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Tetrahedron 60 (2004) 7637–7658
Tetrahedron

Hemisynthesis of methyl pyrethroates from γ-alkoxy-alkylidene malonates and isopropylidenediphenylsulfurane and isopropylidenetriphenylphosphorane

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Received 13 April 2004; revised 31 May 2004; accepted 1 June 2004

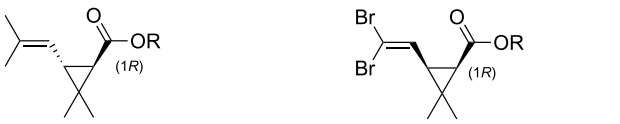
Available online 17 July 2004

Dedicated to Professor Dieter Seebach at the occasion of the 2003 Tetrahedron Prize with admiration for his extremely important contribution to Organic Chemistry

Abstract—Hemisynthesis of methyl pyrethroates from γ-alkoxy-alkylidene malonates and isopropylidenediphenylsulfurane and isopropylidenetriphenylphosphorane is disclosed. It takes advantage of the high degree of stereocontrol observed in the cyclopropanation of γ-alkoxy-alkylidene malonates by the above mentioned ylides.

1. Introduction

We have been interested over the last fifteen years to develop new synthetic routes to chrysanthemic **1** and deltamethrinic acid and related esters **2** (Scheme 1).[1]



1a R= H; Chrysanthemic acid
2a R=Alkyl; Alkyl chrysanthemate

1b R= H; Deltamethrinic acid
2b R=Alkyl; Alkyl deltamethrinate

Scheme 1. Structure of chrysanthemic and deltamethrinic compounds.

One of our strategy involves the use of chiral γ-alkoxy-α,β-unsaturated esters as starting materials and isopropylidene-diphenylsulfurane or isopropylidenetriphenylphosphorane as cyclopropanating agents.[1e,2–6] This interest arose from our original work which involves the synthesis of methyl (*d*,*l*)-*trans*-chrysanthemate in a single step from methyl 4-oxobutenoate and isopropylidenetriphenylphosphorane (Scheme 2, entry a)[2a] and from the work of Mulzer[7] who described the diastereoselective cyclopropanation of ethyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylate which produces, after some functional group manipulation, the enantio-enriched methyl (*d*)-*trans*-chrysanthemate with a 74% ee (Scheme 2, entry b). In such transformation ethyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylate has played the role of chiral masked methyl 4-oxobutenoate.

We have subsequently found that the cyclopropanation reaction takes place from either the *Re* or the *Si*-face of the electrophilic olefin depending not only on the stereochemistry at its allylic carbon bearing the alkoxy group and of its [C,C] double bond but also on the nature of the heteroatomic moiety present on the α-heterosubstituted organometallic (Scheme 3).[5,7]

Important features of the reactions involving methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylate, are collected in Scheme 3.

Isopropylidenetriphenylphosphorane adds from the *Si*-face of the *E*-stereoisomer (Scheme 3, entry a) whereas it adds from the *Re*-face of its *Z*-stereoisomer (Scheme 3, entry c) providing in both cases stereoselectively the *trans*-cyclopropane derivatives.[5a,b,7]

Its sulfur ylide analogue however reacts by the *Re*-face of methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylate, irrespective of its stereochemistry. Furthermore the reaction proved to be completely stereospecific since it leads to the *trans*-cyclopropane carboxylate from the *E*-diastereoisomer of methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylate

Keywords: Asymmetric induction; Insecticide; γ-Alkoxy enoates; