1)
C(6)	1072(3)	4296(1)	2217(1)	33(1)
C(7)	3256(3)	5995(1)	3633(1)	42(1)
C(8)	5914(3)	4885(1)	3128(1)	40(1)
O(9)	1354(2)	3569(1)	4781(1)	40(1)
O(10)	-88(2)	4204(1)	1430(1)	45(1)
C(11)	2143(2)	2927(1)	2718(1)	33(1)
C(12)	3156(3)	2341(1)	3464(1)	32(1)
C(13)	5355(3)	2477(1)	3983(1)	39(1)
C(14)	6354(3)	1907(1)	4624(1)	48(1)
C(15)	5177(3)	1209(1)	4769(1)	51(1)
C(16)	3003(3)	1070(1)	4264(1)	46(1)
C(17)	2022(3)	1628(1)	3599(1)	38(1)
C(18)	1747(3)	2620(1)	1650(1)	54(1)

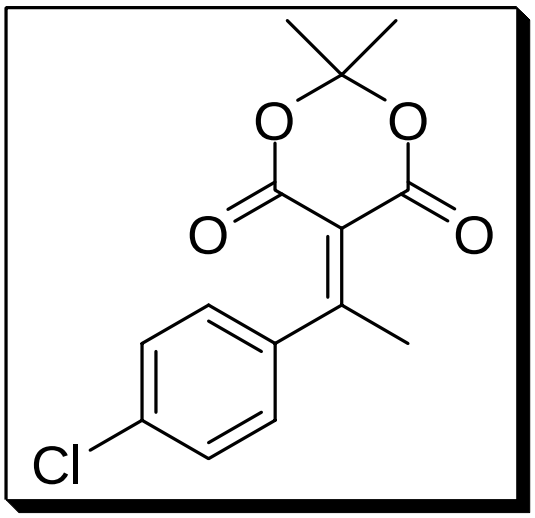
Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

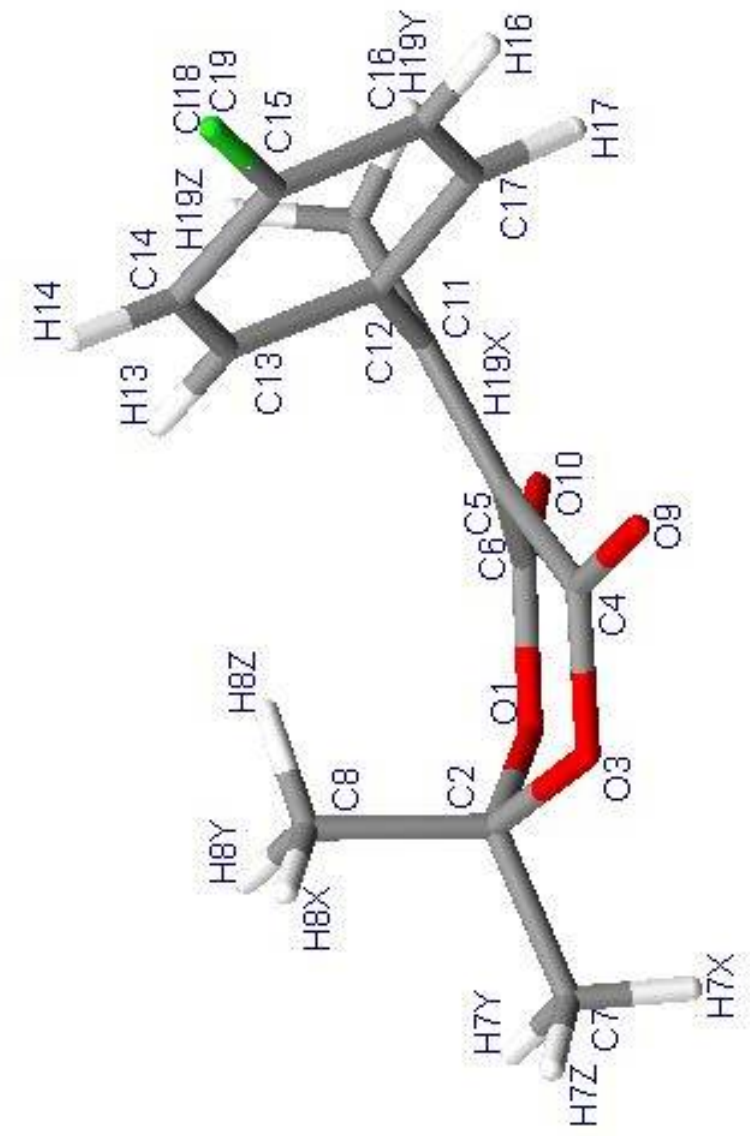
	x	y	z	U(eq)
H(7X)	3617	6320	3042	63
H(7Y)	4416	6110	4201	63
H(7Z)	1631	6113	3841	63
H(8X)	5888	4330	2925	60
H(8Y)	6975	4952	3741	60
H(8Z)	6508	5205	2571	60
H(13)	6169	2962	3896	47
H(14)	7868	1999	4968	57
H(15)	5868	823	5219	62
H(16)	2175	591	4372	55
H(17)	549	1520	3230	45
H(18X)	147	2382	1570	81
H(18Y)	2966	2222	1517	81
H(18Z)	1868	3054	1162	81

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3543(16)
O(1)-C(2)	1.4400(15)
C(2)-O(3)	1.4440(15)
C(2)-C(7)	1.4957(19)
C(2)-C(8)	1.5044(19)
O(3)-C(4)	1.3489(15)
C(4)-O(9)	1.1990(14)
C(4)-C(5)	1.4879(16)
C(5)-C(11)	1.3426(18)
C(5)-C(6)	1.4817(18)
C(6)-O(10)	1.1989(14)
C(11)-C(12)	1.4862(18)
C(11)-C(18)	1.4993(18)
C(12)-C(17)	1.3818(19)
C(12)-C(13)	1.3917(19)
C(13)-C(14)	1.380(2)
C(14)-C(15)	1.374(2)
C(15)-C(16)	1.372(2)
C(16)-C(17)	1.3825(19)
C(6)-O(1)-C(2)	119.01(10)
O(1)-C(2)-O(3)	108.63(10)
O(1)-C(2)-C(7)	106.03(10)
O(3)-C(2)-C(7)	106.06(11)
O(1)-C(2)-C(8)	111.49(11)
O(3)-C(2)-C(8)	110.87(11)
C(7)-C(2)-C(8)	113.46(12)
C(4)-O(3)-C(2)	118.40(9)
O(9)-C(4)-O(3)	118.79(11)
O(9)-C(4)-C(5)	125.26(13)
O(3)-C(4)-C(5)	115.80(11)
C(11)-C(5)-C(6)	123.02(11)
C(11)-C(5)-C(4)	122.33(11)
C(6)-C(5)-C(4)	114.63(11)
O(10)-C(6)-O(1)	118.49(12)
O(10)-C(6)-C(5)	126.27(13)
O(1)-C(6)-C(5)	115.19(11)
C(5)-C(11)-C(12)	122.32(11)
C(5)-C(11)-C(18)	123.20(12)
C(12)-C(11)-C(18)	114.38(12)
C(17)-C(12)-C(13)	118.76(13)
C(17)-C(12)-C(11)	120.66(12)
C(13)-C(12)-C(11)	120.42(13)
C(14)-C(13)-C(12)	119.97(15)
C(15)-C(14)-C(13)	120.58(14)
C(16)-C(15)-C(14)	119.95(14)
C(15)-C(16)-C(17)	119.84(16)
C(12)-C(17)-C(16)	120.85(14)

Crystallographic data for 2.34

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C13
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H19Z
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H16
H17
C17
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C6
C5
O10
O9
C4
O1
O3
C2
C8
H8Z
H8Y
H8X
H7Y
H7Z
C7
H7X

Table 1 Crystal data and structure refinement for $C_{14}H_{13}ClO_4$

Empirical formula	$C_{14}H_{13}ClO_4$
Formula weight	280.69
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Pbca
Unit cell dimensions	a = 17.9005(11) Å alpha = 90º
	b = 5.8609(4) Å beta = 90º
	c = 25.5630(16) Å gamma = 90º
Volume	2681.9(3) $Å^3$
Z, Calculated density	8, 1.390 mg/m^3
Absorption coefficient	0.291 mm^{-1}
F(000)	1168
Crystal size	0.42 x 0.21 x 0.10 mm
Theta range for data collection	1.59 to 28.28º
Limiting indices	-23<=h<=23, -7<=k<=7, -34<=l<=34
Reflections collected / unique	18101 / 3325 [R_{int} = 0.0300]
Completeness to theta = 27.88	100.0%
Absorption correction	None
Max. and min. transmission	0.948 and 0.910
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3325 / 0 / 176
Goodness-of-fit on F^2	1.964
Final R indices [I>2sigma(I)]	R1 = 0.0452, wR2 = 0.0796
R indices (all data)	R1 = 0.0550, wR2 = 0.0810
Extinction coefficient	0.0008(4)
Largest diff. peak and hole	0.399 and -0.317 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	-2140(1)	1328(2)	4949(1)	27(1)
C(2)	-1416(1)	1466(2)	5196(1)	26(1)
O(3)	-936(1)	-247(2)	4973(1)	27(1)
C(4)	-883(1)	-358(2)	4448(1)	24(1)
C(5)	-1456(1)	934(2)	4148(1)	22(1)
C(6)	-2185(1)	1236(2)	4422(1)	24(1)
C(7)	-1537(1)	741(3)	5756(1)	38(1)
C(8)	-1085(1)	3819(2)	5140(1)	31(1)
O(9)	-417(1)	-1574(2)	4254(1)	32(1)
O(10)	-2793(1)	1349(2)	4221(1)	28(1)
C(11)	-1313(1)	1761(2)	3667(1)	24(1)
C(12)	-535(1)	1789(2)	3454(1)	25(1)
C(13)	-77(1)	3611(3)	3582(1)	34(1)
C(14)	639(1)	3768(3)	3379(1)	38(1)
C(15)	890(1)	2089(3)	3048(1)	33(1)
C(16)	443(1)	286(3)	2907(1)	36(1)
C(17)	-273(1)	144(3)	3111(1)	34(1)
Cl(18)	1796(1)	2279(1)	2800(1)	56(1)
C(19)	-1866(1)	2891(3)	3314(1)	34(1)

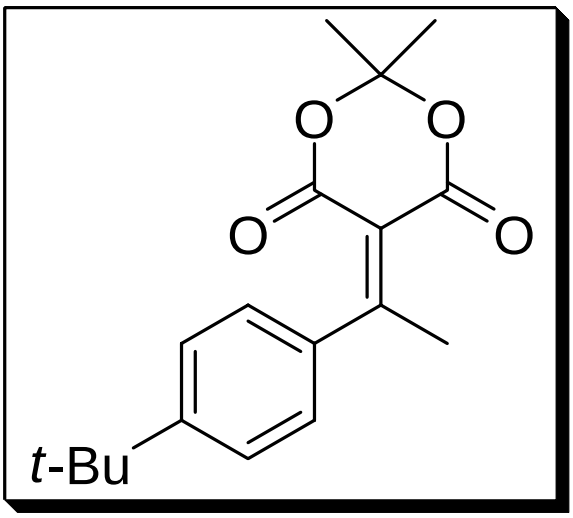
Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
H(7X)	-1751	-799	5763	57
H(7Y)	-1881	1807	5927	57
H(7Z)	-1058	742	5942	57
H(8X)	-593	3860	5308	46
H(8Y)	-1415	4936	5308	46
H(8Z)	-1034	4192	4768	46
H(13)	-256	4764	3812	41
H(14)	952	5019	3468	45
H(16)	623	-848	2673	44
H(17)	-587	-1093	3015	40
H(19X)	-2357	2914	3484	51
H(19Y)	-1898	2042	2985	51
H(19Z)	-1705	4458	3243	51

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3499(15)
O(1)-C(2)	1.4454(16)
C(2)-O(3)	1.4387(16)
C(2)-C(8)	1.5072(19)
C(2)-C(7)	1.5080(19)
O(3)-C(4)	1.3487(15)
C(4)-O(9)	1.2036(15)
C(4)-C(5)	1.4883(17)
C(5)-C(11)	1.3445(18)
C(5)-C(6)	1.4911(18)
C(6)-O(10)	1.2049(15)
C(11)-C(19)	1.4943(18)
C(11)-C(12)	1.4957(18)
C(12)-C(17)	1.3850(18)
C(12)-C(13)	1.3858(19)
C(13)-C(14)	1.386(2)
C(14)-C(15)	1.374(2)
C(15)-C(16)	1.373(2)
C(15)-Cl(18)	1.7442(14)
C(16)-C(17)	1.387(2)
C(6)-O(1)-C(2)	119.51(10)
O(3)-C(2)-O(1)	108.80(10)
O(3)-C(2)-C(8)	111.54(11)
O(1)-C(2)-C(8)	111.17(11)
O(3)-C(2)-C(7)	105.39(11)
O(1)-C(2)-C(7)	105.69(11)
C(8)-C(2)-C(7)	113.87(12)
C(4)-O(3)-C(2)	118.10(10)
O(9)-C(4)-O(3)	119.15(12)
O(9)-C(4)-C(5)	124.57(12)
O(3)-C(4)-C(5)	116.11(11)
C(11)-C(5)-C(4)	121.47(12)
C(11)-C(5)-C(6)	123.62(12)
C(4)-C(5)-C(6)	114.90(11)
O(10)-C(6)-O(1)	118.44(12)
O(10)-C(6)-C(5)	126.58(12)
O(1)-C(6)-C(5)	114.96(11)
C(5)-C(11)-C(19)	125.79(12)
C(5)-C(11)-C(12)	120.96(12)
C(19)-C(11)-C(12)	113.07(11)
C(17)-C(12)-C(13)	119.05(13)
C(17)-C(12)-C(11)	122.59(13)
C(13)-C(12)-C(11)	118.24(12)
C(14)-C(13)-C(12)	120.65(14)
C(15)-C(14)-C(13)	119.06(14)
C(16)-C(15)-C(14)	121.51(14)
C(16)-C(15)-Cl(18)	119.67(12)
C(14)-C(15)-Cl(18)	118.83(12)
C(15)-C(16)-C(17)	119.05(14)
C(12)-C(17)-C(16)	120.66(14)

Crystallographic data for 2.66



H21Y
C21
H21Z
H20X
H20Z
C20
H21X
C18
H20Y
H19Z
C19
C15
C14
H14
H16
H19Y
C13
H19X
C16
C17
H22Y
H13
H17
H22Z
C12
C22
C11
H22X
C5
O9
C4
O10
C6
H8Z
O3
C8
H8Y
O1
H8X
C2
C7
H7ZH7Y
H7X

Table 1 Crystal data and structure refinement for $C_{18}H_{22}O_4$

Empirical formula	$C_{18}H_{22}O_4$
Formula weight	302.36
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 10.4867(4) Å alpha = 90º
	b = 25.6129(9) Å beta = 90.252(1)º
	c = 12.1381(5) Å gamma = 90º
Volume	3260.2(2) $Å^3$
Z, Calculated density	8, 1.232 mg/m^3
Absorption coefficient	0.086 mm^{-1}
F(000)	1296
Crystal size	0.32 x 0.15 x 0.14 mm
Theta range for data collection	1.59 to 28.28º
Limiting indices	-12<=h<=13, -34<=k<=26, -16<=l<=16
Reflections collected / unique	18803 / 8012 [R_{int} = 0.0314]
Completeness to theta = 27.88	99.2%
Absorption correction	None
Max. and min. transmission	0.948 and 0.910
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8012 / 0 / 410
Goodness-of-fit on F^2	1.949
Final R indices [I>2sigma(I)]	R1 = 0.0685, wR2 = 0.1347
R indices (all data)	R1 = 0.0894, wR2 = 0.1381
Extinction coefficient	0.0053(5)
Largest diff. peak and hole	0.706 and -0.571 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	2942(1)	786(1)	7975(1)	37(1)
C(2)	2008(2)	863(1)	8829(2)	35(1)
O(3)	1012(1)	1200(1)	8420(1)	35(1)
C(4)	1346(2)	1648(1)	7897(2)	30(1)
C(5)	2730(2)	1707(1)	7661(2)	27(1)
C(6)	3415(2)	1210(1)	7439(2)	32(1)
C(7)	1377(2)	344(1)	9006(2)	49(1)
C(8)	2615(2)	1084(1)	9856(2)	42(1)
O(9)	516(1)	1941(1)	7615(1)	39(1)
O(10)	4289(1)	1149(1)	6817(1)	40(1)
C(11)	3316(2)	2175(1)	7692(2)	28(1)
C(12)	2650(2)	2654(1)	8083(2)	27(1)
C(13)	1882(2)	2952(1)	7399(2)	35(1)
C(14)	1312(2)	3404(1)	7778(2)	35(1)
C(15)	1496(2)	3580(1)	8849(2)	31(1)
C(16)	2269(2)	3277(1)	9523(2)	38(1)
C(17)	2848(2)	2827(1)	9150(2)	36(1)
C(18)	868(2)	4082(1)	9271(2)	36(1)
C(19)	-288(3)	3939(1)	9957(3)	93(1)
C(20)	361(5)	4411(1)	8324(3)	127(2)
C(21)	1761(3)	4393(1)	9964(4)	142(2)
C(22)	4688(2)	2266(1)	7410(2)	39(1)
O(23)	7989(1)	793(1)	9493(1)	37(1)
C(24)	7057(2)	869(1)	8629(2)	37(1)
O(25)	6049(1)	1194(1)	9038(1)	37(1)
C(26)	6359(2)	1642(1)	9569(2)	31(1)
C(27)	7746(2)	1711(1)	9814(2)	27(1)

C(28)	8442(2)	1216(1)	10040(2)	30(1)
C(29)	6453(2)	344(1)	8445(2)	55(1)
C(30)	7660(2)	1094(1)	7609(2)	46(1)
O(31)	5517(1)	1930(1)	9848(1)	41(1)
O(32)	9308(1)	1158(1)	10678(1)	39(1)
C(33)	8318(2)	2181(1)	9787(2)	27(1)
C(34)	7646(2)	2660(1)	9388(2)	27(1)
C(35)	6853(2)	2950(1)	10057(2)	36(1)
C(36)	6284(2)	3402(1)	9674(2)	35(1)
C(37)	6493(2)	3584(1)	8608(2)	30(1)
C(38)	7295(2)	3288(1)	7954(2)	38(1)
C(39)	7872(2)	2836(1)	8334(2)	36(1)
C(40)	5849(2)	4082(1)	8178(2)	34(1)
C(41)	4621(3)	3934(1)	7619(3)	103(1)
C(42)	6635(3)	4353(1)	7340(4)	136(2)
C(43)	5543(6)	4451(1)	9098(3)	162(2)
C(44)	9695(2)	2274(1)	10068(2)	37(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

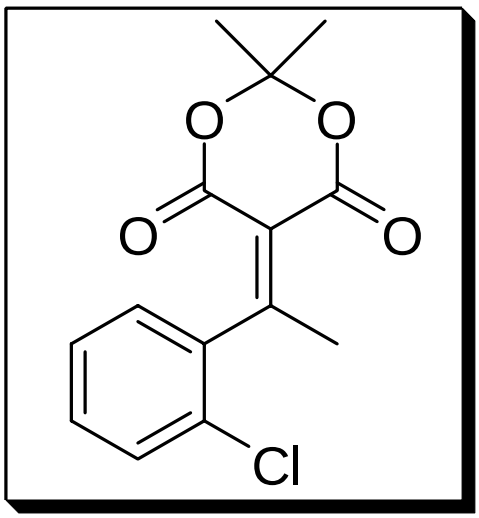
	x	y	z	U(eq)
H(7X)	1021	218	8306	74
H(7Y)	691	382	9545	74
H(7Z)	2008	93	9281	74
H(8X)	3297	851	10107	64
H(8Y)	1971	1117	10434	64
H(8Z)	2973	1429	9694	64
H(13)	1745	2845	6659	42
H(14)	780	3600	7294	42
H(16)	2405	3383	10264	46
H(17)	3387	2634	9631	43
H(19X)	-26	3708	10560	139
H(19Y)	-917	3760	9492	139
H(19Z)	-668	4257	10262	139
H(20X)	-136	4703	8618	191
H(20Y)	-185	4196	7850	191
H(20Z)	1077	4547	7894	191
H(21X)	1942	4204	10649	213
H(21Y)	1371	4731	10138	213
H(21Z)	2557	4450	9562	213
H(22X)	5122	1929	7328	59
H(22Y)	5099	2467	8000	59
H(22Z)	4741	2461	6717	59
H(29X)	6091	217	9139	83
H(29Y)	7100	97	8186	83
H(29Z)	5775	374	7891	83
H(30X)	7012	1130	7030	69
H(30Y)	8337	860	7354	69
H(30Z)	8023	1437	7780	69
H(35)	6696	2837	10790	43
H(36)	5738	3594	10149	42
H(38)	7454	3399	7221	46
H(39)	8426	2646	7864	44
H(41X)	4183	4250	7364	154
H(41Y)	4076	3747	8140	154
H(41Z)	4803	3708	6987	154
H(42X)	6185	4666	7081	204
H(42Y)	6784	4118	6717	204
H(42Z)	7454	4455	7668	204
H(43X)	6337	4569	9447	243
H(43Y)	5015	4272	9644	243
H(43Z)	5078	4752	8804	243
H(42X)	9754	2470	10760	56
H(42Y)	10097	2475	9476	56
H(42Z)	10133	1938	10151	56

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.361(2)
O(1)-C(2)	1.443(2)
C(2)-O(3)	1.441(2)
C(2)-C(7)	1.501(3)
C(2)-C(8)	1.508(3)
O(3)-C(4)	1.359(2)
C(4)-O(9)	1.198(2)
C(4)-C(5)	1.488(3)
C(5)-C(11)	1.348(3)
C(5)-C(6)	1.487(3)
C(6)-O(10)	1.200(2)
C(11)-C(12)	1.491(3)
C(11)-C(22)	1.498(3)
C(12)-C(13)	1.383(3)
C(12)-C(17)	1.383(3)
C(13)-C(14)	1.383(3)
C(14)-C(15)	1.388(3)
C(15)-C(16)	1.386(3)
C(15)-C(18)	1.533(3)
C(16)-C(17)	1.381(3)
C(18)-C(21)	1.488(3)
C(18)-C(19)	1.518(4)
C(18)-C(20)	1.520(3)
O(23)-C(28)	1.356(2)
O(23)-C(24)	1.444(2)
C(24)-O(25)	1.436(2)
C(24)-C(29)	1.503(3)
C(24)-C(30)	1.508(3)
O(25)-C(26)	1.356(2)
C(26)-O(31)	1.199(2)
C(26)-C(27)	1.493(3)
C(27)-C(33)	1.346(3)
C(27)-C(28)	1.486(3)
C(28)-O(32)	1.201(2)
C(33)-C(34)	1.495(3)
C(33)-C(44)	1.501(3)
C(34)-C(39)	1.378(3)
C(34)-C(35)	1.381(3)
C(35)-C(36)	1.383(3)
C(36)-C(37)	1.393(3)
C(37)-C(38)	1.385(3)
C(37)-C(40)	1.534(3)
C(38)-C(39)	1.384(3)
C(40)-C(42)	1.484(4)
C(40)-C(43)	1.497(4)
C(40)-C(41)	1.503(3)
C(6)-O(1)-C(2)	119.03(15)
O(3)-C(2)-O(1)	109.13(15)
O(3)-C(2)-C(7)	105.10(16)
O(1)-C(2)-C(7)	106.43(17)
O(3)-C(2)-C(8)	111.27(16)
O(1)-C(2)-C(8)	111.04(17)
C(7)-C(2)-C(8)	113.56(18)
C(4)-O(3)-C(2)	118.59(15)
O(9)-C(4)-O(3)	118.28(18)
O(9)-C(4)-C(5)	126.13(18)
O(3)-C(4)-C(5)	115.44(16)
C(11)-C(5)-C(6)	123.08(18)
C(11)-C(5)-C(4)	122.00(17)
C(6)-C(5)-C(4)	114.87(17)
O(10)-C(6)-O(1)	118.51(18)
O(10)-C(6)-C(5)	126.70(19)
O(1)-C(6)-C(5)	114.73(17)
C(5)-C(11)-C(12)	121.80(18)
C(5)-C(11)-C(22)	124.72(18)
C(12)-C(11)-C(22)	113.40(17)
C(13)-C(12)-C(17)	118.03(18)
C(13)-C(12)-C(11)	122.41(17)
C(17)-C(12)-C(11)	119.48(16)
C(12)-C(13)-C(14)	120.95(18)
C(13)-C(14)-C(15)	121.57(18)
C(16)-C(15)-C(14)	116.76(18)
C(16)-C(15)-C(18)	121.53(18)

C(14)-C(15)-C(18)	121.71(17)
C(17)-C(16)-C(15)	122.06(18)
C(16)-C(17)-C(12)	120.62(18)
C(21)-C(18)-C(19)	108.7(3)
C(21)-C(18)-C(20)	110.3(3)
C(19)-C(18)-C(20)	105.7(3)
C(21)-C(18)-C(15)	111.60(18)
C(19)-C(18)-C(15)	109.07(18)
C(20)-C(18)-C(15)	111.26(19)
C(28)-O(23)-C(24)	118.88(15)
O(25)-C(24)-O(23)	108.89(16)
O(25)-C(24)-C(29)	105.13(18)
O(23)-C(24)-C(29)	105.73(17)
O(25)-C(24)-C(30)	111.96(17)
O(23)-C(24)-C(30)	111.26(18)
C(29)-C(24)-C(30)	113.48(19)
C(26)-O(25)-C(24)	118.71(15)
O(31)-C(26)-O(25)	118.55(18)
O(31)-C(26)-C(27)	126.12(18)
O(25)-C(26)-C(27)	115.20(17)
C(33)-C(27)-C(28)	123.22(17)
C(33)-C(27)-C(26)	122.29(17)
C(28)-C(27)-C(26)	114.45(16)
O(32)-C(28)-O(23)	118.64(17)
O(32)-C(28)-C(27)	126.44(18)
O(23)-C(28)-C(27)	114.85(16)
C(27)-C(33)-C(34)	122.20(16)
C(27)-C(33)-C(44)	124.42(17)
C(34)-C(33)-C(44)	113.24(16)
C(39)-C(34)-C(35)	118.45(18)
C(39)-C(34)-C(33)	119.10(18)
C(35)-C(34)-C(33)	122.37(18)
C(34)-C(35)-C(36)	120.86(19)
C(35)-C(36)-C(37)	121.53(19)
C(38)-C(37)-C(36)	116.55(18)
C(38)-C(37)-C(40)	121.89(18)
C(36)-C(37)-C(40)	121.55(18)
C(39)-C(38)-C(37)	122.24(19)
C(34)-C(39)-C(38)	120.36(19)
C(42)-C(40)-C(43)	109.8(3)
C(42)-C(40)-C(41)	106.6(3)
C(43)-C(40)-C(41)	108.1(3)
C(42)-C(40)-C(37)	112.17(19)
C(43)-C(40)-C(37)	111.46(19)
C(41)-C(40)-C(37)	108.57(18)

Crystallographic data for 2.71



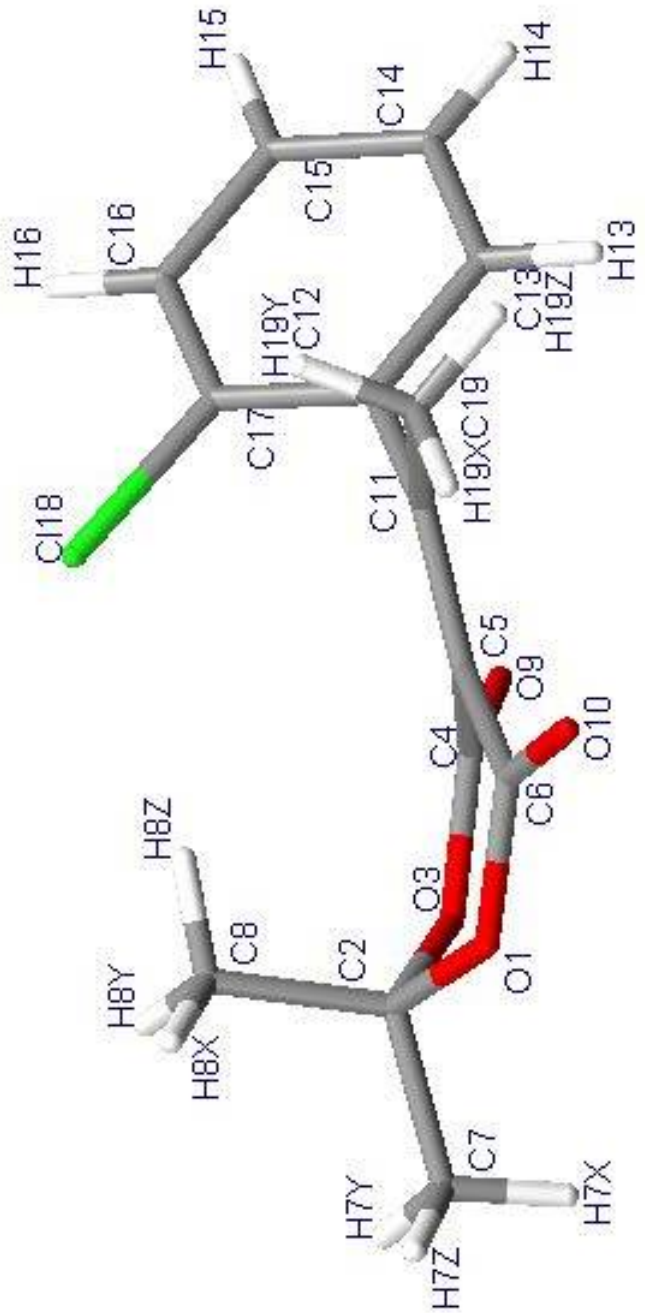

H15
C14
H14
C15
H16
C16
H13
C13
H19Z
H19Y
C12
C17
H19xC19
Cl18
C11
C5
O9
O10
C4
C6
H8Z
O3
C8
C2
O1
H8Y
H8X
C7
H7Y
H7X
H7Z

Table 1 Crystal data and structure refinement for $C_{14}H_{13}ClO_4$

Empirical formula	$C_{14}H_{13}ClO_4$
Formula weight	280.69
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 6.9919(3) Å alpha = 81.573(1)º
	b = 7.4350(3) Å beta = 74.927(1) º
	c = 13.1352(5) Å gamma = 86.963(1)º
Volume	652.14(5) $Å^3$
Z, Calculated density	2, 1.429 mg/m^3
Absorption coefficient	0.300 mm^{-1}
F(000)	292
Crystal size	0.31 x 0.30 x 0.20 mm
Theta range for data collection	1.62 to 28.28º
Limiting indices	-9<=h<=9, -9<=k<=9, -17<=l<=17
Reflections collected / unique	7207 / 3229 [R_{int} = 0. 0262]
Completeness to theta = 27.88	100.0%
Absorption correction	Integration
Max. and min. transmission	0.948 and 0.910
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3229 / 0 / 176
Goodness-of-fit on F^2	2.257
Final R indices [I>2sigma(I)]	R1 = 0.0406, wR2 = 0.1140
R indices (all data)	R1 = 0.0436, wR2 = 0.1148
Extinction coefficient	0.021(7)
Largest diff. peak and hole	0.406 and -0.409 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	9033(1)	8051(1)	2853(1)	28(1)
C(2)	7622(2)	7516(2)	3858(1)	28(1)
O(3)	7575(2)	5561(1)	4079(1)	29(1)
C(4)	7453(2)	4584(2)	3308(1)	25(1)
C(5)	7797(2)	5592(2)	2214(1)	21(1)
C(6)	9015(2)	7251(2)	1996(1)	24(1)
C(7)	8459(3)	8147(2)	4687(1)	42(1)
C(8)	5606(2)	8304(2)	3840(1)	32(1)
O(9)	7183(2)	2980(1)	3536(1)	34(1)
O(10)	10036(2)	7881(2)	1147(1)	35(1)
C(11)	7094(2)	4996(2)	1461(1)	21(1)
C(12)	5828(2)	3356(2)	1668(1)	23(1)
C(13)	6605(2)	1824(2)	1178(1)	29(1)
C(14)	5399(2)	389(2)	1231(1)	34(1)
C(15)	3418(2)	436(2)	1757(1)	34(1)
C(16)	2620(2)	1916(2)	2253(1)	31(1)
C(17)	3838(2)	3358(2)	2199(1)	26(1)
Cl(18)	2784(1)	5244(1)	2786(1)	39(1)
C(19)	7404(2)	5899(2)	336(1)	27(1)

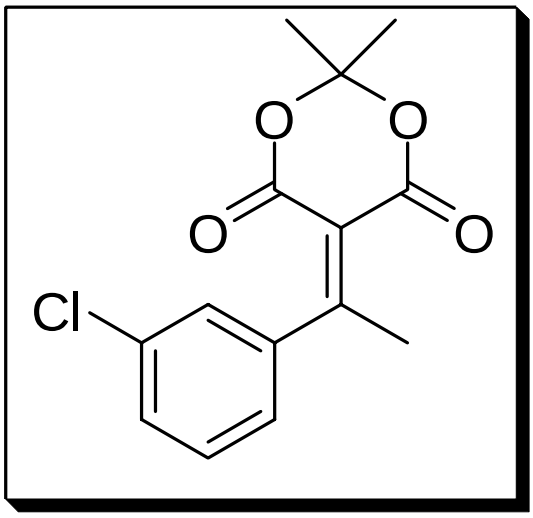
Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
H(7X)	9754	7560	4669	63
H(7Y)	7557	7821	5392	63
H(7Z)	8611	9469	4540	63
H(8X)	5676	9633	3696	49
H(8Y)	4673	7945	4531	49
H(8Z)	5152	7848	3281	49
H(13)	7966	1777	810	35
H(14)	5938	-645	901	41
H(15)	2599	-555	1777	41
H(16)	1260	1946	2626	37
H(19X)	8211	6982	228	40
H(19Y)	6118	6255	194	40
H(19Z)	8085	5051	-151	40

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3501(15)
O(1)-C(2)	1.4437(16)
C(2)-O(3)	1.4410(17)
C(2)-C(8)	1.503(2)
C(2)-C(7)	1.502(2)
O(3)-C(4)	1.3519(15)
C(4)-O(9)	1.1985(16)
C(4)-C(5)	1.4865(18)
C(5)-C(11)	1.3483(17)
C(5)-C(6)	1.4868(17)
C(6)-O(10)	1.2005(16)
C(11)-C(12)	1.4953(17)
C(11)-C(19)	1.4971(17)
C(12)-C(17)	1.3849(19)
C(12)-C(13)	1.4051(19)
C(13)-C(14)	1.378(2)
C(14)-C(15)	1.379(2)
C(15)-C(16)	1.379(2)
C(16)-C(17)	1.3871(19)
C(17)-Cl(18)	1.7365(14)
C(6)-O(1)-C(2)	119.84(10)
O(3)-C(2)-O(1)	109.28(10)
O(3)-C(2)-C(8)	111.13(12)
O(1)-C(2)-C(8)	110.59(11)
O(3)-C(2)-C(7)	106.29(12)
O(1)-C(2)-C(7)	105.69(12)
C(8)-C(2)-C(7)	113.60(12)
C(4)-O(3)-C(2)	119.52(10)
O(9)-C(4)-O(3)	118.74(12)
O(9)-C(4)-C(5)	124.91(12)
O(3)-C(4)-C(5)	116.24(11)
C(11)-C(5)-C(4)	121.65(11)
C(11)-C(5)-C(6)	122.53(11)
C(4)-C(5)-C(6)	115.79(11)
O(10)-C(6)-O(1)	117.93(12)
O(10)-C(6)-C(5)	126.04(12)
O(1)-C(6)-C(5)	115.94(11)
C(5)-C(11)-C(12)	123.46(11)
C(5)-C(11)-C(19)	125.29(12)
C(12)-C(11)-C(19)	111.22(10)
C(17)-C(12)-C(13)	117.80(12)
C(17)-C(12)-C(11)	122.91(12)
C(13)-C(12)-C(11)	118.68(12)
C(14)-C(13)-C(12)	120.18(14)
C(13)-C(14)-C(15)	120.75(14)
C(16)-C(15)-C(14)	120.30(13)
C(15)-C(16)-C(17)	118.81(14)
C(12)-C(17)-C(16)	122.15(13)
C(12)-C(17)-Cl(18)	119.75(10)
C(16)-C(17)-Cl(18)	118.07(11)

Crystallographic data for 2.75



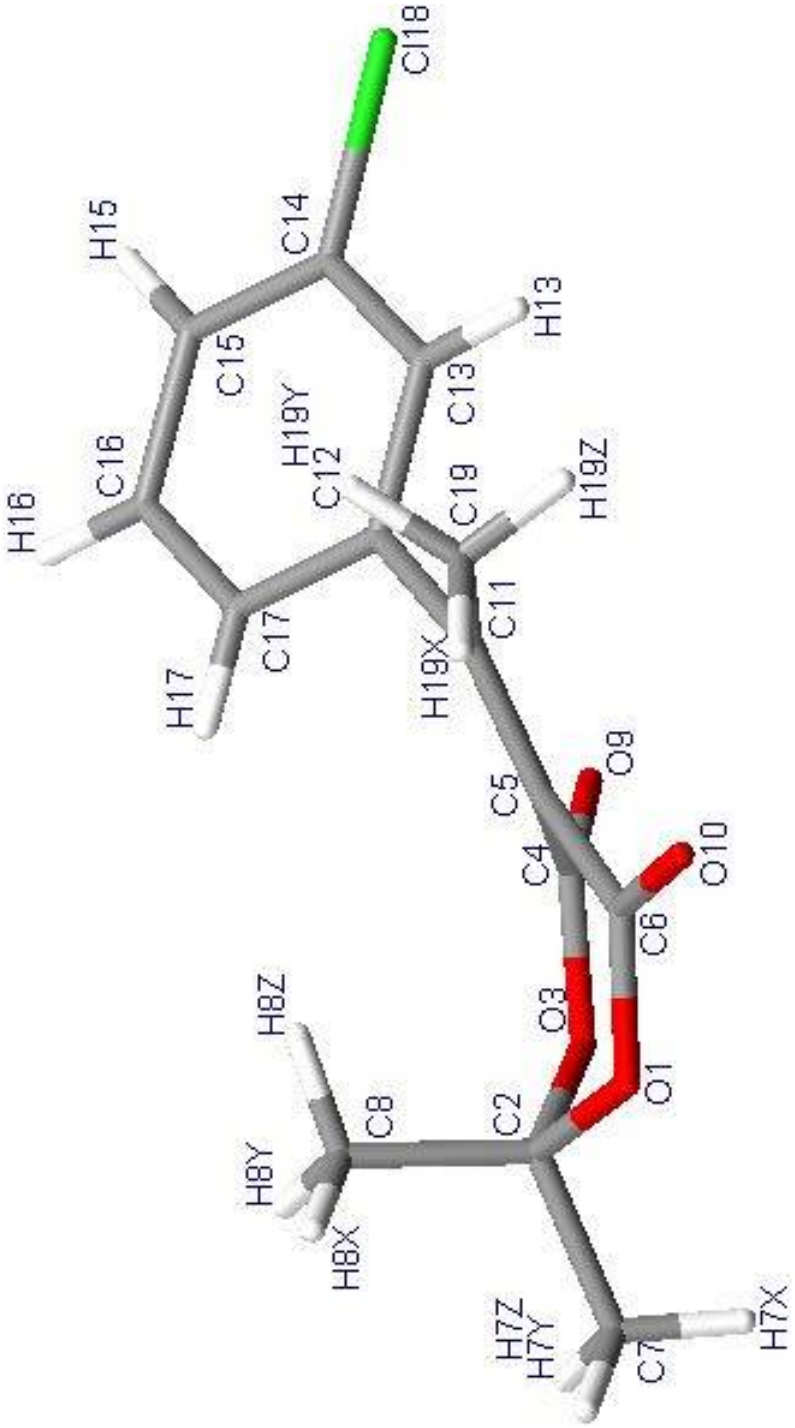

Cl18
H15
C14
H13
C15
C13
H19Y
C12
C16
C19
H19Z
H16
C17
C11
H17
H19X
C5
O9
C4
O10
C6
H8Z
O3
O1
C8
C2
H8Y
H8X
H7Z
H7Y
C7
H7X

Table 1 Crystal data and structure refinement for $C_{14}H_{13}ClO_4$

Empirical formula	$C_{14}H_{13}ClO_4$
Formula weight	280.69
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Pna2(1)
Unit cell dimensions	a = 7.3779(4) Å alpha = 90º
	b = 22.6070(12) Å beta = 90º
	c = 7.9039(4) Å gamma = 90º
Volume	1318.31(12) $Å^3$
Z, Calculated density	4, 1.414 mg/m^3
Absorption coefficient	0.296 mm^{-1}
F(000)	584
Crystal size	0.46 x 0.20 x 0.20 mm
Theta range for data collection	2.73 to 30.03°
Limiting indices	-9<=h<=10, -31<=k<=31, -11<=l<=11
Reflections collected / unique	10430 / 3744 [R_{int} = 0.0271]
Completeness to theta = 27.88	100.0%
Absorption correction	Integration
Max. and min. transmission	0.947 and 0.888
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3744 / 0 / 175
Goodness-of-fit on F^2	1.957
Final R indices [I>2sigma(I)]	R1 = 0.0333, wR2 = 0.0703
R indices (all data)	R1 = 0.0345, wR2 = 0.0705
Extinction coefficient	0.0190(16)
Absolute structure parameter	0.01(4)
Largest diff. peak and hole	0.222 and -0.209 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	9994(1)	2801(1)	4076(2)	37(1)
C(2)	10067(2)	3272(1)	5286(2)	28(1)
O(3)	8244(1)	3396(1)	5862(1)	27(1)
C(4)	6924(2)	3476(1)	4684(2)	23(1)
C(5)	7414(2)	3311(1)	2919(2)	23(1)
C(6)	8776(2)	2831(1)	2782(2)	32(1)
C(7)	11067(2)	3025(1)	6797(2)	40(1)
C(8)	10933(2)	3820(1)	4583(2)	38(1)
O(9)	5461(1)	3641(1)	5157(1)	30(1)
O(10)	8849(2)	2467(1)	1683(2)	50(1)
C(11)	6585(2)	3539(1)	1551(2)	22(1)
C(12)	5326(2)	4053(1)	1666(2)	22(1)
C(13)	3617(2)	4017(1)	928(2)	25(1)
C(14)	2514(2)	4512(1)	934(2)	28(1)
C(15)	3063(2)	5043(1)	1626(2)	32(1)
C(16)	4782(2)	5080(1)	2320(2)	34(1)
C(17)	5909(2)	4589(1)	2350(2)	29(1)
Cl(18)	374(1)	4468(1)	0	45(1)
C(19)	6891(2)	3329(1)	-226(2)	32(1)

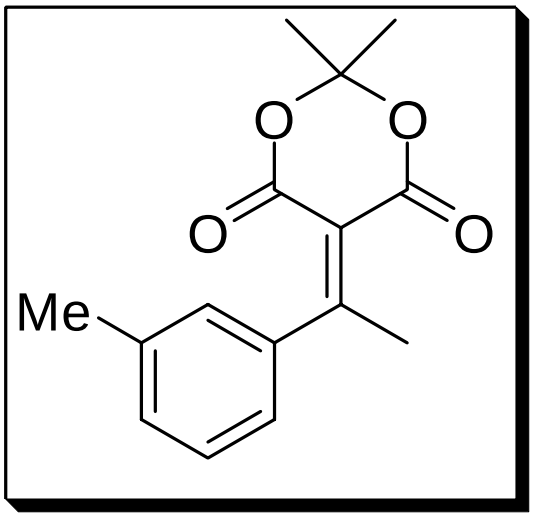
Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
H(7X)	10474	2660	7173	60
H(7Y)	11051	3316	7717	60
H(7Z)	12324	2940	6480	60
H(8X)	12168	3728	4210	57
H(8Y)	10974	4125	5461	57
H(8Z)	10222	3963	3619	57
H(13)	3214	3658	428	30
H(15)	2278	5376	1626	38
H(16)	5193	5444	2779	41
H(17)	7082	4618	2839	35
H(19X)	8113	3162	-322	47
H(19Y)	6767	3662	-1009	47
H(19Z)	5994	3025	-508	47

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3630(18)
O(1)-C(2)	1.4328(17)
C(2)-O(3)	1.4470(15)
C(2)-C(8)	1.499(2)
C(2)-C(7)	1.511(2)
O(3)-C(4)	1.3597(15)
C(4)-O(9)	1.2013(14)
C(4)-C(5)	1.4883(18)
C(5)-C(11)	1.3447(18)
C(5)-C(6)	1.4837(17)
C(6)-O(10)	1.1971(17)
C(11)-C(12)	1.4910(17)
C(11)-C(19)	1.4996(18)
C(12)-C(13)	1.3922(17)
C(12)-C(17)	1.3950(17)
C(13)-C(14)	1.3832(18)
C(14)-C(15)	1.3812(19)
C(14)-Cl(18)	1.7458(14)
C(15)-C(16)	1.384(2)
C(16)-C(17)	1.3861(19)
C(6)-O(1)-C(2)	119.23(10)
O(1)-C(2)-O(3)	108.56(10)
O(1)-C(2)-C(8)	112.48(12)
O(3)-C(2)-C(8)	110.74(11)
O(1)-C(2)-C(7)	105.71(11)
O(3)-C(2)-C(7)	106.04(12)
C(8)-C(2)-C(7)	112.94(12)
C(4)-O(3)-C(2)	118.45(10)
O(9)-C(4)-O(3)	118.16(12)
O(9)-C(4)-C(5)	126.00(12)
O(3)-C(4)-C(5)	115.71(10)
C(11)-C(5)-C(6)	121.97(12)
C(11)-C(5)-C(4)	123.17(11)
C(6)-C(5)-C(4)	114.62(11)
O(10)-C(6)-O(1)	118.72(12)
O(10)-C(6)-C(5)	125.87(13)
O(1)-C(6)-C(5)	115.37(12)
C(5)-C(11)-C(12)	122.17(11)
C(5)-C(11)-C(19)	124.29(11)
C(12)-C(11)-C(19)	113.47(11)
C(13)-C(12)-C(17)	119.54(11)
C(13)-C(12)-C(11)	119.48(11)
C(17)-C(12)-C(11)	120.64(11)
C(14)-C(13)-C(12)	118.90(12)
C(15)-C(14)-C(13)	122.20(13)
C(15)-C(14)-Cl(18)	118.77(10)
C(13)-C(14)-Cl(18)	119.02(10)
C(14)-C(15)-C(16)	118.53(12)
C(15)-C(16)-C(17)	120.56(13)
C(16)-C(17)-C(12)	120.24(13)

Crystallographic data for 2.77



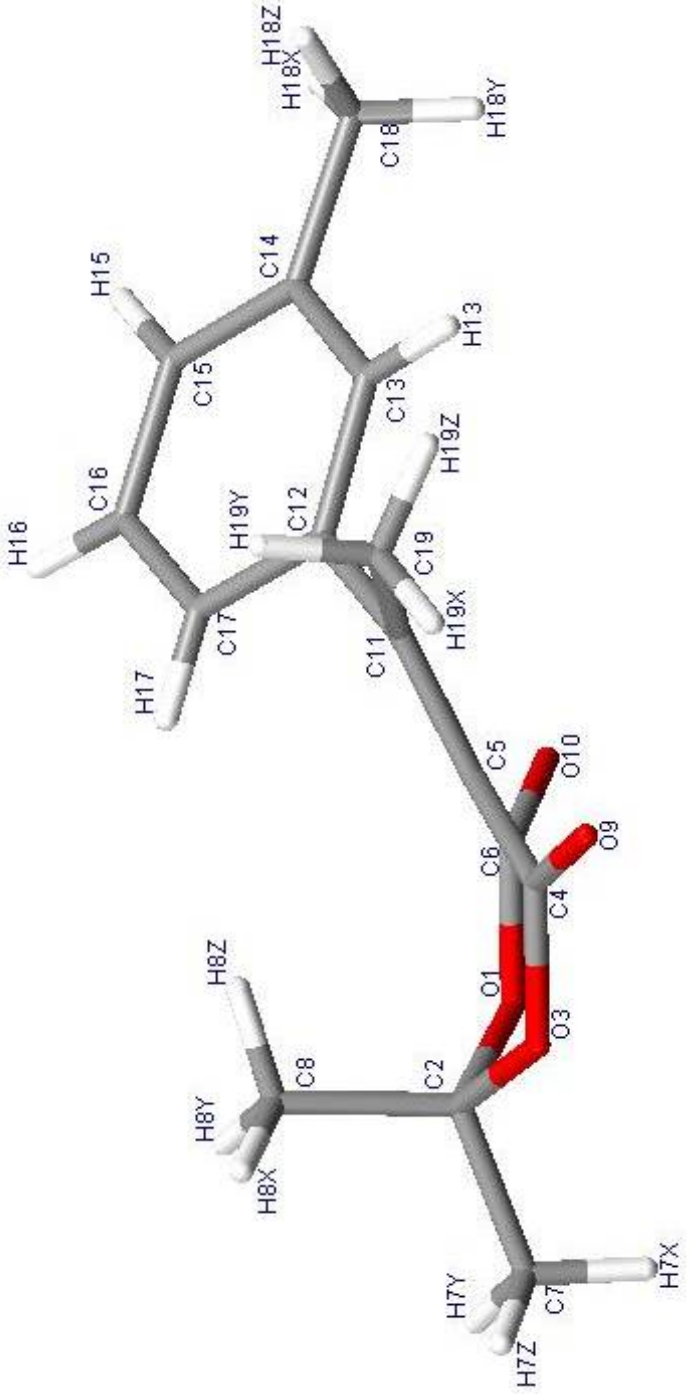

H18Z
H18X
H18Y
C18
C14
H15
H13
C15
C13
H19Z
C16
C12
H19Y
C19
H16
H19X
C17
C11
H17
C5
O10
O9
C6
C4
H8Z
O1
O3
C8
C2
H8Y
H8X
H7Y
C7
H7X
H7Z

Table 1 Crystal data and structure refinement for $C_{15}H_{16}O_4$

Empirical formula	$C_{15}H_{16}O_4$
Formula weight	260.28
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Pna2(1)
Unit cell dimensions	a = 12.6729(6) Å alpha = 90º
	b = 17.6509(8) Å beta = 90º
	c = 5.9633(3) Å gamma = 90º
Volume	1333.92(11) $Å^3$
Z, Calculated density	4, 1.296 mg/m^3
Absorption coefficient	0.094 mm^{-1}
F(000)	552
Crystal size	0.34 x 0.16 x 0.14 mm
Theta range for data collection	1.98 to 30.02°
Limiting indices	-17<=h<=17, -24<=k<=22, -8<=l<=8
Reflections collected / unique	10575 / 3836 [R_{int} = 0.0296]
Completeness to theta = 27.88	99.5%
Absorption correction	None
Max. and min. transmission	0.947 and 0.888
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3836 / 0 / 176
Goodness-of-fit on F^2	1.751
Final R indices [I>2sigma(I)]	R1 = 0.0393, wR2 = 0.0687
R indices (all data)	R1 = 0.0430, wR2 = 0.0690
Extinction coefficient	0.0161(10)
Absolute structure parameter	0.01(4)
Largest diff. peak and hole	0.249 and -0.242 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	4225(1)	5086(1)	3388	30(1)
C(2)	3244(1)	4673(1)	3297(3)	27(1)
O(3)	2575(1)	4923(1)	5103(2)	30(1)
C(4)	2430(1)	5676(1)	5426(3)	26(1)
C(5)	3131(1)	6176(1)	4088(3)	24(1)
C(6)	4193(1)	5850(1)	3628(3)	27(1)
C(7)	3508(1)	3860(1)	3798(3)	36(1)
C(8)	2712(1)	4775(1)	1047(3)	36(1)
O(9)	1786(1)	5876(1)	6789(3)	35(1)
O(10)	5002(1)	6203(1)	3603(2)	34(1)
C(11)	2849(1)	6884(1)	3452(3)	26(1)
C(12)	3516(1)	7336(1)	1899(3)	26(1)
C(13)	3858(1)	8056(1)	2510(3)	27(1)
C(14)	4476(1)	8493(1)	1075(3)	29(1)
C(15)	4715(1)	8207(1)	-1030(3)	33(1)
C(16)	4357(1)	7498(1)	-1684(3)	34(1)
C(17)	3766(1)	7060(1)	-218(3)	31(1)
C(18)	4884(1)	9257(1)	1829(4)	41(1)
C(19)	1836(1)	7262(1)	4122(3)	41(1)

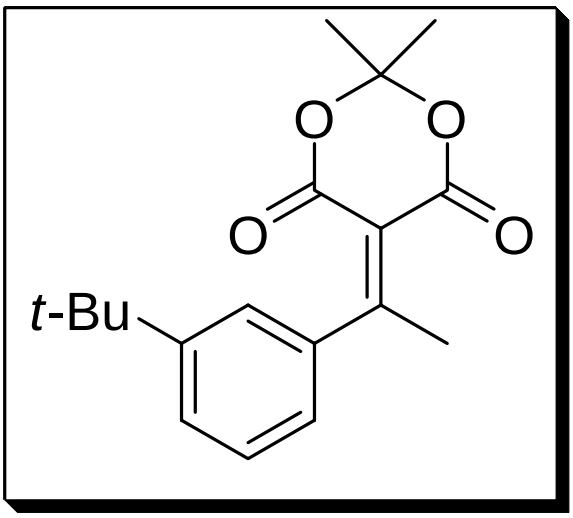
Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
H(7X)	3878	3829	5238	53
H(7Y)	3961	3658	2608	53
H(7Z)	2856	3562	3874	53
H(8X)	2056	4482	1014	54
H(8Y)	3184	4597	-144	54
H(8Z)	2553	5313	813	54
H(13)	3666	8254	3935	33
H(15)	5129	8499	-2037	39
H(16)	4517	7313	-3140	40
H(17)	3531	6572	-662	37
H(18X)	5473	9411	867	61
H(18Y)	5126	9223	3387	61
H(18Z)	4316	9633	1722	61
H(19X)	1445	6930	5146	62
H(19Y)	1409	7359	2783	62
H(19Z)	1992	7742	4875	62

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3579(15)
O(1)-C(2)	1.4419(15)
C(2)-O(3)	1.4397(16)
C(2)-C(7)	1.5041(17)
C(2)-C(8)	1.512(2)
O(3)-C(4)	1.3553(15)
C(4)-O(9)	1.2041(16)
C(4)-C(5)	1.4853(18)
C(5)-C(11)	1.3544(17)
C(5)-C(6)	1.4886(18)
C(6)-O(10)	1.1996(15)
C(11)-C(12)	1.4859(18)
C(11)-C(19)	1.5006(19)
C(12)-C(17)	1.3895(19)
C(12)-C(13)	1.3924(17)
C(13)-C(14)	1.3931(19)
C(14)-C(15)	1.387(2)
C(14)-C(18)	1.5130(19)
C(15)-C(16)	1.386(2)
C(16)-C(17)	1.387(2)
C(6)-O(1)-C(2)	118.67(10)
O(3)-C(2)-O(1)	108.95(10)
O(3)-C(2)-C(7)	105.96(11)
O(1)-C(2)-C(7)	106.39(11)
O(3)-C(2)-C(8)	111.42(11)
O(1)-C(2)-C(8)	110.95(12)
C(7)-C(2)-C(8)	112.89(12)
C(4)-O(3)-C(2)	119.13(10)
O(9)-C(4)-O(3)	118.43(12)
O(9)-C(4)-C(5)	126.40(13)
O(3)-C(4)-C(5)	115.12(11)
C(11)-C(5)-C(4)	122.71(12)
C(11)-C(5)-C(6)	122.94(12)
C(4)-C(5)-C(6)	114.25(11)
O(10)-C(6)-O(1)	119.28(12)
O(10)-C(6)-C(5)	125.05(12)
O(1)-C(6)-C(5)	115.49(11)
C(5)-C(11)-C(12)	121.29(12)
C(5)-C(11)-C(19)	124.15(13)
C(12)-C(11)-C(19)	114.48(11)
C(17)-C(12)-C(13)	119.10(13)
C(17)-C(12)-C(11)	120.55(12)
C(13)-C(12)-C(11)	120.28(12)
C(12)-C(13)-C(14)	121.31(13)
C(15)-C(14)-C(13)	118.51(13)
C(15)-C(14)-C(18)	121.33(13)
C(13)-C(14)-C(18)	120.16(14)
C(16)-C(15)-C(14)	120.79(13)
C(15)-C(16)-C(17)	120.18(14)
C(16)-C(17)-C(12)	120.05(13)

Crystallographic data for 2.81



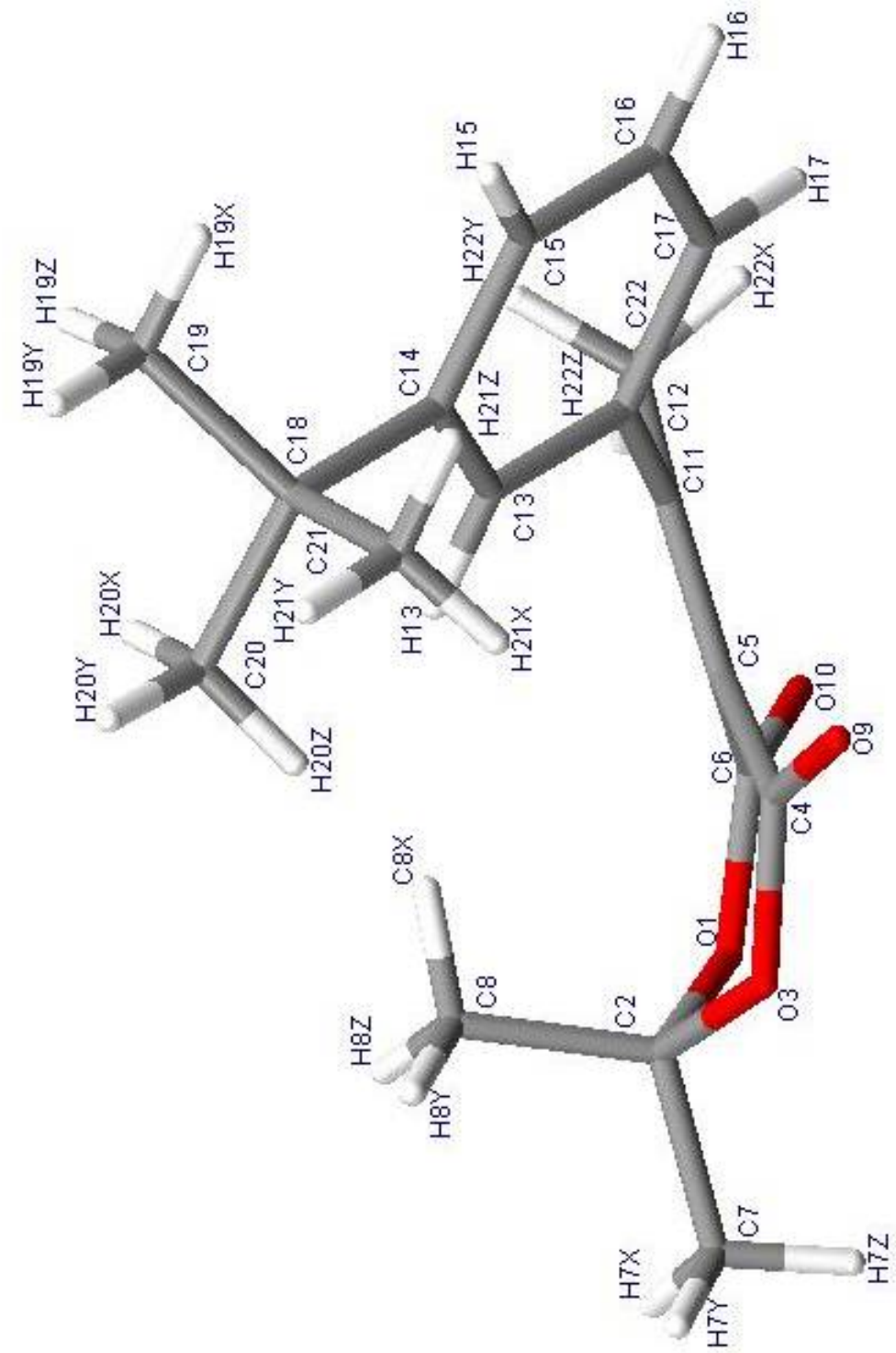

H16
C16
H15
H17
C17
H22Y
C15
H22X
C22
H19X
H19Z
H19Y
C19
C14
H22Z
C12
C18
H21Z
C11
C13
C21
H20X
H21Y
H13
H21X
C5
H20Y
C20
O10
H20Z
C6
O9
C4
C8X
O1
C8
O3
C2
H8Z
H8Y
C7
H7X
H7Y
H7Z

Table 1 Crystal data and structure refinement for $C_{18}H_{22}O_4$

Empirical formula	$C_{18}H_{22}O_4$
Formula weight	302.36
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 7.0650(4) Å alpha = 90º
	b = 26.7547(14) Å beta = 92.108(1)º
	c = 8.9248(5) Å gamma = 90º
Volume	1685.84(16) $Å^3$
Z, Calculated density	4, 1.191 mg/m^3
Absorption coefficient	0.083 mm^{-1}
F(000)	648
Crystal size	0.35 x 0.31 x 0.11 mm
Theta range for data collection	2.41 to 30.05º
Limiting indices	-9<=h<=9, -37<=k<=34, -12<=l<=11
Reflections collected / unique	13687 / 4896 [R_{int} = 0.0399]
Completeness to theta = 27.88	99.2%
Absorption correction	None
Max. and min. transmission	0.948 and 0.910
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4896 / 0 / 206
Goodness-of-fit on F^2	1.768
Final R indices [I>2sigma(I)]	R1 = 0.0499, wR2 = 0.0825
R indices (all data)	R1 = 0.0637, wR2 = 0.0841
Extinction coefficient	0.0134(9)
Largest diff. peak and hole	0.338 and -0.232 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	-2107(1)	3939(1)	7134(1)	32(1)
C(2)	-1801(1)	4348(1)	6108(1)	28(1)
O(3)	206(1)	4461(1)	6133(1)	29(1)
C(4)	1437(2)	4078(1)	5915(1)	26(1)
C(5)	650(1)	3565(1)	6083(1)	25(1)
C(6)	-974(2)	3531(1)	7096(1)	30(1)
C(7)	-2758(2)	4793(1)	6778(2)	38(1)
C(8)	-2515(2)	4228(1)	4530(1)	36(1)
O(9)	3074(1)	4181(1)	5727(1)	35(1)
O(10)	-1305(1)	3183(1)	7910(1)	43(1)
C(11)	1439(2)	3157(1)	5456(1)	27(1)
C(12)	2970(2)	3193(1)	4349(1)	27(1)
C(13)	2702(2)	3477(1)	3038(1)	27(1)
C(14)	4044(2)	3493(1)	1930(1)	27(1)
C(15)	5700(2)	3211(1)	2182(1)	31(1)
C(16)	5990(2)	2927(1)	3468(1)	35(1)
C(17)	4628(2)	2914(1)	4555(1)	34(1)
C(18)	3783(2)	3807(1)	496(1)	31(1)
C(19)	4092(2)	3480(1)	-891(1)	38(1)
C(20)	1801(2)	4040(1)	338(2)	43(1)
C(21)	5265(2)	4232(1)	554(2)	46(1)
C(22)	806(2)	2628(1)	5748(2)	40(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3).

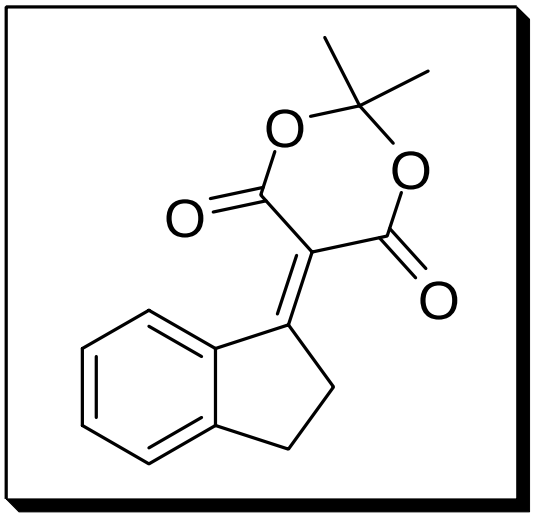
	x	y	z	U(eq)
H(7X)	-4119	4728	6831	56
H(7Y)	-2559	5088	6149	56
H(7Z)	-2220	4855	7789	56
C(8X)	-1832	3938	4156	54
H(8Y)	-2302	4516	3879	54
H(8Z)	-3873	4154	4534	54
H(13)	1567	3665	2898	32
H(15)	6646	3215	1453	37
H(16)	7126	2741	3610	42
H(17)	4825	2716	5431	40
H(19X)	5334	3318	-794	58
H(19Y)	4037	3689	-1793	58
H(19Z)	3100	3224	-970	58
H(20X)	846	3774	305	65
H(20Y)	1698	4236	-589	65
H(20Z)	1592	4258	1198	65
H(21X)	5093	4436	1450	69
H(21Y)	5101	4441	-343	69
H(21Z)	6541	4088	591	69
H(22X)	1733	2463	6425	59
H(22Y)	706	2445	4798	59
H(22Z)	-431	2634	6209	59

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3564(12)
O(1)-C(2)	1.4467(12)
C(2)-O(3)	1.4489(12)
C(2)-C(7)	1.5054(15)
C(2)-C(8)	1.5124(16)
O(3)-C(4)	1.3611(12)
C(4)-O(9)	1.2059(12)
C(4)-C(5)	1.4916(14)
C(5)-C(11)	1.3561(15)
C(5)-C(6)	1.4890(15)
C(6)-O(10)	1.2077(13)
C(11)-C(12)	1.4949(15)
C(11)-C(22)	1.5084(15)
C(12)-C(17)	1.3956(14)
C(12)-C(13)	1.4019(15)
C(13)-C(14)	1.3955(15)
C(14)-C(15)	1.4033(14)
C(14)-C(18)	1.5367(15)
C(15)-C(16)	1.3847(16)
C(16)-C(17)	1.3913(16)
C(18)-C(20)	1.5347(16)
C(18)-C(19)	1.5385(16)
C(18)-C(21)	1.5443(16)
C(6)-O(1)-C(2)	119.39(8)
O(1)-C(2)-O(3)	108.47(8)
O(1)-C(2)-C(7)	105.50(9)
O(3)-C(2)-C(7)	106.41(9)
O(1)-C(2)-C(8)	112.18(9)
O(3)-C(2)-C(8)	110.55(9)
C(7)-C(2)-C(8)	113.40(10)
C(4)-O(3)-C(2)	118.12(8)
O(9)-C(4)-O(3)	118.06(10)
O(9)-C(4)-C(5)	125.88(10)
O(3)-C(4)-C(5)	115.77(9)
C(11)-C(5)-C(6)	122.57(10)
C(11)-C(5)-C(4)	122.64(10)
C(6)-C(5)-C(4)	114.61(9)
O(10)-C(6)-O(1)	118.50(10)
O(10)-C(6)-C(5)	125.70(10)
O(1)-C(6)-C(5)	115.72(9)
C(5)-C(11)-C(12)	122.60(10)
C(5)-C(11)-C(22)	123.68(10)
C(12)-C(11)-C(22)	113.66(10)

C(17)-C(12)-C(13)	119.13(10)
C(17)-C(12)-C(11)	120.14(10)
C(13)-C(12)-C(11)	120.55(9)
C(14)-C(13)-C(12)	122.22(10)
C(13)-C(14)-C(15)	117.03(10)
C(13)-C(14)-C(18)	122.86(10)
C(15)-C(14)-C(18)	120.10(10)
C(16)-C(15)-C(14)	121.62(10)
C(15)-C(16)-C(17)	120.45(11)
C(16)-C(17)-C(12)	119.55(11)
C(20)-C(18)-C(14)	112.31(9)
C(20)-C(18)-C(19)	108.22(10)
C(14)-C(18)-C(19)	110.04(9)
C(20)-C(18)-C(21)	108.65(10)
C(14)-C(18)-C(21)	108.31(9)
C(19)-C(18)-C(21)	109.25(10)

Crystallographic data for 2.105



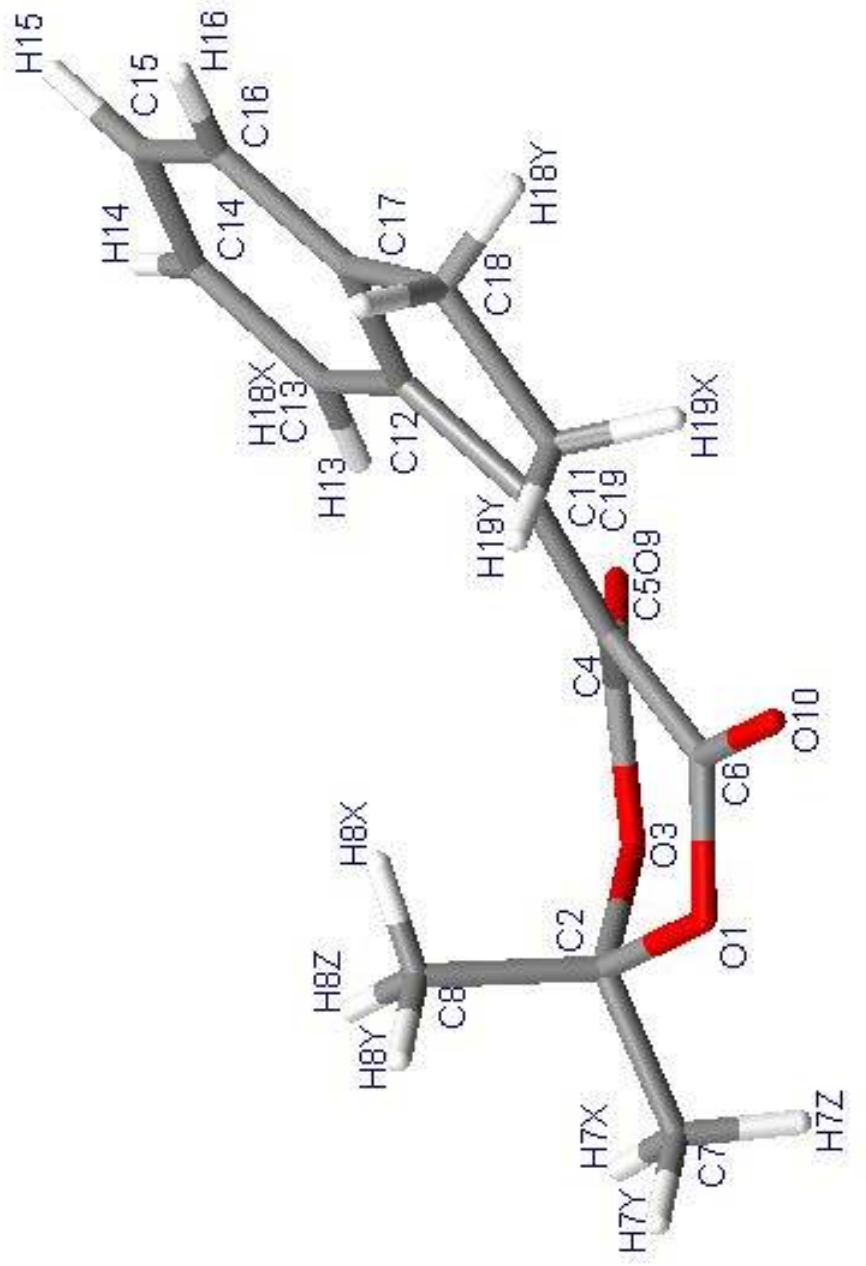

H15
C15
H16
C16
H14
C14
C17
H18Y
C18
H18X
C13
C12
H19X
H13
C11
C19
H19Y
C5O9
C4
O10
C6
H8X
O3
H8Z
C2
O1
H8Y
C8
H7X
H7Z
H7Y

Table 1 Crystal data and structure refinement for $C_{15}H_{14}O_4$

Empirical formula	$C_{15}H_{14}O_4$
Formula weight	258.26
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 12.4109(5) Å alpha = 90º
	b = 7.3211(3) Å beta = 111.371(1)º
	c = 14.7400(5) Å gamma = 90º
Volume	1247.21(8) $Å^3$
Z, Calculated density	4, 1.375 mg/m^3
Absorption coefficient	0.100 mm^{-1}
F(000)	544
Crystal size	0.40 x 0.22 x 0.20 mm
Theta range for data collection	1.84 to 30.03°
Limiting indices	-13<=h<=17, -8<=k<=10, -20<=l<=20
Reflections collected / unique	9977 / 3621 [R_{int} = 0.0291]
Completeness to theta = 27.88	99.2%
Absorption correction	None
Max. and min. transmission	0.947 and 0.888
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3621 / 0 / 175
Goodness-of-fit on F^2	1.982
Final R indices [I>2sigma(I)]	R1 = 0.0443, wR2 = 0.1081
R indices (all data)	R1 = 0.0488, wR2 = 0.1093
Extinction coefficient	0.0161(10)
Absolute structure parameter	0.012(4)
Largest diff. peak and hole	0.407 and -0.229 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	698(1)	2327(1)	5539(1)	28(1)
C(2)	1867(1)	1803(1)	6111(1)	25(1)
O(3)	2627(1)	3306(1)	6142(1)	27(1)
C(4)	2556(1)	4073(1)	5281(1)	25(1)
C(5)	1512(1)	3596(1)	4428(1)	24(1)
C(6)	481(1)	3135(1)	4662(1)	26(1)
C(7)	1902(1)	1571(2)	7138(1)	33(1)
C(8)	2224(1)	121(2)	5700(1)	32(1)
O(9)	3290(1)	5149(1)	5288(1)	36(1)
O(10)	-516(1)	3405(1)	4152(1)	34(1)
C(11)	1444(1)	3568(1)	3482(1)	24(1)
C(12)	2371(1)	3566(1)	3081(1)	25(1)
C(13)	3581(1)	3575(2)	3536(1)	31(1)
C(14)	4254(1)	3413(2)	2970(1)	34(1)
C(15)	3746(1)	3233(2)	1960(1)	35(1)
C(16)	2561(1)	3210(2)	1505(1)	32(1)
C(17)	1873(1)	3385(1)	2063(1)	26(1)
C(18)	580(1)	3355(2)	1701(1)	31(1)
C(19)	303(1)	3356(2)	2632(1)	29(1)

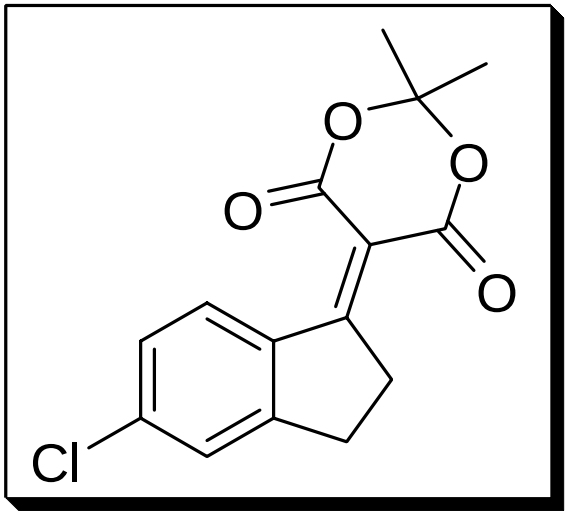
Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
H(7X)	2700	1333	7576	49
H(7Y)	1410	540	7163	49
H(7Z)	1621	2688	7344	49
H(8X)	2180	369	5034	48
H(8Y)	1705	-892	5693	48
H(8Z)	3020	-208	6106	48
H(13)	3934	3690	4224	37
H(14)	5074	3424	3273	41
H(15)	4222	3126	1583	42
H(16)	2217	3076	818	38
H(18X)	271	2245	1309	37
H(18Y)	251	4446	1299	37
H(19X)	-222	4381	2621	35
H(19Y)	-78	2197	2690	35

Table 4 Bond lengths [Å] and angles [º]

O(1)-C(6)	1.3575(11)
O(1)-C(2)	1.4391(12)
C(2)-O(3)	1.4391(12)
C(2)-C(8)	1.5087(14)
C(2)-C(7)	1.5088(13)
O(3)-C(4)	1.3607(11)
C(4)-O(9)	1.2011(12)
C(4)-C(5)	1.4808(13)
C(5)-C(11)	1.3668(12)
C(5)-C(6)	1.4797(14)
C(6)-O(10)	1.2070(12)
C(11)-C(12)	1.4716(14)
C(11)-C(19)	1.5185(13)
C(12)-C(13)	1.4045(14)
C(12)-C(17)	1.4054(12)
C(13)-C(14)	1.3846(15)
C(14)-C(15)	1.3953(15)
C(15)-C(16)	1.3768(16)
C(16)-C(17)	1.3901(14)
C(17)-C(18)	1.4950(15)
C(18)-C(19)	1.5320(13)
C(6)-O(1)-C(2)	118.78(7)
O(3)-C(2)-O(1)	108.90(8)
O(3)-C(2)-C(8)	110.59(8)
O(1)-C(2)-C(8)	111.32(8)
O(3)-C(2)-C(7)	106.01(8)
O(1)-C(2)-C(7)	105.78(8)
C(8)-C(2)-C(7)	113.93(9)
C(4)-O(3)-C(2)	117.85(7)
O(9)-C(4)-O(3)	118.11(8)
O(9)-C(4)-C(5)	126.01(9)
O(3)-C(4)-C(5)	115.68(8)
C(11)-C(5)-C(6)	119.79(9)
C(11)-C(5)-C(4)	125.38(9)
C(6)-C(5)-C(4)	114.83(8)
O(10)-C(6)-O(1)	117.80(9)
O(10)-C(6)-C(5)	126.54(9)
O(1)-C(6)-C(5)	115.67(8)
C(5)-C(11)-C(12)	130.03(9)
C(5)-C(11)-C(19)	122.37(9)
C(12)-C(11)-C(19)	107.41(8)
C(13)-C(12)-C(17)	119.21(9)
C(13)-C(12)-C(11)	131.63(9)
C(17)-C(12)-C(11)	108.96(9)
C(14)-C(13)-C(12)	119.12(9)
C(13)-C(14)-C(15)	120.95(11)
C(16)-C(15)-C(14)	120.51(10)
C(15)-C(16)-C(17)	119.25(10)
C(16)-C(17)-C(12)	120.96(10)
C(16)-C(17)-C(18)	126.70(9)
C(12)-C(17)-C(18)	112.31(9)
C(17)-C(18)-C(19)	104.01(8)
C(11)-C(19)-C(18)	107.01(8)

Crystallographic data for 2.107



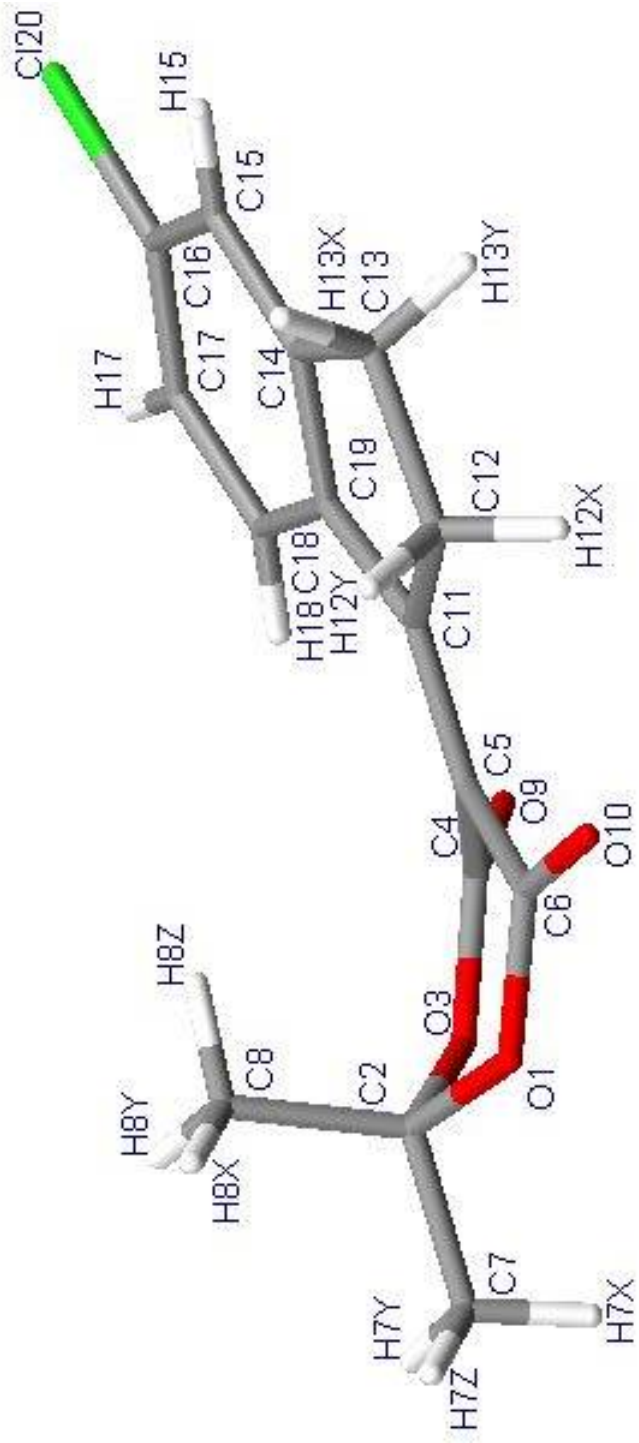

Cl20
H15
C15
C16
H13X
C13
H13Y
H17
C17
C14
C19
C12
H12X
H18
C18
H12Y
C11
C5
O9
C4
O10
C6
H8Z
O3
C8
C2
O1
H8Y
H8X
C7
H7Y
H7X
H7Z

Table 1 Crystal data and structure refinement for $C_{15}H_{13}ClO_4$

Empirical formula	$C_{15}H_{13}ClO_4$
Formula weight	292.70
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 7.1614(3) Å alpha = 76.021(1)º
	b = 7.8727(3) Å beta = 74.192(1)º
	c = 12.7902(5) Å gamma = 78.317(1)º
Volume	666.03(5) $Å^3$
Z, Calculated density	2, 1.460 mg/m^3
Absorption coefficient	0.297 mm^{-1}
F(000)	304
Crystal size	0.30 x 0.26 x 0.20 mm
Theta range for data collection	1.69 to 30.03°
Limiting indices	-10<=h<=10, -10<=k<=11, -18<=l<=18
Reflections collected / unique	6427 / 3721 [R_{int} = 0.0135]
Completeness to theta = 27.88	95.9%
Absorption correction	None
Max. and min. transmission	0.947 and 0.888
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3721 / 0 / 184
Goodness-of-fit on F^2	1.944
Final R indices [I>2sigma(I)]	R1 = 0.0375, wR2 = 0.1183
R indices (all data)	R1 = 0.0399, wR2 = 0.1198
Extinction coefficient	0.0161(10)
Absolute structure parameter	0.022(9)
Largest diff. peak and hole	0.355 and -0.246 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	2664(1)	6340(1)	9725(1)	28(1)
C(2)	3038(2)	8094(1)	9141(1)	25(1)
O(3)	1510(1)	8902(1)	8564(1)	27(1)
C(4)	1004(2)	7973(1)	7945(1)	25(1)
C(5)	1811(2)	6066(1)	8084(1)	24(1)
C(6)	2232(2)	5241(1)	9183(1)	26(1)
C(7)	2797(2)	9128(2)	10026(1)	32(1)
C(8)	5028(2)	8050(2)	8349(1)	32(1)
O(9)	-134(1)	8731(1)	7383(1)	34(1)
O(10)	2194(1)	3718(1)	9636(1)	34(1)
C(11)	2090(2)	5073(1)	7301(1)	24(1)
C(12)	2587(2)	3069(1)	7552(1)	27(1)
C(13)	2698(2)	2438(1)	6488(1)	28(1)
C(14)	2473(2)	4107(1)	5649(1)	25(1)
C(15)	2598(2)	4233(2)	4533(1)	28(1)
C(16)	2363(2)	5906(2)	3876(1)	28(1)
C(17)	2028(2)	7428(2)	4306(1)	30(1)
C(18)	1888(2)	7294(1)	5426(1)	29(1)
C(19)	2088(2)	5614(1)	6117(1)	24(1)
Cl(20)	2458(1)	6099(1)	2486(1)	36(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

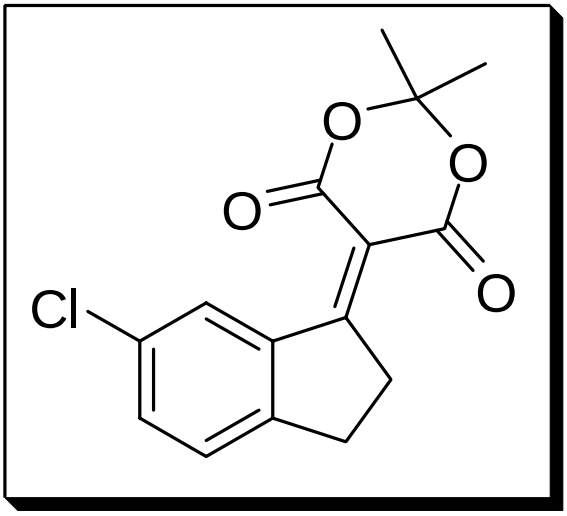
	x	y	z	U(eq)
H(7X)	1507	9044	10538	47
H(7Y)	2903	10371	9683	47
H(7Z)	3825	8643	10435	47
H(8X)	6039	7481	8757	48
H(8Y)	5260	9262	7987	48
H(8Z)	5078	7379	7786	48
H(12X)	1561	2547	8168	32
H(12Y)	3860	2712	7766	32
H(13X)	3975	1702	6257	33
H(13Y)	1631	1741	6596	33
H(15)	2837	3202	4227	34
H(17)	1896	8559	3835	36
H(18)	1657	8332	5724	35

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3560(12)
O(1)-C(2)	1.4419(12)
C(2)-O(3)	1.4408(12)
C(2)-C(7)	1.5025(15)
C(2)-C(8)	1.5062(15)
O(3)-C(4)	1.3551(12)
C(4)-O(9)	1.2050(12)
C(4)-C(5)	1.4816(14)
C(5)-C(11)	1.3640(15)
C(5)-C(6)	1.4832(14)
C(6)-O(10)	1.2008(13)
C(11)-C(19)	1.4710(14)
C(11)-C(12)	1.5195(14)
C(12)-C(13)	1.5347(15)
C(13)-C(14)	1.4942(14)
C(14)-C(15)	1.3860(15)
C(14)-C(19)	1.4007(15)
C(15)-C(16)	1.3857(16)
C(16)-C(17)	1.3883(17)
C(16)-Cl(20)	1.7312(11)
C(17)-C(18)	1.3866(16)
C(18)-C(19)	1.4070(14)
C(6)-O(1)-C(2)	119.28(8)
O(3)-C(2)-O(1)	108.91(8)
O(3)-C(2)-C(7)	106.23(9)
O(1)-C(2)-C(7)	105.45(8)
O(3)-C(2)-C(8)	110.96(9)
O(1)-C(2)-C(8)	111.37(9)
C(7)-C(2)-C(8)	113.60(9)
C(4)-O(3)-C(2)	119.04(8)
O(9)-C(4)-O(3)	117.91(10)
O(9)-C(4)-C(5)	125.76(10)
O(3)-C(4)-C(5)	116.20(9)
C(11)-C(5)-C(4)	124.38(9)
C(11)-C(5)-C(6)	120.53(9)
C(4)-C(5)-C(6)	115.03(9)
O(10)-C(6)-O(1)	117.85(10)
O(10)-C(6)-C(5)	126.26(10)
O(1)-C(6)-C(5)	115.88(9)
C(5)-C(11)-C(19)	130.44(9)
C(5)-C(11)-C(12)	122.20(9)
C(19)-C(11)-C(12)	107.30(9)
C(11)-C(12)-C(13)	106.66(8)
C(14)-C(13)-C(12)	104.29(8)
C(15)-C(14)-C(19)	121.64(10)
C(15)-C(14)-C(13)	126.32(10)
C(19)-C(14)-C(13)	112.03(9)
C(16)-C(15)-C(14)	118.16(10)
C(15)-C(16)-C(17)	121.73(10)
C(15)-C(16)-Cl(20)	119.08(9)
C(17)-C(16)-Cl(20)	119.18(8)
C(18)-C(17)-C(16)	119.87(10)

C(17)-C(18)-C(19)	119.69(11)
C(14)-C(19)-C(18)	118.87(10)
C(14)-C(19)-C(11)	109.38(9)
C(18)-C(19)-C(11)	131.63(10)

Crystallographic data for 2.112



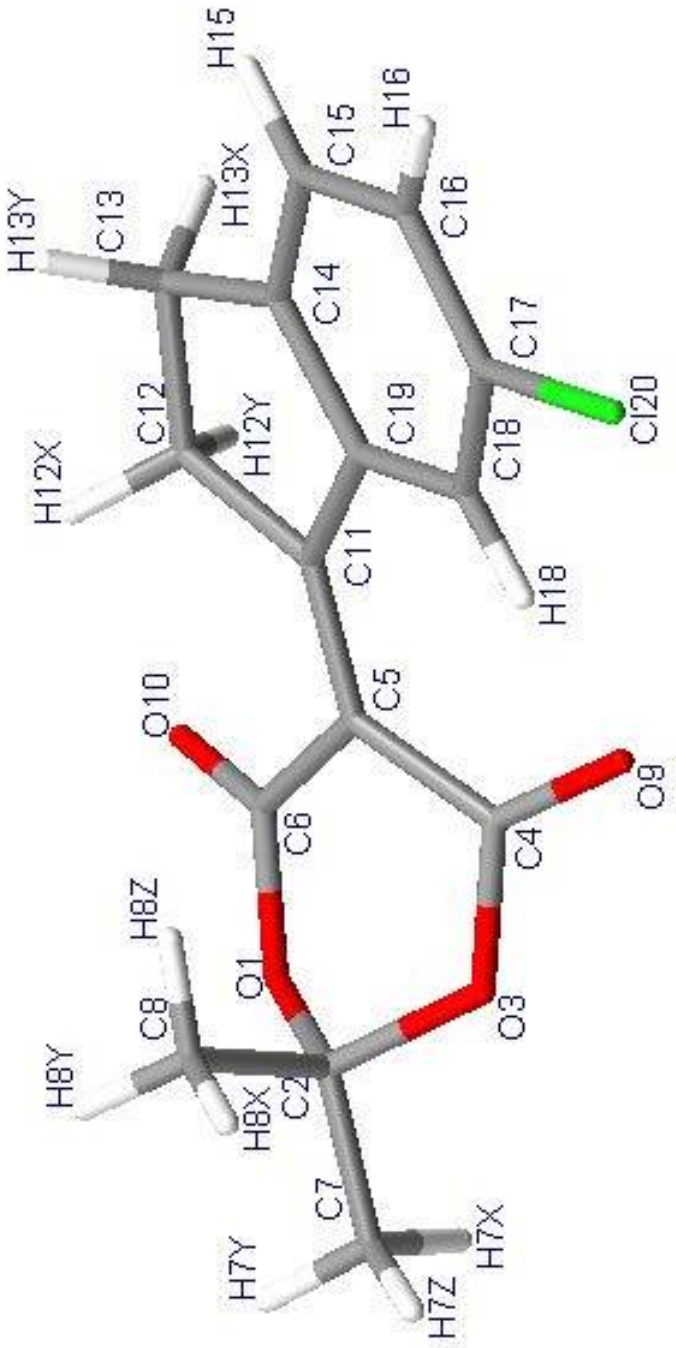

H15
C15
H16
C16
H13X
C13
H13Y
C14
C17
Cl20
C12
H12Y
C19
C18
H12X
C11
H18
O10
C5
O9
C6
C4
H8Z
O1
O3
C8
H8Y
H8X
C2
C7
H7Y
H7X
H7Z

Table 1 Crystal data and structure refinement for $C_{15}H_{13}ClO_4$

Empirical formula	$C_{15}H_{13}ClO_4$
Formula weight	292.70
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 7.2743(4) Å alpha = 84.893(1)º
	b = 7.3437(4) Å beta = 77.594(1)º
	c = 12.4759(6) Å gamma = 86.905(1)º
Volume	647.90(6) $Å^3$
Z, Calculated density	2, 1.500 mg/m^3
Absorption coefficient	0.305 mm^{-1}
F(000)	304
Crystal size	0.24 x 0.23 x 0.20 mm
Theta range for data collection	1.68 to 30.03°
Limiting indices	-10<=h<=10, -10<=k<=9, -17<=l<=17
Reflections collected / unique	5415 / 3641 [R_{int} = 0.0227]
Completeness to theta = 27.88	95.9%
Absorption correction	None
Max. and min. transmission	0.947 and 0.888
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3641 / 0 / 184
Goodness-of-fit on F^2	1.835
Final R indices [I>2sigma(I)]	R1 = 0.0391, wR2 = 0.0761
R indices (all data)	R1 = 0.0462, wR2 = 0.0771
Extinction coefficient	0.0248(19)
Absolute structure parameter	0.022(9)
Largest diff. peak and hole	0.388 and -0.303 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	2589(1)	4431(1)	-4813(1)	30(1)
C(2)	2358(2)	2522(2)	-4455(1)	27(1)
O(3)	3776(1)	1940(1)	-3834(1)	30(1)
C(4)	4062(2)	2986(2)	-3049(1)	26(1)
C(5)	3086(2)	4817(2)	-2999(1)	24(1)
C(6)	2639(2)	5624(2)	-4048(1)	27(1)
C(7)	2809(2)	1522(2)	-5486(1)	36(1)
C(8)	415(2)	2197(2)	-3769(1)	34(1)
O(9)	5161(1)	2404(1)	-2491(1)	36(1)
O(10)	2362(2)	7219(1)	-4288(1)	41(1)
C(11)	2658(2)	5787(2)	-2086(1)	23(1)
C(12)	1927(2)	7765(2)	-2135(1)	28(1)
C(13)	1576(2)	8376(2)	-964(1)	28(1)
C(14)	2054(2)	6716(2)	-287(1)	25(1)
C(15)	1931(2)	6546(2)	845(1)	30(1)
C(16)	2368(2)	4892(2)	1354(1)	30(1)
C(17)	2920(2)	3410(2)	728(1)	26(1)
C(18)	3109(2)	3541(2)	-401(1)	24(1)
C(19)	2674(2)	5230(2)	-922(1)	22(1)
Cl(20)	3446(1)	1313(1)	1394(1)	34(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3).

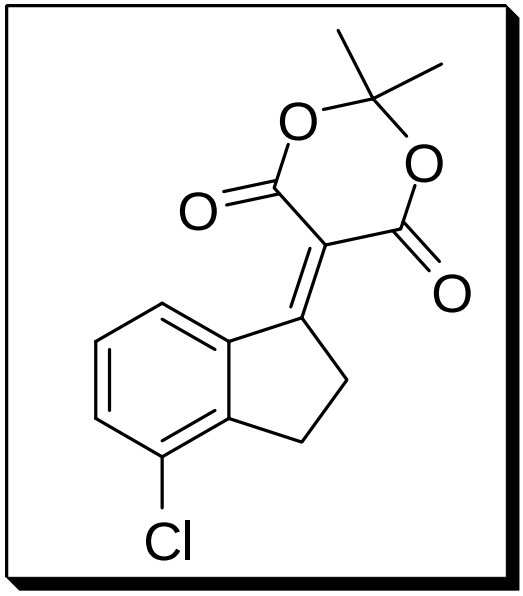
	x	y	z	U(eq)
H(7X)	4083	1805	-5894	54
H(7Y)	1900	1907	-5945	54
H(7Z)	2739	202	-5289	54
H(8X)	283	887	-3554	52
H(8Y)	-527	2625	-4198	52
H(8Z)	226	2869	-3107	52
H(12X)	743	7865	-2409	33
H(12Y)	2865	8544	-2637	33
H(13X)	2394	9393	-926	33
H(13Y)	244	8778	-712	33
H(15)	1547	7570	1264	35
H(16)	2292	4764	2127	35
H(18)	3522	2514	-813	29

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3593(15)
O(1)-C(2)	1.4403(15)
C(2)-O(3)	1.4435(15)
C(2)-C(7)	1.5035(18)
C(2)-C(8)	1.506(2)
O(3)-C(4)	1.3537(15)
C(4)-O(9)	1.2066(15)
C(4)-C(5)	1.4863(17)
C(5)-C(11)	1.3668(17)
C(5)-C(6)	1.4810(17)
C(6)-O(10)	1.2004(15)
C(11)-C(19)	1.4754(17)
C(11)-C(12)	1.5202(17)
C(12)-C(13)	1.5310(18)
C(13)-C(14)	1.4895(18)
C(14)-C(15)	1.3903(18)
C(14)-C(19)	1.4030(17)
C(15)-C(16)	1.3741(19)
C(16)-C(17)	1.3872(18)
C(17)-C(18)	1.3813(18)
C(17)-Cl(20)	1.7468(13)
C(18)-C(19)	1.4016(17)
C(6)-O(1)-C(2)	118.49(10)
O(1)-C(2)-O(3)	108.39(10)
O(1)-C(2)-C(7)	105.86(11)
O(3)-C(2)-C(7)	106.70(11)
O(1)-C(2)-C(8)	111.10(11)
O(3)-C(2)-C(8)	110.65(11)
C(7)-C(2)-C(8)	113.85(12)
C(4)-O(3)-C(2)	119.11(10)
O(9)-C(4)-O(3)	117.67(12)
O(9)-C(4)-C(5)	125.41(12)
O(3)-C(4)-C(5)	116.79(11)
C(11)-C(5)-C(6)	119.70(11)
C(11)-C(5)-C(4)	124.92(11)
C(6)-C(5)-C(4)	115.33(11)
O(10)-C(6)-O(1)	117.67(12)
O(10)-C(6)-C(5)	126.23(12)
O(1)-C(6)-C(5)	116.08(11)
C(5)-C(11)-C(19)	130.93(11)
C(5)-C(11)-C(12)	122.12(11)
C(19)-C(11)-C(12)	106.87(10)
C(11)-C(12)-C(13)	107.23(11)
C(14)-C(13)-C(12)	104.23(10)
C(15)-C(14)-C(19)	120.77(12)
C(15)-C(14)-C(13)	126.91(12)
C(19)-C(14)-C(13)	112.32(11)
C(16)-C(15)-C(14)	119.78(13)
C(15)-C(16)-C(17)	119.29(13)
C(18)-C(17)-C(16)	122.49(13)
C(18)-C(17)-Cl(20)	118.91(10)

C(16)-C(17)-Cl(20)	118.58(10)
C(17)-C(18)-C(19)	118.25(12)
C(18)-C(19)-C(14)	119.37(12)
C(18)-C(19)-C(11)	131.28(11)
C(14)-C(19)-C(11)	109.30(11)

Crystallographic data for 2.114



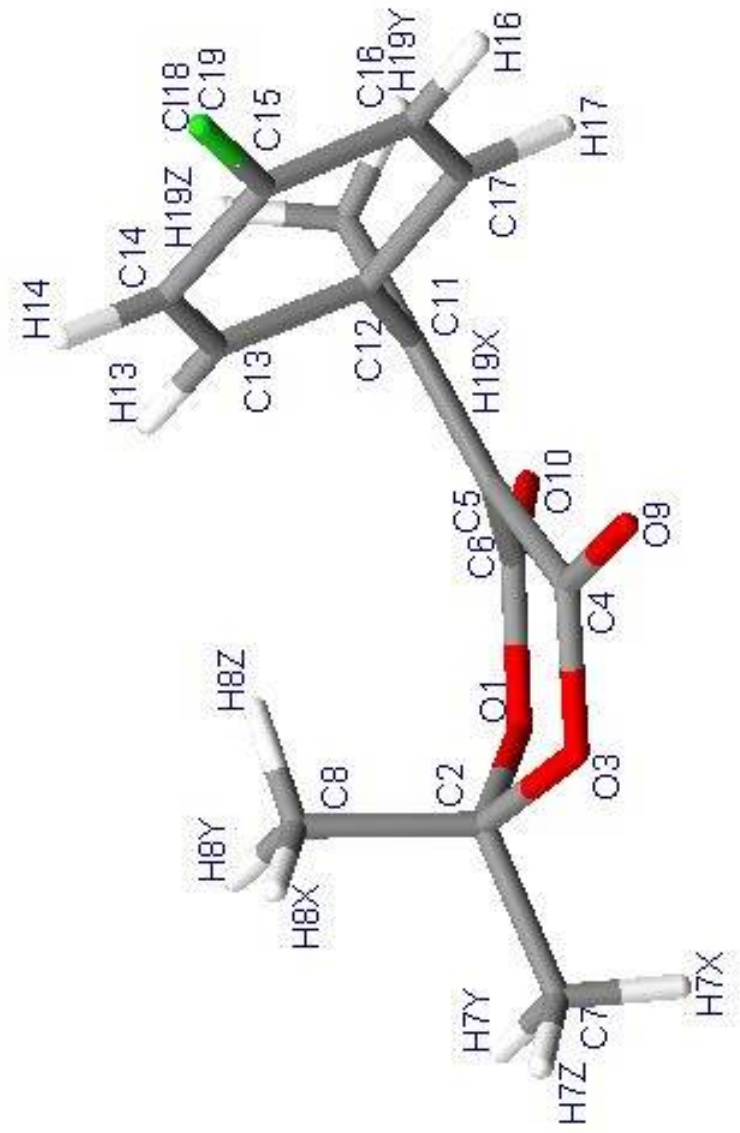

H14
C14
H19Z
Cl18
C19
C15
C16
H19Y
H16
H17
C17
H13
C13
C12
C11
H19X
C6
C5
O10
O9
C4
H8Z
O1
O3
C8
C2
H8Y
H8X
H7Y
C7
H7X
H7Z

Table 1 Crystal data and structure refinement for $C_{15}H_{13}ClO_4$

Empirical formula	$C_{15}H_{13}ClO_4$
Formula weight	292.70
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 8.0094(4) Å alpha = 101.999(1)º
	b = 9.2974(5) Å beta = 105.978(1)º
	c = 10.0005(5) Å gamma = 106.012(1)º
Volume	654.89(6) $Å^3$
Z, Calculated density	2, 1.484 mg/m^3
Absorption coefficient	0.302 mm^{-1}
F(000)	304
Crystal size	0.29 x 0.29 x 0.17 mm
Theta range for data collection	2.23 to 30.03°
Limiting indices	-11<=h<=9, -13<=k<=11, -14<=l<=14
Reflections collected / unique	5450 / 3665 [R_{int} = 0.0253]
Completeness to theta = 27.88	95.6%
Absorption correction	None
Max. and min. transmission	0.947 and 0.888
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3665 / 0 / 188
Goodness-of-fit on F^2	1.919
Final R indices [I>2sigma(I)]	R1 = 0.0382, wR2 = 0.1076
R indices (all data)	R1 = 0.0408, wR2 = 0.1085
Extinction coefficient	0.109(9)
Largest diff. peak and hole	0.334 and -0.322 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	7635(1)	11009(1)	7445(1)	24(1)
C(2)	7245(2)	11270(1)	8771(1)	24(1)
O(3)	7588(1)	10097(1)	9439(1)	28(1)
C(4)	6878(2)	8573(1)	8587(1)	24(1)
C(5)	5958(2)	8272(1)	6998(1)	22(1)
C(6)	6751(2)	9559(1)	6435(1)	22(1)
C(7)	8676(2)	12827(1)	9778(1)	34(1)
C(8)	5270(2)	11214(2)	8476(1)	30(1)
O(9)	7104(1)	7594(1)	9170(1)	31(1)
O(10)	6750(1)	9433(1)	5214(1)	29(1)
C(11)	4543(2)	6935(1)	6072(1)	22(1)
C(12)	3741(2)	6704(1)	4444(1)	26(1)
C(13)	2175(2)	5108(1)	3748(1)	27(1)
C(14)	2141(2)	4478(1)	4996(1)	24(1)
C(15)	991(2)	3030(1)	4945(1)	28(1)
C(16)	1076(2)	2619(1)	6212(1)	32(1)
C(17)	2324(2)	3679(1)	7541(1)	31(1)
C(18)	3526(2)	5124(1)	7631(1)	28(1)
C(19)	3456(2)	5532(1)	6342(1)	23(1)
Cl(20)	-533(1)	1716(1)	3257(1)	40(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3).

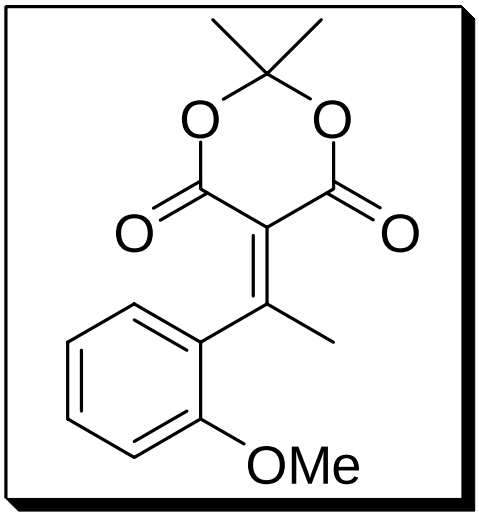
	x	y	z	U(eq)
H(7X)	9921	12782	9936	51
H(7Y)	8489	13056	10716	51
H(7Z)	8549	13657	9336	51
H(8X)	5088	12040	8045	46
H(8Y)	5030	11382	9395	46
H(8Z)	4410	10185	7796	46
H(12X)	4714	6736	4007	31
H(12Y)	3259	7549	4280	31
H(13X)	977	5225	3285	32
H(13Y)	2435	4411	3001	32
H(16)	287	1623	6168	38
H(17)	2359	3411	8412	38
H(18)	4430(20)	5796(16)	8581(15)	33(4)

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3609(13)
O(1)-C(2)	1.4323(12)
C(2)-O(3)	1.4413(13)
C(2)-C(7)	1.5052(15)
C(2)-C(8)	1.5113(16)
O(3)-C(4)	1.3582(13)
C(4)-O(9)	1.2050(13)
C(4)-C(5)	1.4847(14)
C(5)-C(11)	1.3614(15)
C(5)-C(6)	1.4868(14)
C(6)-O(10)	1.2021(13)
C(11)-C(19)	1.4774(15)
C(11)-C(12)	1.5198(14)
C(12)-C(13)	1.5240(16)
C(13)-C(14)	1.4885(15)
C(14)-C(15)	1.3873(16)
C(14)-C(19)	1.4087(15)
C(15)-C(16)	1.3871(17)
C(15)-Cl(20)	1.7372(12)
C(16)-C(17)	1.3849(17)
C(17)-C(18)	1.3888(17)
C(18)-C(19)	1.4090(14)
C(6)-O(1)-C(2)	118.19(8)
O(1)-C(2)-O(3)	108.23(8)
O(1)-C(2)-C(7)	106.02(9)
O(3)-C(2)-C(7)	106.49(9)
O(1)-C(2)-C(8)	110.92(9)
O(3)-C(2)-C(8)	111.38(9)
C(7)-C(2)-C(8)	113.48(10)
C(4)-O(3)-C(2)	118.36(8)
O(9)-C(4)-O(3)	117.78(9)
O(9)-C(4)-C(5)	125.73(10)
O(3)-C(4)-C(5)	116.43(9)
C(11)-C(5)-C(4)	125.26(9)
C(11)-C(5)-C(6)	120.33(9)
C(4)-C(5)-C(6)	114.38(9)
O(10)-C(6)-O(1)	117.83(10)
O(10)-C(6)-C(5)	126.83(10)
O(1)-C(6)-C(5)	115.26(9)
C(5)-C(11)-C(19)	131.47(9)
C(5)-C(11)-C(12)	121.53(9)
C(19)-C(11)-C(12)	106.96(9)
C(11)-C(12)-C(13)	107.66(9)
C(14)-C(13)-C(12)	103.94(8)
C(15)-C(14)-C(19)	119.90(10)
C(15)-C(14)-C(13)	127.30(10)
C(19)-C(14)-C(13)	112.80(10)
C(16)-C(15)-C(14)	120.93(11)
C(16)-C(15)-Cl(20)	120.29(9)
C(14)-C(15)-Cl(20)	118.77(9)
C(17)-C(16)-C(15)	119.11(11)
C(16)-C(17)-C(18)	121.59(11)

C(17)-C(18)-C(19)	119.25(11)
C(14)-C(19)-C(18)	119.16(10)
C(14)-C(19)-C(11)	108.57(9)
C(18)-C(19)-C(11)	132.27(10)

Crystallographic data for 2.148



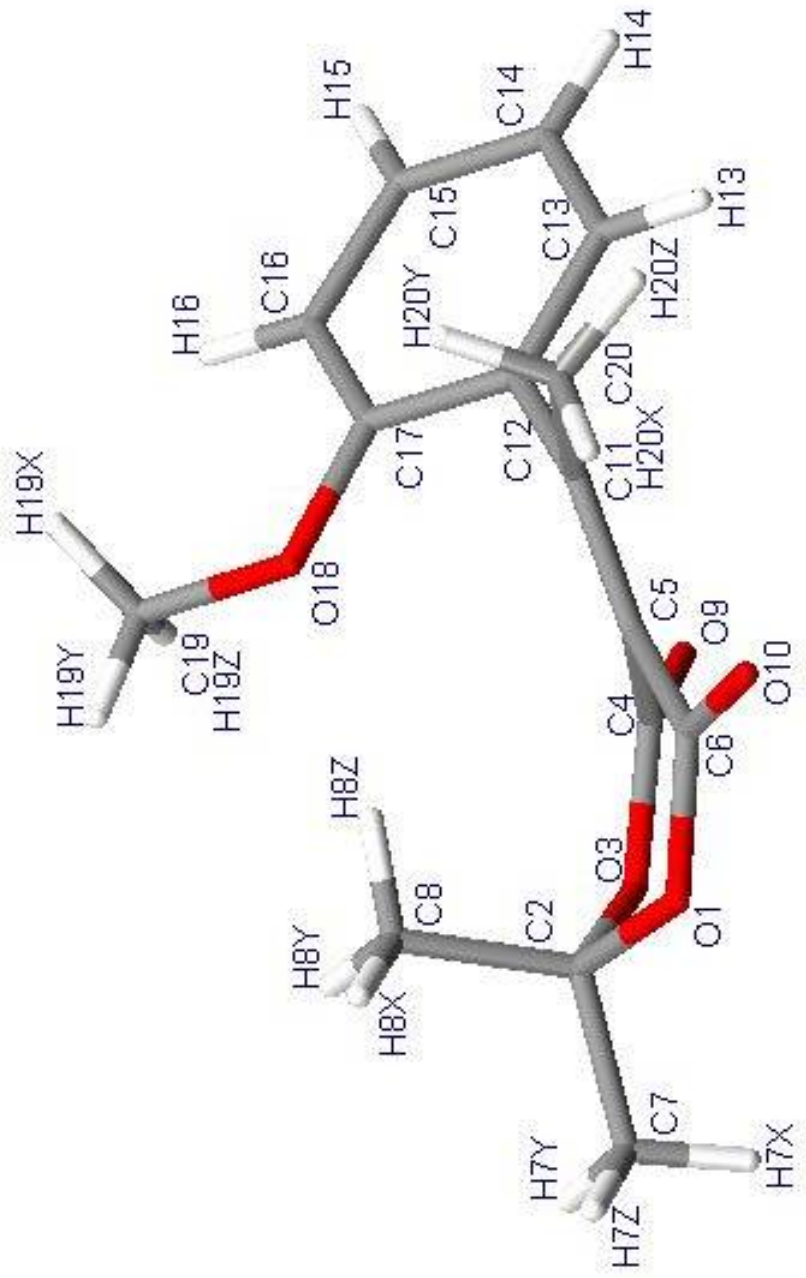

H19X
H19Y
C19
H19Z
O18
C17
H16
C16
H15
C15
C14
H14
C13
H13
H20Y
H20Z
C20
C12
C11
H20X
C5
O9
O10
C6
C4
H8Z
H8Y
H8X
C8
C2
O3
O1
H7Y
H7Z
C7
H7X

Table 1 Crystal data and structure refinement for $C_{15}H_{16}O_5$

Empirical formula	$C_{14}H_{13}ClO_4$
Formula weight	276.28
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 7.7985(5) Å alpha = 90º
	b = 23.3395(14) Å beta = 93.530(1)º
	c = 7.5683(5) Å gamma = 90º
Volume	1374.92(15) $Å^3$
Z, Calculated density	4, 1.335 mg/m^3
Absorption coefficient	0.100 mm^{-1}
F(000)	584
Crystal size	0.36 x 0.22 x 0.06 mm
Theta range for data collection	1.75 to 28.28º
Limiting indices	-10<=h<=9, -31<=k<=28, -10<=l<=10
Reflections collected / unique	9899 / 3400 [R_{int} = 0.0351]
Completeness to theta = 27.88	100.0%
Absorption correction	None
Max. and min. transmission	0.948 and 0.910
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3400 / 0 / 186
Goodness-of-fit on F^2	1.471
Final R indices [I>2sigma(I)]	R1 = 0.0405, wR2 = 0.0679
R indices (all data)	R1 = 0.0552, wR2 = 0.0695
Extinction coefficient	0.0082(9)
Largest diff. peak and hole	0.235 and -0.203 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	4502(1)	2292(1)	8550(1)	36(1)
C(2)	5590(2)	1804(1)	8927(2)	34(1)
O(3)	6142(1)	1581(1)	7280(1)	35(1)
C(4)	4938(2)	1488(1)	5932(2)	27(1)
C(5)	3199(2)	1712(1)	6208(2)	25(1)
C(6)	3147(2)	2230(1)	7343(2)	32(1)
C(7)	7183(2)	2030(1)	9902(2)	53(1)
C(8)	4679(2)	1352(1)	9937(2)	43(1)
O(9)	5385(1)	1262(1)	4615(1)	33(1)
O(10)	2083(1)	2601(1)	7233(1)	47(1)
C(11)	1787(2)	1468(1)	5447(2)	28(1)
C(12)	1849(1)	936(1)	4357(2)	26(1)
C(13)	1313(2)	951(1)	2579(2)	33(1)
C(14)	1298(2)	461(1)	1552(2)	37(1)
C(15)	1783(2)	-52(1)	2323(2)	36(1)
C(16)	2301(2)	-84(1)	4102(2)	31(1)
C(17)	2343(2)	410(1)	5116(2)	27(1)
O(18)	2853(1)	426(1)	6875(1)	35(1)
C(19)	3370(2)	-104(1)	7684(2)	36(1)
C(20)	2(2)	1680(1)	5641(2)	51(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3).

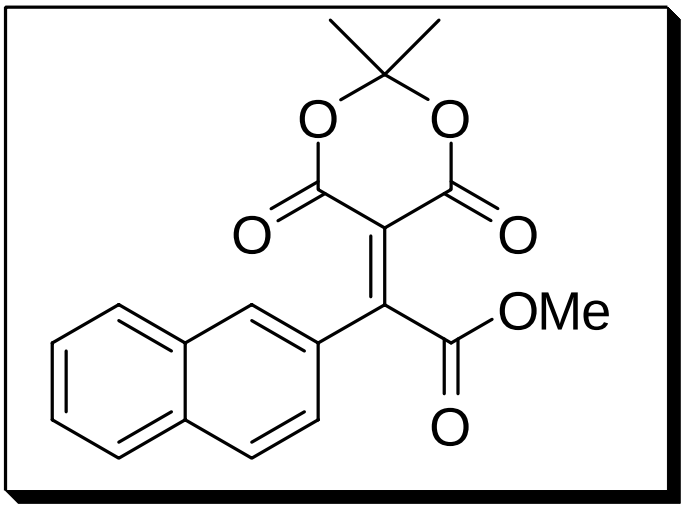
	x	y	z	U(eq)
H(7X)	7710	2323	9179	79

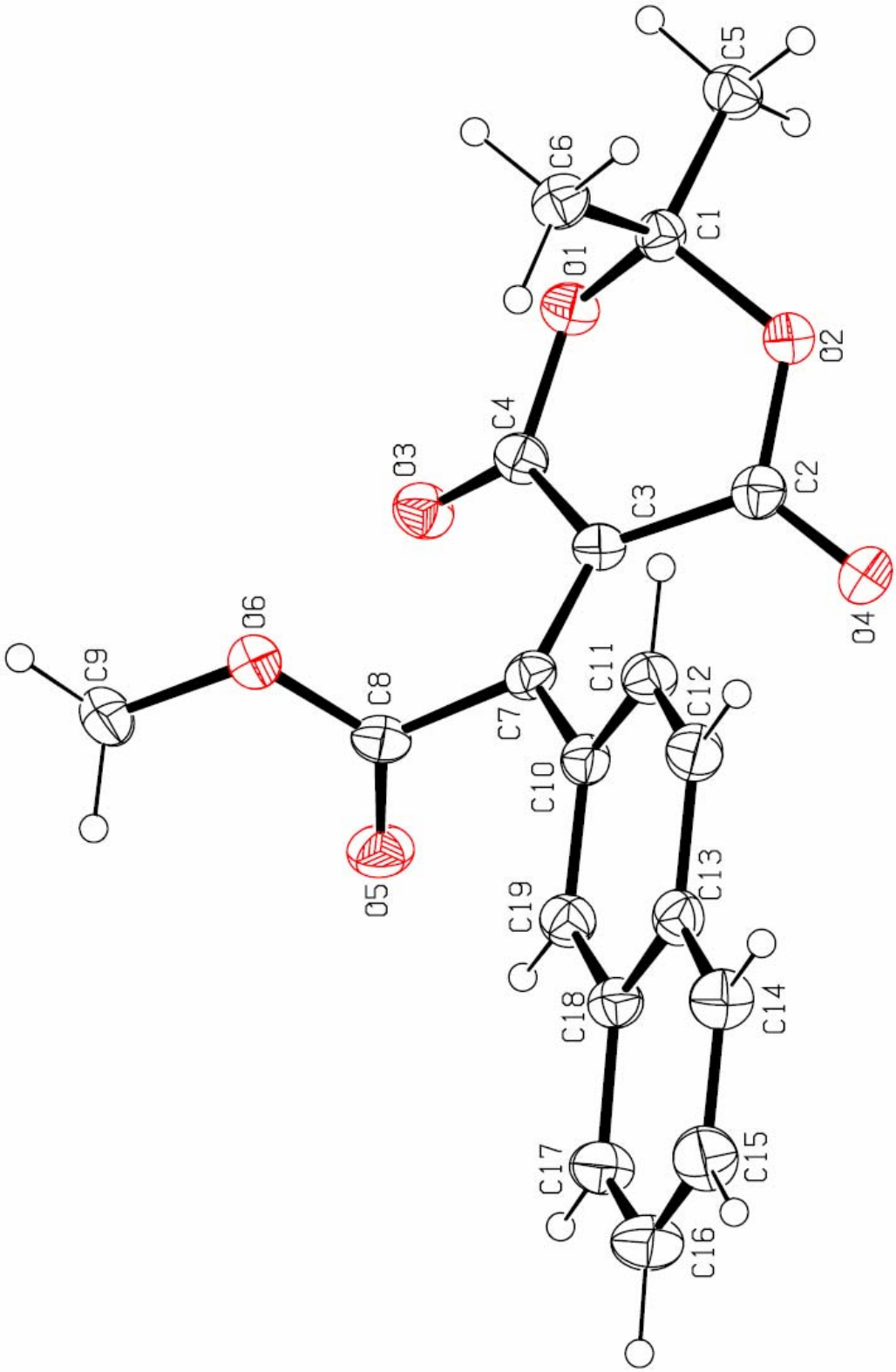
H(7Y)	7998	1716	10138	79
H(7Z)	6881	2201	11024	79
H(8X)	4354	1512	11067	64
H(8Y)	5445	1024	10161	64
H(8Z)	3645	1228	9241	64
H(13)	949	1304	2056	39
H(14)	956	479	326	45
H(15)	1762	-390	1623	43
H(16)	2625	-441	4623	37
H(19X)	2413	-376	7577	54
H(19Y)	3700	-39	8938	54
H(19Z)	4351	-259	7092	54
H(20X)	31	2001	6478	77
H(20Y)	-702	1370	6085	77
H(20Z)	-493	1809	4488	77

Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3611(14)
O(1)-C(2)	1.4383(14)
C(2)-O(3)	1.4400(14)
C(2)-C(7)	1.5019(17)
C(2)-C(8)	1.5051(18)
O(3)-C(4)	1.3607(13)
C(4)-O(9)	1.1981(13)
C(4)-C(5)	1.4803(16)
C(5)-C(11)	1.3389(15)
C(5)-C(6)	1.4841(16)
C(6)-O(10)	1.1992(14)
C(11)-C(12)	1.4912(16)
C(11)-C(20)	1.4935(16)
C(12)-C(13)	1.3847(16)
C(12)-C(17)	1.3999(16)
C(13)-C(14)	1.3819(17)
C(14)-C(15)	1.3748(17)
C(15)-C(16)	1.3840(17)
C(16)-C(17)	1.3844(16)
C(17)-O(18)	1.3665(13)
O(18)-C(19)	1.4255(13)
C(6)-O(1)-C(2)	118.26(9)
O(1)-C(2)-O(3)	108.55(9)
O(1)-C(2)-C(7)	106.17(11)
O(3)-C(2)-C(7)	105.68(11)
O(1)-C(2)-C(8)	111.32(11)
O(3)-C(2)-C(8)	111.25(10)
C(7)-C(2)-C(8)	113.53(11)
C(4)-O(3)-C(2)	118.52(9)
O(9)-C(4)-O(3)	118.13(11)
O(9)-C(4)-C(5)	126.07(11)
O(3)-C(4)-C(5)	115.69(10)
C(11)-C(5)-C(4)	121.67(11)
C(11)-C(5)-C(6)	123.03(11)
C(4)-C(5)-C(6)	115.29(10)
O(10)-C(6)-O(1)	118.37(11)
O(10)-C(6)-C(5)	126.27(12)
O(1)-C(6)-C(5)	115.26(11)
C(5)-C(11)-C(12)	122.61(11)
C(5)-C(11)-C(20)	124.22(11)
C(12)-C(11)-C(20)	113.13(11)
C(13)-C(12)-C(17)	118.63(11)
C(13)-C(12)-C(11)	119.94(11)
C(17)-C(12)-C(11)	121.31(11)
C(14)-C(13)-C(12)	121.20(12)
C(15)-C(14)-C(13)	119.26(12)
C(14)-C(15)-C(16)	121.14(12)
C(15)-C(16)-C(17)	119.27(12)
O(18)-C(17)-C(16)	123.85(11)
O(18)-C(17)-C(12)	115.66(10)
C(16)-C(17)-C(12)	120.49(11)
C(17)-O(18)-C(19)	116.96(9)

Crystallographic data for 3.60




C5
C6
C1
O1
O2
C4
O3
C2
C3
O4
O6
C9
C8
C7
C11
C12
C10
O5
C19
C13
C18
C14
C17
C15
C16

Crystallization solvent: benzene/petroleum ether (diffusion technique)

Table 1 Crystal data and structure refinement for $C_{19}H_{16}O_6$

Empirical formula	$C_{19}H_{16}O_6$
Formula weight	340.32
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, P b c a
Unit cell dimensions	a = 9.9608(6) Å, α= 90°
	b = 9.8561(4) Å, β= 90°
	c = 33.1310(19) Å, γ = 90°
Volume	3252.6(3) $Å^3$
Z, Calculated density	8, 1.390 mg/m^3
Absorption coefficient	0.104 mm^{-1}
F(000)	1424
Crystal size	0.24 x 0.22 x 0.05 mm^3
Theta range for data collection	2.97 to 25.04°.
Index ranges	-8<=h<=11, -8<=k<=11, -39<=l<=35
Reflections collected / unique	13924 / 2869 [R_{int} = 0.0982]
Completeness to theta = 25.04°	99.7%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.998 and 0.778
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2869 / 0 / 229
Goodness-of-fit on F^2	0.971
Final R indices [I>**2s**igma(I)]	R1 = 0.0507, wR2 = 0.1111
R indices (all data)	R1 = 0.1276, wR2 = 0.1434
Largest diff. peak and hole	0.214 and -0.272 $e.Å^{-3}$

Table 2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	2693(2)	1580(2)	209(1)	37(1)
O(2)	5020(2)	1915(2)	230(1)	37(1)
O(3)	1477(2)	1526(2)	765(1)	42(1)
O(4)	6064(2)	1976(2)	818(1)	43(1)
O(5)	1917(2)	2393(2)	1657(1)	50(1)
O(6)	1374(2)	4057(2)	1221(1)	40(1)
C(1)	3816(3)	2198(3)	3(1)	33(1)
C(2)	5022(3)	2132(3)	634(1)	36(1)
C(3)	3698(3)	2424(3)	819(1)	32(1)
C(4)	2526(3)	1831(3)	608(1)	34(1)
C(5)	3953(3)	1457(3)	-391(1)	41(1)
C(6)	3610(3)	3691(3)	-45(1)	38(1)
C(7)	3540(3)	3092(3)	1173(1)	34(1)
C(8)	2177(3)	3107(3)	1377(1)	37(1)
C(9)	38(3)	4112(4)	1401(1)	50(1)
C(10)	4587(3)	3878(3)	1382(1)	34(1)
C(11)	5531(3)	4663(3)	1162(1)	38(1)
C(12)	6469(3)	5444(3)	1349(1)	42(1)
C(13)	6530(3)	5496(3)	1777(1)	37(1)
C(14)	7482(3)	6318(3)	1982(1)	46(1)

C(15)	7516(4)	6330(4)	2395(1)	52(1)
C(16)	6626(3)	5537(4)	2619(1)	53(1)
C(17)	5682(3)	4755(3)	2432(1)	45(1)
C(18)	5607(3)	4719(3)	2005(1)	36(1)
C(19)	4628(3)	3929(3)	1800(1)	37(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
H(5A)	4075	486	-339	62
H(5B)	4733	1807	-538	62
H(5C)	3141	1594	-553	62
H(6A)	3533	4113	222	57
H(6B)	2786	3856	-199	57
H(6C)	4376	4084	-189	57
H(9A)	-471	4859	1280	75
H(9B)	118	4259	1692	75
H(9C)	-430	3253	1350	75
H(11A)	5506	4641	876	45
H(12A)	7086	5957	1192	51
H(14A)	8095	6860	1833	55
H(15A)	8152	6885	2530	62
H(16A)	6679	5541	2905	63
H(17A)	5073	4234	2589	55
H(19A)	3990	3427	1952	45

Table 4 Bond lengths [Å] and angles [º]

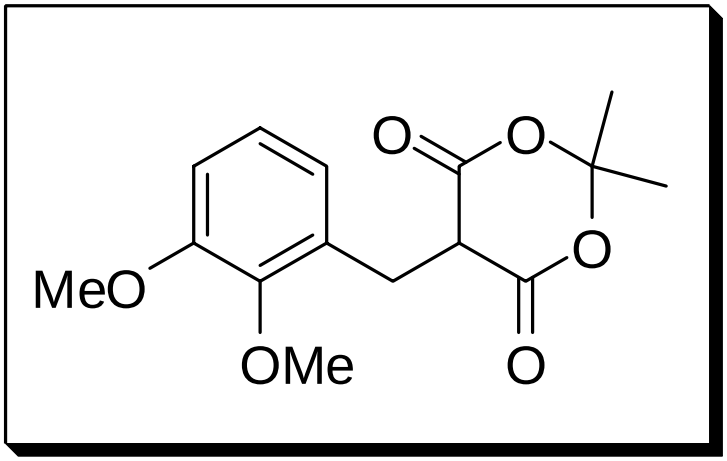
O(1)-C(4)	1.354(3)
O(1)-C(1)	1.447(3)
O(2)-C(2)	1.355(3)
O(2)-C(1)	1.443(3)
O(3)-C(4)	1.205(3)
O(4)-C(2)	1.213(3)
O(5)-C(8)	1.193(3)
O(6)-C(8)	1.335(3)
O(6)-C(9)	1.459(3)
C(1)-C(6)	1.495(4)
C(1)-C(5)	1.500(4)
C(2)-C(3)	1.482(4)
C(3)-C(7)	1.353(4)
C(3)-C(4)	1.482(4)
C(7)-C(10)	1.473(4)
C(7)-C(8)	1.517(4)
C(10)-C(19)	1.385(4)
C(10)-C(11)	1.418(4)
C(11)-C(12)	1.360(4)
C(12)-C(13)	1.420(4)
C(13)-C(18)	1.415(4)
C(13)-C(14)	1.421(4)
C(14)-C(15)	1.366(4)
C(15)-C(16)	1.396(5)
C(16)-C(17)	1.364(4)
C(17)-C(18)	1.418(4)
C(18)-C(19)	1.421(4)
C(4)-O(1)-C(1)	118.7(2)
C(2)-O(2)-C(1)	119.1(2)
C(8)-O(6)-C(9)	114.5(2)
O(2)-C(1)-O(1)	108.3(2)
O(2)-C(1)-C(6)	111.1(2)
O(1)-C(1)-C(6)	111.0(2)
O(2)-C(1)-C(5)	106.5(2)
O(1)-C(1)-C(5)	106.0(2)
C(6)-C(1)-C(5)	113.6(3)
O(4)-C(2)-O(2)	118.5(3)
O(4)-C(2)-C(3)	125.3(3)

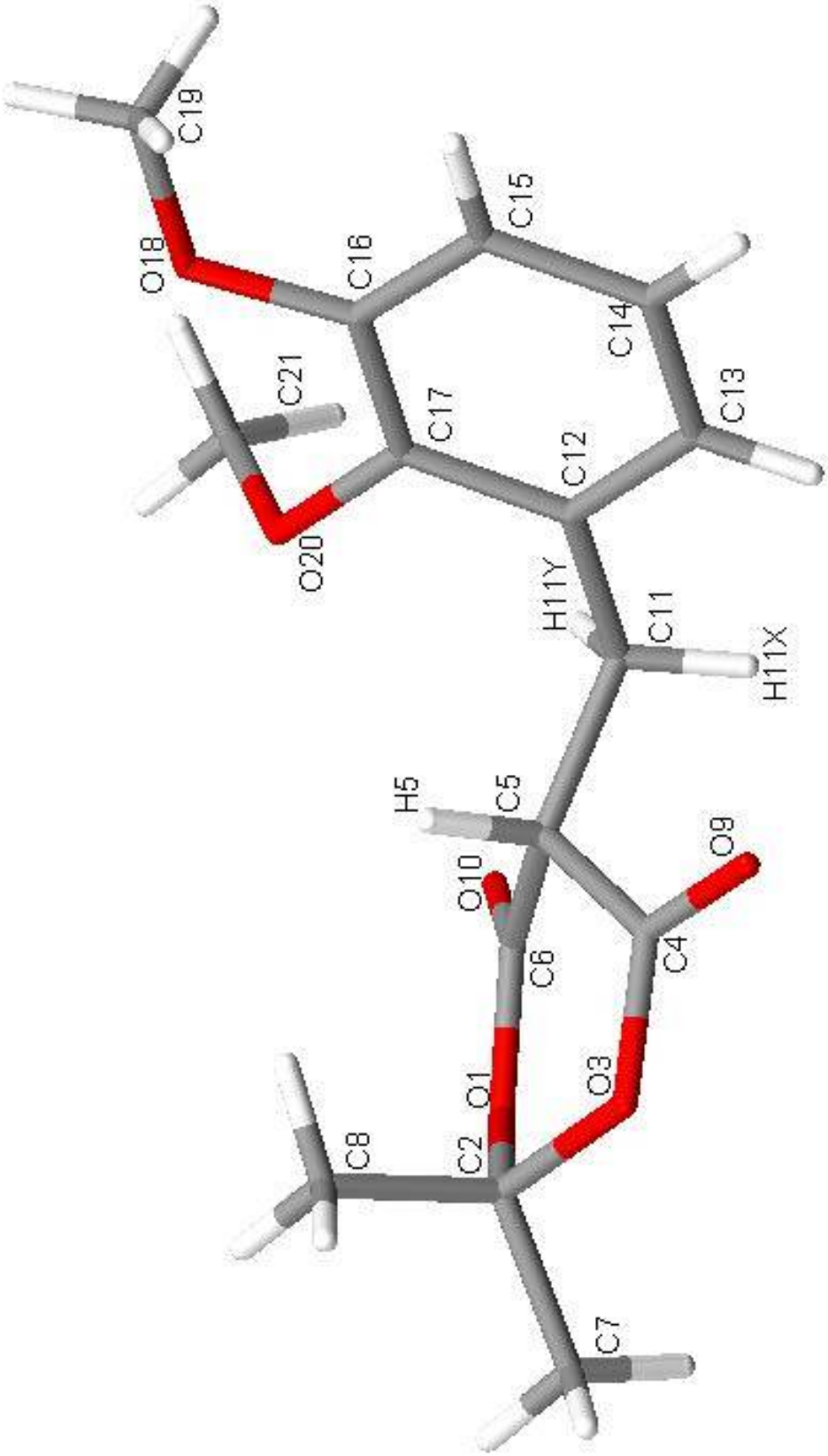
O(2)-C(2)-C(3)	116.0(3)
C(7)-C(3)-C(4)	120.6(3)
C(7)-C(3)-C(2)	123.8(3)
C(4)-C(3)-C(2)	115.4(3)
O(3)-C(4)-O(1)	118.9(3)
O(3)-C(4)-C(3)	125.2(3)
O(1)-C(4)-C(3)	115.8(3)
C(3)-C(7)-C(10)	125.6(3)
C(3)-C(7)-C(8)	119.7(3)
C(10)-C(7)-C(8)	114.7(3)
O(5)-C(8)-O(6)	125.7(3)
O(5)-C(8)-C(7)	122.4(3)
O(6)-C(8)-C(7)	111.7(3)
C(19)-C(10)-C(11)	118.2(3)
C(19)-C(10)-C(7)	120.8(3)
C(11)-C(10)-C(7)	120.9(3)
C(12)-C(11)-C(10)	122.1(3)
C(11)-C(12)-C(13)	120.2(3)
C(18)-C(13)-C(12)	119.1(3)
C(18)-C(13)-C(14)	119.1(3)
C(12)-C(13)-C(14)	121.8(3)
C(15)-C(14)-C(13)	120.0(3)
C(14)-C(15)-C(16)	120.8(3)
C(17)-C(16)-C(15)	120.8(3)
C(16)-C(17)-C(18)	120.2(3)
C(13)-C(18)-C(17)	119.0(3)
C(13)-C(18)-C(19)	119.1(3)
C(17)-C(18)-C(19)	121.9(3)
C(10)-C(19)-C(18)	121.2(3)

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$).

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	40(1)	36(1)	34(1)	-2(1)	1(1)	-5(1)
O(2)	37(1)	41(1)	34(1)	0(1)	1(1)	6(1)
O(3)	38(1)	49(1)	39(1)	-1(1)	3(1)	-8(1)
O(4)	37(1)	49(2)	43(1)	3(1)	-6(1)	7(1)
O(5)	49(1)	63(2)	37(2)	14(1)	2(1)	-6(1)
O(6)	37(1)	46(1)	37(1)	0(1)	1(1)	4(1)
C(1)	28(2)	36(2)	35(2)	2(2)	-1(2)	-2(1)
C(2)	41(2)	28(2)	38(2)	3(2)	-1(2)	1(2)
C(3)	35(2)	33(2)	28(2)	2(2)	0(1)	-1(1)
C(4)	38(2)	31(2)	33(2)	-3(1)	1(2)	-2(2)
C(5)	48(2)	39(2)	37(2)	-4(2)	2(2)	1(2)
C(6)	44(2)	31(2)	40(2)	3(2)	-3(2)	0(2)
C(7)	36(2)	33(2)	32(2)	8(2)	-1(1)	3(1)
C(8)	43(2)	39(2)	28(2)	-4(2)	-2(2)	-4(2)
C(9)	39(2)	68(3)	42(2)	-5(2)	8(2)	6(2)
C(10)	34(2)	34(2)	34(2)	-2(2)	-2(2)	4(2)
C(11)	41(2)	37(2)	35(2)	4(2)	2(2)	0(2)
C(12)	41(2)	43(2)	43(2)	5(2)	3(2)	1(2)
C(13)	38(2)	33(2)	40(2)	-3(2)	-1(2)	4(2)
C(14)	46(2)	45(2)	47(2)	-1(2)	-2(2)	-7(2)
C(15)	49(2)	54(2)	53(3)	-14(2)	-6(2)	-5(2)
C(16)	61(2)	58(2)	39(2)	-5(2)	-5(2)	-8(2)
C(17)	48(2)	53(2)	35(2)	-1(2)	0(2)	-5(2)
C(18)	40(2)	35(2)	33(2)	-1(2)	-3(2)	0(2)
C(19)	40(2)	36(2)	36(2)	2(2)	3(2)	-1(2)

Crystallographic data for 5.2




C19
O18
C16
C15
C14
C13
C21
C17
C12
O20
H11Y
C11
H11X
H5
C5
O9
O10
C6
C4
O1
O3
C8
C2
C7

Crystallization solvent: methanol

Table 1 Crystal data and structure refinement for $C_{15}H_{18}O_6$

Empirical formula	$C_{15}H_{18}O_6$
Formula weight	294.29
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 7.4134(14) Å alpha = 90º
	b = 20.429(4) Å beta = 104.548(4)º
	c = 9.8491(19) Å gamma = 90º
Volume	1443.8(5) $Å^3$
Z, Calculated density	4, 1.354 mg/m^3
Absorption coefficient	0.105 mm^{-1}
F(000)	624
Crystal size	0.34 x 0.29 x 0.10 mm
Theta range for data collection	1.99 to 27.88º
Limiting indices	-9<=h<=9, -26<=k<=26, -12<=l<=12
Reflections collected / unique	10218 / 3431 [R_{int} = 0.0306]
Completeness to theta = 27.88	99.7%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3431 / 0 / 199
Goodness-of-fit on F^2	2.156
Final R indices [I>2sigma(I)]	R1 = 0.0414, wR2 = 0.0756
R indices (all data)	R1 = 0.0480, wR2 = 0.0765
Extinction coefficient	0.0168(12)
Largest diff. peak and hole	0.259 and -0.218 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	-959(1)	3427(1)	1921(1)	32(1)
C(2)	-1048(2)	3831(1)	704(1)	30(1)
O(3)	801(1)	3941(1)	516(1)	33(1)
C(4)	2093(2)	3457(1)	750(1)	30(1)
C(5)	1549(2)	2817(1)	1293(1)	26(1)
C(6)	205(2)	2911(1)	2204(1)	28(1)
C(7)	-1713(2)	4490(1)	1074(2)	44(1)
C(8)	-2293(2)	3526(1)	-582(1)	35(1)
O(9)	3588(1)	3570(1)	536(1)	44(1)
O(10)	103(1)	2551(1)	3144(1)	38(1)
C(11)	3229(2)	2391(1)	2018(1)	33(1)
C(12)	4062(2)	1990(1)	1041(1)	28(1)
C(13)	5849(2)	2115(1)	890(1)	36(1)
C(14)	6626(2)	1728(1)	41(1)	39(1)
C(15)	5645(2)	1208(1)	-689(1)	36(1)
C(16)	3862(2)	1073(1)	-557(1)	30(1)
C(17)	3087(2)	1464(1)	319(1)	26(1)
O(18)	2761(1)	570(1)	-1223(1)	42(1)
C(19)	3566(2)	130(1)	-2033(1)	48(1)
O(20)	1288(1)	1345(1)	438(1)	32(1)
C(21)	1155(2)	801(1)	1327(2)	51(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3).

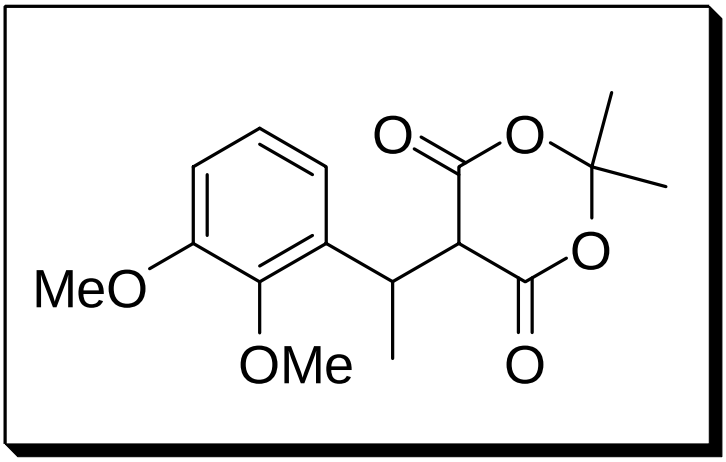
	x	y	z	U(eq)
H(7X)	-2994	4451	1169	66
H(7Y)	-1677	4805	331	66
H(7Z)	-901	4642	1963	66
H(8X)	-1789	3099	-752	52
H(8Y)	-2356	3812	-1392	52
H(8Z)	-3546	3469	-441	52
H(11X)	4211	2679	2579	39
H(11Y)	2835	2090	2678	39
H(13)	6540	2472	1378	43
H(14)	7849	1820	-44	47
H(15)	6188	944	-1276	43
H(19X)	3903	371	-2794	72
H(19Y)	2663	-213	-2430	72
H(19Z)	4685	-70	-1430	72
H(21X)	1532	399	928	76
H(21Y)	-134	757	1398	76
H(21Z)	1976	875	2262	76
H(5)	815(15)	2588(5)	473(13)	28(3)

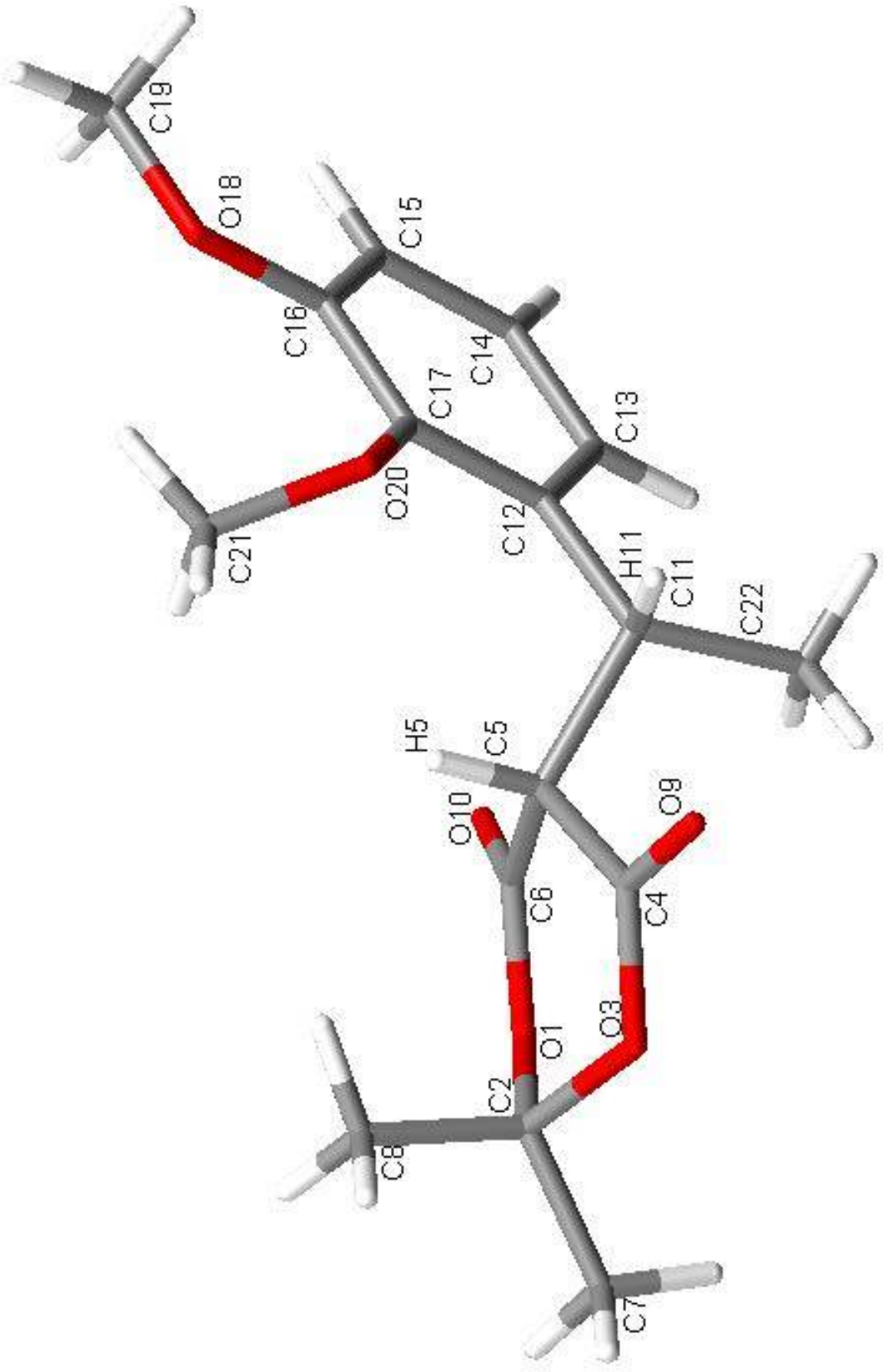
Table 4 Bond lengths [Å] and angles [º]

O(1)-C(6)	1.3469(14)
O(1)-C(2)	1.4422(14)
C(2)-O(3)	1.4462(13)
C(2)-C(8)	1.5021(17)
C(2)-C(7)	1.5091(16)
O(3)-C(4)	1.3553(13)
C(4)-O(9)	1.2006(13)
C(4)-C(5)	1.5068(16)
C(5)-C(6)	1.5118(16)
C(5)-C(11)	1.5401(16)
C(6)-O(10)	1.1999(13)
C(11)-C(12)	1.5086(16)
C(12)-C(17)	1.3873(15)
C(12)-C(13)	1.3934(16)
C(13)-C(14)	1.3775(18)
C(14)-C(15)	1.3832(18)
C(15)-C(16)	1.3878(16)
C(16)-O(18)	1.3731(14)
C(16)-C(17)	1.4002(16)
C(17)-O(20)	1.3893(12)
O(18)-C(19)	1.4279(14)
O(20)-C(21)	1.4334(14)
C(6)-O(1)-C(2)	120.92(9)
O(1)-C(2)-O(3)	110.36(9)
O(1)-C(2)-C(8)	110.73(9)
O(3)-C(2)-C(8)	110.92(10)
O(1)-C(2)-C(7)	105.04(10)
O(3)-C(2)-C(7)	105.67(9)
C(8)-C(2)-C(7)	113.86(11)
C(4)-O(3)-C(2)	121.16(9)
O(9)-C(4)-O(3)	118.36(11)
O(9)-C(4)-C(5)	124.70(11)
O(3)-C(4)-C(5)	116.93(10)
C(4)-C(5)-C(6)	112.02(10)
C(4)-C(5)-C(11)	113.45(10)
C(6)-C(5)-C(11)	111.91(10)
O(10)-C(6)-O(1)	118.63(10)
O(10)-C(6)-C(5)	123.98(11)
O(1)-C(6)-C(5)	117.38(10)
C(12)-C(11)-C(5)	115.03(10)
C(17)-C(12)-C(13)	118.29(11)
C(17)-C(12)-C(11)	120.21(10)
C(13)-C(12)-C(11)	121.42(11)

C(14)-C(13)-C(12)	120.91(12)
C(13)-C(14)-C(15)	120.73(12)
C(14)-C(15)-C(16)	119.49(12)
O(18)-C(16)-C(15)	124.71(11)
O(18)-C(16)-C(17)	115.77(10)
C(15)-C(16)-C(17)	119.52(11)
C(12)-C(17)-O(20)	118.71(10)
C(12)-C(17)-C(16)	121.06(10)
O(20)-C(17)-C(16)	120.19(10)
C(16)-O(18)-C(19)	117.16(10)
C(17)-O(20)-C(21)	113.71(9)

Crystallographic data for 5.3




C19
O18
C15
C16
C14
C17
C13
O20
C12
C21
H11
C11
C22
H5
C5
O10
O9
C6
C4
O1
O3
C2
C8
C7

Crystallization solvent: benzene/petroleum ether (diffusion technique)

Table 1 Crystal data and structure refinement for $C_{16}H_{20}O_6$

Empirical formula	$C_{16}H_{20}O_6$
Formula weight	308.32
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 11.5072(7) Å, alpha = 90º
	b = 9.0242(6) Å, beta = 107.625(1)º
	c = 15.2500(10) Å, gamma = 90º
Volume	1509.27(17) $Å^3$
Z, Calculated density	4, 1.357 mg/m^3
Absorption coefficient	0.104 mm^{-1}
F(000)	656
Crystal size	0.38 x 0.35 x 0.18 mm
Theta range for data collection	1.96 to 27.87º
Limiting indices	-15<=h<=15, -11<=k<=11, -20<=l<=20
Reflections collected / unique	15672 / 3593 [R_{int} = 0.0384]
Completeness to theta = 27.87	99.9%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3593 / 0 / 209
Goodness-of-fit on F^2	2.700
Final R indices [I>2sigma(I)]	R1 = 0.0409, wR2 = 0.0848
R indices (all data)	R1 = 0.0462, wR2 = 0.0853
Extinction coefficient	0.0169(18)
Largest diff. peak and hole	0.257 and -0.259 $e.A^{-3}$

Table 2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	1898(1)	938(1)	3692(1)	38(1)
C(2)	1035(1)	2123(1)	3404(1)	35(1)
O(3)	1644(1)	3522(1)	3658(1)	35(1)
C(4)	2700(1)	3787(1)	3473(1)	29(1)
C(5)	3401(1)	2472(1)	3273(1)	25(1)
C(6)	2992(1)	993(1)	3538(1)	27(1)
C(7)	177(1)	1981(2)	3972(1)	53(1)
C(8)	421(1)	2087(2)	2389(1)	44(1)
O(9)	3057(1)	5037(1)	3516(1)	40(1)
O(10)	3585(1)	-113(1)	3646(1)	37(1)
C(11)	4787(1)	2750(1)	3726(1)	29(1)
C(12)	5607(1)	1716(1)	3390(1)	28(1)
C(13)	6380(1)	695(1)	3976(1)	35(1)
C(14)	7151(1)	-185(1)	3667(1)	39(1)
C(15)	7191(1)	-77(1)	2770(1)	37(1)
C(16)	6449(1)	933(1)	2179(1)	32(1)
C(17)	5653(1)	1827(1)	2490(1)	29(1)
O(18)	6442(1)	1160(1)	1287(1)	43(1)
C(19)	7246(1)	279(2)	954(1)	49(1)
O(20)	4968(1)	2928(1)	1939(1)	33(1)
C(21)	4098(1)	2459(1)	1092(1)	35(1)
C(22)	5078(1)	2794(1)	4773(1)	40(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3).

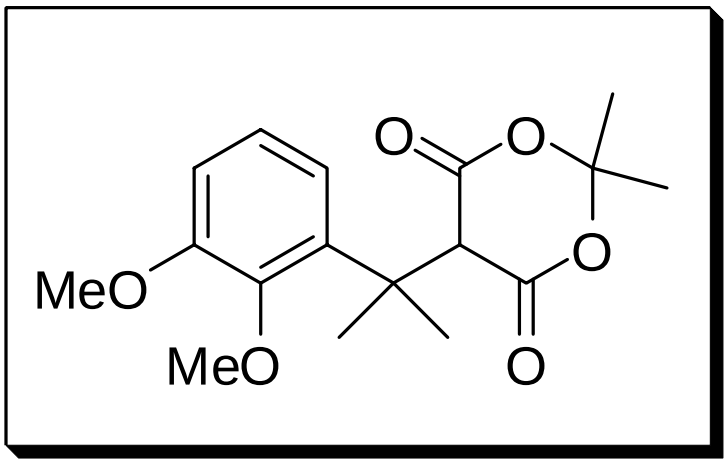
	x	y	z	U(eq)
H(7X)	-235	1019	3852	80
H(7Y)	-431	2776	3807	80
H(7Z)	638	2057	4626	80
H(8X)	1031	2219	2065	67
H(8Y)	-181	2887	2218	67
H(8Z)	12	1130	2218	67
H(11)	4950	3771	3536	35
H(13)	6373	609	4595	42
H(14)	7663	-878	4074	46
H(15)	7724	-693	2564	45
H(19X)	8091	479	1320	73
H(19Y)	7138	523	308	73
H(19Z)	7063	-773	1006	73
H(21X)	4522	2236	639	53
H(21Y)	3502	3251	857	53
H(21Z)	3675	1568	1203	53
H(22X)	4906	1824	4994	60
H(22Y)	4574	3551	4942	60
H(22Z)	5942	3036	5053	60
H(5)	3242(11)	2449(11)	2623(9)	28(3)

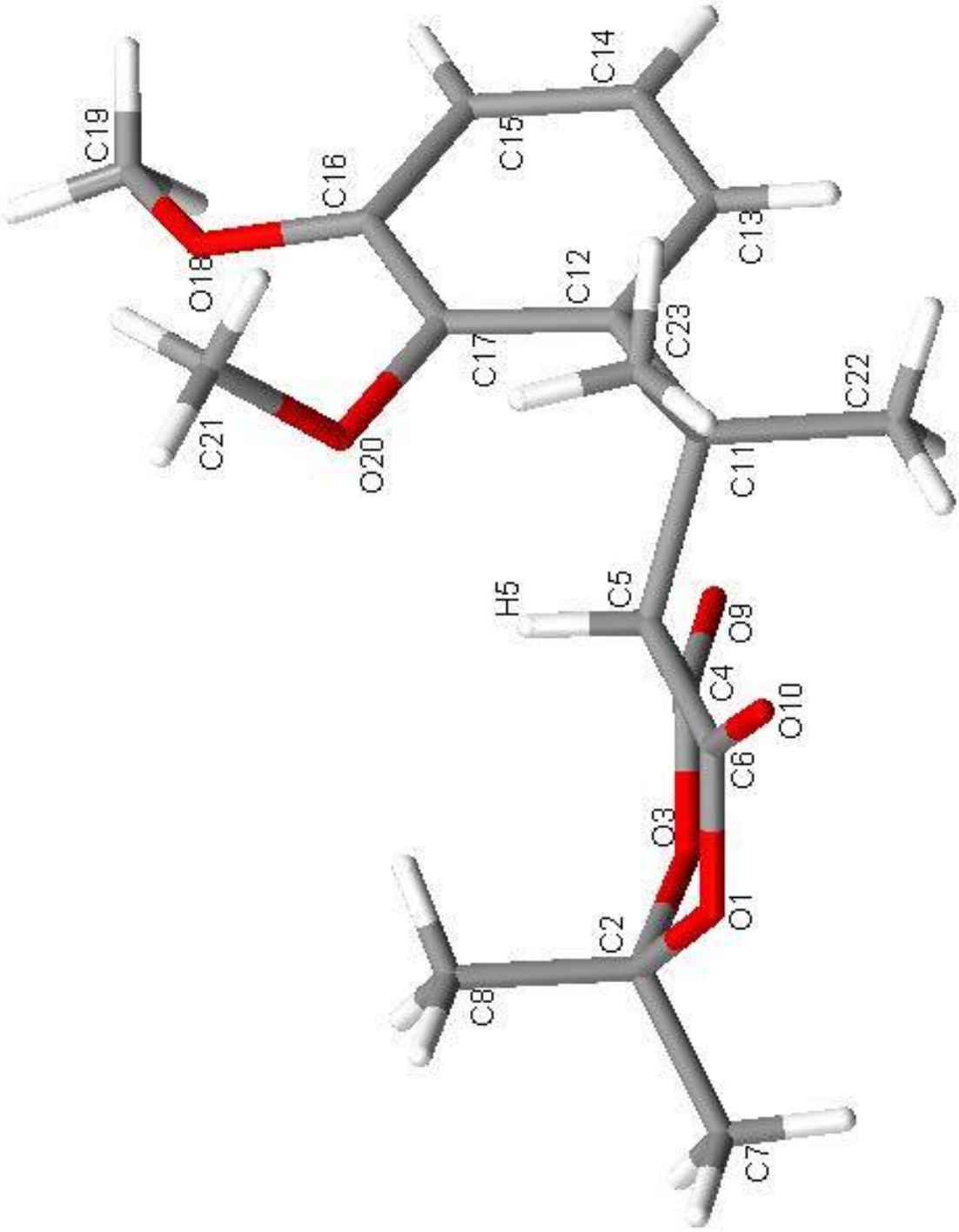
Table 4 Bond lengths [Å] and angles [°]

O(1)-C(6)	1.3490(13)
O(1)-C(2)	1.4342(14)
C(2)-O(3)	1.4392(14)
C(2)-C(8)	1.4942(19)
C(2)-C(7)	1.5032(18)
O(3)-C(4)	1.3491(14)
C(4)-O(9)	1.1958(13)
C(4)-C(5)	1.5172(15)
C(5)-C(6)	1.5111(15)
C(5)-C(11)	1.5548(16)
C(6)-O(10)	1.1917(13)
C(11)-C(12)	1.5219(16)
C(11)-C(22)	1.5288(17)
C(12)-C(17)	1.3937(16)
C(12)-C(13)	1.3988(16)
C(13)-C(14)	1.3755(17)
C(14)-C(15)	1.3858(18)
C(15)-C(16)	1.3812(17)
C(16)-O(18)	1.3731(14)
C(16)-C(17)	1.4057(16)
C(17)-O(20)	1.3830(13)
O(18)-C(19)	1.4251(15)
O(20)-C(21)	1.4376(14)
C(6)-O(1)-C(2)	121.04(9)
O(1)-C(2)-O(3)	109.63(9)
O(1)-C(2)-C(8)	111.54(10)
O(3)-C(2)-C(8)	109.67(10)
O(1)-C(2)-C(7)	105.96(10)
O(3)-C(2)-C(7)	105.70(10)
C(8)-C(2)-C(7)	114.09(11)
C(4)-O(3)-C(2)	119.69(9)
O(9)-C(4)-O(3)	118.15(10)
O(9)-C(4)-C(5)	123.67(11)
O(3)-C(4)-C(5)	118.09(10)
C(6)-C(5)-C(4)	114.15(9)
C(6)-C(5)-C(11)	112.63(9)
C(4)-C(5)-C(11)	108.70(9)
O(10)-C(6)-O(1)	118.12(10)
O(10)-C(6)-C(5)	124.36(10)
O(1)-C(6)-C(5)	117.49(10)
C(12)-C(11)-C(22)	113.91(10)
C(12)-C(11)-C(5)	114.11(9)

C(22)-C(11)-C(5)	109.83(10)
C(17)-C(12)-C(13)	118.05(11)
C(17)-C(12)-C(11)	119.99(10)
C(13)-C(12)-C(11)	121.86(11)
C(14)-C(13)-C(12)	120.84(12)
C(13)-C(14)-C(15)	121.00(12)
C(16)-C(15)-C(14)	119.47(11)
O(18)-C(16)-C(15)	124.20(11)
O(18)-C(16)-C(17)	116.08(11)
C(15)-C(16)-C(17)	119.71(12)
O(20)-C(17)-C(12)	117.74(10)
O(20)-C(17)-C(16)	121.12(11)
C(12)-C(17)-C(16)	120.92(11)
C(16)-O(18)-C(19)	117.37(10)
C(17)-O(20)-C(21)	116.61(9)

Crystallographic data for 5.4




C19
C16
C15
C14
O18
C12
C13
C17
C23
C21
O20
C22
C11
H5
C5
O9
C4
O10
C6
O3
O1
C2
C8
C7

Crystallization solvent: benzene/petroleum ether (diffusion technique)
A major phase change occurs at 291K: Orthorhombic to monoclinic
Phase 1 – Orthorhombic

Table 1 Crystal data and structure refinement for $C_{17}H_{22}O_6$

Empirical formula	$C_{17}H_{22}O_6$
Formula weight	322.35
Temperature	297(1) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Pbcn
Unit cell dimensions	a = 22.5294(12) Å, b = 13.8214(8) Å, c = 10.7410(6) Å
Volume	3344.6(3) $Å^3$
Z, Calculated density	8, 1.280 mg/m^3
Absorption coefficient	0.097 mm^{-1}
F(000)	1376
Crystal size	0.50 x 0.22 x 0.20 mm
Theta range for data collection	1.73 to 26.37º
Limiting indices	-28<=h<=27, -17<=k<=17, -13<=l<=12
Reflections collected / unique	22868 / 3421 [R_{int} = 0.0591]
Completeness to theta = 27.87	99.9%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3421 / 0 / 219
Goodness-of-fit on F^2	1.992
Final R indices [I>2sigma(I)]	R1 = 0.0552, wR2 = 0.1219
R indices (all data)	R1 = 0.0662, wR2 = 0.1239
Extinction coefficient	0.0041(7)
Largest diff. peak and hole	0.236 and -0.165 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	934(1)	557(1)	8023(1)	63(1)
C(2)	1091(1)	-31(1)	6981(2)	62(1)
O(3)	1617(1)	343(1)	6416(1)	64(1)
C(4)	1689(1)	1302(1)	6242(2)	50(1)
C(5)	1217(1)	1958(1)	6787(2)	49(1)
C(6)	956(1)	1527(1)	7958(2)	62(1)
C(7)	1258(1)	-1001(2)	7506(3)	99(1)
C(8)	590(1)	-66(2)	6061(2)	85(1)
O(9)	2113(1)	1560(1)	5678(1)	68(1)
O(10)	766(1)	1963(1)	8829(2)	103(1)
C(11)	1418(1)	3036(1)	6895(2)	51(1)
C(12)	1631(1)	3408(1)	5619(2)	46(1)
C(13)	2173(1)	3888(1)	5496(2)	56(1)
C(14)	2365(1)	4239(1)	4372(2)	60(1)
C(15)	2036(1)	4110(1)	3312(2)	54(1)
C(16)	1496(1)	3642(1)	3386(2)	49(1)
C(17)	1289(1)	3323(1)	4543(2)	48(1)
O(18)	1140(1)	3453(1)	2387(1)	63(1)
C(19)	1386(1)	3584(2)	1178(2)	70(1)
O(20)	750(1)	2842(1)	4600(1)	65(1)
C(21)	237(1)	3405(2)	4286(2)	104(1)
C(22)	1908(1)	3095(2)	7885(2)	67(1)
C(23)	895(1)	3686(1)	7304(2)	68(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
H(7X)	1578	-925	8088	149
H(7Y)	1381	-1421	6843	149
H(7Z)	921	-1278	7923	149
H(8X)	698	-475	5375	128
H(8Y)	509	575	5762	128
H(8Z)	242	-321	6459	128
H(13)	2411	3971	6196	67
H(14)	2723	4570	4329	72
H(15)	2175	4336	2550	65
H(19X)	1757	3244	1123	105
H(19Y)	1451	4261	1031	105
H(19Z)	1116	3335	565	105
H(21X)	237	3534	3408	156
H(21Y)	247	4005	4736	156
H(21Z)	-115	3053	4505	156
H(22X)	2004	3761	8039	100
H(22Y)	2254	2760	7593	100
H(22Z)	1771	2800	8641	100
H(23X)	554	3550	6795	101
H(23Y)	1003	4354	7212	101
H(23Z)	800	3557	8160	101
H(5)	906(7)	1950(10)	6205(15)	37(4)

Table 4 Bond lengths [Å] and angles [º]

O(1)-C(6)	1.343(2)
O(1)-C(2)	1.428(2)
C(2)-O(3)	1.428(2)
C(2)-C(8)	1.501(3)
C(2)-C(7)	1.502(3)
O(3)-C(4)	1.349(2)
C(4)-O(9)	1.185(2)
C(4)-C(5)	1.515(2)
C(5)-C(6)	1.510(2)
C(5)-C(11)	1.563(3)
C(6)-O(10)	1.192(2)
C(11)-C(22)	1.534(3)
C(11)-C(12)	1.540(2)
C(11)-C(23)	1.547(2)
C(12)-C(17)	1.393(2)
C(12)-C(13)	1.397(2)
C(13)-C(14)	1.371(3)
C(14)-C(15)	1.370(3)
C(15)-C(16)	1.380(2)
C(16)-O(18)	1.365(2)
C(16)-C(17)	1.399(2)
C(17)-O(20)	1.3865(19)
O(18)-C(19)	1.424(2)
O(20)-C(21)	1.432(2)
C(6)-O(1)-C(2)	121.21(14)
O(3)-C(2)-O(1)	109.44(14)
O(3)-C(2)-C(8)	110.89(16)
O(1)-C(2)-C(8)	110.30(16)
O(3)-C(2)-C(7)	106.00(16)
O(1)-C(2)-C(7)	106.01(17)
C(8)-C(2)-C(7)	113.96(19)
C(4)-O(3)-C(2)	120.94(14)
O(9)-C(4)-O(3)	117.53(15)
O(9)-C(4)-C(5)	125.72(17)
O(3)-C(4)-C(5)	116.75(15)
C(6)-C(5)-C(4)	111.10(15)
C(6)-C(5)-C(11)	115.30(14)
C(4)-C(5)-C(11)	113.29(14)
O(10)-C(6)-O(1)	116.77(17)

O(10)-C(6)-C(5)	126.43(18)
O(1)-C(6)-C(5)	116.80(15)
C(22)-C(11)-C(12)	112.10(15)
C(22)-C(11)-C(23)	108.71(15)
C(12)-C(11)-C(23)	107.25(14)
C(22)-C(11)-C(5)	108.06(15)
C(12)-C(11)-C(5)	110.03(13)
C(23)-C(11)-C(5)	110.70(14)
C(17)-C(12)-C(13)	116.46(15)
C(17)-C(12)-C(11)	122.56(15)
C(13)-C(12)-C(11)	120.94(15)
C(14)-C(13)-C(12)	121.76(17)
C(15)-C(14)-C(13)	121.08(17)
C(14)-C(15)-C(16)	119.29(16)
O(18)-C(16)-C(15)	124.25(15)
O(18)-C(16)-C(17)	116.21(15)
C(15)-C(16)-C(17)	119.53(16)
O(20)-C(17)-C(12)	119.25(14)
O(20)-C(17)-C(16)	118.83(14)
C(12)-C(17)-C(16)	121.72(15)
C(16)-O(18)-C(19)	117.58(14)
C(17)-O(20)-C(21)	115.83(17)

Phase 2 – Monoclinic

Table 1 Crystal data and structure refinement for $C_{17}H_{22}O_6$

Empirical formula	$C_{17}H_{22}O_6$
Formula weight	322.35
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 10.6791(7) Å, alpha = 90º; b = 22.3042(15) Å, beta = 91.130(1)º; c = 13.7749(9) Å, gamma = 90º
Volume	3280.4(4) $Å^3$
Z, Calculated density	8, 1.305 mg/m^3
Absorption coefficient	0.099 mm^{-1}
F(000)	1376
Crystal size	0.50 x 0.22 x 0.20 mm
Theta range for data collection	1.74 to 27.87º
Limiting indices	-13<=h<=14, -29<=k<=29, -18<=l<=17
Reflections collected / unique	29876 / 7791 [R_{int} = 0.0484]
Completeness to theta = 27.87	99.6%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7791 / 0 / 436
Goodness-of-fit on F^2	2.241
Final R indices [I>2sigma(I)]	R1 = 0.0583, wR2 = 0.1208
R indices (all data)	R1 = 0.0689, wR2 = 0.1222
Extinction coefficient	0.0034(5)
Largest diff. peak and hole	0.388 and -0.241 $e.A^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
O(1)	3684(1)	6602(1)	4977(1)	35(1)
C(2)	3071(2)	6077(1)	5336(1)	34(1)
O(3)	1993(1)	5947(1)	4733(1)	35(1)
C(4)	2059(2)	5959(1)	3755(1)	32(1)
C(5)	3259(2)	6212(1)	3339(1)	26(1)
C(6)	3840(2)	6680(1)	4009(1)	27(1)
C(7)	2579(2)	6245(1)	6319(1)	53(1)
C(8)	3948(2)	5549(1)	5371(1)	43(1)
O(9)	1185(1)	5770(1)	3304(1)	54(1)
O(10)	4423(1)	7107(1)	3760(1)	37(1)
C(11)	3144(2)	6426(1)	2256(1)	28(1)
C(12)	4426(2)	6637(1)	1892(1)	25(1)
C(13)	4548(2)	7192(1)	1425(1)	30(1)
C(14)	5680(2)	7381(1)	1072(1)	32(1)
C(15)	6751(2)	7039(1)	1191(1)	30(1)
C(16)	6668(2)	6489(1)	1660(1)	27(1)
C(17)	5502(2)	6284(1)	1977(1)	26(1)
O(18)	7672(1)	6125(1)	1846(1)	33(1)
C(19)	8885(2)	6384(1)	1746(1)	38(1)
O(20)	5443(1)	5733(1)	2442(1)	34(1)
C(21)	5758(2)	5220(1)	1860(2)	54(1)
C(22)	2155(2)	6925(1)	2198(1)	35(1)
C(23)	2711(2)	5900(1)	1594(1)	36(1)
O(24)	11330(1)	3362(1)	4371(1)	33(1)
C(25)	11929(2)	3893(1)	4757(1)	32(1)
O(26)	12990(1)	4037(1)	4177(1)	33(1)
C(27)	12929(2)	4007(1)	3201(1)	34(1)
C(28)	11724(2)	3763(1)	2751(1)	27(1)
C(29)	11148(2)	3291(1)	3403(1)	27(1)
C(30)	12450(2)	3719(1)	5737(1)	49(1)
C(31)	11025(2)	4409(1)	4785(1)	41(1)
O(32)	13829(2)	4172(1)	2770(1)	60(1)
O(33)	10568(1)	2866(1)	3132(1)	36(1)
C(34)	11808(2)	3564(1)	1664(1)	28(1)
C(35)	10510(2)	3360(1)	1282(1)	26(1)
C(36)	10367(2)	2814(1)	793(1)	31(1)
C(37)	9222(2)	2627(1)	439(1)	33(1)
C(38)	8152(2)	2964(1)	573(1)	29(1)
C(39)	8262(2)	3509(1)	1052(1)	27(1)
C(40)	9434(2)	3713(1)	1376(1)	26(1)
O(41)	7262(1)	3876(1)	1240(1)	34(1)
C(42)	6041(2)	3631(1)	1079(1)	40(1)
O(43)	9510(1)	4255(1)	1866(1)	36(1)
C(44)	9204(2)	4777(1)	1293(2)	59(1)
C(45)	12794(2)	3064(1)	1596(1)	37(1)
C(46)	12225(2)	4098(1)	1027(1)	36(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
H(7X)	2039	6599	6255	79
H(7Y)	3283	6335	6763	79
H(7Z)	2094	5910	6578	79
H(8X)	4683	5647	5777	65
H(8Y)	4214	5452	4712	65
H(8Z)	3517	5202	5647	65
H(13)	3835	7443	1351	36
H(14)	5724	7753	740	38
H(15)	7530	7178	956	36
H(19X)	8921	6768	2092	56
H(19Y)	9048	6450	1057	56
H(19Z)	9519	6112	2021	56
H(21X)	6657	5137	1930	81

H(21Y)	5550	5302	1177	81
H(21Z)	5283	4870	2077	81
H(22X)	1992	7031	1517	53
H(22Y)	2463	7279	2552	53
H(22Z)	1378	6785	2489	53
H(23X)	3228	5546	1735	54
H(23Y)	2800	6014	912	54
H(23Z)	1832	5807	1718	54
H(30X)	13032	3383	5667	73
H(30Y)	11763	3599	6157	73
H(30Z)	12893	4061	6027	73
H(31X)	10318	4304	5194	62
H(31Y)	10718	4498	4126	62
H(31Z)	11451	4763	5055	62
H(36)	11080	2567	703	37
H(37)	9163	2258	95	40
H(38)	7359	2825	342	35
H(42X)	5980	3245	1414	61
H(42Y)	5891	3573	382	61
H(42Z)	5413	3907	1333	61
H(44X)	8325	4756	1077	88
H(44Y)	9743	4792	726	88
H(44Z)	9335	5138	1687	88
H(45X)	12933	2968	912	55
H(45Y)	12496	2706	1933	55
H(45Z)	13582	3199	1900	55
H(46X)	12126	3992	340	53
H(46Y)	13106	4191	1172	53
H(46Z)	11708	4449	1167	53
H(5)	3845(18)	5878(8)	3352(11)	26(4)
H(28)	11100(20)	4101(8)	2783(12)	34(5)

Table 4 Bond lengths [Å] and angles [°]

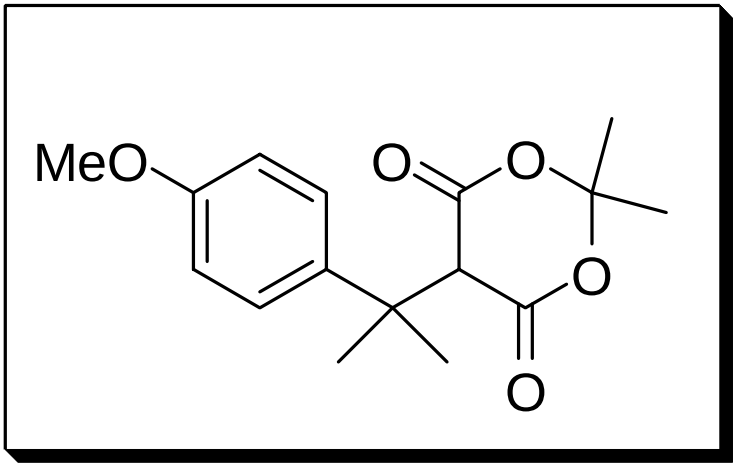
O(1)-C(6)	1.3580(19)
O(1)-C(2)	1.434(2)
C(2)-O(3)	1.436(2)
C(2)-C(8)	1.506(3)
C(2)-C(7)	1.510(3)
O(3)-C(4)	1.351(2)
C(4)-O(9)	1.188(2)
C(4)-C(5)	1.523(2)
C(5)-C(6)	1.517(2)
C(5)-C(11)	1.569(2)
C(6)-O(10)	1.1931(19)
C(11)-C(22)	1.537(2)
C(11)-C(12)	1.541(2)
C(11)-C(23)	1.550(2)
C(12)-C(17)	1.397(2)
C(12)-C(13)	1.400(2)
C(13)-C(14)	1.378(2)
C(14)-C(15)	1.381(3)
C(15)-C(16)	1.391(2)
C(16)-O(18)	1.366(2)
C(16)-C(17)	1.404(2)
C(17)-O(20)	1.3876(18)
O(18)-C(19)	1.428(2)
O(20)-C(21)	1.441(2)
O(24)-C(29)	1.3537(19)
O(24)-C(25)	1.442(2)
C(25)-O(26)	1.435(2)
C(25)-C(30)	1.501(2)
C(25)-C(31)	1.504(3)
O(26)-C(27)	1.347(2)
C(27)-O(32)	1.198(2)
C(27)-C(28)	1.518(2)
C(28)-C(29)	1.520(2)
C(28)-C(34)	1.566(2)
C(29)-O(33)	1.1889(19)

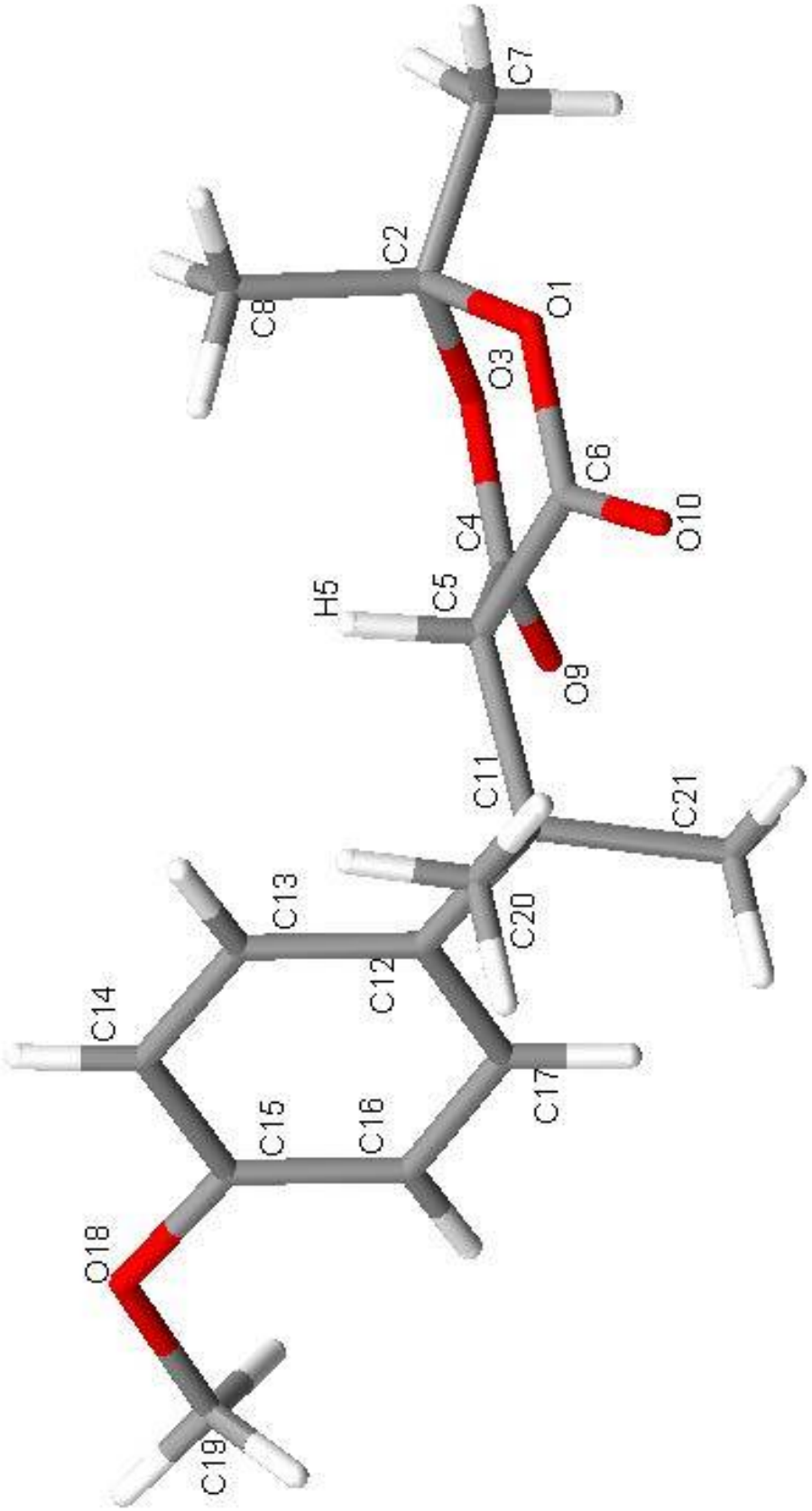
C(34)-C(45)	1.538(2)
C(34)-C(35)	1.542(2)
C(34)-C(46)	1.550(2)
C(35)-C(36)	1.398(2)
C(35)-C(40)	1.401(2)
C(36)-C(37)	1.373(3)
C(37)-C(38)	1.384(3)
C(38)-C(39)	1.386(2)
C(39)-O(41)	1.374(2)
C(39)-C(40)	1.397(2)
C(40)-O(43)	1.3857(18)
O(41)-C(42)	1.427(2)
O(43)-C(44)	1.440(2)

C(6)-O(1)-C(2)	120.56(12)
O(1)-C(2)-O(3)	109.43(13)
O(1)-C(2)-C(8)	111.24(16)
O(3)-C(2)-C(8)	110.56(14)
O(1)-C(2)-C(7)	106.04(14)
O(3)-C(2)-C(7)	106.22(17)
C(8)-C(2)-C(7)	113.11(16)
C(4)-O(3)-C(2)	121.02(14)
O(9)-C(4)-O(3)	117.28(16)
O(9)-C(4)-C(5)	126.38(16)
O(3)-C(4)-C(5)	116.34(14)
C(6)-C(5)-C(4)	111.28(13)
C(6)-C(5)-C(11)	113.16(13)
C(4)-C(5)-C(11)	114.83(14)
O(10)-C(6)-O(1)	117.34(14)
O(10)-C(6)-C(5)	125.73(14)
O(1)-C(6)-C(5)	116.93(13)
C(22)-C(11)-C(12)	112.03(13)
C(22)-C(11)-C(23)	108.78(14)
C(12)-C(11)-C(23)	107.28(13)
C(22)-C(11)-C(5)	108.08(13)
C(12)-C(11)-C(5)	110.41(13)
C(23)-C(11)-C(5)	110.25(13)
C(17)-C(12)-C(13)	116.92(15)
C(17)-C(12)-C(11)	122.30(14)
C(13)-C(12)-C(11)	120.74(15)
C(14)-C(13)-C(12)	121.52(16)
C(13)-C(14)-C(15)	121.32(15)
C(14)-C(15)-C(16)	118.71(16)
O(18)-C(16)-C(15)	123.66(16)
O(18)-C(16)-C(17)	116.44(14)
C(15)-C(16)-C(17)	119.89(16)
O(20)-C(17)-C(12)	119.58(14)
O(20)-C(17)-C(16)	118.80(15)
C(12)-C(17)-C(16)	121.48(14)
C(16)-O(18)-C(19)	116.89(13)
C(17)-O(20)-C(21)	115.66(13)
C(29)-O(24)-C(25)	120.84(12)
O(26)-C(25)-O(24)	109.21(13)
O(26)-C(25)-C(30)	106.01(16)
O(24)-C(25)-C(30)	105.87(14)
O(26)-C(25)-C(31)	110.84(14)
O(24)-C(25)-C(31)	110.99(16)
C(30)-C(25)-C(31)	113.64(15)
C(27)-O(26)-C(25)	121.40(14)
O(32)-C(27)-O(26)	117.17(16)
O(32)-C(27)-C(28)	126.13(15)
O(26)-C(27)-C(28)	116.69(15)
C(27)-C(28)-C(29)	110.91(13)
C(27)-C(28)-C(34)	115.35(14)
C(29)-C(28)-C(34)	113.61(13)
O(33)-C(29)-O(24)	117.76(14)
O(33)-C(29)-C(28)	125.50(14)
O(24)-C(29)-C(28)	116.73(13)
C(45)-C(34)-C(35)	112.15(14)
C(45)-C(34)-C(46)	108.54(14)
C(35)-C(34)-C(46)	107.51(13)

C(45)-C(34)-C(28)	108.35(13)
C(35)-C(34)-C(28)	110.02(13)
C(46)-C(34)-C(28)	110.25(13)
C(36)-C(35)-C(40)	116.86(15)
C(36)-C(35)-C(34)	120.71(15)
C(40)-C(35)-C(34)	122.40(14)
C(37)-C(36)-C(35)	121.63(17)
C(36)-C(37)-C(38)	121.25(16)
C(37)-C(38)-C(39)	118.55(16)
O(41)-C(39)-C(38)	123.58(16)
O(41)-C(39)-C(40)	116.13(14)
C(38)-C(39)-C(40)	120.29(16)
O(43)-C(40)-C(39)	118.90(14)
O(43)-C(40)-C(35)	119.64(15)
C(39)-C(40)-C(35)	121.27(14)
C(39)-O(41)-C(42)	116.96(13)
C(40)-O(43)-C(44)	115.34(14)

Crystallographic data for 5.10




C7
C2
C8
O1
O3
C6
O10
C4
C5
H5
O9
C11
C21
C20
C13
C12
C14
C17
C15
C16
O18
C19

Crystallization solvent: benzene/petroleum ether (diffusion technique)

Table 1 Crystal data and structure refinement for $C_{16}H_{20}O_5$

Empirical formula	$C_{16}H_{20}O_5$
Formula weight	292.32
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Pbca
Unit cell dimensions	a = 8.2119(4) Å, b = 9.6137(4) Å, c = 38.6588(18) Å
Volume	3052.0(2) $Å^3$
Z, Calculated density	8, 1.272 mg/m^3
Absorption coefficient	0.094 mm^{-1}
F(000)	1248
Crystal size	0.36 x 0.17 x 0.10 mm
Theta range for data collection	2.11 to 28.28º
Limiting indices	-9<=h<=10, -12<=k<=12, -49<=l<=51
Reflections collected / unique	18787 / 3781 [R_{int} = 0.0423]
Completeness to theta = 28.28	99.9%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3781 / 0 / 195
Goodness-of-fit on F^2	1.960
Final R indices [I>2sigma(I)]	R1 = 0.0783, wR2 = 0.1261
R indices (all data)	R1 = 0.0895, wR2 = 0.1282
Largest diff. peak and hole	0.263 and -0.312 e. $Å^{-3}$

Table 2. Atomic coordinates (Åx 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	3503(2)	4421(1)	2177(1)	28(1)
C(2)	2191(2)	5404(2)	2130(1)	26(1)
O(3)	2711(2)	6460(1)	1887(1)	28(1)
C(4)	3598(2)	6111(2)	1605(1)	26(1)
C(5)	3930(2)	4566(2)	1556(1)	23(1)
C(6)	4421(2)	3980(2)	1907(1)	27(1)
C(7)	2021(2)	6135(2)	2473(1)	31(1)
C(8)	632(2)	4705(2)	2014(1)	32(1)
O(9)	4054(2)	7032(1)	1418(1)	35(1)
O(10)	5526(2)	3205(1)	1966(1)	33(1)
C(11)	5044(2)	4203(2)	1247(1)	31(1)
C(12)	4299(2)	4833(2)	914(1)	30(1)
C(13)	2765(3)	4426(2)	800(1)	38(1)
C(14)	2118(3)	4924(2)	494(1)	44(1)
C(15)	3001(3)	5838(2)	291(1)	41(1)
C(16)	4511(3)	6267(2)	401(1)	44(1)
C(17)	5133(3)	5771(2)	710(1)	40(1)
O(18)	2292(2)	6242(2)	-16(1)	56(1)
C(19)	3270(4)	7076(3)	-240(1)	66(1)
C(20)	5094(3)	2609(2)	1199(1)	39(1)
C(21)	6797(2)	4729(2)	1316(1)	44(1)

Table 3. Hydrogen coordinates (Å x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3).

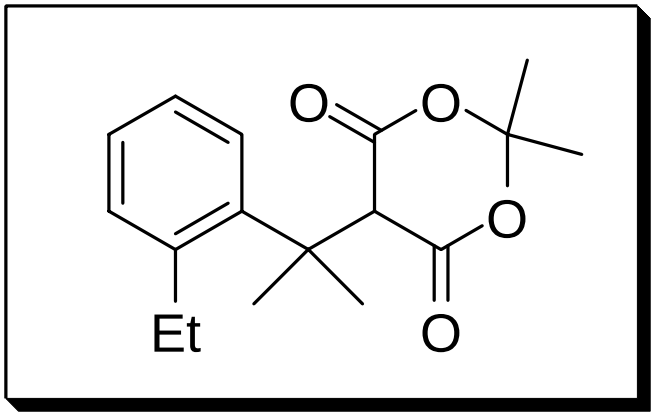
	x	y	z	U(eq)
H(5)	2850	4138	1502	28
H(7X)	1806	5448	2655	46
H(7Y)	1114	6796	2461	46
H(7Z)	3030	6635	2526	46
H(8X)	834	4186	1800	48
H(8Y)	-204	5413	1973	48
H(8Z)	258	4064	2195	48
H(13)	2148	3790	935	46
H(14)	1062	4638	423	53
H(16)	5126	6903	265	53
H(17)	6172	6087	784	48
H(19X)	3434	7994	-135	99
H(19Y)	2721	7182	-463	99
H(19Z)	4328	6625	-274	99
H(20X)	5548	2176	1407	58
H(20Y)	5779	2378	999	58
H(20Z)	3988	2259	1160	58
H(21X)	6777	5738	1354	66
H(21Y)	7490	4515	1117	66
H(21Z)	7232	4269	1523	66

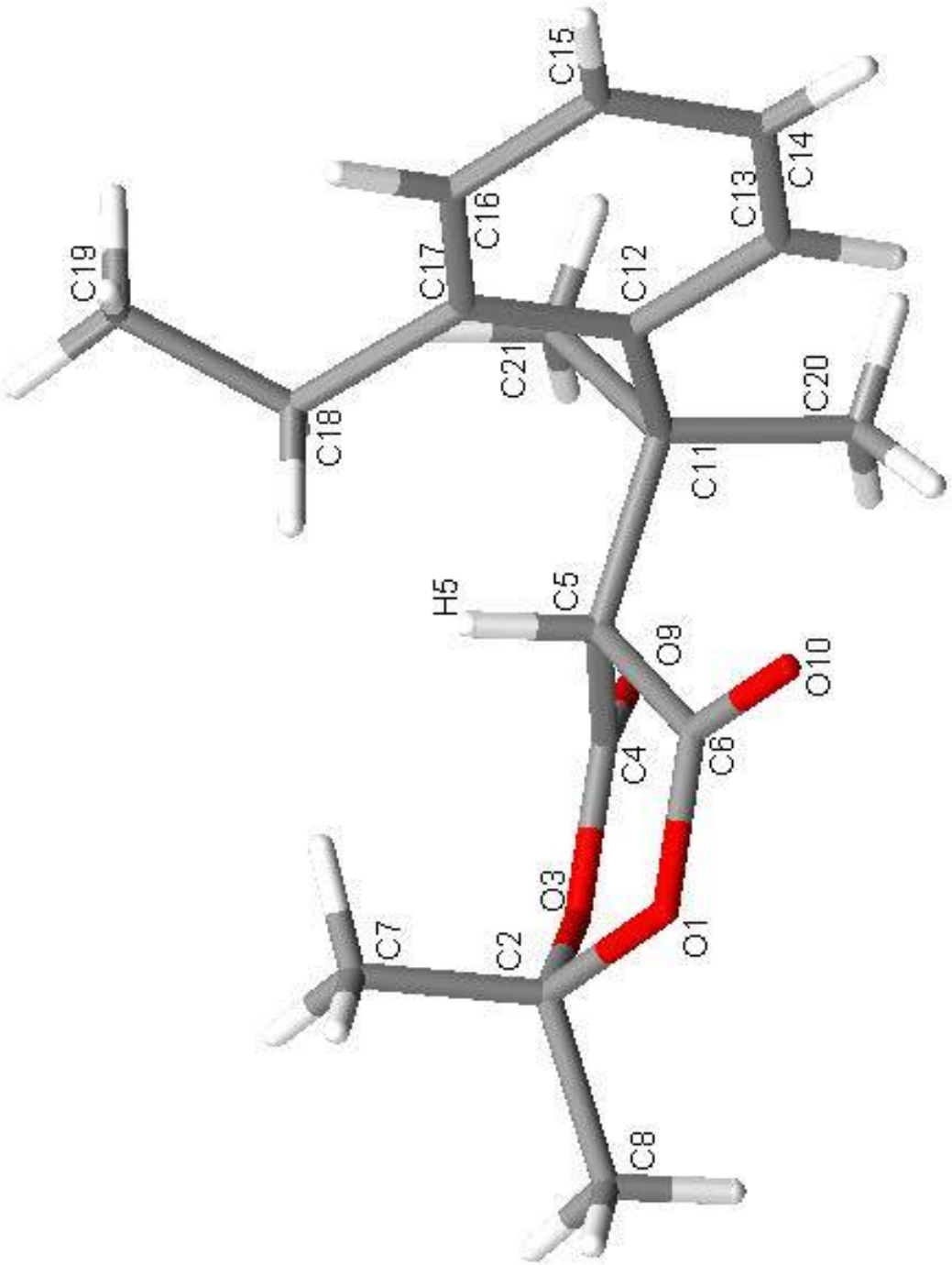
Table 4. Bond lengths [Å] and angles [º].

O(1)-C(6)	1.356(2)
O(1)-C(2)	1.444(2)
C(2)-O(3)	1.450(2)
C(2)-C(7)	1.506(2)
C(2)-C(8)	1.514(2)
O(3)-C(4)	1.353(2)
C(4)-O(9)	1.201(2)
C(4)-C(5)	1.522(2)
C(5)-C(6)	1.524(2)
C(5)-C(11)	1.547(2)
C(6)-O(10)	1.196(2)
C(11)-C(20)	1.544(3)
C(11)-C(12)	1.546(3)
C(11)-C(21)	1.549(3)
C(12)-C(17)	1.380(3)
C(12)-C(13)	1.391(3)
C(13)-C(14)	1.383(3)
C(14)-C(15)	1.383(3)
C(15)-C(16)	1.374(3)
C(15)-O(18)	1.377(2)
C(16)-C(17)	1.385(3)
O(18)-C(19)	1.427(3)
C(6)-O(1)-C(2)	121.49(13)
O(1)-C(2)-O(3)	108.70(13)
O(1)-C(2)-C(7)	105.32(14)
O(3)-C(2)-C(7)	105.82(13)
O(1)-C(2)-C(8)	112.19(14)
O(3)-C(2)-C(8)	111.51(14)
C(7)-C(2)-C(8)	112.89(15)
C(4)-O(3)-C(2)	120.59(13)
O(9)-C(4)-O(3)	117.90(16)
O(9)-C(4)-C(5)	126.19(16)
O(3)-C(4)-C(5)	115.91(14)
C(4)-C(5)-C(6)	107.38(14)
C(4)-C(5)-C(11)	114.92(14)
C(6)-C(5)-C(11)	116.72(14)
O(10)-C(6)-O(1)	118.16(16)
O(10)-C(6)-C(5)	126.79(17)
O(1)-C(6)-C(5)	115.04(14)
C(20)-C(11)-C(12)	107.51(15)
C(20)-C(11)-C(5)	109.38(15)
C(12)-C(11)-C(5)	108.68(14)

C(20)-C(11)-C(21)	108.66(16)
C(12)-C(11)-C(21)	112.62(16)
C(5)-C(11)-C(21)	109.92(15)
C(17)-C(12)-C(13)	116.82(18)
C(17)-C(12)-C(11)	122.30(18)
C(13)-C(12)-C(11)	120.83(17)
C(14)-C(13)-C(12)	121.51(19)
C(13)-C(14)-C(15)	120.3(2)
C(16)-C(15)-O(18)	124.3(2)
C(16)-C(15)-C(14)	119.23(19)
O(18)-C(15)-C(14)	116.5(2)
C(15)-C(16)-C(17)	119.8(2)
C(12)-C(17)-C(16)	122.4(2)
C(15)-O(18)-C(19)	116.26(19)

Crystallographic data for 5.22




C15
C14
C13
C16
C17
C12
C19
C21
C20
C18
C11
H5
C5
O9
O10
C4
C6
O3
O1
C7
C2
C8

Crystallization solvent: benzene/hexane (diffusion technique)

Table 1 Crystal data and structure refinement for $C_{17}H_{22}O_4$

Empirical formula	$C_{17}H_{22}O_4$
Formula weight	290.35
Temperature	180(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Fdd2
Unit cell dimensions	a = 21.6856(12) Å, b = 39.832(2) Å, c = 6.9889(4) Å
Volume	6036.8(6) $Å^3$
Z, Calculated density	16, 1.278 mg/m^3
Absorption coefficient	0.090 mm^{-1}
F(000)	2496
Crystal size	0.24 x 0.18 x 0.05 mm
Theta range for data collection	3.10 to 30.00º
Limiting indices	-30<=h<=30, -50<=k<=56, -9<=l<=9
Reflections collected / unique	14559 / 2339 [R_{int} = 0.0284]
Completeness to theta = 30.00	98.8%
Absorption correction	Empirical
Max. and min. transmission	0.9960 and 0.9787
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2339 / 1 / 191
Goodness-of-fit on F^2	1.460
Final R indices [I>2sigma(I)]	R1 = 0.0372, wR2 = 0.0976
R indices (all data)	R1 = 0.0403, wR2 = 0.1111
Largest diff. peak and hole	0.321 and -0.259 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(9)	1502(1)	1074(1)	5306(3)	30(1)
O(10)	310(1)	1332(1)	240(3)	32(1)
O(1)	762(1)	840(1)	373(3)	25(1)
O(3)	1403(1)	708(1)	2989(3)	26(1)
C(17)	1480(1)	1981(1)	-121(3)	21(1)
C(16)	1379(1)	2249(1)	-1360(4)	25(1)
C(15)	851(1)	2447(1)	-1299(4)	28(1)
C(14)	405(1)	2372(1)	23(4)	29(1)
C(13)	492(1)	2109(1)	1289(4)	24(1)
C(12)	1031(1)	1912(1)	1294(3)	19(1)
C(18)	2065(1)	1772(1)	-437(3)	23(1)
C(19)	2606(1)	1957(1)	-1324(5)	36(1)
C(11)	1118(1)	1656(1)	2960(3)	19(1)
C(20)	558(1)	1641(1)	4308(4)	28(1)
C(21)	1671(1)	1783(1)	4177(3)	25(1)
C(5)	1241(1)	1297(1)	2165(3)	18(1)
C(6)	730(1)	1169(1)	854(3)	21(1)
C(2)	1272(1)	636(1)	1012(3)	23(1)
C(8)	1039(1)	278(1)	980(4)	33(1)
C(7)	1834(1)	687(1)	-243(4)	27(1)
C(4)	1393(1)	1027(1)	3655(3)	21(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
H(16)	1679	2298	-2270	30
H(15)	802	2626	-2137	34
H(14)	44	2497	68	35
H(13)	183	2061	2171	29
H(18Y)	2195	1682	787	28
H(18X)	1961	1583	-1253	28
H(19Z)	2948	1806	-1463	53
H(19Y)	2724	2141	-512	53
H(19X)	2489	2042	-2558	53
H(20Z)	633	1479	5299	42
H(20Y)	199	1576	3594	42
H(20X)	492	1858	4872	42
H(21Z)	1741	1630	5218	37
H(21Y)	1579	2002	4674	37
H(21X)	2033	1794	3391	37
H(5)	1609	1316	1358	22
H(8Z)	682	259	1787	49
H(8Y)	1356	130	1438	49
H(8X)	930	217	-306	49
H(7Z)	1963	917	-179	40
H(7Y)	1733	630	-1541	40
H(7X)	2162	544	197	40

Table 4 Bond lengths [Å] and angles [º]

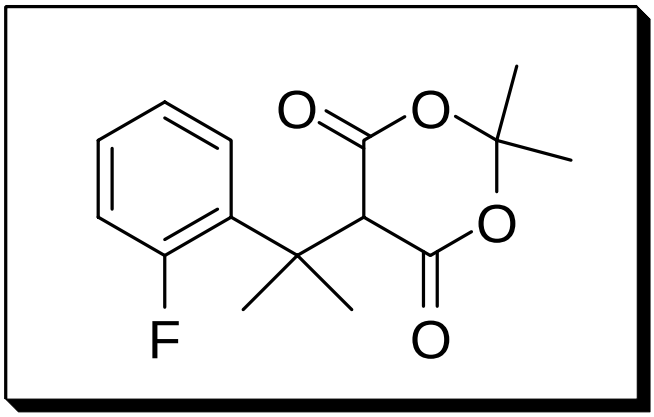
O(9)-C(4)	1.192(3)
O(10)-C(6)	1.198(3)
O(1)-C(6)	1.355(3)
O(1)-C(2)	1.441(3)
O(3)-C(4)	1.355(3)
O(3)-C(2)	1.439(3)
C(17)-C(16)	1.392(3)
C(17)-C(12)	1.415(3)
C(17)-C(18)	1.532(3)
C(16)-C(15)	1.392(3)
C(16)-H(16)	0.9300
C(15)-C(14)	1.370(4)
C(15)-H(15)	0.9300
C(14)-C(13)	1.384(3)
C(14)-H(14)	0.9300
C(13)-C(12)	1.406(3)
C(13)-H(13)	0.9300
C(12)-C(11)	1.559(3)
C(18)-C(19)	1.519(3)
C(18)-H(18Y)	0.9700
C(18)-H(18X)	0.9700
C(19)-H(19Z)	0.9600
C(19)-H(19Y)	0.9600
C(19)-H(19X)	0.9600
C(11)-C(20)	1.539(3)
C(11)-C(21)	1.553(3)
C(11)-C(5)	1.560(3)
C(20)-H(20Z)	0.9600
C(20)-H(20Y)	0.9600
C(20)-H(20X)	0.9600
C(21)-H(21Z)	0.9600
C(21)-H(21Y)	0.9600
C(21)-H(21X)	0.9600
C(5)-C(6)	1.525(3)
C(5)-C(4)	1.530(3)
C(5)-H(5)	0.9800
C(2)-C(7)	1.515(3)
C(2)-C(8)	1.516(3)
C(8)-H(8Z)	0.9600

C(8)-H(8Y)	0.9600
C(8)-H(8X)	0.9600
C(7)-H(7Z)	0.9600
C(7)-H(7Y)	0.9600
C(7)-H(7X)	0.9600

C(6)-O(1)-C(2)	120.42(17)
C(4)-O(3)-C(2)	120.84(18)
C(16)-C(17)-C(12)	118.31(18)
C(16)-C(17)-C(18)	117.14(19)
C(12)-C(17)-C(18)	124.51(19)
C(15)-C(16)-C(17)	123.0(2)
C(15)-C(16)-H(16)	118.5
C(17)-C(16)-H(16)	118.5
C(14)-C(15)-C(16)	118.5(2)
C(14)-C(15)-H(15)	120.7
C(16)-C(15)-H(15)	120.7
C(15)-C(14)-C(13)	120.0(2)
C(15)-C(14)-H(14)	120.0
C(13)-C(14)-H(14)	120.0
C(14)-C(13)-C(12)	122.5(2)
C(14)-C(13)-H(13)	118.8
C(12)-C(13)-H(13)	118.8
C(13)-C(12)-C(17)	117.57(19)
C(13)-C(12)-C(11)	117.87(18)
C(17)-C(12)-C(11)	124.32(17)
C(19)-C(18)-C(17)	115.83(18)
C(19)-C(18)-H(18Y)	108.3
C(17)-C(18)-H(18Y)	108.3
C(19)-C(18)-H(18X)	108.3
C(17)-C(18)-H(18X)	108.3
H(18Y)-C(18)-H(18X)	107.4
C(18)-C(19)-H(19Z)	109.5
C(18)-C(19)-H(19Y)	109.5
H(19Z)-C(19)-H(19Y)	109.5
C(18)-C(19)-H(19X)	109.5
H(19Z)-C(19)-H(19X)	109.5
H(19Y)-C(19)-H(19X)	109.5
C(20)-C(11)-C(21)	106.66(19)
C(20)-C(11)-C(12)	112.76(17)
C(21)-C(11)-C(12)	106.95(16)
C(20)-C(11)-C(5)	108.41(17)
C(21)-C(11)-C(5)	111.17(16)
C(12)-C(11)-C(5)	110.83(17)
C(11)-C(20)-H(20Z)	109.5
C(11)-C(20)-H(20Y)	109.5
H(20Z)-C(20)-H(20Y)	109.5
C(11)-C(20)-H(20X)	109.5
H(20Z)-C(20)-H(20X)	109.5
H(20Y)-C(20)-H(20X)	109.5
C(11)-C(21)-H(21Z)	109.5
C(11)-C(21)-H(21Y)	109.5
H(21Z)-C(21)-H(21Y)	109.5
C(11)-C(21)-H(21X)	109.5
H(21Z)-C(21)-H(21X)	109.5
H(21Y)-C(21)-H(21X)	109.5
C(6)-C(5)-C(4)	109.36(16)
C(6)-C(5)-C(11)	113.40(16)
C(4)-C(5)-C(11)	116.01(18)
C(6)-C(5)-H(5)	105.7
C(4)-C(5)-H(5)	105.7
C(11)-C(5)-H(5)	105.7
O(10)-C(6)-O(1)	118.30(19)
O(10)-C(6)-C(5)	125.92(19)
O(1)-C(6)-C(5)	115.78(17)
O(3)-C(2)-O(1)	109.74(18)
O(3)-C(2)-C(7)	111.72(18)
O(1)-C(2)-C(7)	111.31(19)
O(3)-C(2)-C(8)	105.5(2)
O(1)-C(2)-C(8)	105.62(17)
C(7)-C(2)-C(8)	112.62(19)

C(2)-C(8)-H(8Z)	109.5
C(2)-C(8)-H(8Y)	109.5
H(8Z)-C(8)-H(8Y)	109.5
C(2)-C(8)-H(8X)	109.5
H(8Z)-C(8)-H(8X)	109.5
H(8Y)-C(8)-H(8X)	109.5
C(2)-C(7)-H(7Z)	109.5
C(2)-C(7)-H(7Y)	109.5
H(7Z)-C(7)-H(7Y)	109.5
C(2)-C(7)-H(7X)	109.5
H(7Z)-C(7)-H(7X)	109.5
H(7Y)-C(7)-H(7X)	109.5
O(9)-C(4)-O(3)	118.3(2)
O(9)-C(4)-C(5)	126.3(2)
O(3)-C(4)-C(5)	115.34(19)

Crystallographic data for 5.24



C7
C2
C8
O3
O1
C4
C6
O9
O10
H5
C5
C11
C19
F18
C12
C17
C16
C14
C13
C20
C15

Crystallization solvent: benzene/hexane (diffusion technique)

Table 1 Crystal data and structure refinement for $C_{15}H_{17}FO_4$

Empirical formula	$C_{15}H_{17}FO_4$
Formula weight	280.29 g/mol
Temperature	180(2) K
Wavelength	0.71073 A
Crystal system, space group	monoclinic, $P2_1/c$
Unit cell dimensions	a = 6.8109(17) Å, b = 20.468(5) Å, c = 10.125(3) Å
	β = 98.917(5) º
Volume	1394.4(6) $Å^3$
Z, Calculated density	4, 1.335 g/cm^3
Absorption coefficient	0.105 mm^{-1}
F(000)	592
Crystal size	0.25 x 0.20 x 0.08 mm
Theta range for data collection	2.85 to 30.00 º
Limiting indices	-9<=h<=9, -28<=k<=28, -12<=l<=14
Reflections collected / unique	12854 / 4064 [R(int) = 0.0247]
Completeness to theta = 30.00	99.8%
Max. and min. transmission	1.00 and 0.9743
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4064 / 0 / 182
Goodness-of-fit on F^2	1.189
Final R indices [I>2σ(I)]	R1 = 0.0412, wR2 = 0.0900
R indices (all data)	R1 = 0.0549, wR2 = 0.0958
Extinction coefficient	0.0054(12)
Largest diff. peak and hole	0.278 and -0.198 e. $Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	8290(1)	5572(1)	6023(1)	37(1)
C(2)	8388(2)	6243(1)	6445(1)	38(1)
O(3)	8889(1)	6652(1)	5389(1)	37(1)
C(4)	8009(2)	6561(1)	4117(1)	29(1)
C(5)	6685(2)	5960(1)	3846(1)	27(1)
C(6)	7464(2)	5400(1)	4771(1)	33(1)
C(7)	10141(3)	6284(1)	7553(2)	60(1)
C(8)	6464(2)	6466(1)	6861(1)	47(1)
O(9)	8323(1)	6950(1)	3294(1)	35(1)
O(10)	7364(2)	4831(1)	4502(1)	47(1)
C(11)	6185(2)	5796(1)	2325(1)	29(1)
C(12)	5072(2)	6372(1)	1584(1)	28(1)
C(13)	5667(2)	6673(1)	474(1)	34(1)
C(14)	4539(2)	7155(1)	-247(1)	38(1)
C(15)	2765(2)	7362(1)	121(1)	39(1)
C(16)	2132(2)	7082(1)	1221(1)	37(1)
C(17)	3278(2)	6603(1)	1908(1)	32(1)
F(18)	2583(1)	6340(1)	2989(1)	43(1)
C(19)	8111(2)	5626(1)	1789(1)	37(1)
C(20)	4774(2)	5201(1)	2077(1)	40(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3).

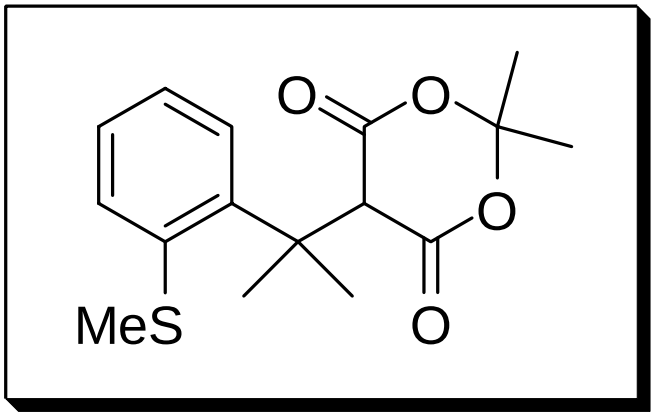
	x	y	z	U(eq)
H(5)	5389	6087	4120	33
H(7X)	11339	6130	7224	90
H(7Y)	9892	6010	8304	90
H(7Z)	10330	6738	7852	90
H(8X)	5388	6428	6101	71
H(8Y)	6591	6922	7154	71
H(8Z)	6162	6192	7598	71
H(13)	6883	6543	203	40
H(14)	4988	7346	-1002	46
H(15)	1995	7691	-376	47
H(16)	926	7218	1498	44
H(19X)	7803	5522	835	56
H(19Y)	8741	5247	2274	56
H(19Z)	9020	6000	1917	56
H(20X)	4490	5109	1116	60
H(20Y)	3530	5297	2411	60
H(20Z)	5408	4818	2546	60

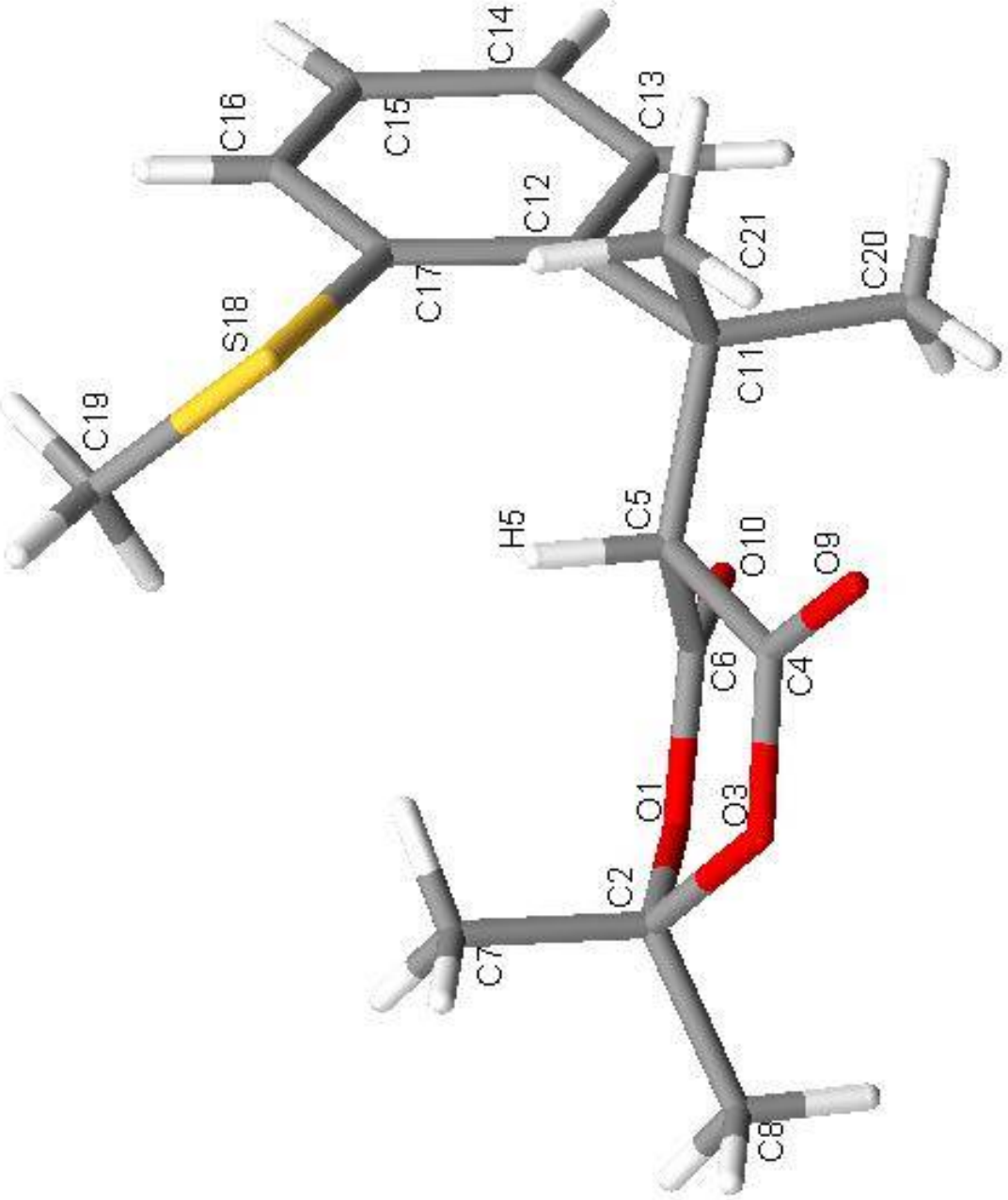
Table 4 Bond lengths [Å] and angles [º]

O(1)-C(6)	1.3511(15)
O(1)-C(2)	1.4366(15)
C(2)-O(3)	1.4392(15)
C(2)-C(8)	1.508(2)
C(2)-C(7)	1.509(2)
O(3)-C(4)	1.3465(14)
C(4)-O(9)	1.1953(14)
C(4)-C(5)	1.5261(16)
C(5)-C(6)	1.5220(17)
C(5)-C(11)	1.5606(16)
C(6)-O(10)	1.1958(15)
C(11)-C(12)	1.5337(17)
C(11)-C(19)	1.5353(16)
C(11)-C(20)	1.5482(16)
C(12)-C(13)	1.3953(16)
C(12)-C(17)	1.3955(16)
C(13)-C(14)	1.3874(18)
C(14)-C(15)	1.3842(18)
C(15)-C(16)	1.3788(18)
C(16)-C(17)	1.3740(18)
C(17)-F(18)	1.3684(13)
C(6)-O(1)-C(2)	121.44(9)
O(1)-C(2)-O(3)	109.87(10)
O(1)-C(2)-C(8)	111.71(11)
O(3)-C(2)-C(8)	110.37(11)
O(1)-C(2)-C(7)	105.63(11)
O(3)-C(2)-C(7)	105.58(11)
C(8)-C(2)-C(7)	113.40(12)
C(4)-O(3)-C(2)	120.61(9)
O(9)-C(4)-O(3)	118.32(10)
O(9)-C(4)-C(5)	125.22(10)
O(3)-C(4)-C(5)	116.47(10)
C(6)-C(5)-C(4)	110.91(9)
C(6)-C(5)-C(11)	116.57(9)
C(4)-C(5)-C(11)	112.55(9)
O(10)-C(6)-O(1)	117.91(11)
O(10)-C(6)-C(5)	126.22(11)
O(1)-C(6)-C(5)	115.84(10)
C(12)-C(11)-C(19)	112.67(10)
C(12)-C(11)-C(20)	106.14(9)
C(19)-C(11)-C(20)	107.91(10)
C(12)-C(11)-C(5)	109.47(9)
C(19)-C(11)-C(5)	109.24(9)

C(20)-C(11)-C(5)	111.39(9)
C(13)-C(12)-C(17)	114.45(11)
C(13)-C(12)-C(11)	123.37(10)
C(17)-C(12)-C(11)	121.98(10)
C(14)-C(13)-C(12)	122.09(11)
C(15)-C(14)-C(13)	120.72(12)
C(16)-C(15)-C(14)	119.09(12)
C(17)-C(16)-C(15)	118.71(12)
F(18)-C(17)-C(16)	116.44(10)
F(18)-C(17)-C(12)	118.63(11)
C(16)-C(17)-C(12)	124.93(11)

Crystallographic data for 5.27




C14
C13
C16
C15
C12
C21
C20
C17
S18
C11
C19
H5
C5
O10
O9
C6
C4
O1
O3
C2
C7
C8

Crystallization solvent: benzene/petroleum ether (diffusion technique)

Table 1 Crystal data and structure refinement for $C_{16}H_{20}O_4S$

Empirical formula	$C_{16}H_{20}O_4S$
Formula weight	308.38
Temperature	180(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Pbca
Unit cell dimensions	a = 9.6108(6) Å, b = 9.9743(6) Å, c = 33.578(2) Å
Volume	3218.8(3) $Å^3$
Z, Calculated density	8, 1.273 mg/m^3
Absorption coefficient	0.213 mm^{-1}
F(000)	1312
Crystal size	0.28 x 0.24 x 0.20 mm
Theta range for data collection	3.01 to 30.00º
Limiting indices	-11<h<13, -13<k<13, -47<l<47
Reflections collected / unique	29314 / 4676 [R_{int} = 0.0349]
Completeness to theta = 30.00	99.6%
Max. and min. transmission	0.9586 and 0.9427
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4676 / 0 / 192
Goodness-of-fit on F^2	1.178
Final R indices [I>2sigma(I)]	R1 = 0.0458, wR2 = 0.0996
R indices (all data)	R1 = 0.0554, wR2 = 0.1053
Largest diff. peak and hole	0.324 and -0.286 e. $Å^{-3}$

Table 2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
S(18)	2323(1)	7473(1)	3281(1)	45(1)
O(9)	-304(1)	7129(1)	4515(1)	45(1)
O(10)	310(1)	11069(1)	3903(1)	48(1)
O(1)	1742(1)	10527(1)	4384(1)	35(1)
O(3)	1321(1)	8494(1)	4721(1)	35(1)
C(17)	1084(2)	8672(2)	3105(1)	38(1)
C(12)	-137(2)	8999(2)	3316(1)	37(1)
C(13)	-1019(2)	9944(2)	3140(1)	50(1)
C(14)	-718(2)	10557(2)	2781(1)	60(1)
C(15)	485(2)	10234(2)	2581(1)	59(1)
C(16)	1361(2)	9284(2)	2739(1)	51(1)
C(19)	3937(2)	8339(2)	3207(1)	64(1)
C(11)	-538(2)	8354(2)	3719(1)	35(1)
C(21)	-651(2)	6822(2)	3654(1)	50(1)
C(20)	-1961(2)	8831(2)	3873(1)	51(1)
C(5)	609(1)	8696(1)	4029(1)	27(1)
C(4)	475(2)	8026(1)	4432(1)	32(1)
C(2)	2344(2)	9515(1)	4639(1)	32(1)
C(8)	2605(2)	10208(2)	5032(1)	43(1)
C(7)	3642(2)	8920(2)	4460(1)	38(1)
C(6)	840(2)	10188(1)	4090(1)	32(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
H(13)	-1859	10174	3273	59
H(14)	-1341	11199	2672	72
H(15)	709	10663	2337	71
H(16)	2175	9036	2597	61
H(19Z)	4708	7770	3296	96
H(19Y)	3934	9173	3362	96
H(19X)	4050	8549	2924	96
H(21Z)	-1381	6634	3458	75
H(21Y)	-885	6386	3907	75
H(21X)	240	6475	3557	75
H(20Z)	-1933	9802	3918	76
H(20Y)	-2176	8374	4124	76
H(20X)	-2680	8622	3676	76
H(5)	1496	8348	3913	33
H(8Z)	1727	10571	5134	64
H(8Y)	3271	10940	4993	64
H(8X)	2984	9562	5223	64
H(7Z)	3412	8490	4206	57
H(7Y)	4030	8252	4642	57
H(7X)	4327	9632	4414	57

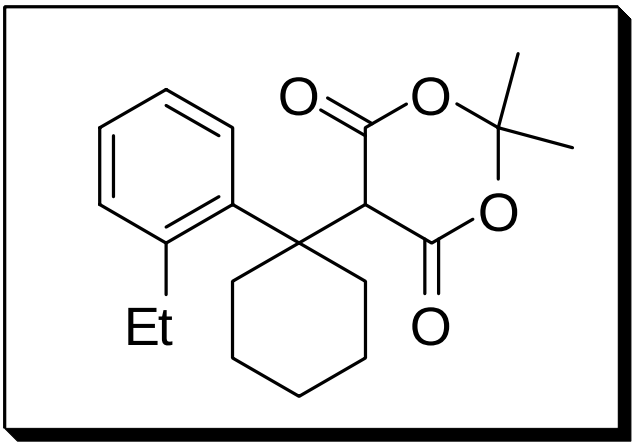
Table 4 Bond lengths [Å] and angles [°]

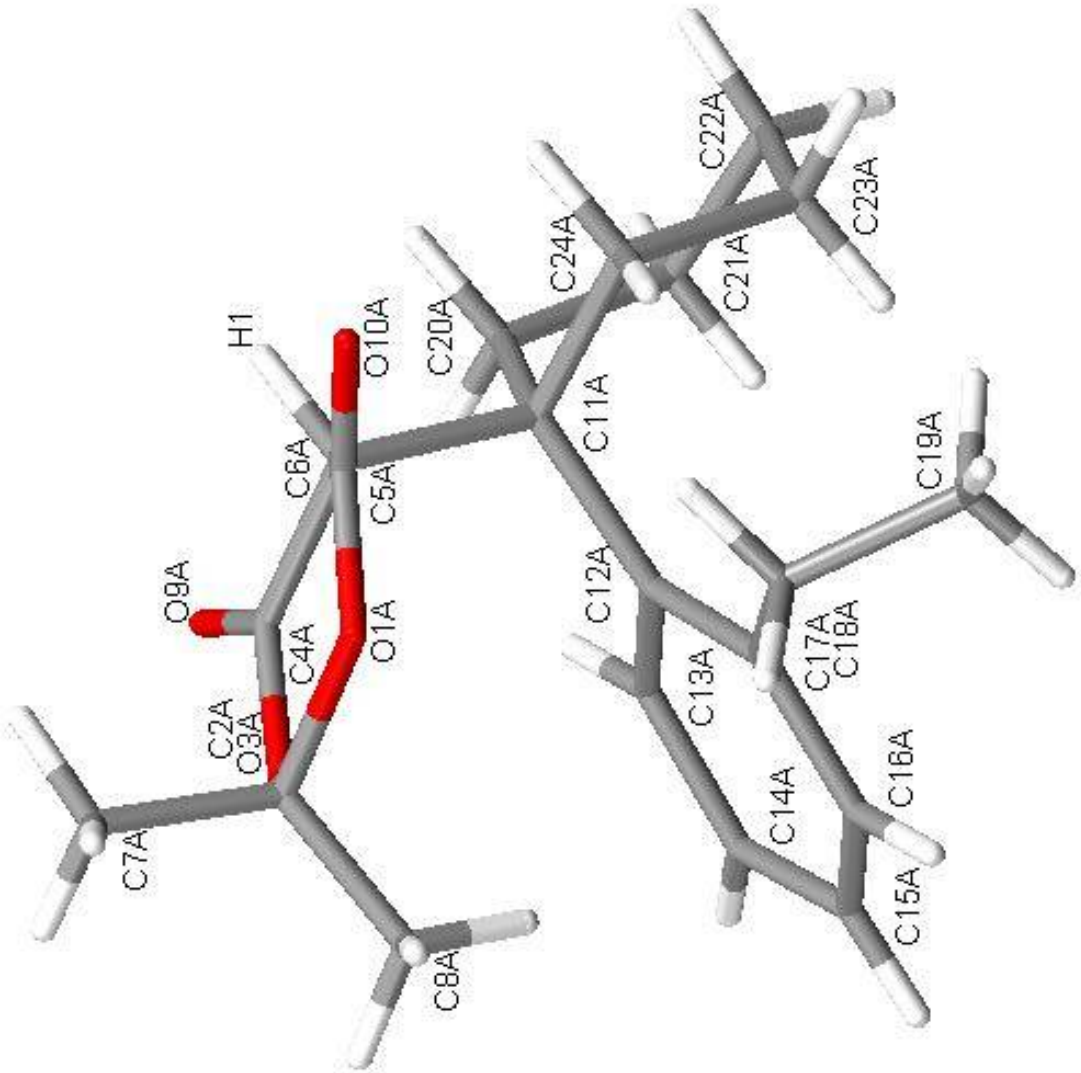
S(18)-C(17)	1.7891(17)
S(18)-C(19)	1.792(2)
O(9)-C(4)	1.1993(17)
O(10)-C(6)	1.1950(16)
O(1)-C(6)	1.3547(16)
O(1)-C(2)	1.4447(16)
O(3)-C(4)	1.3481(18)
O(3)-C(2)	1.4422(17)
C(17)-C(16)	1.395(2)
C(17)-C(12)	1.408(2)
C(12)-C(13)	1.398(2)
C(12)-C(11)	1.547(2)
C(13)-C(14)	1.384(3)
C(13)-H(13)	0.9500
C(14)-C(15)	1.375(3)
C(14)-H(14)	0.9500
C(15)-C(16)	1.375(3)
C(15)-H(15)	0.9500
C(16)-H(16)	0.9500
C(19)-H(19Z)	0.9800
C(19)-H(19Y)	0.9800
C(19)-H(19X)	0.9800
C(11)-C(20)	1.538(2)
C(11)-C(21)	1.547(2)
C(11)-C(5)	1.5551(19)
C(21)-H(21Z)	0.9800
C(21)-H(21Y)	0.9800
C(21)-H(21X)	0.9800
C(20)-H(20Z)	0.9800
C(20)-H(20Y)	0.9800
C(20)-H(20X)	0.9800
C(5)-C(4)	1.5140(18)
C(5)-C(6)	1.5193(18)
C(5)-H(5)	1.0000
C(2)-C(7)	1.506(2)
C(2)-C(8)	1.5112(19)
C(8)-H(8Z)	0.9800
C(8)-H(8Y)	0.9800
C(8)-H(8X)	0.9800
C(7)-H(7Z)	0.9800
C(7)-H(7Y)	0.9800

C(7)-H(7X)	0.9800
C(17)-S(18)-C(19)	102.01(9)
C(6)-O(1)-C(2)	120.84(10)
C(4)-O(3)-C(2)	121.25(10)
C(16)-C(17)-C(12)	119.99(16)
C(16)-C(17)-S(18)	117.12(14)
C(12)-C(17)-S(18)	122.88(12)
C(13)-C(12)-C(17)	116.70(15)
C(13)-C(12)-C(11)	119.85(15)
C(17)-C(12)-C(11)	123.44(14)
C(14)-C(13)-C(12)	122.59(19)
C(14)-C(13)-H(13)	118.7
C(12)-C(13)-H(13)	118.7
C(15)-C(14)-C(13)	119.83(19)
C(15)-C(14)-H(14)	120.1
C(13)-C(14)-H(14)	120.1
C(14)-C(15)-C(16)	119.21(17)
C(14)-C(15)-H(15)	120.4
C(16)-C(15)-H(15)	120.4
C(15)-C(16)-C(17)	121.64(18)
C(15)-C(16)-H(16)	119.2
C(17)-C(16)-H(16)	119.2
S(18)-C(19)-H(19Z)	109.5
S(18)-C(19)-H(19Y)	109.5
H(19Z)-C(19)-H(19Y)	109.5
S(18)-C(19)-H(19X)	109.5
H(19Z)-C(19)-H(19X)	109.5
H(19Y)-C(19)-H(19X)	109.5
C(20)-C(11)-C(12)	112.83(14)
C(20)-C(11)-C(21)	106.87(14)
C(12)-C(11)-C(21)	107.86(12)
C(20)-C(11)-C(5)	109.61(12)
C(12)-C(11)-C(5)	108.58(11)
C(21)-C(11)-C(5)	111.10(13)
C(11)-C(21)-H(21Z)	109.5
C(11)-C(21)-H(21Y)	109.5
H(21Z)-C(21)-H(21Y)	109.5
C(11)-C(21)-H(21X)	109.5
H(21Z)-C(21)-H(21X)	109.5
H(21Y)-C(21)-H(21X)	109.5
C(11)-C(20)-H(20Z)	109.5
C(11)-C(20)-H(20Y)	109.5
H(20Z)-C(20)-H(20Y)	109.5
C(11)-C(20)-H(20X)	109.5
H(20Z)-C(20)-H(20X)	109.5
H(20Y)-C(20)-H(20X)	109.5
C(4)-C(5)-C(6)	108.90(11)
C(4)-C(5)-C(11)	116.25(11)
C(6)-C(5)-C(11)	114.17(11)
C(4)-C(5)-H(5)	105.5
C(6)-C(5)-H(5)	105.5
C(11)-C(5)-H(5)	105.5
O(9)-C(4)-O(3)	117.96(13)
O(9)-C(4)-C(5)	126.08(14)
O(3)-C(4)-C(5)	115.97(12)
O(3)-C(2)-O(1)	109.44(11)
O(3)-C(2)-C(7)	111.30(11)
O(1)-C(2)-C(7)	111.77(12)
O(3)-C(2)-C(8)	105.61(12)
O(1)-C(2)-C(8)	105.30(11)
C(7)-C(2)-C(8)	113.07(13)
C(2)-C(8)-H(8Z)	109.5
C(2)-C(8)-H(8Y)	109.5
H(8Z)-C(8)-H(8Y)	109.5
C(2)-C(8)-H(8X)	109.5
H(8Z)-C(8)-H(8X)	109.5
H(8Y)-C(8)-H(8X)	109.5
C(2)-C(7)-H(7Z)	109.5
C(2)-C(7)-H(7Y)	109.5
H(7Z)-C(7)-H(7Y)	109.5

C(2)-C(7)-H(7X)	109.5
H(7Z)-C(7)-H(7X)	109.5
H(7Y)-C(7)-H(7X)	109.5
O(10)-C(6)-O(1)	118.23(12)
O(10)-C(6)-C(5)	125.88(13)
O(1)-C(6)-C(5)	115.89(11)

Crystallographic data for 5.35

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C5A
C20A
C24A
C22A
C23A
C21A
C11A
O9A
O1A
C4A
C2A
O3A
C12A
C19A
C17A
C18A
C13A
C14A
C16A
C7A
C15A
C8A

Crystallization solvent: benzene/hexane (diffusion technique)

Table 1. Crystal data and structure refinement for $C_{20}H_{26}O_4$

Empirical formula	$C_{20}H_{26}O_4$	
Formula weight	330.41	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system, space group	Triclinic, P -1	
Unit cell dimensions	a = 15.3157(7) Å	α= 108.696(3)°
	b = 16.1213(11) Å	β= 112.449(3)°
	c = 17.3561(8) Å	γ = 101.980(3)°
Volume	3474.9(3) $Å^3$	
Z, Calculated density	8, 1.263 g/cm^3	
Absorption coefficient	0.087 mm^{-1}	
F(000)	1424	
Crystal size	0.30 x 0.24 x 0.20 mm	
Theta range for data collection	2.56 to 25.00º	
Limiting indices	-18<=h<=17, -19<=k<=19, -20<=l<=20	
Reflections collected / unique	2768 / 12190 [R_{int} = 0.0639]	
Completeness to theta = 28.00	99.6%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.983 and 0.837	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12190 / 0 / 877	
Goodness-of-fit on F^2	1.036	
Final R indices [I>2σ(I)]	R1 = 0.0736, wR2 = 0.1779	
R indices (all data)	R1 = 0.1758, wR2 = 0.2364	
Largest diff. peak and hole	0.686 and -0.454 $e^-.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

	x	y	z	U(eq)
O(1A)	12264(2)	-11655(2)	12799(2)	47(1)
O(3A)	11487(2)	-10571(2)	13227(2)	41(1)
O(9A)	12376(2)	-9250(2)	14519(2)	41(1)
O(10A)	13886(2)	-11338(2)	13681(2)	47(1)
C(2A)	11335(3)	-11539(3)	12751(2)	35(1)
C(4A)	12387(3)	-9919(3)	13966(2)	31(1)
C(5A)	13346(2)	-10043(3)	13995(2)	29(1)
C(6A)	13206(3)	-11056(3)	13513(2)	36(1)
C(7A)	10941(3)	-12082(3)	13187(3)	56(1)
C(8A)	10606(3)	-11876(3)	11740(2)	56(1)
C(11A)	13837(2)	-9378(2)	13635(2)	28(1)
C(12A)	13003(2)	-9486(3)	12708(2)	28(1)
C(13A)	12490(2)	-8868(3)	12765(2)	34(1)
C(14A)	11714(3)	-8890(3)	11999(3)	43(1)
C(15A)	11435(3)	-9541(3)	11122(3)	47(1)
C(16A)	11921(3)	-10166(3)	11043(2)	42(1)
C(17A)	12686(3)	-10174(3)	11804(2)	35(1)
C(18A)	13042(3)	-10990(3)	11522(2)	44(1)
C(19A)	13710(3)	-10833(3)	11067(3)	62(1)
C(20A)	14301(3)	-8350(3)	14420(2)	37(1)

C(21A)	14883(3)	-7614(3)	14233(3)	45(1)
C(22A)	15737(3)	-7849(3)	14096(3)	47(1)
C(23A)	15326(3)	-8851(3)	13357(2)	40(1)
C(24A)	14777(2)	-9558(3)	13590(2)	36(1)
O(1B)	8417(2)	-15888(2)	8420(2)	47(1)
O(3B)	7646(2)	-14771(2)	8779(2)	45(1)
O(9B)	8568(2)	-13272(2)	9695(2)	39(1)
O(10B)	10076(2)	-15436(2)	9061(2)	39(1)
C(2B)	7523(3)	-15749(3)	8450(3)	40(1)
C(4B)	8535(3)	-14038(3)	9252(2)	32(1)
C(5B)	9428(2)	-14199(3)	9151(2)	29(1)
C(6B)	9353(3)	-15202(3)	8898(2)	31(1)
C(7B)	7364(3)	-16096(3)	9107(3)	61(1)
C(8B)	6653(3)	-16259(3)	7484(3)	59(1)
C(11B)	9645(2)	-13798(3)	8483(2)	29(1)
C(12B)	8638(3)	-14214(3)	7524(2)	35(1)
C(13B)	8019(3)	-13684(3)	7429(3)	40(1)
C(14B)	7123(3)	-13959(3)	6632(3)	48(1)
C(15B)	6784(3)	-14801(4)	5894(3)	58(1)
C(16B)	7365(4)	-15364(3)	5955(3)	65(2)
C(17B)	8258(3)	-15081(3)	6762(3)	49(1)
C(18B)	8699(4)	-15863(4)	6692(3)	79(2)
C(19B)	9099(4)	-16049(4)	6035(3)	67(1)
C(20B)	9985(3)	-12717(3)	8977(2)	40(1)
C(21B)	10335(3)	-12212(3)	8474(3)	48(1)
C(22B)	11214(3)	-12408(4)	8381(3)	61(2)
C(23B)	10911(3)	-13484(4)	7895(3)	70(2)
C(24B)	10563(3)	-13968(4)	8414(3)	57(1)
O(1C)	13494(2)	-15851(2)	8306(2)	46(1)
O(3C)	12626(2)	-14817(2)	8645(2)	43(1)
O(9C)	13484(2)	-13315(2)	9629(2)	43(1)
O(10C)	15155(2)	-15350(2)	9096(2)	39(1)
C(2C)	12560(3)	-15776(3)	8273(3)	39(1)
C(4C)	13510(3)	-14050(3)	9185(2)	32(1)
C(5C)	14454(2)	-14151(2)	9162(2)	28(1)
C(6C)	14413(3)	-15145(3)	8881(2)	31(1)
C(7C)	12316(3)	-16222(3)	8841(3)	55(1)
C(8C)	11767(3)	-16243(3)	7266(3)	57(1)
C(11C)	14744(2)	-13678(2)	8565(2)	29(1)
C(12C)	13833(3)	-14135(3)	7550(2)	38(1)
C(13C)	13073(3)	-13745(3)	7401(3)	40(1)
C(14C)	12214(3)	-14067(3)	6548(3)	49(1)
C(15C)	12087(3)	-14831(3)	5813(3)	56(1)
C(16C)	12831(3)	-15250(3)	5935(3)	49(1)
C(17C)	13668(3)	-14914(3)	6778(2)	46(1)
C(18C)	14419(3)	-15446(3)	6800(3)	55(1)
C(19C)	14109(4)	-16252(3)	5925(3)	65(1)
C(20C)	14963(3)	-12602(3)	9047(2)	35(1)
C(21C)	15351(2)	-12060(3)	8592(3)	41(1)
C(22C)	16325(3)	-12127(3)	8631(3)	41(1)
C(23C)	16188(3)	-13159(3)	8217(3)	48(1)
C(24C)	15782(3)	-13693(3)	8673(3)	40(1)
O(1D)	17406(2)	-11578(2)	12782(2)	44(1)
O(3D)	16574(2)	-10576(2)	13248(2)	40(1)
O(9D)	17408(2)	-9278(2)	14558(2)	38(1)
O(10)	19036(2)	-11234(2)	13680(2)	45(1)
C(2D)	16470(3)	-11529(3)	12764(2)	40(1)
C(4D)	17452(3)	-9916(3)	13997(2)	32(1)
C(5D)	18442(2)	-9983(3)	14041(2)	30(1)
C(6D)	18335(3)	-10970(3)	13522(2)	33(1)
C(7D)	16178(3)	-12097(3)	13225(3)	58(1)
C(8D)	15700(3)	-11891(3)	11761(2)	58(1)
C(11D)	18910(2)	-9261(3)	13713(2)	27(1)
C(12D)	18071(2)	-9371(3)	12785(2)	28(1)
C(13D)	17539(2)	-8770(3)	12858(2)	33(1)
C(14D)	16764(3)	-8790(3)	12093(3)	39(1)
C(15D)	16500(3)	-9420(3)	11212(3)	43(1)
C(16D)	17003(3)	-10022(3)	11124(2)	41(1)
C(17D)	17781(2)	-10035(3)	11885(2)	33(1)
C(18D)	18180(3)	-10809(3)	11587(2)	43(1)
C(19D)	18856(3)	-10584(3)	11168(3)	52(1)

C(20D)	19327(3)	-8252(2)	14525(2)	34(1)
C(21D)	19892(3)	-7474(3)	14377(3)	45(1)
C(22D)	20780(3)	-7637(3)	14252(3)	49(1)
C(23D)	20409(3)	-8626(3)	13490(2)	41(1)
C(24D)	19872(2)	-9388(3)	13680(2)	37(1)

Table 3. Hydrogen coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

	x	y	z	U(eq)
H(1)	13846	-9811	14665	35
H(2)	11464	-11858	13831	84
H(3)	10776	-12757	12837	84
H(4)	10326	-11986	13176	84
H(5)	10882	-11469	11507	84
H(6)	9947	-11851	11669	84
H(7)	10514	-12528	11387	84
H(13A)	12684	-8403	13364	41
H(14A)	11379	-8460	12080	51
H(15A)	10921	-9558	10586	57
H(16A)	11727	-10618	10438	50
H(18A)	12436	-11583	11080	53
H(18B)	13434	-11068	12080	53
H(19A)	13811	-11417	10801	93
H(19B)	14373	-10326	11538	93
H(19C)	13372	-10656	10575	93
H(20A)	13743	-8180	14494	44
H(20B)	14769	-8331	15012	44
H(21A)	14407	-7590	13671	54
H(21B)	15171	-6983	14764	54
H(22A)	16052	-7405	13908	56
H(22B)	16269	-7777	14689	56
H(23A)	15896	-9007	13298	49
H(23B)	14847	-8902	12752	49
H(24A)	15255	-9506	14196	43
H(24B)	14552	-10207	13111	43
H(8)	10039	-13810	9781	34
H(9)	7972	-15746	9721	92
H(10)	7244	-16771	8876	92
H(11)	6773	-15999	9154	92
H(12)	6777	-15956	7108	88
H(13)	6023	-16238	7494	88
H(14)	6587	-16919	7213	88
H(13B)	8229	-13102	7945	48
H(14B)	6745	-13561	6600	57
H(15B)	6162	-15005	5344	70
H(16B)	7143	-15949	5437	78
H(18C)	9255	-15688	7317	95
H(18D)	8157	-16456	6511	95
H(19D)	9324	-16579	6015	100
H(19E)	9677	-15485	6236	100
H(19F)	8562	-16210	5414	100
H(20C)	9410	-12563	9028	48
H(20D)	10551	-12475	9615	48
H(21C)	9759	-12424	7848	57
H(21D)	10540	-11522	8823	57
H(22C)	11819	-12135	9003	73
H(22D)	11389	-12114	8012	73
H(23C)	10352	-13742	7251	84
H(23D)	11501	-13621	7866	84
H(24C)	10384	-14656	8089	68
H(24D)	11135	-13729	9048	68
H(15)	15023	-13775	9816	34
H(16)	12860	-15874	9489	82
H(17)	12260	-16880	8596	82
H(18)	11667	-16203	8807	82
H(19)	11988	-15924	6939	86
H(20)	11119	-16199	7212	86

H(21)	11677	-16909	6989	86
H(13C)	13155	-13229	7917	47
H(14C)	11733	-13771	6476	58
H(15C)	11502	-15080	5221	67
H(16C)	12742	-15771	5420	59
H(18E)	15090	-14986	6994	66
H(18F)	14512	-15673	7282	66
H(19G)	14613	-16550	6022	97
H(19H)	14067	-16033	5452	97
H(19I)	13441	-16713	5717	97
H(20E)	14329	-12522	9017	42
H(20F)	15477	-12334	9711	42
H(21E)	14825	-12313	7935	49
H(21F)	15460	-11386	8910	49
H(22E)	16880	-11797	9284	50
H(22F)	16514	-11818	8278	50
H(23E)	16851	-13201	8301	58
H(23F)	15706	-13461	7542	58
H(24E)	16281	-13407	9343	48
H(24F)	15718	-14358	8392	48
H(22)	18936	-9767	14709	36
H(23)	16733	-11852	13861	86
H(24)	16053	-12760	12874	86
H(25)	15558	-12049	13243	86
H(26)	15916	-11467	11515	87
H(27)	15034	-11915	11709	87
H(28)	15647	-12526	11404	87
H(13D)	17716	-8325	13460	39
H(14D)	16417	-8372	12176	47
H(15D)	15982	-9436	10679	51
H(16D)	16817	-10458	10516	49
H(18G)	18574	-10901	12135	52
H(18H)	17593	-11410	11125	52
H(19J)	18972	-11150	10878	79
H(19K)	19511	-10077	11659	79
H(19L)	18520	-10380	10698	79
H(20G)	18749	-8121	14590	41
H(20H)	19793	-8243	15113	41
H(21G)	19412	-7444	13820	54
H(21H)	20150	-6858	14919	54
H(22G)	21316	-7566	14842	59
H(22H)	21077	-7162	14083	59
H(23G)	20998	-8743	13439	49
H(23H)	19932	-8667	12889	49
H(24G)	20348	-9350	14280	44
H(24H)	19674	-10020	13184	44

Table 4. Bond lengths [Å] and angles [º]

O(1A)-C(6A)	1.356(4)
O(1A)-C(2A)	1.448(4)
O(3A)-C(4A)	1.354(4)
O(3A)-C(2A)	1.431(4)
O(9A)-C(4A)	1.199(4)
O(10A)-C(6A)	1.194(4)
C(2A)-C(7A)	1.502(5)
C(2A)-C(8A)	1.503(5)
C(4A)-C(5A)	1.509(5)
C(5A)-C(6A)	1.501(5)
C(5A)-C(11A)	1.599(5)
C(5A)-H(1)	1.0000
C(7A)-H(2)	0.9800
C(7A)-H(3)	0.9800
C(7A)-H(4)	0.9800
C(8A)-H(5)	0.9800
C(8A)-H(6)	0.9800
(8A)-H(7)	0.9800
C(11A)-C(24A)	1.551(5)
C(11A)-C(12A)	1.552(4)

C(11A)-C(20A)	1.559(5)
C(12A)-C(13A)	1.393(5)
C(12A)-C(17A)	1.417(5)
C(13A)-C(14A)	1.388(5)
C(13A)-H(13A)	0.9500
C(14A)-C(15A)	1.377(5)
C(14A)-H(14A)	0.9500
C(15A)-C(16A)	1.375(6)
C(15A)-H(15A)	0.9500
C(16A)-C(17A)	1.398(5)
C(16A)-H(16A)	0.9500
C(17A)-C(18A)	1.535(5)
C(18A)-C(19A)	1.539(5)
C(18A)-H(18A)	0.9900
C(18A)-H(18B)	0.9900
C(19A)-H(19A)	0.9800
C(19A)-H(19B)	0.9800
C(19A)-H(19C)	0.9800
C(20A)-C(21A)	1.528(5)
C(20A)-H(20A)	0.9900
C(20A)-H(20B)	0.9900
C(21A)-C(22A)	1.515(5)
C(21A)-H(21A)	0.9900
C(21A)-H(21B)	0.9900
C(22A)-C(23A)	1.512(5)
C(22A)-H(22A)	0.9900
C(22A)-H(22B)	0.9900
C(23A)-C(24A)	1.525(5)
C(23A)-H(23A)	0.9900
C(23A)-H(23B)	0.9900
C(24A)-H(24A)	0.9900
C(24A)-H(24B)	0.9900
O(1B)-C(6B)	1.347(4)
O(1B)-C(2B)	1.449(4)
O(3B)-C(4B)	1.335(4)
O(3B)-C(2B)	1.437(5)
O(9B)-C(4B)	1.206(4)
O(10B)-C(6B)	1.205(4)
C(2B)-C(8B)	1.489(5)
C(2B)-C(7B)	1.496(5)
C(4B)-C(5B)	1.506(5)
C(5B)-C(6B)	1.499(5)
C(5B)-C(11B)	1.599(4)
C(5B)-H(8)	1.0000
C(7B)-H(9)	0.9800
C(7B)-H(10)	0.9800
C(7B)-H(11)	0.9800
C(8B)-H(12)	0.9800
C(8B)-H(13)	0.9800
C(8B)-H(14)	0.9800
C(11B)-C(24B)	1.528(5)
C(11B)-C(20B)	1.539(5)
C(11B)-C(12B)	1.578(4)
C(12B)-C(17B)	1.390(5)
C(12B)-C(13B)	1.401(5)
C(13B)-C(14B)	1.378(5)
C(13B)-H(13B)	0.9500
C(14B)-C(15B)	1.355(6)
C(14B)-H(14B)	0.9500
C(15B)-C(16B)	1.397(6)
C(15B)-H(15B)	0.9500
C(16B)-C(17B)	1.381(5)
C(16B)-H(16B)	0.9500
C(17B)-C(18B)	1.542(6)
C(18B)-C(19B)	1.469(6)
C(18B)-H(18C)	0.9900
C(18B)-H(18D)	0.9900
C(19B)-H(19D)	0.9800
C(19B)-H(19E)	0.9800
C(19B)-H(19F)	0.9800
C(20B)-C(21B)	1.531(5)

C(20B)-H(20C)	0.9900
C(20B)-H(20D)	0.9900
C(21B)-C(22B)	1.499(6)
C(21B)-H(21C)	0.9900
C(21B)-H(21D)	0.9900
C(22B)-C(23B)	1.538(7)
C(22B)-H(22C)	0.9900
C(22B)-H(22D)	0.9900
C(23B)-C(24B)	1.532(5)
C(23B)-H(23C)	0.9900
C(23B)-H(23D)	0.9900
C(24B)-H(24C)	0.9900
C(24B)-H(24D)	0.9900
O(1C)-C(6C)	1.344(4)
O(1C)-C(2C)	1.441(4)
O(3C)-C(4C)	1.354(4)
O(3C)-C(2C)	1.438(5)
O(9C)-C(4C)	1.207(4)
O(10C)-C(6C)	1.205(4)
C(2C)-C(7C)	1.500(5)
C(2C)-C(8C)	1.501(5)
C(4C)-C(5C)	1.502(5)
C(5C)-C(6C)	1.498(5)
C(5C)-C(11C)	1.605(4)
C(5C)-H(15)	1.0000
C(7C)-H(16)	0.9800
C(7C)-H(17)	0.9800
C(7C)-H(18)	0.9800
C(8C)-H(19)	0.9800
C(8C)-H(20)	0.9800
C(8C)-H(21)	0.9800
C(11C)-C(24C)	1.534(5)
C(11C)-C(20C)	1.560(5)
C(11C)-C(12C)	1.568(4)
C(12C)-C(17C)	1.402(5)
C(12C)-C(13C)	1.413(5)
C(13C)-C(14C)	1.388(5)
C(13C)-H(13C)	0.9500
C(14C)-C(15C)	1.373(6)
C(14C)-H(14C)	0.9500
C(15C)-C(16C)	1.423(6)
C(15C)-H(15C)	0.9500
C(16C)-C(17C)	1.360(5)
C(16C)-H(16C)	0.9500
C(17C)-C(18C)	1.567(6)
C(18C)-C(19C)	1.466(6)
C(18C)-H(18E)	0.9900
C(18C)-H(18F)	0.9900
C(19C)-H(19G)	0.9800
C(19C)-H(19H)	0.9800
C(19C)-H(19I)	0.9800
C(20C)-C(21C)	1.525(5)
C(20C)-H(20E)	0.9900
C(20C)-H(20F)	0.9900
C(21C)-C(22C)	1.495(5)
C(21C)-H(21E)	0.9900
C(21C)-H(21F)	0.9900
C(22C)-C(23C)	1.518(6)
C(22C)-H(22E)	0.9900
C(22C)-H(22F)	0.9900
C(23C)-C(24C)	1.531(5)
C(23C)-H(23E)	0.9900
C(23C)-H(23F)	0.9900
C(24C)-H(24E)	0.9900
C(24C)-H(24F)	0.9900
O(1D)-C(6D)	1.361(4)
O(1D)-C(2D)	1.441(4)
O(3D)-C(4D)	1.348(4)
O(3D)-C(2D)	1.435(5)
O(9D)-C(4D)	1.202(4)
O(10)-C(6D)	1.204(4)

C(2D)-C(7D)	1.501(5)
C(2D)-C(8D)	1.502(5)
C(4D)-C(5D)	1.516(5)
C(5D)-C(6D)	1.494(5)
C(5D)-C(11D)	1.606(5)
C(5D)-H(22)	1.0000
C(7D)-H(23)	0.9800
C(7D)-H(24)	0.9800
C(7D)-H(25)	0.9800
C(8D)-H(26)	0.9800
C(8D)-H(27)	0.9800
C(8D)-H(28)	0.9800
C(11D)-C(24D)	1.550(5)
C(11D)-C(12D)	1.556(4)
C(11D)-C(20D)	1.566(5)
C(12D)-C(13D)	1.395(5)
C(12D)-C(17D)	1.408(5)
C(13D)-C(14D)	1.388(5)
C(13D)-H(13D)	0.9500
C(14D)-C(15D)	1.376(5)
C(14D)-H(14D)	0.9500
C(15D)-C(16D)	1.364(6)
C(15D)-H(15D)	0.9500
C(16D)-C(17D)	1.410(5)
C(16D)-H(16D)	0.9500
C(17D)-C(18D)	1.530(5)
C(18D)-C(19D)	1.524(5)
C(18D)-H(18G)	0.9900
C(18D)-H(18H)	0.9900
C(19D)-H(19J)	0.9800
C(19D)-H(19K)	0.9800
C(19D)-H(19L)	0.9800
C(20D)-C(21D)	1.523(5)
C(20D)-H(20G)	0.9900
C(20D)-H(20H)	0.9900
C(21D)-C(22D)	1.517(5)
C(21D)-H(21G)	0.9900
C(21D)-H(21H)	0.9900
C(22D)-C(23D)	1.521(5)
C(22D)-H(22G)	0.9900
C(22D)-H(22H)	0.9900
C(23D)-C(24D)	1.529(5)
C(23D)-H(23G)	0.9900
C(23D)-H(23H)	0.9900
C(24D)-H(24G)	0.9900
C(24D)-H(24H)	0.9900

C(6A)-O(1A)-C(2A)	123.2(3)
C(4A)-O(3A)-C(2A)	123.1(3)
O(3A)-C(2A)-O(1A)	112.5(3)
O(3A)-C(2A)-C(7A)	108.1(3)
O(1A)-C(2A)-C(7A)	109.4(3)
O(3A)-C(2A)-C(8A)	107.3(3)
O(1A)-C(2A)-C(8A)	106.5(3)
C(7A)-C(2A)-C(8A)	113.2(3)
O(9A)-C(4A)-O(3A)	118.5(3)
O(9A)-C(4A)-C(5A)	124.1(3)
O(3A)-C(4A)-C(5A)	117.2(3)
C(6A)-C(5A)-C(4A)	113.6(3)
C(6A)-C(5A)-C(11A)	113.0(3)
C(4A)-C(5A)-C(11A)	110.4(3)
C(6A)-C(5A)-H(1)	106.4
C(4A)-C(5A)-H(1)	106.4
C(11A)-C(5A)-H(1)	106.4
O(10A)-C(6A)-O(1A)	119.2(4)
O(10A)-C(6A)-C(5A)	123.7(3)
O(1A)-C(6A)-C(5A)	116.9(3)
C(2A)-C(7A)-H(2)	109.5
C(2A)-C(7A)-H(3)	109.5
H(2)-C(7A)-H(3)	109.5
C(2A)-C(7A)-H(4)	109.5

H(2)-C(7A)-H(4)	109.5
H(3)-C(7A)-H(4)	109.5
C(2A)-C(8A)-H(5)	109.5
C(2A)-C(8A)-H(6)	109.5
H(5)-C(8A)-H(6)	109.5
C(2A)-C(8A)-H(7)	109.5
H(5)-C(8A)-H(7)	109.5
H(6)-C(8A)-H(7)	109.5
C(24A)-C(11A)-C(12A)	114.4(3)
C(24A)-C(11A)-C(20A)	103.7(3)
C(12A)-C(11A)-C(20A)	111.6(3)
C(24A)-C(11A)-C(5A)	110.8(3)
C(12A)-C(11A)-C(5A)	109.9(2)
C(20A)-C(11A)-C(5A)	106.0(2)
C(13A)-C(12A)-C(17A)	116.3(3)
C(13A)-C(12A)-C(11A)	117.3(3)
C(17A)-C(12A)-C(11A)	126.3(3)
C(14A)-C(13A)-C(12A)	124.0(4)
C(14A)-C(13A)-H(13A)	118.0
C(12A)-C(13A)-H(13A)	118.0
C(15A)-C(14A)-C(13A)	119.2(4)
C(15A)-C(14A)-H(14A)	120.4
C(13A)-C(14A)-H(14A)	120.4
C(16A)-C(15A)-C(14A)	118.2(4)
C(16A)-C(15A)-H(15A)	120.9
C(14A)-C(15A)-H(15A)	120.9
C(15A)-C(16A)-C(17A)	123.6(4)
C(15A)-C(16A)-H(16A)	118.2
C(17A)-C(16A)-H(16A)	118.2
C(16A)-C(17A)-C(12A)	118.6(4)
C(16A)-C(17A)-C(18A)	112.7(3)
C(12A)-C(17A)-C(18A)	128.6(3)
C(17A)-C(18A)-C(19A)	113.0(4)
C(17A)-C(18A)-H(18A)	109.0
C(19A)-C(18A)-H(18A)	109.0
C(17A)-C(18A)-H(18B)	109.0
C(19A)-C(18A)-H(18B)	109.0
H(18A)-C(18A)-H(18B)	107.8
C(18A)-C(19A)-H(19A)	109.5
C(18A)-C(19A)-H(19B)	109.5
H(19A)-C(19A)-H(19B)	109.5
C(18A)-C(19A)-H(19C)	109.5
H(19A)-C(19A)-H(19C)	109.5
H(19B)-C(19A)-H(19C)	109.5
C(21A)-C(20A)-C(11A)	113.7(3)
C(21A)-C(20A)-H(20A)	108.8
C(11A)-C(20A)-H(20A)	108.8
C(21A)-C(20A)-H(20B)	108.8
C(11A)-C(20A)-H(20B)	108.8
H(20A)-C(20A)-H(20B)	107.7
C(22A)-C(21A)-C(20A)	111.1(4)
C(22A)-C(21A)-H(21A)	109.4
C(20A)-C(21A)-H(21A)	109.4
C(22A)-C(21A)-H(21B)	109.4
C(20A)-C(21A)-H(21B)	109.4
H(21A)-C(21A)-H(21B)	108.0
C(23A)-C(22A)-C(21A)	110.1(3)
C(23A)-C(22A)-H(22A)	109.6
C(21A)-C(22A)-H(22A)	109.6
C(23A)-C(22A)-H(22B)	109.6
C(21A)-C(22A)-H(22B)	109.6
H(22A)-C(22A)-H(22B)	108.2
C(22A)-C(23A)-C(24A)	111.6(3)
C(22A)-C(23A)-H(23A)	109.3
C(24A)-C(23A)-H(23A)	109.3
C(22A)-C(23A)-H(23B)	109.3
C(24A)-C(23A)-H(23B)	109.3
H(23A)-C(23A)-H(23B)	108.0
C(23A)-C(24A)-C(11A)	111.4(3)
C(23A)-C(24A)-H(24A)	109.4
C(11A)-C(24A)-H(24A)	109.4

C(23A)-C(24A)-H(24B)	109.4
C(11A)-C(24A)-H(24B)	109.4
H(24A)-C(24A)-H(24B)	108.0
C(6B)-O(1B)-C(2B)	124.2(3)
C(4B)-O(3B)-C(2B)	125.4(3)
O(3B)-C(2B)-O(1B)	112.3(3)
O(3B)-C(2B)-C(8B)	107.1(3)
O(1B)-C(2B)-C(8B)	108.0(3)
O(3B)-C(2B)-C(7B)	108.4(3)
O(1B)-C(2B)-C(7B)	107.3(3)
C(8B)-C(2B)-C(7B)	113.8(3)
O(9B)-C(4B)-O(3B)	118.4(3)
O(9B)-C(4B)-C(5B)	123.4(3)
O(3B)-C(4B)-C(5B)	118.1(3)
C(6B)-C(5B)-C(4B)	113.1(3)
C(6B)-C(5B)-C(11B)	113.4(3)
C(4B)-C(5B)-C(11B)	111.6(3)
C(6B)-C(5B)-H(8)	106.0
C(4B)-C(5B)-H(8)	106.0
C(11B)-C(5B)-H(8)	106.0
O(10B)-C(6B)-O(1B)	117.8(4)
O(10B)-C(6B)-C(5B)	124.1(3)
O(1B)-C(6B)-C(5B)	118.0(3)
C(2B)-C(7B)-H(9)	109.5
C(2B)-C(7B)-H(10)	109.5
H(9)-C(7B)-H(10)	109.5
C(2B)-C(7B)-H(11)	109.5
H(9)-C(7B)-H(11)	109.5
H(10)-C(7B)-H(11)	109.5
C(2B)-C(8B)-H(12)	109.5
C(2B)-C(8B)-H(13)	109.5
H(12)-C(8B)-H(13)	109.5
C(2B)-C(8B)-H(14)	109.5
H(12)-C(8B)-H(14)	109.5
H(13)-C(8B)-H(14)	109.5
C(24B)-C(11B)-C(20B)	105.3(3)
C(24B)-C(11B)-C(12B)	115.2(3)
C(20B)-C(11B)-C(12B)	109.7(3)
C(24B)-C(11B)-C(5B)	109.6(3)
C(20B)-C(11B)-C(5B)	106.7(3)
C(12B)-C(11B)-C(5B)	109.9(3)
C(17B)-C(12B)-C(13B)	115.0(3)
C(17B)-C(12B)-C(11B)	127.3(4)
C(13B)-C(12B)-C(11B)	117.6(3)
C(14B)-C(13B)-C(12B)	123.8(4)
C(14B)-C(13B)-H(13B)	118.1
C(12B)-C(13B)-H(13B)	118.1
C(15B)-C(14B)-C(13B)	119.6(4)
C(15B)-C(14B)-H(14B)	120.2
C(13B)-C(14B)-H(14B)	120.2
C(14B)-C(15B)-C(16B)	119.0(4)
C(14B)-C(15B)-H(15B)	120.5
C(16B)-C(15B)-H(15B)	120.5
C(17B)-C(16B)-C(15B)	120.7(4)
C(17B)-C(16B)-H(16B)	119.7
C(15B)-C(16B)-H(16B)	119.7
C(16B)-C(17B)-C(12B)	121.8(4)
C(16B)-C(17B)-C(18B)	110.8(4)
C(12B)-C(17B)-C(18B)	127.3(4)
C(19B)-C(18B)-C(17B)	115.7(4)
C(19B)-C(18B)-H(18C)	108.4
C(17B)-C(18B)-H(18C)	108.4
C(19B)-C(18B)-H(18D)	108.4
C(17B)-C(18B)-H(18D)	108.4
H(18C)-C(18B)-H(18D)	107.4
C(18B)-C(19B)-H(19D)	109.5
C(18B)-C(19B)-H(19E)	109.5
H(19D)-C(19B)-H(19E)	109.5
C(18B)-C(19B)-H(19F)	109.5
H(19D)-C(19B)-H(19F)	109.5
H(19E)-C(19B)-H(19F)	109.5

C(21B)-C(20B)-C(11B)	113.2(3)
C(21B)-C(20B)-H(20C)	108.9
C(11B)-C(20B)-H(20C)	108.9
C(21B)-C(20B)-H(20D)	108.9
C(11B)-C(20B)-H(20D)	108.9
H(20C)-C(20B)-H(20D)	107.8
C(22B)-C(21B)-C(20B)	111.8(4)
C(22B)-C(21B)-H(21C)	109.3
C(20B)-C(21B)-H(21C)	109.3
C(22B)-C(21B)-H(21D)	109.3
C(20B)-C(21B)-H(21D)	109.3
H(21C)-C(21B)-H(21D)	107.9
C(21B)-C(22B)-C(23B)	108.8(3)
C(21B)-C(22B)-H(22C)	109.9
C(23B)-C(22B)-H(22C)	109.9
C(21B)-C(22B)-H(22D)	109.9
C(23B)-C(22B)-H(22D)	109.9
H(22C)-C(22B)-H(22D)	108.3
C(24B)-C(23B)-C(22B)	111.2(4)
C(24B)-C(23B)-H(23C)	109.4
C(22B)-C(23B)-H(23C)	109.4
C(24B)-C(23B)-H(23D)	109.4
C(22B)-C(23B)-H(23D)	109.4
H(23C)-C(23B)-H(23D)	108.0
C(11B)-C(24B)-C(23B)	112.8(3)
C(11B)-C(24B)-H(24C)	109.0
C(23B)-C(24B)-H(24C)	109.0
C(11B)-C(24B)-H(24D)	109.0
C(23B)-C(24B)-H(24D)	109.0
H(24C)-C(24B)-H(24D)	107.8
C(6C)-O(1C)-C(2C)	123.6(3)
C(4C)-O(3C)-C(2C)	124.5(3)
O(3C)-C(2C)-O(1C)	113.3(3)
O(3C)-C(2C)-C(7C)	107.9(3)
O(1C)-C(2C)-C(7C)	108.0(3)
O(3C)-C(2C)-C(8C)	106.6(3)
O(1C)-C(2C)-C(8C)	106.8(3)
C(7C)-C(2C)-C(8C)	114.2(3)
O(9C)-C(4C)-O(3C)	117.9(3)
O(9C)-C(4C)-C(5C)	123.9(3)
O(3C)-C(4C)-C(5C)	118.2(3)
C(6C)-C(5C)-C(4C)	113.4(3)
C(6C)-C(5C)-C(11C)	113.1(3)
C(4C)-C(5C)-C(11C)	111.5(3)
C(6C)-C(5C)-H(15)	106.1
C(4C)-C(5C)-H(15)	106.1
C(11C)-C(5C)-H(15)	106.1
O(10C)-C(6C)-O(1C)	118.0(4)
O(10C)-C(6C)-C(5C)	124.0(3)
O(1C)-C(6C)-C(5C)	117.8(3)
C(2C)-C(7C)-H(16)	109.5
C(2C)-C(7C)-H(17)	109.5
H(16)-C(7C)-H(17)	109.5
C(2C)-C(7C)-H(18)	109.5
H(16)-C(7C)-H(18)	109.5
H(17)-C(7C)-H(18)	109.5
C(2C)-C(8C)-H(19)	109.5
C(2C)-C(8C)-H(20)	109.5
H(19)-C(8C)-H(20)	109.5
C(2C)-C(8C)-H(21)	109.5
H(19)-C(8C)-H(21)	109.5
H(20)-C(8C)-H(21)	109.5
C(24C)-C(11C)-C(20C)	103.4(3)
C(24C)-C(11C)-C(12C)	117.1(3)
C(20C)-C(11C)-C(12C)	109.6(3)
C(24C)-C(11C)-C(5C)	108.7(3)
C(20C)-C(11C)-C(5C)	107.5(3)
C(12C)-C(11C)-C(5C)	110.1(3)
C(17C)-C(12C)-C(13C)	116.2(3)
C(17C)-C(12C)-C(11C)	127.1(4)
C(13C)-C(12C)-C(11C)	116.6(3)

C(14C)-C(13C)-C(12C)	124.1(4)
C(14C)-C(13C)-H(13C)	118.0
C(12C)-C(13C)-H(13C)	118.0
C(15C)-C(14C)-C(13C)	117.5(4)
C(15C)-C(14C)-H(14C)	121.2
C(13C)-C(14C)-H(14C)	121.2
C(14C)-C(15C)-C(16C)	120.1(4)
C(14C)-C(15C)-H(15C)	119.9
C(16C)-C(15C)-H(15C)	119.9
C(17C)-C(16C)-C(15C)	121.0(4)
C(17C)-C(16C)-H(16C)	119.5
C(15C)-C(16C)-H(16C)	119.5
C(16C)-C(17C)-C(12C)	121.0(4)
C(16C)-C(17C)-C(18C)	114.9(4)
C(12C)-C(17C)-C(18C)	124.0(3)
C(19C)-C(18C)-C(17C)	116.1(3)
C(19C)-C(18C)-H(18E)	108.3
C(17C)-C(18C)-H(18E)	108.3
C(19C)-C(18C)-H(18F)	108.3
C(17C)-C(18C)-H(18F)	108.3
H(18E)-C(18C)-H(18F)	107.4
C(18C)-C(19C)-H(19G)	109.5
C(18C)-C(19C)-H(19H)	109.5
H(19G)-C(19C)-H(19H)	109.5
C(18C)-C(19C)-H(19I)	109.5
H(19G)-C(19C)-H(19I)	109.5
H(19H)-C(19C)-H(19I)	109.5
C(21C)-C(20C)-C(11C)	112.0(3)
C(21C)-C(20C)-H(20E)	109.2
C(11C)-C(20C)-H(20E)	109.2
C(21C)-C(20C)-H(20F)	109.2
C(11C)-C(20C)-H(20F)	109.2
H(20E)-C(20C)-H(20F)	107.9
C(22C)-C(21C)-C(20C)	112.4(3)
C(22C)-C(21C)-H(21E)	109.1
C(20C)-C(21C)-H(21E)	109.1
C(22C)-C(21C)-H(21F)	109.1
C(20C)-C(21C)-H(21F)	109.1
H(21E)-C(21C)-H(21F)	107.8
C(21C)-C(22C)-C(23C)	109.4(3)
C(21C)-C(22C)-H(22E)	109.8
C(23C)-C(22C)-H(22E)	109.8
C(21C)-C(22C)-H(22F)	109.8
C(23C)-C(22C)-H(22F)	109.8
H(22E)-C(22C)-H(22F)	108.2
C(22C)-C(23C)-C(24C)	111.7(3)
C(22C)-C(23C)-H(23E)	109.3
C(24C)-C(23C)-H(23E)	109.3
C(22C)-C(23C)-H(23F)	109.3
C(24C)-C(23C)-H(23F)	109.3
H(23E)-C(23C)-H(23F)	107.9
C(23C)-C(24C)-C(11C)	112.9(3)
C(23C)-C(24C)-H(24E)	109.0
C(11C)-C(24C)-H(24E)	109.0
C(23C)-C(24C)-H(24F)	109.0
C(11C)-C(24C)-H(24F)	109.0
H(24E)-C(24C)-H(24F)	107.8
C(6D)-O(1D)-C(2D)	121.9(3)
C(4D)-O(3D)-C(2D)	122.5(3)
O(3D)-C(2D)-O(1D)	112.1(3)
O(3D)-C(2D)-C(7D)	108.5(3)
O(1D)-C(2D)-C(7D)	108.4(3)
O(3D)-C(2D)-C(8D)	107.6(3)
O(1D)-C(2D)-C(8D)	106.5(3)
C(7D)-C(2D)-C(8D)	113.8(3)
O(9D)-C(4D)-O(3D)	118.4(3)
O(9D)-C(4D)-C(5D)	123.9(3)
O(3D)-C(4D)-C(5D)	117.6(3)
C(6D)-C(5D)-C(4D)	113.0(3)
C(6D)-C(5D)-C(11D)	112.6(3)
C(4D)-C(5D)-C(11D)	109.9(3)

C(6D)-C(5D)-H(22)	107.0
C(4D)-C(5D)-H(22)	107.0
C(11D)-C(5D)-H(22)	107.0
O(10)-C(6D)-O(1D)	118.6(4)
O(10)-C(6D)-C(5D)	123.7(3)
O(1D)-C(6D)-C(5D)	117.5(3)
C(2D)-C(7D)-H(23)	109.5
C(2D)-C(7D)-H(24)	109.5
H(23)-C(7D)-H(24)	109.5
C(2D)-C(7D)-H(25)	109.5
H(23)-C(7D)-H(25)	109.5
H(24)-C(7D)-H(25)	109.5
C(2D)-C(8D)-H(26)	109.5
C(2D)-C(8D)-H(27)	109.5
H(26)-C(8D)-H(27)	109.5
C(2D)-C(8D)-H(28)	109.5
H(26)-C(8D)-H(28)	109.5
H(27)-C(8D)-H(28)	109.5
C(24D)-C(11D)-C(12D)	114.3(3)
C(24D)-C(11D)-C(20D)	104.3(3)
C(12D)-C(11D)-C(20D)	112.1(3)
C(24D)-C(11D)-C(5D)	109.9(3)
C(12D)-C(11D)-C(5D)	110.1(2)
C(20D)-C(11D)-C(5D)	105.6(2)
C(13D)-C(12D)-C(17D)	117.3(3)
C(13D)-C(12D)-C(11D)	116.5(3)
C(17D)-C(12D)-C(11D)	126.2(3)
C(14D)-C(13D)-C(12D)	123.1(3)
C(14D)-C(13D)-H(13D)	118.4
C(12D)-C(13D)-H(13D)	118.4
C(15D)-C(14D)-C(13D)	119.6(4)
C(15D)-C(14D)-H(14D)	120.2
C(13D)-C(14D)-H(14D)	120.2
C(16D)-C(15D)-C(14D)	118.3(4)
C(16D)-C(15D)-H(15D)	120.9
C(14D)-C(15D)-H(15D)	120.9
C(15D)-C(16D)-C(17D)	123.8(4)
C(15D)-C(16D)-H(16D)	118.1
C(17D)-C(16D)-H(16D)	118.1
C(12D)-C(17D)-C(16D)	117.9(4)
C(12D)-C(17D)-C(18D)	129.3(3)
C(16D)-C(17D)-C(18D)	112.8(3)
C(19D)-C(18D)-C(17D)	113.3(3)
C(19D)-C(18D)-H(18G)	108.9
C(17D)-C(18D)-H(18G)	108.9
C(19D)-C(18D)-H(18H)	108.9
C(17D)-C(18D)-H(18H)	108.9
H(18G)-C(18D)-H(18H)	107.7
C(18D)-C(19D)-H(19J)	109.5
C(18D)-C(19D)-H(19K)	109.5
H(19J)-C(19D)-H(19K)	109.5
C(18D)-C(19D)-H(19L)	109.5
H(19J)-C(19D)-H(19L)	109.5
H(19K)-C(19D)-H(19L)	109.5
C(21D)-C(20D)-C(11D)	113.2(3)
C(21D)-C(20D)-H(20G)	108.9
C(11D)-C(20D)-H(20G)	108.9
C(21D)-C(20D)-H(20H)	108.9
C(11D)-C(20D)-H(20H)	108.9
H(20G)-C(20D)-H(20H)	107.8
C(22D)-C(21D)-C(20D)	112.1(4)
C(22D)-C(21D)-H(21G)	109.2
C(20D)-C(21D)-H(21G)	109.2
C(22D)-C(21D)-H(21H)	109.2
C(20D)-C(21D)-H(21H)	109.2
H(21G)-C(21D)-H(21H)	107.9
C(21D)-C(22D)-C(23D)	109.5(3)
C(21D)-C(22D)-H(22G)	109.8
C(23D)-C(22D)-H(22G)	109.8
C(21D)-C(22D)-H(22H)	109.8
C(23D)-C(22D)-H(22H)	109.8

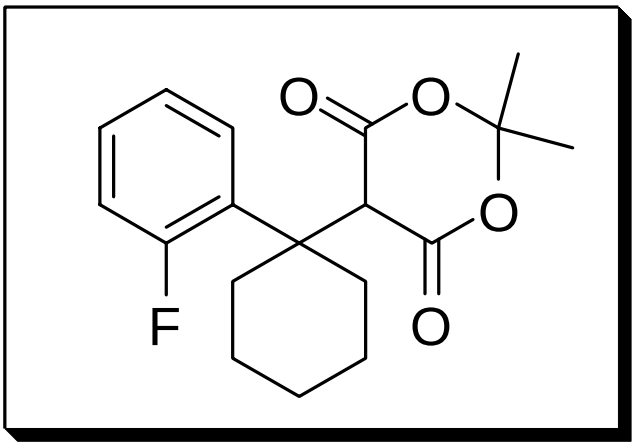
H(22G)-C(22D)-H(22H)	108.2
C(22D)-C(23D)-C(24D)	112.1(3)
C(22D)-C(23D)-H(23G)	109.2
C(24D)-C(23D)-H(23G)	109.2
C(22D)-C(23D)-H(23H)	109.2
C(24D)-C(23D)-H(23H)	109.2
H(23G)-C(23D)-H(23H)	107.9
C(23D)-C(24D)-C(11D)	110.9(3)
C(23D)-C(24D)-H(24G)	109.5
C(11D)-C(24D)-H(24G)	109.5
C(23D)-C(24D)-H(24H)	109.5
C(11D)-C(24D)-H(24H)	109.5
H(24G)-C(24D)-H(24H)	108.0

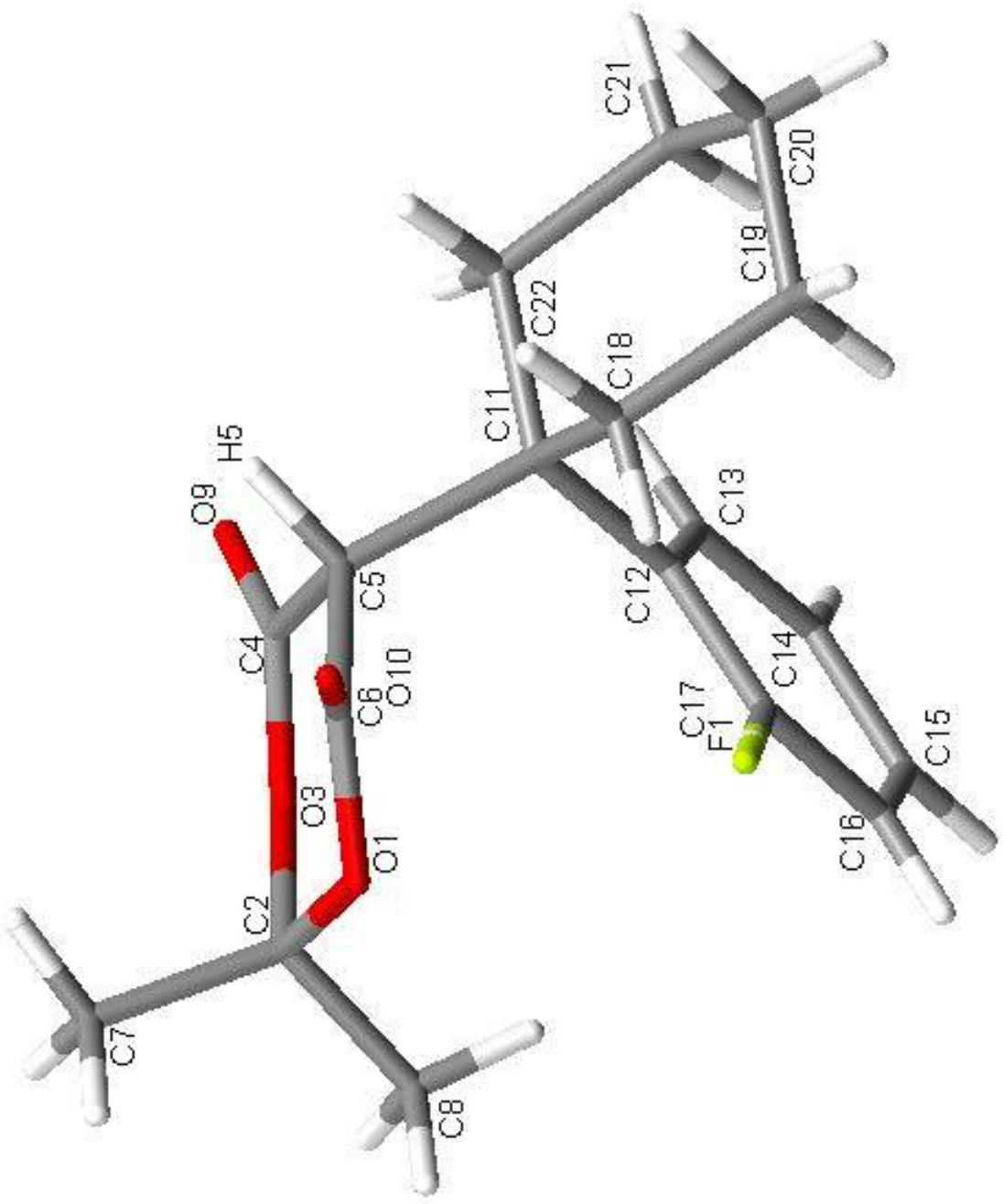
Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$).

	U11	U22	U33	U23	U13	U12
O(1A)	45(2)	30(2)	52(2)	8(1)	18(1)	15(1)
O(3A)	30(1)	31(2)	57(2)	20(1)	16(1)	10(1)
O(9A)	45(2)	41(2)	48(2)	21(1)	30(1)	22(1)
O(10A)	50(2)	42(2)	56(2)	27(2)	22(1)	29(2)
C(2A)	36(2)	27(2)	39(2)	13(2)	16(2)	10(2)
C(4A)	34(2)	32(2)	34(2)	22(2)	18(2)	13(2)
C(5A)	33(2)	31(2)	24(2)	16(2)	10(2)	14(2)
C(6A)	40(2)	35(2)	38(2)	23(2)	18(2)	17(2)
C(7A)	69(3)	43(3)	50(2)	24(2)	27(2)	6(2)
C(8A)	56(3)	57(3)	42(2)	25(2)	15(2)	10(2)
C(11A)	28(2)	30(2)	26(2)	13(2)	11(2)	11(2)
C(12A)	29(2)	30(2)	27(2)	14(2)	14(2)	10(2)
C(13A)	34(2)	40(2)	42(2)	24(2)	24(2)	17(2)
C(14A)	33(2)	60(3)	60(3)	45(2)	25(2)	25(2)
C(15A)	28(2)	67(3)	47(3)	40(2)	10(2)	10(2)
C(16A)	39(2)	46(3)	30(2)	19(2)	10(2)	5(2)
C(17A)	36(2)	35(2)	36(2)	18(2)	17(2)	11(2)
C(18A)	58(3)	37(3)	32(2)	11(2)	21(2)	17(2)
C(19A)	78(3)	62(3)	53(3)	22(2)	37(2)	33(3)
C(20A)	34(2)	36(2)	34(2)	13(2)	15(2)	9(2)
C(21A)	41(2)	35(2)	47(2)	12(2)	20(2)	2(2)
C(22A)	34(2)	53(3)	44(2)	20(2)	17(2)	4(2)
C(23A)	31(2)	54(3)	45(2)	25(2)	23(2)	19(2)
C(24A)	28(2)	45(3)	33(2)	16(2)	12(2)	17(2)
O(1B)	42(2)	29(2)	60(2)	10(1)	27(1)	10(1)
O(3B)	34(1)	31(2)	70(2)	18(1)	28(1)	10(1)
O(9B)	44(2)	32(2)	43(2)	12(1)	27(1)	14(1)
O(10B)	47(2)	44(2)	40(2)	28(1)	24(1)	26(1)
C(2B)	35(2)	33(2)	52(2)	17(2)	22(2)	13(2)
C(4B)	38(2)	30(2)	29(2)	16(2)	18(2)	10(2)
C(5B)	30(2)	34(2)	25(2)	15(2)	15(2)	12(2)
C(6B)	39(2)	33(2)	26(2)	17(2)	18(2)	17(2)
C(7B)	59(3)	74(4)	77(3)	50(3)	40(2)	32(3)
C(8B)	42(2)	54(3)	55(3)	15(2)	11(2)	10(2)
C(11B)	35(2)	33(2)	31(2)	20(2)	20(2)	15(2)
C(12B)	39(2)	42(3)	35(2)	22(2)	21(2)	18(2)
C(13B)	41(2)	48(3)	47(2)	26(2)	27(2)	25(2)
C(14B)	41(2)	66(3)	40(2)	25(2)	20(2)	22(2)
C(15B)	57(3)	61(3)	41(3)	32(3)	8(2)	11(3)
C(16B)	99(4)	43(3)	30(2)	16(2)	13(2)	19(3)
C(17B)	68(3)	51(3)	37(2)	25(2)	24(2)	32(2)
C(18B)	133(5)	73(4)	56(3)	34(3)	49(3)	70(4)
C(19B)	100(4)	79(4)	68(3)	47(3)	61(3)	56(3)
C(20B)	40(2)	37(3)	41(2)	21(2)	16(2)	11(2)
C(21B)	51(2)	40(3)	51(2)	27(2)	25(2)	6(2)
C(22B)	36(2)	87(4)	66(3)	56(3)	23(2)	6(2)
C(23B)	70(3)	116(5)	110(4)	92(4)	73(3)	64(3)
C(24B)	61(3)	84(4)	83(3)	67(3)	52(3)	50(3)
O(1C)	36(2)	29(2)	61(2)	9(1)	24(1)	9(1)
O(3C)	33(1)	30(2)	64(2)	16(1)	25(1)	9(1)

O(9C)	52(2)	36(2)	54(2)	18(1)	38(1)	17(1)
O(10C)	41(2)	44(2)	43(2)	26(1)	22(1)	20(1)
C(2C)	37(2)	30(2)	48(2)	14(2)	22(2)	9(2)
C(4C)	38(2)	31(2)	39(2)	21(2)	26(2)	14(2)
C(5C)	33(2)	28(2)	27(2)	15(2)	16(2)	11(2)
C(6C)	37(2)	34(2)	29(2)	16(2)	21(2)	12(2)
C(7C)	55(3)	50(3)	64(3)	31(2)	31(2)	16(2)
C(8C)	44(2)	50(3)	54(3)	15(2)	13(2)	8(2)
C(11C)	29(2)	31(2)	26(2)	13(2)	15(2)	6(2)
C(12C)	42(2)	37(2)	35(2)	18(2)	20(2)	9(2)
C(13C)	39(2)	46(3)	48(2)	25(2)	28(2)	21(2)
C(14C)	47(2)	58(3)	48(2)	26(2)	26(2)	24(2)
C(15C)	50(3)	57(3)	36(2)	19(2)	8(2)	3(2)
C(16C)	55(3)	49(3)	34(2)	16(2)	18(2)	15(2)
C(17C)	59(3)	43(3)	25(2)	13(2)	14(2)	13(2)
C(18C)	71(3)	56(3)	69(3)	43(3)	41(3)	42(3)
C(19C)	88(3)	77(4)	51(3)	34(3)	43(3)	43(3)
C(20C)	32(2)	34(2)	42(2)	20(2)	19(2)	11(2)
C(21C)	35(2)	40(3)	54(2)	28(2)	22(2)	11(2)
C(22C)	33(2)	49(3)	44(2)	28(2)	18(2)	8(2)
C(23C)	50(2)	58(3)	65(3)	36(2)	43(2)	28(2)
C(24C)	42(2)	46(3)	55(2)	31(2)	32(2)	26(2)
O(1D)	48(2)	35(2)	41(2)	12(1)	18(1)	14(1)
O(3D)	30(1)	29(2)	51(2)	16(1)	15(1)	6(1)
O(9D)	42(2)	38(2)	42(2)	20(1)	25(1)	17(1)
O(10)	54(2)	43(2)	54(2)	29(1)	28(1)	29(2)
C(2D)	36(2)	32(2)	39(2)	11(2)	14(2)	4(2)
C(4D)	36(2)	32(2)	31(2)	18(2)	16(2)	11(2)
C(5D)	28(2)	35(2)	27(2)	16(2)	11(2)	13(2)
C(6D)	40(2)	32(2)	33(2)	20(2)	18(2)	15(2)
C(7D)	78(3)	35(3)	45(2)	15(2)	30(2)	-1(2)
C(8D)	50(2)	63(3)	40(2)	19(2)	14(2)	9(2)
C(11D)	24(2)	34(2)	28(2)	17(2)	12(2)	13(2)
C(12D)	28(2)	31(2)	29(2)	17(2)	13(2)	10(2)
C(13D)	30(2)	40(2)	38(2)	23(2)	20(2)	15(2)
C(14D)	34(2)	53(3)	53(2)	36(2)	26(2)	24(2)
C(15D)	27(2)	61(3)	47(2)	36(2)	14(2)	18(2)
C(16D)	39(2)	43(3)	27(2)	15(2)	9(2)	5(2)
C(17D)	35(2)	36(2)	35(2)	20(2)	20(2)	11(2)
C(18D)	57(2)	43(3)	35(2)	18(2)	24(2)	22(2)
C(19D)	64(3)	61(3)	50(2)	28(2)	37(2)	30(2)
C(20D)	34(2)	33(2)	32(2)	13(2)	16(2)	9(2)
C(21D)	41(2)	35(2)	45(2)	13(2)	19(2)	2(2)
C(22D)	34(2)	56(3)	41(2)	23(2)	12(2)	-1(2)
C(23D)	29(2)	60(3)	46(2)	31(2)	22(2)	21(2)
C(24D)	31(2)	51(3)	37(2)	27(2)	17(2)	17(2)

Crystallographic data for 5.36




C21
C20
C19
C22
C18
C11
H5
O9
C5
C13
C12
C4
C6
O10
C14
C17
F1
C15
C16
O3
O1
C2
C7
C8

Crystallization solvent: benzene/hexane (diffusion technique)

Table 1. Crystal data and structure refinement for $C_{18}H_{21}FO_4$

Empirical formula	$C_{18}H_{21}FO_4$
Formula weight	320.35
Temperature	150(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P 21/c
Unit cell dimensions	a = 15.5125(6) Å α= 90°
	b = 7.6198(2) Å β= 98.5560(19)°
	c = 14.4039(7) Å γ = 90°
Volume	1683.62(11) $Å^3$
Z, Calculated density	4, 1.264 g/cm^3
Absorption coefficient	0.095 mm^{-1}
F(000)	680
Crystal size	0.20 x 0.20 x 0.04 mm
Theta range for data collection	2.66 to 25.00º
Limiting indices	-18<=h<=18, -9<=k<=8, -17<=l<=16
Reflections collected / unique	8563 / 2945 [R_{int} = 0.0771]
Completeness to theta = 28.00	99.5%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.997 and 0.820
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2945 / 0 / 220
Goodness-of-fit on F^2	1.005
Final R indices [I>2σ(I)]	R1 = 0.0534, wR2 = 0.1096
R indices (all data)	R1 = 0.1345, wR2 = 0.1420
Largest diff. peak and hole	0.179 and -0.207 $e^-.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

	x	y	z	U(eq)
F(1)	2366(2)	554(3)	2599(2)	63(1)
F(1*)	3973(4)	-2289(8)	296(4)	51(2)
O(1)	749(2)	-1398(2)	1686(1)	52(1)
O(3)	1459(1)	-3682(2)	904(1)	49(1)
C(2)	830(2)	-3272(4)	1549(2)	41(1)
C(4)	1664(2)	-2612(4)	224(2)	36(1)
C(5)	1524(2)	-657(3)	344(2)	36(1)
C(6)	845(2)	-231(4)	1006(2)	38(1)
C(7)	-117(2)	-3977(4)	1168(2)	54(1)
C(8)	1239(2)	-4027(4)	2481(2)	53(1)
O(9)	1993(1)	-3234(2)	-421(1)	46(1)
O(10)	422(1)	1134(3)	980(1)	48(1)
C(11)	2503(2)	317(3)	603(2)	35(1)
C(12)	3120(2)	-700(3)	1380(2)	33(1)
C(13)	3801(2)	-1889(4)	1198(2)	37(1)
C(14)	4358(2)	-2820(4)	1894(2)	47(1)
C(15)	4233(2)	-2618(4)	2818(2)	51(1)
C(16)	3567(2)	-1496(4)	3037(2)	50(1)
C(17)	3030(2)	-560(4)	2327(2)	43(1)
C(18)	2346(2)	2233(3)	888(2)	47(1)

C(19)	3249(2)	3267(4)	1032(2)	55(1)
C(20)	3700(2)	3331(4)	151(2)	62(1)
C(21)	3830(2)	1487(4)	-212(2)	52(1)
C(22)	2931(2)	431(4)	-318(2)	42(1)

Table 3. Hydrogen coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

x	y	z	U(eq)	
H(5)	1268	-209	-289	43
H(7X)	-334	-3403	570	81
H(7Y)	-508	-3714	1625	81
H(7Z)	-95	-5248	1073	81
H(8X)	1817	-3505	2666	80
H(8Y)	1297	-5301	2423	80
H(8Z)	869	-3763	2959	80
H(13)	3880	-2057	563	45
H(14)	4805	-3561	1732	56
H(15)	4593	-3231	3303	61
H(16)	3478	-1370	3672	60
H(17*)	2592	192	2500	51
H(18A)	2090	2249	1478	56
H(18B)	1931	2809	393	56
H(19A)	3144	4483	1229	66
H(19B)	3648	2702	1547	66
H(20A)	3340	4023	-344	74
H(20B)	4273	3919	304	74
H(21A)	4276	863	231	63
H(21B)	4038	1554	-828	63
H(22A)	2512	1000	-813	51
H(22B)	3033	-776	-531	51

Table 4. Bond lengths [Å] and angles [º]

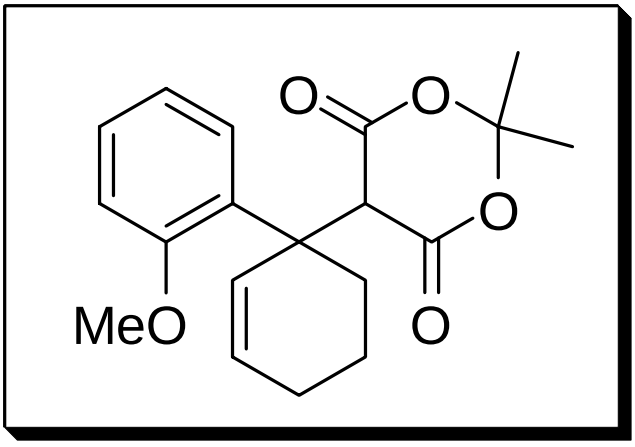
F(1)-C(17)	1.433(4)
O(1)-C(6)	1.347(3)
O(1)-C(2)	1.450(3)
O(3)-C(4)	1.349(3)
O(3)-C(2)	1.476(3)
C(2)-C(8)	1.511(4)
C(2)-C(7)	1.584(4)
C(4)-O(9)	1.221(3)
C(4)-C(5)	1.519(4)
C(5)-C(6)	1.556(4)
C(5)-C(11)	1.682(4)
C(6)-O(10)	1.227(3)
C(11)-C(18)	1.546(4)
C(11)-C(12)	1.566(4)
C(11)-C(22)	1.571(3)
C(12)-C(17)	1.396(4)
C(12)-C(13)	1.444(4)
C(13)-C(14)	1.413(4)
C(14)-C(15)	1.382(4)
C(15)-C(16)	1.412(4)
C(16)-C(17)	1.413(4)
C(18)-C(19)	1.594(4)
C(19)-C(20)	1.538(4)
C(20)-C(21)	1.523(4)
C(21)-C(22)	1.598(4)
C(6)-O(1)-C(2)	122.0(2)
C(4)-O(3)-C(2)	125.3(2)
O(1)-C(2)-O(3)	111.9(2)
O(1)-C(2)-C(8)	106.7(2)
O(3)-C(2)-C(8)	104.4(2)
O(1)-C(2)-C(7)	106.7(2)
O(3)-C(2)-C(7)	112.1(2)
C(8)-C(2)-C(7)	115.1(2)

O(9)-C(4)-O(3)	119.2(3)
O(9)-C(4)-C(5)	123.4(3)
O(3)-C(4)-C(5)	117.2(2)
C(4)-C(5)-C(6)	113.3(2)
C(4)-C(5)-C(11)	108.6(2)
C(6)-C(5)-C(11)	116.3(2)
O(10)-C(6)-O(1)	117.7(3)
O(10)-C(6)-C(5)	124.5(3)
O(1)-C(6)-C(5)	117.7(3)
C(18)-C(11)-C(12)	112.5(2)
C(18)-C(11)-C(22)	106.0(2)
C(12)-C(11)-C(22)	109.9(2)
C(18)-C(11)-C(5)	107.6(2)
C(12)-C(11)-C(5)	112.1(2)
C(22)-C(11)-C(5)	108.5(2)
C(17)-C(12)-C(13)	114.1(2)
C(17)-C(12)-C(11)	121.4(3)
C(13)-C(12)-C(11)	124.5(2)
C(14)-C(13)-C(12)	124.9(3)
C(15)-C(14)-C(13)	117.9(3)
C(14)-C(15)-C(16)	119.7(3)
C(15)-C(16)-C(17)	121.0(3)
C(12)-C(17)-C(16)	122.3(3)
C(12)-C(17)-F(1)	119.6(3)
C(16)-C(17)-F(1)	118.1(3)
C(11)-C(18)-C(19)	109.3(2)
C(20)-C(19)-C(18)	114.0(3)
C(21)-C(20)-C(19)	110.7(2)
C(20)-C(21)-C(22)	109.8(3)
C(11)-C(22)-C(21)	114.8(2)

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$).

	U11	U22	U33	U23	U13	U12
F(1)	71(2)	76(2)	44(1)	-12(1)	19(1)	11(2)
F(1*)	55(5)	56(4)	40(3)	-6(3)	7(3)	11(3)
O(1)	78(2)	37(1)	47(1)	-2(1)	27(1)	-2(1)
O(3)	69(2)	38(1)	46(1)	4(1)	30(1)	4(1)
C(2)	53(2)	33(2)	39(2)	-3(1)	17(2)	-2(2)
C(4)	33(2)	41(2)	33(2)	-1(2)	1(1)	-5(2)
C(5)	42(2)	34(2)	32(2)	1(1)	8(1)	2(1)
C(6)	40(2)	38(2)	37(2)	-3(2)	2(1)	-5(2)
C(7)	57(2)	55(2)	50(2)	-4(2)	4(2)	-4(2)
C(8)	65(3)	57(2)	38(2)	4(2)	7(2)	-4(2)
O(9)	56(2)	45(1)	40(1)	-7(1)	15(1)	1(1)
O(10)	48(2)	39(1)	58(1)	-5(1)	10(1)	5(1)
C(11)	37(2)	30(2)	37(2)	1(1)	5(1)	-1(1)
C(12)	37(2)	27(2)	34(2)	-2(1)	3(1)	-2(1)
C(13)	43(2)	33(2)	36(2)	1(1)	6(1)	2(2)
C(13*)	43(2)	33(2)	36(2)	1(1)	6(1)	2(2)
C(14)	43(2)	40(2)	55(2)	3(2)	1(2)	-4(2)
C(15)	53(2)	47(2)	48(2)	11(2)	-9(2)	-11(2)
C(16)	57(2)	57(2)	34(2)	4(2)	-1(2)	-11(2)
C(17)	45(2)	45(2)	38(2)	-5(2)	9(2)	-4(2)
C(17*)	45(2)	45(2)	38(2)	-5(2)	9(2)	-4(2)
C(18)	43(2)	34(2)	63(2)	-4(2)	3(2)	-1(2)
C(19)	44(2)	31(2)	88(2)	-4(2)	7(2)	0(2)
C(20)	50(2)	45(2)	88(3)	18(2)	1(2)	-8(2)
C(21)	51(2)	55(2)	52(2)	14(2)	14(2)	-4(2)
C(22)	44(2)	46(2)	37(2)	9(1)	7(1)	-3(2)

Crystallographic data for 5.38



C19
O18
C17
C16
C15
C14
C12
C13
C21
C22
C23
C24
C20
C11
H5
C5
O9
O10
C4
C6
O3
O1
C8
C2
C7

Crystallization solvent: benzene/petroleum ether (diffusion technique)

Table 1. Crystal data and structure refinement for $C_{19}H_{22}O_5$

Empirical formula	$C_{19}H_{22}O_5$	
Formula weight	330.37	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system, space group	Triclinic, P -1	
Unit cell dimensions	a = 6.0581(5) Å	α= 94.029(5)°
	b = 9.1995(10) Å	β= 100.953(6)°
	c = 15.9090(17) Å	γ = 100.439(6)°
Volume	851.03(15) $Å^3$	
Z, Calculated density	2, 1.289 g/cm^3	
Absorption coefficient	0.093 mm^{-1}	
F(000)	352	
Crystal size	0.24 x 0.20 x 0.12 mm	
Theta range for data collection	2.62 to 25.00º	
Limiting indices	-7<=h<=7, -10<=k<=10, -7<=l<=18	
Reflections collected / unique	2917 / 2917 [R_{int} = 0.0104]	
Completeness to theta = 28.00	97.5%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.019 and 0.640	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2917 / 0 / 221	
Goodness-of-fit on F^2	1.129	
Final R indices [I>2σ(I)]	R1 = 0.0851, wR2 = 0.2371	
R indices (all data)	R1 = 0.1108, wR2 = 0.2538	
Largest diff. peak and hole	0.274 and -0.265 $e^-.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

	x	y	z	U(eq)
O(1)	7448(6)	1142(3)	5663(2)	53(1)
O(3)	10394(5)	3087(4)	5519(2)	52(1)
O(9)	13103(5)	3877(4)	6675(2)	58(1)
O(10)	7290(6)	406(3)	6940(2)	58(1)
O(18)	8557(5)	5818(3)	7315(2)	54(1)
C(2)	8059(8)	2309(5)	5151(3)	52(1)
C(4)	11107(8)	3357(5)	6387(3)	46(1)
C(5)	9267(7)	2947(4)	6896(3)	41(1)
C(6)	7930(8)	1404(5)	6547(3)	47(1)
C(7)	8181(10)	1559(7)	4288(3)	69(2)
C(8)	6369(9)	3352(6)	5066(3)	63(1)
C(11)	10091(7)	3233(4)	7900(3)	41(1)
C(12)	11476(7)	4828(5)	8169(3)	43(1)
C(13)	13558(7)	5101(5)	8749(3)	45(1)
C(14)	14801(8)	6532(5)	9040(3)	53(1)
C(15)	13956(9)	7732(5)	8750(3)	56(1)
C(16)	11866(8)	7516(5)	8171(3)	53(1)
C(17)	10639(8)	6083(5)	7886(3)	45(1)
C(19)	7371(9)	7017(5)	7176(3)	55(1)
C(20)	7954(7)	3059(5)	8308(3)	45(1)
C(21)	8601(8)	2946(5)	9269(3)	50(1)
C(22)	9550(8)	1552(5)	9427(3)	53(1)

C(23)	11258(8)	1368(5)	8882(3)	50(1)
C(24)	11518(8)	2096(5)	8211(3)	46(1)

Table 3. Hydrogen coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

	x	y	z	U(eq)
H(5)	8120(80)	3630(50)	6780(30)	44(11)
H(7X)	9346	939	4370	103
H(7Y)	8592	2316	3910	103
H(7Z)	6686	934	4023	103
H(8X)	6414	3856	5635	95
H(8Y)	4818	2780	4829	95
H(8Z)	6784	4093	4680	95
H(13)	14162	4280	8957	54
H(14)	16227	6677	9438	63
H(15)	14798	8711	8946	67
H(16)	11279	8347	7971	64
H(19X)	5773	6621	6888	82
H(19Y)	8114	7685	6814	82
H(19Z)	7414	7567	7731	82
H(20X)	7212	3925	8213	54
H(20Y)	6838	2153	8026	54
H(21X)	9767	3831	9549	60
H(21Y)	7232	2921	9527	60
H(22X)	10294	1607	10042	63
H(22Y)	8276	675	9296	63
H(23)	12223	678	9029	60
H(24)	12654	1901	7905	55

Table 4. Bond lengths [Å] and angles [º]

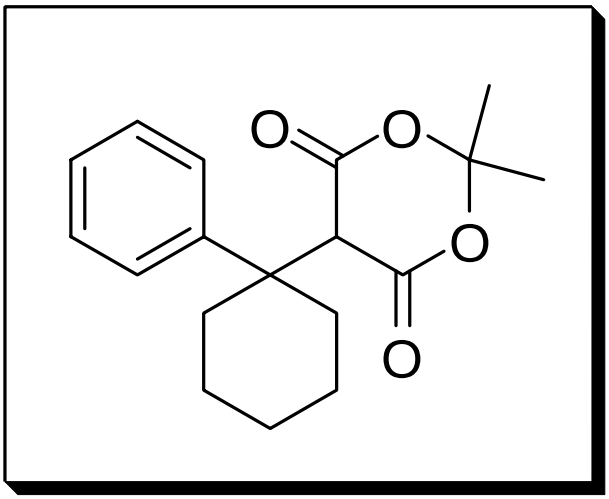
O(1)-C(6)	1.375(6)
O(1)-C(2)	1.430(6)
O(3)-C(4)	1.357(5)
O(3)-C(2)	1.455(6)
O(9)-C(4)	1.204(6)
O(10)-C(6)	1.195(5)
O(18)-C(17)	1.378(5)
O(18)-C(19)	1.429(5)
C(2)-C(7)	1.514(7)
C(2)-C(8)	1.520(7)
C(4)-C(5)	1.508(6)
C(5)-C(6)	1.510(6)
C(5)-C(11)	1.569(6)
C(11)-C(24)	1.525(6)
C(11)-C(12)	1.539(6)
C(11)-C(20)	1.543(6)
C(12)-C(13)	1.385(6)
C(12)-C(17)	1.410(6)
C(13)-C(14)	1.391(6)
C(14)-C(15)	1.371(7)
C(15)-C(16)	1.389(7)
C(16)-C(17)	1.389(6)
C(20)-C(21)	1.520(6)
C(21)-C(22)	1.515(6)
C(22)-C(23)	1.495(7)
C(23)-C(24)	1.318(7)
C(6)-O(1)-C(2)	120.5(3)
C(4)-O(3)-C(2)	119.7(3)
C(17)-O(18)-C(19)	118.8(3)
O(1)-C(2)-O(3)	108.7(4)
O(1)-C(2)-C(7)	106.4(4)
O(3)-C(2)-C(7)	104.9(4)
O(1)-C(2)-C(8)	111.9(4)
O(3)-C(2)-C(8)	112.2(4)
C(7)-C(2)-C(8)	112.3(5)
O(9)-C(4)-O(3)	118.2(4)

O(9)-C(4)-C(5)	126.6(4)
O(3)-C(4)-C(5)	115.2(4)
C(4)-C(5)-C(6)	108.4(3)
C(4)-C(5)-C(11)	115.4(3)
C(6)-C(5)-C(11)	115.8(4)
O(10)-C(6)-O(1)	117.5(4)
O(10)-C(6)-C(5)	128.2(4)
O(1)-C(6)-C(5)	114.2(4)
C(24)-C(11)-C(12)	110.9(4)
C(24)-C(11)-C(20)	109.4(4)
C(12)-C(11)-C(20)	108.0(3)
C(24)-C(11)-C(5)	109.5(3)
C(12)-C(11)-C(5)	110.6(3)
C(20)-C(11)-C(5)	108.3(3)
C(13)-C(12)-C(17)	116.7(4)
C(13)-C(12)-C(11)	120.9(4)
C(17)-C(12)-C(11)	122.3(4)
C(12)-C(13)-C(14)	122.5(4)
C(15)-C(14)-C(13)	119.6(5)
C(14)-C(15)-C(16)	120.0(4)
C(17)-C(16)-C(15)	119.9(4)
O(18)-C(17)-C(16)	121.8(4)
O(18)-C(17)-C(12)	116.9(4)
C(16)-C(17)-C(12)	121.3(4)
C(21)-C(20)-C(11)	110.9(4)
C(22)-C(21)-C(20)	110.3(4)
C(23)-C(22)-C(21)	111.3(4)
C(24)-C(23)-C(22)	124.6(4)
C(23)-C(24)-C(11)	123.5(4)

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$).

	U11	U22	U33	U23	U13	U12
O(1)	62(2)	41(2)	52(2)	-1(1)	9(2)	4(2)
O(3)	49(2)	57(2)	50(2)	0(1)	13(1)	7(2)
O(9)	46(2)	64(2)	58(2)	-7(2)	15(2)	1(2)
O(10)	69(2)	36(2)	63(2)	8(2)	5(2)	3(2)
O(18)	56(2)	36(2)	67(2)	1(1)	-1(2)	19(1)
C(2)	47(3)	53(3)	52(3)	3(2)	10(2)	4(2)
C(4)	52(3)	35(2)	52(3)	1(2)	14(2)	11(2)
C(5)	40(2)	33(2)	52(2)	1(2)	12(2)	11(2)
C(6)	46(2)	34(2)	61(3)	1(2)	8(2)	13(2)
C(7)	70(3)	78(4)	55(3)	-5(3)	15(3)	9(3)
C(8)	64(3)	73(4)	58(3)	12(3)	14(2)	23(3)
C(11)	43(2)	31(2)	49(2)	1(2)	11(2)	11(2)
C(12)	45(2)	40(2)	45(2)	-3(2)	14(2)	12(2)
C(13)	43(2)	43(2)	50(3)	0(2)	12(2)	11(2)
C(14)	48(3)	51(3)	57(3)	-5(2)	15(2)	6(2)
C(15)	59(3)	41(3)	64(3)	-12(2)	16(2)	2(2)
C(16)	60(3)	37(2)	63(3)	-1(2)	17(2)	10(2)
C(17)	48(2)	38(2)	49(2)	-1(2)	11(2)	13(2)
C(19)	63(3)	42(3)	67(3)	9(2)	18(2)	24(2)
C(20)	43(2)	40(2)	57(3)	6(2)	15(2)	14(2)
C(21)	53(3)	45(3)	56(3)	5(2)	15(2)	14(2)
C(22)	58(3)	41(3)	56(3)	10(2)	6(2)	7(2)
C(23)	55(3)	34(2)	59(3)	3(2)	2(2)	17(2)
C(24)	45(2)	38(2)	57(3)	0(2)	11(2)	14(2)

Crystallographic data for 5.43



C20A
C19A
C21A
C22A
C11A
C18A
C12A
C13A
C14A
C5A
O10A
C17A
C16A
C15A
O9A
C4A
C6A
O3A
O1A
C2A
C8A
C7A

Crystallization solvent: benzene/hexane (diffusion technique)

Table 1. Crystal data and structure refinement for $C_{18}H_{22}O_4$

Empirical formula	$C_{18}H_{22}O_4$	
Formula weight	302.36	
Temperature	150(1) K	
Wavelength	0.71073 Å	
Crystal system, space group	Triclinic, P -1	
Unit cell dimensions	a = 14.688(3) Å	α= 75.32(3)°
	b = 15.063(3) Å	β= 89.96(3)°
	c = 29.361(6) Å	γ = 89.50(3)°
Volume	6284(2) $Å^3$	
Z, Calculated density	16, 1.278 g/cm^3	
Absorption coefficient	0.089 mm^{-1}	
F(000)	2592	
Crystal size	0.40 x 0.35 x 0.16 mm	
Theta range for data collection	2.56 to 25.00º	
Limiting indices	-17<=h<=17, -17<=k<=17, -17<=l<=34	
Reflections collected / unique	21528 / 21528 [R_{int} = 0.091]	
Completeness to theta = 28.00	97.3%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.661	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	21528 / 0 / 1602	
Goodness-of-fit on F^2	1.030	
Final R indices [I>2σ(I)]	R1 = 0.0533, wR2 = 0.1212	
R indices (all data)	R1 = 0.0885, wR2 = 0.1403	
Largest diff. peak and hole	0.261 and -0.224 $e^-.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

	x	y	z	U(eq)
O(1A)	10697(1)	226(1)	742(1)	40(1)
C(2A)	11483(2)	511(2)	449(1)	32(1)
O(3A)	11712(1)	1459(1)	405(1)	39(1)
C(4A)	11076(2)	2089(2)	427(1)	31(1)
C(5A)	10293(2)	1793(2)	759(1)	28(1)
C(6A)	10041(2)	804(2)	822(1)	30(1)
C(7A)	11278(2)	393(2)	-35(1)	39(1)
C(8A)	12275(2)	-62(2)	688(1)	45(1)
O(9A)	11180(1)	2878(1)	205(1)	40(1)
O(10A)	9311(1)	498(1)	954(1)	38(1)
C(11A)	10470(2)	2002(2)	1261(1)	27(1)
C(12A)	11107(2)	1267(2)	1563(1)	27(1)
C(13A)	10775(2)	476(2)	1871(1)	33(1)
C(14A)	11356(2)	-183(2)	2138(1)	41(1)
C(15A)	12290(2)	-64(2)	2104(1)	40(1)
C(16A)	12633(2)	709(2)	1802(1)	36(1)
C(17A)	12052(2)	1366(2)	1532(1)	32(1)
C(18A)	9527(2)	2030(2)	1491(1)	34(1)
C(19A)	9565(2)	2321(2)	1952(1)	41(1)
C(20A)	10021(2)	3246(2)	1886(1)	43(1)
C(21A)	10940(2)	3263(2)	1649(1)	38(1)
C(22A)	10867(2)	2975(2)	1187(1)	33(1)

O(1B)	1687(1)	1835(1)	4630(1)	41(1)
C(2B)	1460(2)	946(2)	4567(1)	33(1)
O(3B)	652(1)	966(1)	4283(1)	40(1)
C(4B)	45(2)	1661(2)	4176(1)	30(1)
C(5B)	326(2)	2584(2)	4233(1)	29(1)
C(6B)	1068(2)	2515(2)	4593(1)	31(1)
C(7B)	1268(2)	319(2)	5044(1)	39(1)
C(8B)	2237(2)	638(2)	4310(1)	45(1)
O(9B)	-681(1)	1526(1)	4016(1)	39(1)
O(10B)	1174(1)	3074(1)	4819(1)	39(1)
C(11B)	572(2)	3275(2)	3743(1)	30(1)
C(12B)	1210(2)	2807(2)	3453(1)	28(1)
C(13B)	2148(2)	2881(2)	3470(1)	33(1)
C(14B)	2721(2)	2473(2)	3206(1)	38(1)
C(15B)	2370(2)	1956(2)	2924(1)	38(1)
C(16B)	1432(2)	1856(2)	2908(1)	37(1)
C(17B)	868(2)	2286(2)	3165(1)	32(1)
C(18B)	1003(2)	4145(2)	3835(1)	34(1)
C(19B)	1135(2)	4907(2)	3381(1)	43(1)
C(20B)	242(2)	5170(2)	3121(1)	46(1)
C(21B)	-215(2)	4332(2)	3030(1)	44(1)
C(22B)	-340(2)	3582(2)	3483(1)	35(1)
O(1C)	6630(1)	10547(1)	365(1)	36(1)
C(2C)	6418(2)	11463(2)	404(1)	34(1)
O(3C)	5701(1)	11467(1)	741(1)	37(1)
C(4C)	5035(2)	10833(2)	837(1)	31(1)
C(5C)	5251(2)	9900(2)	764(1)	28(1)
C(6C)	5968(2)	9923(2)	396(1)	31(1)
C(7C)	6087(2)	12022(2)	-72(1)	46(1)
C(8C)	7246(2)	11827(2)	580(1)	48(1)
O(9C)	4330(1)	11022(1)	1004(1)	40(1)
O(10C)	6006(1)	9383(1)	155(1)	40(1)
C(11C)	5506(2)	9190(2)	1254(1)	30(1)
C(12C)	6150(2)	9638(2)	1542(1)	28(1)
C(13C)	7092(2)	9611(2)	1490(1)	34(1)
C(14C)	7670(2)	10019(2)	1747(1)	38(1)
C(15C)	7325(2)	10484(2)	2060(1)	38(1)
C(16C)	6395(2)	10526(2)	2114(1)	36(1)
C(17C)	5816(2)	10104(2)	1861(1)	32(1)
C(18C)	5933(2)	8316(2)	1154(1)	34(1)
C(19C)	6075(2)	7557(2)	1604(1)	39(1)
C(20C)	5182(2)	7294(2)	1862(1)	45(1)
C(21C)	4715(2)	8128(2)	1961(1)	41(1)
C(22C)	4596(2)	8888(2)	1510(1)	35(1)
O(1D)	11379(1)	7128(1)	4630(1)	41(1)
C(2D)	11385(2)	6198(2)	4590(1)	35(1)
O(3D)	10742(1)	6054(1)	4250(1)	41(1)
C(4D)	9947(2)	6523(2)	4160(1)	30(1)
C(5D)	9919(2)	7486(2)	4219(1)	28(1)
C(6D)	10618(2)	7656(2)	4562(1)	30(1)
C(7D)	11135(2)	5581(2)	5060(1)	54(1)
C(8D)	12305(2)	6019(2)	4420(1)	53(1)
O(9D)	9323(1)	6173(1)	4011(1)	39(1)
O(10D)	10557(1)	8260(1)	4761(1)	40(1)
C(11D)	9980(2)	8222(2)	3721(1)	27(1)
C(12D)	10851(2)	8059(2)	3465(1)	33(1)
C(13D)	11674(2)	8426(2)	3561(1)	55(1)
C(14D)	12465(2)	8268(3)	3339(2)	87(2)
C(15D)	12462(3)	7760(3)	3015(2)	89(2)
C(16D)	11664(3)	7389(2)	2918(1)	76(1)
C(17D)	10860(2)	7531(2)	3139(1)	46(1)
C(18D)	9933(2)	9196(2)	3797(1)	40(1)
C(19D)	9880(2)	9938(2)	3335(1)	45(1)
C(20D)	9049(2)	9824(2)	3049(1)	45(1)
C(21D)	9028(2)	8869(2)	2974(1)	40(1)
C(22D)	9109(2)	8128(2)	3439(1)	35(1)
O(1E)	5745(1)	2214(1)	4233(1)	37(1)
C(2E)	6443(2)	1868(2)	4581(1)	34(1)
O(3E)	6655(1)	917(1)	4613(1)	37(1)
C(4E)	5982(2)	326(2)	4591(1)	33(1)
C(5E)	5234(2)	674(2)	4242(1)	30(1)

C(6E)	5043(2)	1689(2)	4165(1)	32(1)
C(7E)	6100(2)	1948(2)	5052(1)	48(1)
C(8E)	7288(2)	2403(2)	4414(1)	48(1)
O(9E)	6030(1)	-459(1)	4827(1)	42(1)
O(10E)	4337(1)	2052(1)	4016(1)	40(1)
C(11E)	5420(2)	437(2)	3746(1)	28(1)
C(12E)	6068(2)	1150(2)	3448(1)	27(1)
C(13E)	5742(2)	1925(2)	3115(1)	31(1)
C(14E)	6329(2)	2570(2)	2858(1)	38(1)
C(15E)	7258(2)	2468(2)	2918(1)	39(1)
C(16E)	7595(2)	1709(2)	3244(1)	39(1)
C(17E)	7007(2)	1059(2)	3505(1)	32(1)
C(18E)	4477(2)	415(2)	3517(1)	33(1)
C(19E)	4521(2)	100(2)	3063(1)	38(1)
C(20E)	4982(2)	-841(2)	3143(1)	42(1)
C(21E)	5904(2)	-854(2)	3378(1)	38(1)
C(22E)	5818(2)	-550(2)	3838(1)	32(1)
O(1F)	6387(1)	5375(1)	350(1)	41(1)
C(2F)	6400(2)	6271(2)	436(1)	33(1)
O(3F)	5648(1)	6440(1)	719(1)	40(1)
C(4F)	4916(2)	5909(2)	832(1)	28(1)
C(5F)	4960(2)	4936(2)	782(1)	27(1)
C(6F)	5691(2)	4794(2)	444(1)	29(1)
C(7F)	6333(2)	6966(2)	-33(1)	45(1)
C(8F)	7252(2)	6337(2)	703(1)	43(1)
O(9F)	4264(1)	6224(1)	985(1)	35(1)
O(10F)	5686(1)	4162(1)	257(1)	37(1)
C(11F)	5019(2)	4206(2)	1281(1)	27(1)
C(12F)	5881(2)	4380(2)	1540(1)	31(1)
C(13F)	6717(2)	3985(2)	1461(1)	52(1)
C(14F)	7491(2)	4136(3)	1691(2)	77(1)
C(15F)	7470(3)	4666(3)	2008(2)	86(2)
C(16F)	6664(3)	5061(2)	2089(1)	67(1)
C(17F)	5871(2)	4920(2)	1858(1)	43(1)
C(18F)	5008(2)	3228(2)	1207(1)	38(1)
C(19F)	4962(2)	2493(2)	1668(1)	42(1)
C(20F)	4114(2)	2601(2)	1948(1)	43(1)
C(21F)	4066(2)	3555(2)	2022(1)	39(1)
C(22F)	4145(2)	4295(2)	1558(1)	34(1)
O(1G)	806(1)	5302(1)	752(1)	39(1)
C(2G)	1441(2)	5789(2)	412(1)	33(1)
O(3G)	1429(1)	6759(1)	375(1)	41(1)
C(4G)	659(2)	7212(2)	438(1)	30(1)
C(5G)	-52(2)	6689(2)	763(1)	27(1)
C(6G)	-19(2)	5671(2)	815(1)	29(1)
C(7G)	1197(2)	5641(2)	-60(1)	54(1)
C(8G)	2366(2)	5444(2)	584(1)	52(1)
O(9G)	603(1)	8020(1)	246(1)	40(1)
O(10G)	-644(1)	5166(1)	936(1)	39(1)
C(11G)	-38(2)	6924(2)	1265(1)	27(1)
C(12G)	885(2)	6636(2)	1501(1)	33(1)
C(13G)	1037(2)	5767(2)	1794(1)	46(1)
C(14G)	1896(3)	5509(3)	1988(1)	68(1)
C(15G)	2601(3)	6102(4)	1891(1)	81(2)
C(16G)	2468(2)	6961(3)	1602(1)	79(1)
C(17G)	1620(2)	7224(2)	1410(1)	55(1)
C(18G)	-836(2)	6421(2)	1558(1)	33(1)
C(19G)	-978(2)	6696(2)	2017(1)	39(1)
C(20G)	-1128(2)	7722(2)	1933(1)	47(1)
C(21G)	-350(2)	8234(2)	1652(1)	46(1)
C(22G)	-231(2)	7960(2)	1189(1)	39(1)
O(1H)	5657(1)	7144(1)	4298(1)	42(1)
C(2H)	6412(2)	6687(2)	4572(1)	32(1)
O(3H)	6380(1)	5699(1)	4662(1)	43(1)
C(4H)	5684(2)	5221(2)	4559(1)	29(1)
C(5H)	4946(2)	5718(2)	4233(1)	25(1)
C(6H)	4907(2)	6733(2)	4199(1)	28(1)
C(7H)	6374(2)	6922(2)	5041(1)	43(1)
C(8H)	7256(2)	7002(2)	4297(1)	44(1)
O(9H)	5684(1)	4403(1)	4728(1)	37(1)
O(10H)	4240(1)	7201(1)	4072(1)	35(1)

C(11H)	4983(2)	5510(2)	3726(1)	25(1)
C(12H)	5893(2)	5841(2)	3490(1)	32(1)
C(13H)	5993(2)	6712(2)	3190(1)	43(1)
C(14H)	6834(3)	7000(3)	2987(1)	66(1)
C(15H)	7576(3)	6429(3)	3083(1)	74(1)
C(16H)	7497(2)	5573(3)	3372(1)	69(1)
C(17H)	6664(2)	5272(2)	3577(1)	50(1)
C(18H)	4158(2)	5999(2)	3439(1)	33(1)
C(19H)	4042(2)	5751(2)	2972(1)	38(1)
C(20H)	3952(2)	4731(2)	3036(1)	44(1)
C(21H)	4755(2)	4228(2)	3314(1)	44(1)
C(22H)	4848(2)	4477(2)	3785(1)	36(1)

Table 3. Hydrogen coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

	x	y	z	U(eq)
H(5AA)	9753	2170	617	33
H(7AA)	10758	783	-169	59
H(7AB)	11133	-251	-12	59
H(7AC)	11811	569	-237	59
H(8AA)	12332	-1	1011	68
H(8AB)	12836	149	514	68
H(8AC)	12174	-707	693	68
H(13A)	10136	385	1897	39
H(14A)	11114	-718	2345	49
H(15A)	12689	-514	2288	48
H(16A)	13273	795	1779	43
H(17A)	12302	1893	1321	38
H(18A)	9127	2464	1267	41
(18B)	9250	1414	1551	41
H(19A)	8939	2356	2072	49
H(19B)	9907	1852	2189	49
H(20A)	9623	3731	1693	52
H(20B)	10101	3378	2197	52
H(21A)	11365	2842	1863	46
H(21B)	11192	3890	1585	46
H(22A)	11478	2991	1043	40
H(22B)	10472	3420	965	40
H(5BA)	-219	2849	4357	35
H(7BA)	760	569	5191	58
H(7BB)	1811	271	5243	58
H(7BC)	1109	-291	5010	58
H(8BA)	2307	1069	4001	67
H(8BB)	2113	24	4271	67
H(8BC)	2798	621	4492	67
H(13B)	2406	3222	3668	40
H(14B)	3360	2551	3219	45
H(15B)	2762	1673	2744	45
H(16B)	1178	1493	2719	44
H(17B)	228	2223	3144	38
H(18C)	607	4380	4052	41
H(18D)	1600	3982	3990	41
H(19C)	1395	5454	3460	51
H(19D)	1572	4694	3174	51
H(20C)	357	5622	2817	55
H(20D)	-167	5461	3310	55
H(21C)	160	4090	2807	53
H(21D)	-817	4512	2882	53
H(22C)	-629	3045	3407	42
H(22D)	-756	3810	3694	42
H(5CA)	4681	9672	648	34
H(7CA)	5536	11744	-161	70
H(7CB)	6562	12033	-308	70
H(7CC)	5950	12650	-55	70
H(8CA)	7399	11446	894	72
H(8CB)	7131	12460	597	72
H(8CC)	7754	11815	365	72
H(13C)	7343	9305	1273	41
H(14C)	8310	9980	1707	45

H(15C)	7721	10768	2235	46
H(16C)	6147	10847	2326	43
H(17C)	5177	10134	1907	38
H(18E)	5530	8090	938	41
H(18F)	6526	8472	994	41
H(19E)	6347	7011	1525	47
H(19F)	6506	7768	1813	47
H(20E)	4777	7015	1668	54
H(20F)	5299	6831	2162	54
H(21E)	5082	8357	2189	50
H(21F)	4111	7951	2103	50
H(22E)	4303	9425	1588	42
H(22F)	4183	8672	1295	42
H(5DA)	9309	7572	4354	34
H(7DA)	10527	5748	5151	80
H(7DB)	11579	5650	5297	80
H(7DC)	11135	4942	5040	80
H(8DA)	12413	6439	4111	80
H(8DB)	12342	5384	4394	80
H(8DC)	12766	6116	4643	80
H(13D)	11692	8790	3782	66
H(14D)	13021	8517	3413	104
H(15D)	13008	7666	2859	107
H(16D)	11658	7029	2695	91
H(17D)	10312	7265	3067	55
H(18G)	9391	9247	3990	48
H(18H)	10479	9298	3974	48
H(19G)	9856	10548	3403	54
H(19H)	10436	9909	3148	54
H(20G)	8491	9935	3217	54
H(20H)	9063	10282	2741	54
H(21G)	9536	8796	2764	48
H(21H)	8451	8787	2816	48
H(22G)	9113	7516	3371	42
H(22H)	8568	8164	3635	42
H(5EA)	4667	345	4375	36
H(7EA)	5535	1601	5129	72
H(7EB)	5982	2595	5040	72
H(7EC)	6559	1700	5294	72
H(8EA)	7451	2337	4101	72
H(8EB)	7788	2169	4634	72
H(8EC)	7178	3052	4399	72
H(13E)	5104	2007	3065	37
H(14E)	6089	3092	2636	45
H(15E)	7659	2913	2738	47
H(16E)	8233	1631	3290	46
H(17E)	7251	541	3727	39
H(18I)	4077	-4	3744	40
H(18J)	4201	1036	3449	40
H(19I)	4864	554	2823	45
H(19J)	3896	69	2942	45
H(20I)	4588	-1313	3343	50
H(20J)	5061	-994	2836	50
H(21I)	6323	-437	3161	46
H(21J)	6167	-1481	3446	46
H(22I)	6425	-573	3987	39
H(22J)	5416	-980	4058	39
H(5FA)	4367	4826	640	32
H(7FA)	5766	6873	-190	68
H(7FB)	6852	6889	-230	68
H(7FC)	6336	7586	15	68
H(8FA)	7234	5889	1010	65
H(8FB)	7301	6956	749	65
H(8FC)	7779	6208	524	65
H(13F)	6747	3610	1245	63
H(14F)	8051	3868	1630	93
H(15F)	8008	4759	2169	103
H(16F)	6644	5435	2305	80
H(17F)	5316	5197	1919	51
H(18K)	4475	3168	1010	46
H(18L)	5564	3129	1035	46

H(19K)	5509	2531	1859	50
H(19L)	4961	1880	1602	50
H(20K)	3566	2487	1776	52
H(20L)	4129	2143	2257	52
H(21K)	4565	3630	2235	46
H(21L)	3481	3635	2175	46
H(22K)	4133	4906	1627	40
H(22L)	3609	4260	1359	40
H(5GA)	-654	6908	616	33
H(7GA)	585	5887	-149	80
H(7GB)	1211	4983	-42	80
H(7GC)	1636	5957	-296	80
H(8GA)	2483	5581	887	77
H(8GB)	2823	5747	355	77
H(8GC)	2399	4780	621	77
H(13G)	550	5343	1863	55
H(14G)	1987	4913	2189	81
H(15G)	3185	5922	2023	98
H(16G)	2961	7378	1532	95
H(17G)	1538	7824	1211	65
H(18M)	-1401	6554	1368	40
H(18N)	-721	5751	1629	40
H(19M)	-1511	6369	2184	47
H(19N)	-437	6509	2222	47
H(20M)	-1707	7902	1760	57
H(20N)	-1174	7884	2238	57
H(21M)	219	8098	1838	55
H(21N)	-469	8903	1585	55
H(22M)	279	8310	1011	46
H(22N)	-791	8126	998	46
H(5HA)	4357	5463	4377	30
H(7HA)	5808	6688	5202	65
H(7HB)	6393	7590	4991	65
H(7HC)	6896	6641	5233	65
H(8HA)	7227	6841	3994	65
H(8HB)	7788	6703	4474	65
H(8HC)	7308	7669	4242	65
H(13H)	5483	7116	3123	52
H(14H)	6892	7595	2782	79
H(15H)	8149	6632	2947	89
H(16H)	8014	5176	3434	83
H(17H)	6618	4672	3779	60
H(18O)	3598	5832	3629	40
H(18P)	4235	6671	3379	40
H(19O)	3492	6064	2810	45
H(19P)	4573	5973	2769	45
H(20O)	3927	4593	2724	53
H(20P)	3379	4517	3204	53
H(21O)	5321	4393	3129	53
H(21P)	4670	3558	3370	53
H(22O)	5373	4138	3959	43
H(22P)	4294	4281	3974	43

Table 4. Bond lengths [Å] and angles [°]

O(1A)-C(6A)	1.351(3)
O(1A)-C(2A)	1.441(3)
C(2A)-O(3A)	1.443(3)
C(2A)-C(8A)	1.505(4)
C(2A)-C(7A)	1.507(4)
O(3A)-C(4A)	1.340(3)
C(4A)-O(9A)	1.213(3)
C(4A)-C(5A)	1.502(4)
C(5A)-C(6A)	1.504(3)
C(5A)-C(11A)	1.605(3)
C(6A)-O(10A)	1.196(3)
C(11A)-C(12A)	1.540(3)
C(11A)-C(18A)	1.544(3)
C(11A)-C(22A)	1.546(3)

C(12A)-C(13A)	1.392(4)
C(12A)-C(17A)	1.398(3)
C(13A)-C(14A)	1.387(4)
C(14A)-C(15A)	1.385(4)
C(15A)-C(16A)	1.370(4)
C(16A)-C(17A)	1.388(3)
C(18A)-C(19A)	1.527(4)
C(19A)-C(20A)	1.519(4)
C(20A)-C(21A)	1.517(4)
C(21A)-C(22A)	1.529(4)
O(1B)-C(6B)	1.347(3)
O(1B)-C(2B)	1.440(3)
C(2B)-O(3B)	1.445(3)
C(2B)-C(8B)	1.500(4)
C(2B)-C(7B)	1.507(4)
O(3B)-C(4B)	1.343(3)
C(4B)-O(9B)	1.205(3)
C(4B)-C(5B)	1.504(3)
C(5B)-C(6B)	1.504(3)
C(5B)-C(11B)	1.592(4)
C(6B)-O(10B)	1.208(3)
C(11B)-C(18B)	1.544(3)
C(11B)-C(12B)	1.546(3)
C(11B)-C(22B)	1.552(3)
C(12B)-C(13B)	1.385(3)
C(12B)-C(17B)	1.388(3)
C(13B)-C(14B)	1.385(4)
C(14B)-C(15B)	1.374(4)
C(15B)-C(16B)	1.389(4)
C(16B)-C(17B)	1.384(4)
C(18B)-C(19B)	1.536(4)
C(19B)-C(20B)	1.517(4)
C(20B)-C(21B)	1.517(4)
C(21B)-C(22B)	1.522(4)
O(1C)-C(6C)	1.345(3)
O(1C)-C(2C)	1.445(3)
C(2C)-O(3C)	1.445(3)
C(2C)-C(8C)	1.484(4)
C(2C)-C(7C)	1.515(4)
O(3C)-C(4C)	1.352(3)
C(4C)-O(9C)	1.207(3)
C(4C)-C(5C)	1.505(3)
C(5C)-C(6C)	1.502(4)
C(5C)-C(11C)	1.600(4)
C(6C)-O(10C)	1.207(3)
C(11C)-C(12C)	1.538(3)
C(11C)-C(18C)	1.547(3)
C(11C)-C(22C)	1.549(4)
C(12C)-C(17C)	1.392(3)
C(12C)-C(13C)	1.393(3)
C(13C)-C(14C)	1.382(4)
C(14C)-C(15C)	1.384(4)
C(15C)-C(16C)	1.378(4)
C(16C)-C(17C)	1.389(3)
C(18C)-C(19C)	1.528(4)
C(19C)-C(20C)	1.519(4)
C(20C)-C(21C)	1.518(4)
C(21C)-C(22C)	1.523(4)
O(1D)-C(6D)	1.351(3)
O(1D)-C(2D)	1.435(3)
C(2D)-O(3D)	1.432(3)
C(2D)-C(8D)	1.487(4)
C(2D)-C(7D)	1.503(4)
O(3D)-C(4D)	1.350(3)
C(4D)-O(9D)	1.199(3)
C(4D)-C(5D)	1.505(3)
C(5D)-C(6D)	1.507(3)
C(5D)-C(11D)	1.597(4)
C(6D)-O(10D)	1.202(3)
C(11D)-C(12D)	1.535(4)
C(11D)-C(18D)	1.540(3)

C(11D)-C(22D)	1.552(3)
C(12D)-C(17D)	1.389(4)
C(12D)-C(13D)	1.393(4)
C(13D)-C(14D)	1.380(5)
C(14D)-C(15D)	1.362(6)
C(15D)-C(16D)	1.365(6)
C(16D)-C(17D)	1.387(4)
C(18D)-C(19D)	1.524(4)
C(19D)-C(20D)	1.517(4)
C(20D)-C(21D)	1.511(4)
C(21D)-C(22D)	1.533(4)
O(1E)-C(6E)	1.350(3)
O(1E)-C(2E)	1.445(3)
C(2E)-O(3E)	1.443(3)
C(2E)-C(8E)	1.498(4)
C(2E)-C(7E)	1.506(4)
O(3E)-C(4E)	1.348(3)
C(4E)-O(9E)	1.210(3)
C(4E)-C(5E)	1.500(4)
C(5E)-C(6E)	1.512(3)
C(5E)-C(11E)	1.608(3)
C(6E)-O(10E)	1.198(3)
C(11E)-C(12E)	1.537(4)
C(11E)-C(18E)	1.545(3)
C(11E)-C(22E)	1.552(3)
C(12E)-C(17E)	1.391(3)
C(12E)-C(13E)	1.400(3)
C(13E)-C(14E)	1.377(4)
C(14E)-C(15E)	1.379(4)
C(15E)-C(16E)	1.379(4)
C(16E)-C(17E)	1.387(4)
C(18E)-C(19E)	1.525(4)
C(19E)-C(20E)	1.530(4)
C(20E)-C(21E)	1.519(4)
C(21E)-C(22E)	1.536(3)
O(1F)-C(6F)	1.333(3)
O(1F)-C(2F)	1.436(3)
C(2F)-O(3F)	1.440(3)
C(2F)-C(8F)	1.493(4)
C(2F)-C(7F)	1.508(4)
O(3F)-C(4F)	1.337(3)
C(4F)-O(9F)	1.202(3)
C(4F)-C(5F)	1.510(3)
C(5F)-C(6F)	1.513(3)
C(5F)-C(11F)	1.595(4)
C(6F)-O(10F)	1.215(3)
C(11F)-C(12F)	1.537(3)
C(11F)-C(22F)	1.543(4)
C(11F)-C(18F)	1.543(3)
C(12F)-C(17F)	1.384(4)
C(12F)-C(13F)	1.405(4)
C(13F)-C(14F)	1.373(5)
C(14F)-C(15F)	1.371(6)
C(15F)-C(16F)	1.368(6)
C(16F)-C(17F)	1.393(4)
C(18F)-C(19F)	1.518(4)
C(19F)-C(20F)	1.520(4)
C(20F)-C(21F)	1.509(4)
C(21F)-C(22F)	1.530(4)
O(1G)-C(6G)	1.361(3)
O(1G)-C(2G)	1.429(3)
C(2G)-O(3G)	1.437(3)
C(2G)-C(8G)	1.491(4)
C(2G)-C(7G)	1.502(4)
O(3G)-C(4G)	1.353(3)
C(4G)-O(9G)	1.207(3)
C(4G)-C(5G)	1.499(4)
C(5G)-C(6G)	1.502(3)
C(5G)-C(11G)	1.601(3)
C(6G)-O(10G)	1.191(3)
C(11G)-C(12G)	1.533(3)

C(11G)-C(18G)	1.540(4)
C(11G)-C(22G)	1.543(3)
C(12G)-C(17G)	1.385(4)
C(12G)-C(13G)	1.388(4)
C(13G)-C(14G)	1.396(4)
C(14G)-C(15G)	1.357(6)
C(15G)-C(16G)	1.368(6)
C(16G)-C(17G)	1.380(4)
C(18G)-C(19G)	1.523(4)
C(19G)-C(20G)	1.516(4)
C(20G)-C(21G)	1.509(4)
C(21G)-C(22G)	1.525(4)
O(1H)-C(6H)	1.336(3)
O(1H)-C(2H)	1.435(3)
C(2H)-O(3H)	1.444(3)
C(2H)-C(8H)	1.493(4)
C(2H)-C(7H)	1.506(4)
O(3H)-C(4H)	1.333(3)
C(4H)-O(9H)	1.207(3)
C(4H)-C(5H)	1.508(3)
C(5H)-C(6H)	1.507(3)
C(5H)-C(11H)	1.600(3)
C(6H)-O(10H)	1.204(3)
C(11H)-C(12H)	1.532(4)
C(11H)-C(22H)	1.535(3)
C(11H)-C(18H)	1.546(3)
C(12H)-C(13H)	1.392(4)
C(12H)-C(17H)	1.398(4)
C(13H)-C(14H)	1.395(4)
C(14H)-C(15H)	1.366(5)
C(15H)-C(16H)	1.358(5)
C(16H)-C(17H)	1.392(5)
C(18H)-C(19H)	1.522(3)
C(19H)-C(20H)	1.507(4)
C(20H)-C(21H)	1.518(4)
C(21H)-C(22H)	1.528(4)

C(6A)-O(1A)-C(2A)	124.3(2)
O(1A)-C(2A)-O(3A)	112.67(19)
O(1A)-C(2A)-C(8A)	107.0(2)
O(3A)-C(2A)-C(8A)	107.1(2)
O(1A)-C(2A)-C(7A)	108.2(2)
O(3A)-C(2A)-C(7A)	108.2(2)
C(8A)-C(2A)-C(7A)	113.7(2)
C(4A)-O(3A)-C(2A)	121.7(2)
O(9A)-C(4A)-O(3A)	119.3(2)
O(9A)-C(4A)-C(5A)	122.8(2)
O(3A)-C(4A)-C(5A)	117.7(2)
C(4A)-C(5A)-C(6A)	113.3(2)
C(4A)-C(5A)-C(11A)	112.0(2)
C(6A)-C(5A)-C(11A)	110.4(2)
O(10A)-C(6A)-O(1A)	118.7(2)
O(10A)-C(6A)-C(5A)	123.9(2)
O(1A)-C(6A)-C(5A)	117.4(2)
C(12A)-C(11A)-C(18A)	112.6(2)
C(12A)-C(11A)-C(22A)	111.49(19)
C(18A)-C(11A)-C(22A)	106.0(2)
C(12A)-C(11A)-C(5A)	110.38(19)
C(18A)-C(11A)-C(5A)	106.69(19)
C(22A)-C(11A)-C(5A)	109.4(2)
C(13A)-C(12A)-C(17A)	117.2(2)
C(13A)-C(12A)-C(11A)	121.9(2)
C(17A)-C(12A)-C(11A)	120.8(2)
C(14A)-C(13A)-C(12A)	121.4(2)
C(15A)-C(14A)-C(13A)	120.2(3)
C(16A)-C(15A)-C(14A)	119.5(3)
C(15A)-C(16A)-C(17A)	120.5(2)
C(16A)-C(17A)-C(12A)	121.3(3)
C(19A)-C(18A)-C(11A)	113.4(2)
C(20A)-C(19A)-C(18A)	111.4(2)
C(21A)-C(20A)-C(19A)	111.4(2)

C(20A)-C(21A)-C(22A)	111.5(2)
C(21A)-C(22A)-C(11A)	112.0(2)
C(6B)-O(1B)-C(2B)	122.87(19)
O(1B)-C(2B)-O(3B)	112.74(19)
O(1B)-C(2B)-C(8B)	107.4(2)
O(3B)-C(2B)-C(8B)	107.4(2)
O(1B)-C(2B)-C(7B)	108.0(2)
O(3B)-C(2B)-C(7B)	107.2(2)
C(8B)-C(2B)-C(7B)	114.3(2)
C(4B)-O(3B)-C(2B)	125.24(19)
O(9B)-C(4B)-O(3B)	118.5(2)
O(9B)-C(4B)-C(5B)	123.1(2)
O(3B)-C(4B)-C(5B)	118.3(2)
C(4B)-C(5B)-C(6B)	112.5(2)
C(4B)-C(5B)-C(11B)	112.0(2)
C(6B)-C(5B)-C(11B)	112.3(2)
O(10B)-C(6B)-O(1B)	119.1(2)
O(10B)-C(6B)-C(5B)	123.4(2)
O(1B)-C(6B)-C(5B)	117.2(2)
C(18B)-C(11B)-C(12B)	111.8(2)
C(18B)-C(11B)-C(22B)	106.5(2)
C(12B)-C(11B)-C(22B)	111.6(2)
C(18B)-C(11B)-C(5B)	109.2(2)
C(12B)-C(11B)-C(5B)	110.64(19)
C(22B)-C(11B)-C(5B)	106.9(2)
C(13B)-C(12B)-C(17B)	116.7(2)
C(13B)-C(12B)-C(11B)	121.8(2)
C(17B)-C(12B)-C(11B)	121.5(2)
C(14B)-C(13B)-C(12B)	122.0(2)
C(15B)-C(14B)-C(13B)	120.4(2)
C(14B)-C(15B)-C(16B)	118.8(3)
C(17B)-C(16B)-C(15B)	120.0(3)
C(16B)-C(17B)-C(12B)	122.0(2)
C(19B)-C(18B)-C(11B)	112.6(2)
C(20B)-C(19B)-C(18B)	111.4(2)
C(19B)-C(20B)-C(21B)	110.8(2)
C(20B)-C(21B)-C(22B)	111.7(2)
C(21B)-C(22B)-C(11B)	112.6(2)
C(6C)-O(1C)-C(2C)	120.56(19)
O(3C)-C(2C)-O(1C)	112.0(2)
O(3C)-C(2C)-C(8C)	107.2(2)
O(1C)-C(2C)-C(8C)	107.6(2)
O(3C)-C(2C)-C(7C)	107.6(2)
O(1C)-C(2C)-C(7C)	108.0(2)
C(8C)-C(2C)-C(7C)	114.4(2)
C(4C)-O(3C)-C(2C)	123.3(2)
O(9C)-C(4C)-O(3C)	118.7(2)
O(9C)-C(4C)-C(5C)	123.8(2)
O(3C)-C(4C)-C(5C)	117.3(2)
C(6C)-C(5C)-C(4C)	113.0(2)
C(6C)-C(5C)-C(11C)	112.0(2)
C(4C)-C(5C)-C(11C)	110.8(2)
O(10C)-C(6C)-O(1C)	119.6(2)
O(10C)-C(6C)-C(5C)	123.6(2)
O(1C)-C(6C)-C(5C)	116.6(2)
C(12C)-C(11C)-C(18C)	111.8(2)
C(12C)-C(11C)-C(22C)	112.6(2)
C(18C)-C(11C)-C(22C)	106.1(2)
C(12C)-C(11C)-C(5C)	110.4(2)
C(18C)-C(11C)-C(5C)	109.1(2)
C(22C)-C(11C)-C(5C)	106.6(2)
C(17C)-C(12C)-C(13C)	116.8(2)
C(17C)-C(12C)-C(11C)	121.5(2)
C(13C)-C(12C)-C(11C)	121.8(2)
C(14C)-C(13C)-C(12C)	121.8(2)
C(13C)-C(14C)-C(15C)	120.5(2)
C(16C)-C(15C)-C(14C)	118.7(2)
C(15C)-C(16C)-C(17C)	120.6(3)
C(16C)-C(17C)-C(12C)	121.6(2)
C(19C)-C(18C)-C(11C)	112.0(2)
C(20C)-C(19C)-C(18C)	111.1(2)

C(21C)-C(20C)-C(19C)	110.9(2)
C(20C)-C(21C)-C(22C)	111.0(2)
C(21C)-C(22C)-C(11C)	113.1(2)
C(6D)-O(1D)-C(2D)	122.38(19)
O(3D)-C(2D)-O(1D)	112.5(2)
O(3D)-C(2D)-C(8D)	107.0(2)
O(1D)-C(2D)-C(8D)	106.8(2)
O(3D)-C(2D)-C(7D)	107.9(2)
O(1D)-C(2D)-C(7D)	108.4(2)
C(8D)-C(2D)-C(7D)	114.3(2)
C(4D)-O(3D)-C(2D)	122.8(2)
O(9D)-C(4D)-O(3D)	118.5(2)
O(9D)-C(4D)-C(5D)	123.7(2)
O(3D)-C(4D)-C(5D)	117.7(2)
C(4D)-C(5D)-C(6D)	113.4(2)
C(4D)-C(5D)-C(11D)	111.0(2)
C(6D)-C(5D)-C(11D)	111.96(19)
O(10D)-C(6D)-O(1D)	118.2(2)
O(10D)-C(6D)-C(5D)	123.8(2)
O(1D)-C(6D)-C(5D)	117.9(2)
C(12D)-C(11D)-C(18D)	112.2(2)
C(12D)-C(11D)-C(22D)	112.1(2)
C(18D)-C(11D)-C(22D)	105.4(2)
C(12D)-C(11D)-C(5D)	109.9(2)
C(18D)-C(11D)-C(5D)	109.4(2)
C(22D)-C(11D)-C(5D)	107.6(2)
C(17D)-C(12D)-C(13D)	117.6(3)
C(17D)-C(12D)-C(11D)	122.1(2)
C(13D)-C(12D)-C(11D)	120.3(3)
C(14D)-C(13D)-C(12D)	120.7(4)
C(15D)-C(14D)-C(13D)	121.2(4)
C(14D)-C(15D)-C(16D)	119.0(4)
C(15D)-C(16D)-C(17D)	121.0(4)
C(16D)-C(17D)-C(12D)	120.5(3)
C(19D)-C(18D)-C(11D)	112.6(2)
C(20D)-C(19D)-C(18D)	111.6(2)
C(21D)-C(20D)-C(19D)	110.4(2)
C(20D)-C(21D)-C(22D)	111.9(2)
C(21D)-C(22D)-C(11D)	113.0(2)
C(6E)-O(1E)-C(2E)	121.9(2)
O(3E)-C(2E)-O(1E)	111.58(19)
O(3E)-C(2E)-C(8E)	107.0(2)
O(1E)-C(2E)-C(8E)	106.9(2)
O(3E)-C(2E)-C(7E)	108.6(2)
O(1E)-C(2E)-C(7E)	108.3(2)
C(8E)-C(2E)-C(7E)	114.5(2)
C(4E)-O(3E)-C(2E)	119.97(19)
O(9E)-C(4E)-O(3E)	119.8(2)
O(9E)-C(4E)-C(5E)	123.2(2)
O(3E)-C(4E)-C(5E)	116.8(2)
C(4E)-C(5E)-C(6E)	113.4(2)
C(4E)-C(5E)-C(11E)	112.2(2)
C(6E)-C(5E)-C(11E)	110.0(2)
O(10E)-C(6E)-O(1E)	119.1(2)
O(10E)-C(6E)-C(5E)	123.9(2)
O(1E)-C(6E)-C(5E)	116.7(2)
C(12E)-C(11E)-C(18E)	113.7(2)
C(12E)-C(11E)-C(22E)	111.7(2)
C(18E)-C(11E)-C(22E)	106.3(2)
C(12E)-C(11E)-C(5E)	109.68(19)
C(18E)-C(11E)-C(5E)	106.1(2)
C(22E)-C(11E)-C(5E)	109.1(2)
C(17E)-C(12E)-C(13E)	117.0(2)
C(17E)-C(12E)-C(11E)	121.2(2)
C(13E)-C(12E)-C(11E)	121.8(2)
C(14E)-C(13E)-C(12E)	121.2(2)
C(13E)-C(14E)-C(15E)	121.0(3)
C(14E)-C(15E)-C(16E)	118.8(3)
C(15E)-C(16E)-C(17E)	120.5(2)
C(16E)-C(17E)-C(12E)	121.5(2)
C(19E)-C(18E)-C(11E)	113.0(2)

C(18E)-C(19E)-C(20E)	111.4(2)
C(21E)-C(20E)-C(19E)	111.2(2)
C(20E)-C(21E)-C(22E)	110.9(2)
C(21E)-C(22E)-C(11E)	111.2(2)
C(6F)-O(1F)-C(2F)	125.2(2)
O(1F)-C(2F)-O(3F)	113.3(2)
O(1F)-C(2F)-C(8F)	107.5(2)
O(3F)-C(2F)-C(8F)	107.2(2)
O(1F)-C(2F)-C(7F)	107.7(2)
O(3F)-C(2F)-C(7F)	107.3(2)
C(8F)-C(2F)-C(7F)	114.0(2)
C(4F)-O(3F)-C(2F)	125.51(19)
O(9F)-C(4F)-O(3F)	117.8(2)
O(9F)-C(4F)-C(5F)	123.3(2)
O(3F)-C(4F)-C(5F)	118.8(2)
C(4F)-C(5F)-C(6F)	112.9(2)
C(4F)-C(5F)-C(11F)	111.9(2)
C(6F)-C(5F)-C(11F)	112.88(19)
O(10F)-C(6F)-O(1F)	117.7(2)
O(10F)-C(6F)-C(5F)	123.0(2)
O(1F)-C(6F)-C(5F)	119.3(2)
C(12F)-C(11F)-C(22F)	112.1(2)
C(12F)-C(11F)-C(18F)	112.0(2)
C(22F)-C(11F)-C(18F)	105.8(2)
C(12F)-C(11F)-C(5F)	109.3(2)
C(22F)-C(11F)-C(5F)	108.18(19)
C(18F)-C(11F)-C(5F)	109.3(2)
C(17F)-C(12F)-C(13F)	117.6(3)
C(17F)-C(12F)-C(11F)	122.2(2)
C(13F)-C(12F)-C(11F)	120.3(2)
C(14F)-C(13F)-C(12F)	120.7(4)
C(15F)-C(14F)-C(13F)	121.2(4)
C(16F)-C(15F)-C(14F)	119.0(3)
C(15F)-C(16F)-C(17F)	120.8(4)
C(12F)-C(17F)-C(16F)	120.8(3)
C(19F)-C(18F)-C(11F)	112.4(2)
C(18F)-C(19F)-C(20F)	111.7(2)
C(21F)-C(20F)-C(19F)	110.1(2)
C(20F)-C(21F)-C(22F)	112.0(2)
C(21F)-C(22F)-C(11F)	113.3(2)
C(6G)-O(1G)-C(2G)	121.5(2)
O(1G)-C(2G)-O(3G)	112.5(2)
O(1G)-C(2G)-C(8G)	106.7(2)
O(3G)-C(2G)-C(8G)	106.8(2)
O(1G)-C(2G)-C(7G)	108.4(2)
O(3G)-C(2G)-C(7G)	108.3(2)
C(8G)-C(2G)-C(7G)	114.2(2)
C(4G)-O(3G)-C(2G)	122.0(2)
O(9G)-C(4G)-O(3G)	118.0(2)
O(9G)-C(4G)-C(5G)	124.1(2)
O(3G)-C(4G)-C(5G)	117.9(2)
C(4G)-C(5G)-C(6G)	114.1(2)
C(4G)-C(5G)-C(11G)	111.8(2)
C(6G)-C(5G)-C(11G)	111.3(2)
O(10G)-C(6G)-O(1G)	118.5(2)
O(10G)-C(6G)-C(5G)	124.8(2)
O(1G)-C(6G)-C(5G)	116.6(2)
C(12G)-C(11G)-C(18G)	112.3(2)
C(12G)-C(11G)-C(22G)	112.3(2)
C(18G)-C(11G)-C(22G)	106.4(2)
C(12G)-C(11G)-C(5G)	109.10(19)
C(18G)-C(11G)-C(5G)	108.07(19)
C(22G)-C(11G)-C(5G)	108.5(2)
C(17G)-C(12G)-C(13G)	117.1(3)
C(17G)-C(12G)-C(11G)	120.8(3)
C(13G)-C(12G)-C(11G)	122.0(2)
C(12G)-C(13G)-C(14G)	120.8(3)
C(15G)-C(14G)-C(13G)	120.5(4)
C(14G)-C(15G)-C(16G)	119.7(3)
C(15G)-C(16G)-C(17G)	120.3(4)
C(16G)-C(17G)-C(12G)	121.6(4)

C(19G)-C(18G)-C(11G)	113.0(2)
C(20G)-C(19G)-C(18G)	111.6(2)
C(21G)-C(20G)-C(19G)	110.1(2)
C(20G)-C(21G)-C(22G)	110.8(2)
C(21G)-C(22G)-C(11G)	112.6(2)
C(6H)-O(1H)-C(2H)	125.2(2)
O(1H)-C(2H)-O(3H)	113.28(19)
O(1H)-C(2H)-C(8H)	107.2(2)
O(3H)-C(2H)-C(8H)	107.8(2)
O(1H)-C(2H)-C(7H)	107.2(2)
O(3H)-C(2H)-C(7H)	107.5(2)
C(8H)-C(2H)-C(7H)	114.0(2)
C(4H)-O(3H)-C(2H)	125.54(19)
O(9H)-C(4H)-O(3H)	117.8(2)
O(9H)-C(4H)-C(5H)	123.1(2)
O(3H)-C(4H)-C(5H)	119.1(2)
C(6H)-C(5H)-C(4H)	113.3(2)
C(6H)-C(5H)-C(11H)	112.0(2)
C(4H)-C(5H)-C(11H)	112.67(19)
O(10H)-C(6H)-O(1H)	118.1(2)
O(10H)-C(6H)-C(5H)	123.3(2)
O(1H)-C(6H)-C(5H)	118.6(2)
C(12H)-C(11H)-C(22H)	112.1(2)
C(12H)-C(11H)-C(18H)	112.4(2)
C(22H)-C(11H)-C(18H)	106.5(2)
C(12H)-C(11H)-C(5H)	109.22(19)
C(22H)-C(11H)-C(5H)	108.8(2)
C(18H)-C(11H)-C(5H)	107.63(18)
C(13H)-C(12H)-C(17H)	117.4(3)
C(13H)-C(12H)-C(11H)	122.1(2)
C(17H)-C(12H)-C(11H)	120.5(3)
C(12H)-C(13H)-C(14H)	120.8(3)
C(15H)-C(14H)-C(13H)	120.3(4)
C(16H)-C(15H)-C(14H)	120.2(3)
C(15H)-C(16H)-C(17H)	120.4(4)
C(16H)-C(17H)-C(12H)	120.9(3)
C(19H)-C(18H)-C(11H)	112.8(2)
C(20H)-C(19H)-C(18H)	112.0(2)
C(19H)-C(20H)-C(21H)	110.3(2)
C(20H)-C(21H)-C(22H)	110.8(2)
C(21H)-C(22H)-C(11H)	112.6(2)

Table 5. Anisotropic displacement parameters ($Å^2 x\ 10^3$).

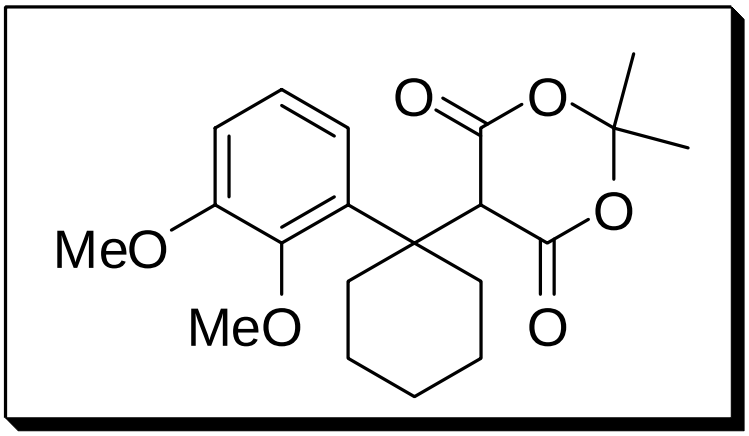
	U11	U22	U33	U23	U13	U12
O(1A)	46(1)	34(1)	43(1)	-15(1)	18(1)	-8(1)
C(2A)	36(2)	33(1)	28(2)	-9(1)	9(1)	-6(1)
O(3A)	41(1)	36(1)	45(1)	-16(1)	14(1)	-8(1)
C(4A)	39(2)	32(2)	23(2)	-7(1)	-2(1)	-9(1)
C(5A)	34(1)	31(1)	20(2)	-9(1)	-1(1)	0(1)
C(6A)	38(2)	34(2)	20(2)	-9(1)	3(1)	-5(1)
C(7A)	45(2)	44(2)	30(2)	-11(1)	0(1)	3(1)
C(8A)	42(2)	53(2)	40(2)	-10(2)	-3(1)	1(1)
O(9A)	52(1)	38(1)	28(1)	-4(1)	5(1)	-8(1)
O(10A)	38(1)	43(1)	35(1)	-13(1)	6(1)	-12(1)
C(11A)	33(1)	28(1)	21(2)	-7(1)	0(1)	-2(1)
C(12A)	35(1)	26(1)	21(2)	-10(1)	0(1)	-2(1)
C(13A)	36(2)	34(2)	28(2)	-7(1)	1(1)	-3(1)
C(14A)	54(2)	31(2)	33(2)	-2(1)	0(1)	-3(1)
C(15A)	47(2)	39(2)	31(2)	-5(1)	-8(1)	6(1)
C(16A)	33(2)	41(2)	35(2)	-11(1)	-4(1)	-1(1)
C(17A)	38(2)	29(1)	27(2)	-6(1)	-1(1)	-5(1)
C(18A)	37(2)	38(2)	30(2)	-11(1)	1(1)	3(1)
C(19A)	45(2)	48(2)	32(2)	-15(1)	2(1)	7(1)
C(20A)	61(2)	40(2)	33(2)	-18(1)	-2(2)	11(1)
C(21A)	52(2)	33(2)	33(2)	-14(1)	-8(1)	-1(1)

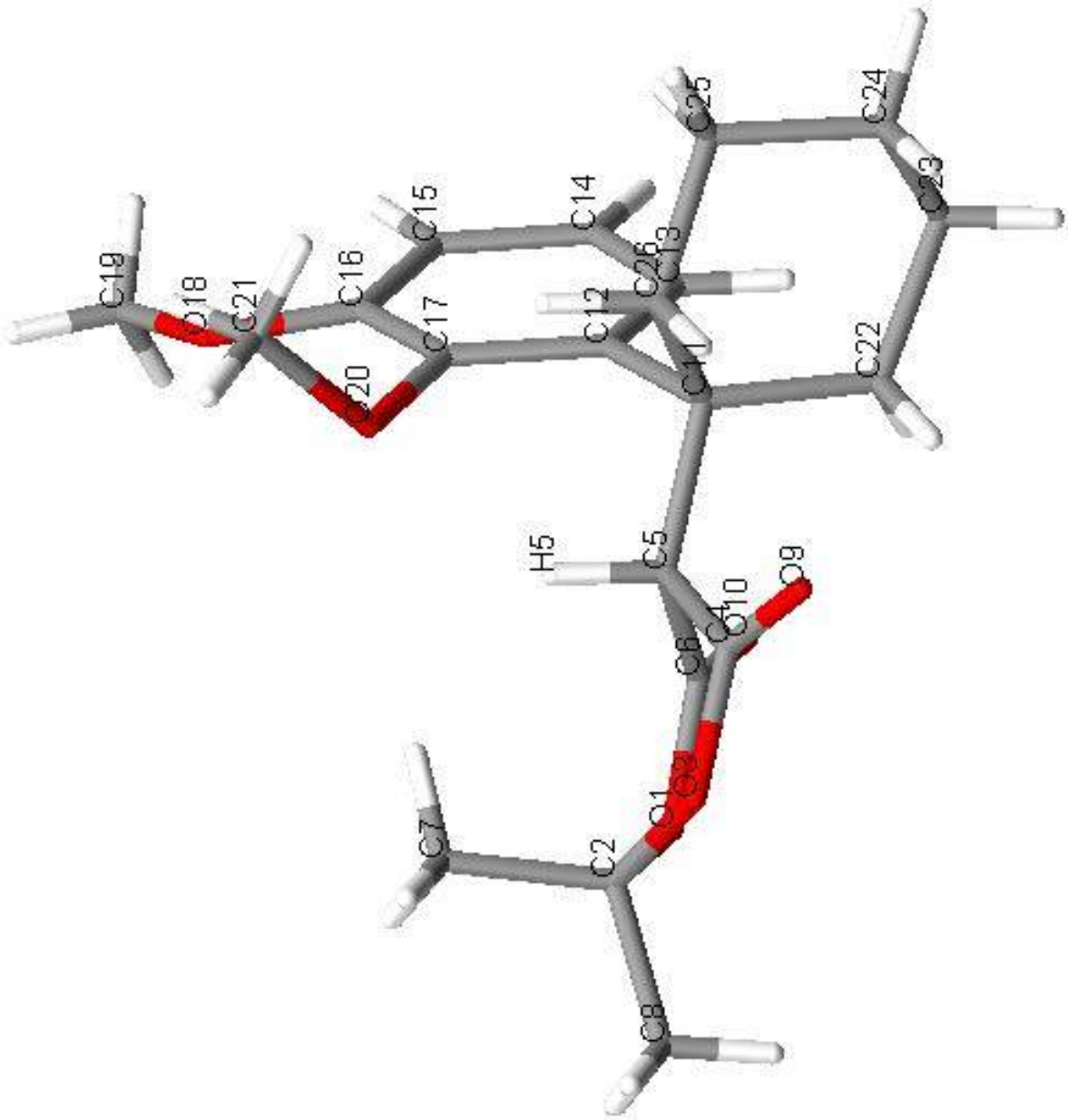
C(22A)	46(2)	28(1)	26(2)	-6(1)	-6(1)	-2(1)
O(1B)	41(1)	33(1)	49(1)	-9(1)	-19(1)	-2(1)
C(2B)	35(2)	33(2)	32(2)	-8(1)	-6(1)	-4(1)
O(3B)	41(1)	34(1)	46(1)	-13(1)	-15(1)	0(1)
C(4B)	32(2)	39(2)	19(2)	-4(1)	2(1)	-3(1)
C(5B)	32(1)	34(1)	25(2)	-12(1)	1(1)	-1(1)
C(6B)	35(2)	35(2)	23(2)	-6(1)	2(1)	-7(1)
C(7B)	43(2)	41(2)	33(2)	-9(1)	0(1)	-2(1)
C(8B)	46(2)	53(2)	36(2)	-12(2)	6(1)	-1(1)
O(9B)	35(1)	46(1)	36(1)	-12(1)	-6(1)	-7(1)
O(10B)	52(1)	41(1)	24(1)	-13(1)	-3(1)	-8(1)
C(11B)	38(2)	30(1)	22(2)	-8(1)	-1(1)	3(1)
C(12B)	39(2)	25(1)	19(2)	-3(1)	0(1)	-5(1)
C(13B)	38(2)	36(2)	25(2)	-9(1)	-4(1)	-2(1)
C(14B)	33(2)	40(2)	38(2)	-6(1)	3(1)	1(1)
C(15B)	44(2)	38(2)	30(2)	-7(1)	7(1)	1(1)
C(16B)	47(2)	38(2)	28(2)	-13(1)	1(1)	-5(1)
C(17B)	38(2)	34(1)	24(2)	-9(1)	0(1)	-1(1)
C(18B)	49(2)	33(1)	22(2)	-10(1)	-1(1)	1(1)
C(19B)	67(2)	35(2)	26(2)	-7(1)	0(1)	3(1)
C(20B)	71(2)	38(2)	28(2)	-7(1)	-3(2)	14(2)
C(21B)	57(2)	49(2)	25(2)	-11(1)	-10(1)	18(1)
C(22B)	40(2)	42(2)	26(2)	-13(1)	-4(1)	8(1)
O(1C)	39(1)	34(1)	34(1)	-10(1)	9(1)	3(1)
C(2C)	41(2)	31(1)	30(2)	-6(1)	8(1)	2(1)
O(3C)	45(1)	33(1)	35(1)	-12(1)	12(1)	-3(1)
C(4C)	38(2)	34(2)	21(2)	-6(1)	-3(1)	2(1)
C(5C)	31(1)	33(1)	21(2)	-8(1)	1(1)	0(1)
C(6C)	42(2)	30(1)	19(2)	-4(1)	-2(1)	4(1)
C(7C)	60(2)	40(2)	36(2)	-5(1)	2(2)	8(1)
C(8C)	48(2)	44(2)	51(2)	-9(2)	-1(2)	-9(1)
O(9C)	37(1)	47(1)	38(1)	-14(1)	6(1)	6(1)
O(10C)	59(1)	40(1)	24(1)	-11(1)	6(1)	4(1)
C(11C)	37(2)	29(1)	23(2)	-8(1)	1(1)	0(1)
C(12C)	34(1)	26(1)	23(2)	-5(1)	1(1)	1(1)
C(13C)	38(2)	35(2)	31(2)	-9(1)	6(1)	0(1)
C(14C)	31(2)	40(2)	41(2)	-7(1)	-1(1)	-3(1)
C(15C)	42(2)	38(2)	34(2)	-8(1)	-8(1)	-3(1)
C(16C)	44(2)	38(2)	28(2)	-13(1)	-2(1)	3(1)
C(17C)	34(1)	34(1)	27(2)	-8(1)	0(1)	2(1)
C(18C)	46(2)	31(1)	25(2)	-9(1)	3(1)	-3(1)
C(19C)	59(2)	30(2)	28(2)	-7(1)	3(1)	-4(1)
C(20C)	71(2)	35(2)	29(2)	-6(1)	4(2)	-13(1)
C(21C)	54(2)	42(2)	29(2)	-10(1)	12(1)	-17(1)
C(22C)	37(2)	38(2)	31(2)	-12(1)	4(1)	-7(1)
O(1D)	42(1)	39(1)	45(1)	-16(1)	-12(1)	2(1)
C(2D)	37(2)	35(2)	32(2)	-10(1)	-4(1)	-1(1)
O(3D)	45(1)	38(1)	45(1)	-20(1)	-12(1)	8(1)
C(4D)	35(2)	32(1)	22(2)	-6(1)	3(1)	-5(1)
C(5D)	29(1)	31(1)	26(2)	-10(1)	4(1)	-2(1)
C(6D)	38(2)	29(1)	24(2)	-7(1)	4(1)	-5(1)
C(7D)	68(2)	54(2)	35(2)	-5(2)	-1(2)	-14(2)
C(8D)	45(2)	57(2)	60(2)	-21(2)	8(2)	-1(2)
O(9D)	44(1)	36(1)	39(1)	-12(1)	-2(1)	-8(1)
O(10D)	54(1)	40(1)	30(1)	-14(1)	-1(1)	-3(1)
C(11D)	33(1)	30(1)	20(2)	-9(1)	0(1)	-4(1)
C(12D)	35(2)	31(1)	27(2)	2(1)	4(1)	3(1)
C(13D)	36(2)	72(2)	44(2)	10(2)	2(2)	-7(2)
C(14D)	32(2)	109(4)	81(3)	43(3)	10(2)	8(2)
C(15D)	67(3)	75(3)	88(4)	47(3)	49(3)	38(2)
C(16D)	109(3)	43(2)	60(3)	13(2)	49(2)	32(2)
C(17D)	61(2)	32(2)	40(2)	-2(1)	22(2)	10(1)
C(18D)	61(2)	31(2)	30(2)	-10(1)	-1(1)	-4(1)
C(19D)	72(2)	27(1)	37(2)	-11(1)	1(2)	-1(1)
C(20D)	50(2)	44(2)	38(2)	-3(1)	1(1)	12(1)
C(21D)	40(2)	48(2)	30(2)	-6(1)	-8(1)	0(1)
C(22D)	34(2)	42(2)	29(2)	-9(1)	0(1)	1(1)
O(1E)	44(1)	33(1)	33(1)	-10(1)	-8(1)	2(1)
C(2E)	41(2)	35(2)	30(2)	-14(1)	-6(1)	4(1)
O(3E)	41(1)	36(1)	36(1)	-14(1)	-7(1)	6(1)
C(4E)	45(2)	35(2)	20(2)	-11(1)	3(1)	6(1)

C(5E)	34(1)	32(1)	24(2)	-8(1)	1(1)	0(1)
C(6E)	41(2)	38(2)	19(2)	-10(1)	2(1)	4(1)
C(7E)	67(2)	51(2)	31(2)	-18(2)	-2(2)	10(2)
C(8E)	49(2)	47(2)	51(2)	-18(2)	-1(2)	-5(1)
O(9E)	63(1)	35(1)	25(1)	-5(1)	-1(1)	7(1)
O(10E)	41(1)	43(1)	36(1)	-12(1)	-5(1)	12(1)
C(11E)	37(1)	29(1)	20(2)	-8(1)	1(1)	1(1)
C(12E)	35(2)	27(1)	20(2)	-8(1)	0(1)	0(1)
C(13E)	36(2)	33(1)	24(2)	-7(1)	-2(1)	3(1)
C(14E)	46(2)	36(2)	28(2)	-3(1)	-3(1)	2(1)
C(15E)	45(2)	37(2)	35(2)	-7(1)	7(1)	-10(1)
C(16E)	35(2)	43(2)	39(2)	-11(1)	0(1)	-3(1)
C(17E)	39(2)	33(1)	25(2)	-6(1)	-3(1)	4(1)
C(18E)	34(2)	37(2)	29(2)	-10(1)	1(1)	-4(1)
C(19E)	42(2)	44(2)	29(2)	-11(1)	0(1)	-7(1)
C(20E)	59(2)	40(2)	31(2)	-17(1)	3(1)	-11(1)
C(21E)	60(2)	28(1)	29(2)	-11(1)	5(1)	1(1)
C(22E)	45(2)	27(1)	25(2)	-8(1)	3(1)	-1(1)
O(1F)	41(1)	40(1)	46(1)	-21(1)	16(1)	-8(1)
C(2F)	31(1)	37(2)	33(2)	-12(1)	7(1)	-3(1)
O(3F)	41(1)	37(1)	48(1)	-21(1)	15(1)	-10(1)
C(4F)	33(2)	29(1)	21(2)	-3(1)	-3(1)	-1(1)
C(5F)	31(1)	31(1)	19(2)	-9(1)	-1(1)	0(1)
C(6F)	35(2)	30(1)	22(2)	-7(1)	-3(1)	2(1)
C(7F)	49(2)	51(2)	36(2)	-10(2)	-5(1)	1(1)
C(8F)	42(2)	52(2)	35(2)	-9(2)	-4(1)	0(1)
O(9F)	36(1)	32(1)	35(1)	-7(1)	5(1)	5(1)
O(10F)	49(1)	36(1)	27(1)	-13(1)	2(1)	2(1)
C(11F)	31(1)	27(1)	24(2)	-8(1)	-1(1)	1(1)
C(12F)	33(2)	31(1)	25(2)	1(1)	-1(1)	-4(1)
C(13F)	36(2)	60(2)	49(2)	6(2)	-1(2)	6(1)
C(14F)	34(2)	84(3)	84(3)	33(2)	-17(2)	-5(2)
C(15F)	68(3)	70(3)	87(4)	40(2)	-46(3)	-36(2)
C(16F)	102(3)	43(2)	46(2)	7(2)	-37(2)	33(2)
C(17F)	59(2)	33(2)	33(2)	-2(1)	-13(2)	-11(1)
C(18F)	58(2)	29(1)	28(2)	-9(1)	-1(1)	-1(1)
C(19F)	69(2)	27(1)	31(2)	-9(1)	-2(2)	0(1)
C(20F)	55(2)	39(2)	31(2)	-1(1)	-1(1)	-16(1)
C(21F)	37(2)	45(2)	31(2)	-3(1)	5(1)	-5(1)
C(22F)	33(1)	37(2)	30(2)	-6(1)	2(1)	-2(1)
O(1G)	44(1)	31(1)	41(1)	-7(1)	12(1)	1(1)
C(2G)	35(2)	37(2)	30(2)	-11(1)	5(1)	-1(1)
O(3G)	43(1)	37(1)	42(1)	-9(1)	11(1)	-5(1)
C(4G)	39(2)	31(2)	20(2)	-6(1)	-2(1)	-1(1)
C(5G)	32(1)	32(1)	18(2)	-6(1)	-3(1)	0(1)
C(6G)	35(2)	33(1)	21(2)	-9(1)	-1(1)	-5(1)
C(7G)	66(2)	65(2)	32(2)	-18(2)	0(2)	-11(2)
C(8G)	45(2)	59(2)	52(2)	-16(2)	-6(2)	5(2)
O(9G)	53(1)	34(1)	29(1)	-3(1)	3(1)	-4(1)
O(10G)	44(1)	39(1)	37(1)	-14(1)	7(1)	-13(1)
C(11G)	32(1)	28(1)	23(2)	-9(1)	-1(1)	-1(1)
C(12G)	34(2)	48(2)	23(2)	-18(1)	-2(1)	2(1)
C(13G)	56(2)	48(2)	37(2)	-19(2)	-14(2)	23(2)
C(14G)	81(3)	89(3)	44(2)	-38(2)	-24(2)	48(2)
C(15G)	46(2)	167(5)	52(3)	-68(3)	-16(2)	33(3)
C(16G)	43(2)	145(4)	59(3)	-43(3)	-4(2)	-12(2)
C(17G)	43(2)	85(2)	39(2)	-21(2)	-4(2)	-15(2)
C(18G)	33(1)	39(2)	29(2)	-12(1)	3(1)	-5(1)
C(19G)	43(2)	43(2)	33(2)	-13(1)	8(1)	-6(1)
C(20G)	56(2)	52(2)	37(2)	-18(2)	5(2)	8(2)
C(21G)	71(2)	31(2)	38(2)	-13(1)	7(2)	-1(1)
C(22G)	54(2)	31(1)	32(2)	-9(1)	3(1)	2(1)
O(1H)	40(1)	29(1)	54(1)	-6(1)	-15(1)	-3(1)
C(2H)	30(1)	34(2)	32(2)	-8(1)	-5(1)	0(1)
O(3H)	41(1)	34(1)	52(1)	-9(1)	-16(1)	-1(1)
C(4H)	37(2)	30(2)	19(2)	-7(1)	2(1)	0(1)
C(5H)	29(1)	29(1)	17(1)	-5(1)	3(1)	-2(1)
C(6H)	33(2)	35(1)	17(2)	-10(1)	1(1)	-2(1)
C(7H)	49(2)	50(2)	31(2)	-13(1)	6(1)	-4(1)
C(8H)	39(2)	59(2)	32(2)	-9(2)	3(1)	-5(1)
O(9H)	50(1)	32(1)	26(1)	-4(1)	-1(1)	2(1)

O(10H)	36(1)	39(1)	31(1)	-13(1)	-4(1)	8(1)
C(11H)	29(1)	30(1)	17(1)	-6(1)	4(1)	-1(1)
C(12H)	31(1)	44(2)	24(2)	-17(1)	3(1)	-4(1)
C(13H)	55(2)	50(2)	29(2)	-17(2)	10(1)	-21(1)
C(14H)	91(3)	82(3)	30(2)	-25(2)	18(2)	-51(2)
C(15H)	58(2)	131(4)	55(3)	-62(3)	25(2)	-43(3)
C(16H)	33(2)	127(4)	65(3)	-55(3)	7(2)	-1(2)
C(17H)	41(2)	74(2)	40(2)	-24(2)	4(1)	8(2)
C(18H)	36(2)	41(2)	24(2)	-13(1)	-2(1)	2(1)
C(19H)	43(2)	45(2)	28(2)	-14(1)	-6(1)	1(1)
C(20H)	52(2)	54(2)	30(2)	-18(2)	0(1)	-11(1)
C(21H)	69(2)	33(2)	35(2)	-16(1)	1(2)	-7(1)
C(22H)	49(2)	29(1)	30(2)	-9(1)	1(1)	-6(1)

Crystallographic data for 5.45




C19
O18
C21
C16
C15
C14
C25
C24
C23
C26
C13
C12
C17
O20
C11
C22
H5
C5
O9
O10
C4
O6
O3
O1
C7
C2
C8

Crystallization solvent: benzene/petroleum ether (diffusion technique)

Table 1. Crystal data and structure refinement for $C_{20}H_{26}O_6$

Empirical formula	$C_{20}H_{26}O_6$
Formula weight	362.41
Temperature	180(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P21/n
Unit cell dimensions	a = 8.017(3) Å, b = 12.411(5) Å, c = 18.403(7) Å,
	β = 97.923(7)º
Volume	1813.6(11) $Å^3$
Z, Calculated density	4, 1.327 g/cm^3
Absorption coefficient	0.097 mm^{-1}
F(000)	776
Crystal size	0.28 x 0.22 x 0.04 mm
Theta range for data collection	2.94 to 28.00º
Limiting indices	-10<h<10, -16<k<16, -24<l<21
Reflections collected / unique	13217 / 4241 [R_{int} = 0.0354]
Completeness to theta = 28.00	96.7%
Max. and min. transmission	0.9961 and 0.9733
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4241 / 0 / 237
Goodness-of-fit on F^2	1.396
Final R indices [I>2σ(I)]	R1 = 0.0556, wR2 = 0.1048
R indices (all data)	R1 = 0.0806, wR2 = 0.1257
Extinction coefficient	0.0032(6)
Largest diff. peak and hole	0.288 and -0.331 $e^-.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

	x	y	z	U(eq)
O(20)	9105(2)	4660(1)	1408(1)	31(1)
O(18)	7054(2)	4083(1)	201(1)	44(1)
O(1)	8365(2)	3046(1)	3476(1)	36(1)
O(3)	10322(2)	4352(1)	3953(1)	39(1)
O(10)	9120(2)	1875(1)	2688(1)	40(1)
O(9)	12848(2)	4285(1)	3638(1)	41(1)
C(5)	10544(3)	3608(2)	2756(1)	26(1)
C(17)	9324(3)	3655(2)	1106(1)	28(1)
C(11)	11676(3)	3243(2)	2179(1)	28(1)
C(26)	12814(3)	4191(2)	1996(1)	33(1)
C(12)	10494(3)	2929(2)	1474(1)	28(1)
C(16)	8243(3)	3341(2)	478(1)	35(1)
C(6)	9305(3)	2754(2)	2948(1)	30(1)
C(4)	11391(3)	4100(2)	3464(1)	32(1)
C(22)	12837(3)	2314(2)	2502(1)	34(1)
C(13)	10543(3)	1897(2)	1172(1)	35(1)
C(2)	8547(3)	4098(2)	3806(1)	38(1)
C(7)	7567(3)	4946(2)	3333(1)	39(1)
C(25)	14096(3)	3849(2)	1506(2)	44(1)
C(14)	9540(3)	1615(2)	537(2)	43(1)
C(15)	8392(3)	2329(2)	181(1)	42(1)
C(21)	9351(3)	5582(2)	957(1)	44(1)

C(23)	14268(3)	2010(2)	2070(2)	43(1)
C(24)	15260(3)	2983(2)	1882(2)	47(1)
C(8)	7961(4)	3989(2)	4543(2)	55(1)
C(19)	5800(4)	3722(3)	-373(2)	59(1)

Table 3. Hydrogen coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3)

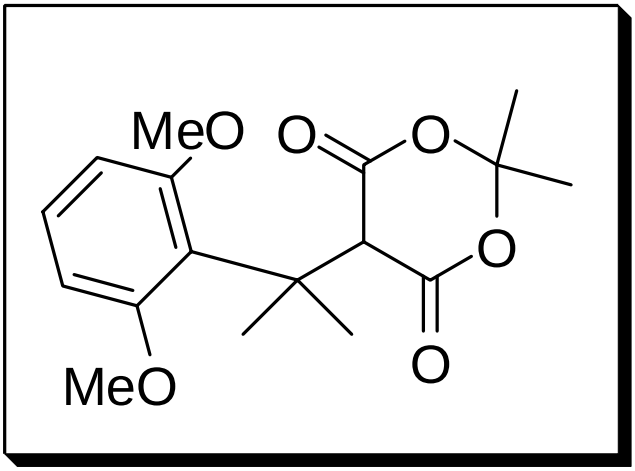
	x	y	z	U(eq)
H(5)	9837	4184	2514	31
H(26X)	12111	4758	1754	39
H(26Y)	13401	4484	2449	39
H(22X)	13326	2514	2995	41
H(22Y)	12147	1680	2541	41
H(13)	11277	1388	1409	42
H(7X)	7981	4988	2869	59
H(7Y)	7703	5633	3575	59
H(7Z)	6395	4756	3256	59
H(25X)	14757	4468	1397	52
H(25Y)	13517	3571	1047	52
H(14)	9635	929	343	51
H(15)	7727	2132	-253	50
H(21X)	9165	6231	1219	66
H(21Y)	8571	5552	513	66
H(21Z)	10482	5579	840	66
H(23X)	15020	1510	2358	52
H(23Y)	13800	1648	1620	52
H(24X)	16062	2767	1560	57
H(24Y)	15887	3275	2327	57
H(8X)	8614	3445	4824	82
H(8Y)	6794	3788	4479	82
H(8Z)	8100	4665	4799	82
H(19X)	5039	4303	-523	88
H(19Y)	5186	3134	-199	88
H(19Z)	6329	3487	-783	88

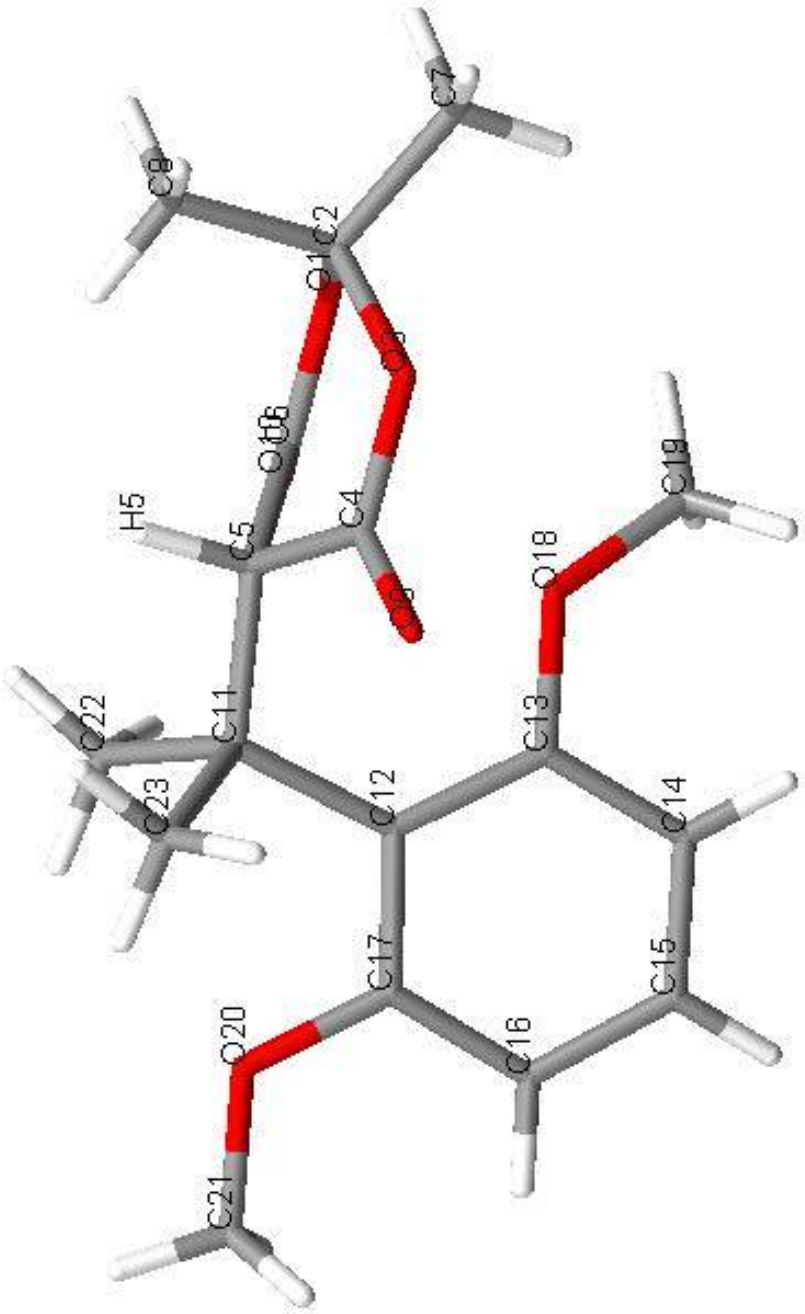
Table 4. Bond lengths [Å] and angles [º]

O(20)-C(17)	1.387(2)
O(20)-C(21)	1.442(3)
O(18)-C(16)	1.371(3)
O(18)-C(19)	1.426(3)
O(1)-C(6)	1.359(2)
O(1)-C(2)	1.440(3)
O(3)-C(4)	1.362(3)
O(3)-C(2)	1.446(3)
O(10)-C(6)	1.193(3)
O(9)-C(4)	1.190(3)
C(5)-C(4)	1.514(3)
C(5)-C(6)	1.526(3)
C(5)-C(11)	1.556(3)
C(17)-C(16)	1.401(3)
C(17)-C(12)	1.405(3)
C(11)-C(12)	1.548(3)
C(11)-C(22)	1.548(3)
C(11)-C(26)	1.554(3)
C(26)-C(25)	1.519(3)
C(12)-C(13)	1.399(3)
C(16)-C(15)	1.382(3)
C(22)-C(23)	1.531(3)
C(13)-C(14)	1.370(4)
C(2)-C(8)	1.502(3)
C(2)-C(7)	1.515(3)
C(25)-C(24)	1.525(4)
C(14)-C(15)	1.376(4)
C(23)-C(24)	1.513(3)

C(17)-O(20)-C(21)	116.66(18)
C(16)-O(18)-C(19)	116.6(2)
C(6)-O(1)-C(2)	120.64(17)
C(4)-O(3)-C(2)	121.28(18)
C(4)-C(5)-C(6)	108.01(18)
C(4)-C(5)-C(11)	118.06(18)
C(6)-C(5)-C(11)	114.56(17)
O(20)-C(17)-C(16)	118.8(2)
O(20)-C(17)-C(12)	119.82(19)
C(16)-C(17)-C(12)	121.0(2)
C(12)-C(11)-C(22)	113.65(18)
C(12)-C(11)-C(26)	108.61(18)
C(22)-C(11)-C(26)	107.90(17)
C(12)-C(11)-C(5)	107.33(17)
C(22)-C(11)-C(5)	109.31(18)
C(26)-C(11)-C(5)	110.01(17)
C(25)-C(26)-C(11)	112.45(19)
C(13)-C(12)-C(17)	116.7(2)
C(13)-C(12)-C(11)	121.1(2)
C(17)-C(12)-C(11)	122.23(18)
O(18)-C(16)-C(15)	123.8(2)
O(18)-C(16)-C(17)	116.1(2)
C(15)-C(16)-C(17)	120.1(2)
O(10)-C(6)-O(1)	118.7(2)
O(10)-C(6)-C(5)	126.2(2)
O(1)-C(6)-C(5)	115.08(18)
O(9)-C(4)-O(3)	117.5(2)
O(9)-C(4)-C(5)	128.1(2)
O(3)-C(4)-C(5)	114.42(19)
C(23)-C(22)-C(11)	116.0(2)
C(14)-C(13)-C(12)	121.8(2)
O(1)-C(2)-O(3)	108.47(17)
O(1)-C(2)-C(8)	105.9(2)
O(3)-C(2)-C(8)	105.9(2)
O(1)-C(2)-C(7)	111.9(2)
O(3)-C(2)-C(7)	112.0(2)
C(8)-C(2)-C(7)	112.3(2)
C(26)-C(25)-C(24)	110.5(2)
C(13)-C(14)-C(15)	121.1(2)
C(14)-C(15)-C(16)	119.1(2)
C(24)-C(23)-C(22)	112.2(2)
C(23)-C(24)-C(25)	111.0(2)

Crystallographic data for 5.46




C7
C8
O1
C2
O3
O6
H5
C5
C4
O18
C19
C22
C11
C13
O23
C12
C14
C17
C15
O20
C16
C21

Crystallization solvent: benzene/petroleum ether (diffusion technique)

Table 1 Crystal data and structure refinement for $C_{23}H_{28}O_6$

Empirical formula	$C_{23}H_{28}O_6$
Formula weight	400.45
Temperature	180(1) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 13.3229(7) Å alpha = 90º
	b = 9.9293(5) Å beta = 110.720(1)º
	c = 16.8309(9) Å gamma = 90º
Volume	2082.50(19) $Å^3$
Z, Calculated density	4, 1.277 mg/m^3
Absorption coefficient	0.092 mm^{-1}
F(000)	856
Crystal size	0.17 x 0.17 x 0.08 mm
Theta range for data collection	1.69 to 28.28º
Limiting indices	-17<=h<=12, -7<=k<=13, -22<=l<=22
Reflections collected / unique	12701 / 5050 [R_{int} = 0.0360]
Completeness to theta = 28.28	97.8%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5050 / 0 / 269
Goodness-of-fit on F^2	1.356
Final R indices [I>2sigma(I)]	R1 = 0.0489, wR2 = 0.0743
R indices (all data)	R1 = 0.0771, wR2 = 0.0774
Extinction coefficient	0.0101(5)
Largest diff. peak and hole	0.234 and -0.261 e. $Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3).

	x	y	z	U(eq)
O(1)	6750(1)	7104(1)	2381(1)	39(1)
C(2)	7364(1)	5879(2)	2505(1)	35(1)
O(3)	6681(1)	4796(1)	2056(1)	35(1)
C(4)	5678(1)	4652(2)	2071(1)	31(1)
C(5)	5275(1)	5764(1)	2502(1)	29(1)
C(6)	5736(1)	7111(2)	2382(1)	35(1)
C(7)	8159(1)	6093(2)	2068(1)	46(1)
C(8)	7895(1)	5553(2)	3432(1)	49(1)
O(9)	5190(1)	3658(1)	1754(1)	40(1)
O(10)	5285(1)	8179(1)	2298(1)	46(1)
C(11)	4049(1)	5729(2)	2347(1)	30(1)
C(12)	3310(1)	5937(1)	1409(1)	28(1)
C(13)	3645(1)	6165(1)	719(1)	30(1)
C(14)	2937(1)	6277(1)	-113(1)	35(1)
C(15)	1854(1)	6214(2)	-278(1)	40(1)
C(16)	1470(1)	6037(2)	372(1)	39(1)
C(17)	2187(1)	5895(1)	1200(1)	33(1)
O(18)	4733(1)	6249(1)	889(1)	39(1)
C(19)	5103(1)	6931(2)	301(1)	55(1)
O(20)	1836(1)	5713(1)	1864(1)	44(1)
C(21)	723(1)	5641(2)	1707(1)	49(1)

C(22)	3831(1)	6827(2)	2926(1)	39(1)
C(23)	3812(1)	4342(2)	2671(1)	40(1)
C(24)	3393(2)	1176(3)	834(1)	68(1)
C(25)	2801(2)	2247(2)	486(1)	61(1)
C(26)	1764(2)	2130(2)	49(1)	69(1)
C(27)	1278(2)	933(4)	-59(1)	86(1)
C(28)	1857(3)	-202(3)	293(2)	102(1)
C(29)	2941(3)	-52(3)	748(2)	88(1)

Table 3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3).

	x	y	z	U(eq)
H(5)	5626	5571	3123	35
H(7X)	8580	5270	2108	69
H(7Y)	8640	6838	2341	69
H(7Z)	7775	6312	1468	69
H(8X)	7346	5451	3691	74
H(8Y)	8385	6283	3716	74
H(8Z)	8299	4710	3494	74
H(14)	3200	6396	-564	42
H(15)	1365	6293	-846	48
H(16)	719	6011	256	46
H(19X)	4935	6392	-218	83
H(19Y)	5881	7061	555	83
H(19Z)	4748	7809	161	83
H(21X)	384	6497	1468	73
H(21Y)	607	5464	2241	73
H(21Z)	406	4912	1304	73
H(22X)	3771	7709	2652	59
H(22Y)	4426	6843	3474	59
H(22Z)	3161	6620	3018	59
H(23X)	3119	4380	2752	60
H(23Y)	4379	4128	3213	60
H(23Z)	3788	3644	2253	60
H(24)	4139	1279	1145	81
H(25)	3128	3110	553	74
H(26)	1358	2909	-194	83
H(27)	532	865	-378	104
H(28)	1523	-1061	225	123
H(29)	3365	-815	998	106

Table 4 Bond lengths [Å] and angles [º]

O(1)-C(6)	1.3516(16)
O(1)-C(2)	1.4389(17)
C(2)-O(3)	1.4382(16)
C(2)-C(8)	1.503(2)
C(2)-C(7)	1.503(2)
O(3)-C(4)	1.3534(17)
C(4)-O(9)	1.1979(16)
C(4)-C(5)	1.5204(19)
C(5)-C(6)	1.515(2)
C(5)-C(11)	1.5600(19)
C(6)-O(10)	1.2027(16)
C(11)-C(12)	1.5502(19)
C(11)-C(23)	1.5549(19)
C(11)-C(22)	1.5569(19)
C(12)-C(13)	1.402(2)
C(12)-C(17)	1.4102(19)
C(13)-O(18)	1.3776(16)
C(13)-C(14)	1.389(2)
C(14)-C(15)	1.3709(19)
C(15)-C(16)	1.372(2)
C(16)-C(17)	1.391(2)
C(17)-O(20)	1.3676(17)
O(18)-C(19)	1.4230(17)
O(20)-C(21)	1.4134(16)

C(24)-C(25)	1.331(3)
C(24)-C(29)	1.346(3)
C(25)-C(26)	1.320(3)
C(26)-C(27)	1.335(3)
C(27)-C(28)	1.376(3)
C(28)-C(29)	1.382(3)

C(6)-O(1)-C(2)	121.45(12)
O(3)-C(2)-O(1)	109.51(11)
O(3)-C(2)-C(8)	111.23(13)
O(1)-C(2)-C(8)	111.52(13)
O(3)-C(2)-C(7)	105.82(12)
O(1)-C(2)-C(7)	105.81(13)
C(8)-C(2)-C(7)	112.65(13)
C(4)-O(3)-C(2)	121.00(11)
O(9)-C(4)-O(3)	117.57(14)
O(9)-C(4)-C(5)	125.69(14)
O(3)-C(4)-C(5)	116.73(13)
C(6)-C(5)-C(4)	110.41(12)
C(6)-C(5)-C(11)	116.52(12)
C(4)-C(5)-C(11)	115.45(12)
O(10)-C(6)-O(1)	117.56(14)
O(10)-C(6)-C(5)	125.81(15)
O(1)-C(6)-C(5)	116.62(13)
C(12)-C(11)-C(23)	109.91(12)
C(12)-C(11)-C(22)	110.65(12)
C(23)-C(11)-C(22)	107.08(12)
C(12)-C(11)-C(5)	114.74(12)
C(23)-C(11)-C(5)	106.92(12)
C(22)-C(11)-C(5)	107.18(12)
C(13)-C(12)-C(17)	114.74(14)
C(13)-C(12)-C(11)	126.18(13)
C(17)-C(12)-C(11)	119.08(13)
O(18)-C(13)-C(14)	119.60(14)
O(18)-C(13)-C(12)	117.31(13)
C(14)-C(13)-C(12)	123.08(14)
C(15)-C(14)-C(13)	119.46(15)
C(14)-C(15)-C(16)	120.41(15)
C(15)-C(16)-C(17)	119.62(15)
O(20)-C(17)-C(16)	121.34(14)
O(20)-C(17)-C(12)	116.03(14)
C(16)-C(17)-C(12)	122.62(15)
C(13)-O(18)-C(19)	118.88(12)
C(17)-O(20)-C(21)	119.61(13)
C(25)-C(24)-C(29)	120.2(2)
C(26)-C(25)-C(24)	121.0(2)
C(25)-C(26)-C(27)	121.1(2)
C(26)-C(27)-C(28)	120.0(2)
C(27)-C(28)-C(29)	117.8(2)
C(24)-C(29)-C(28)	119.9(2)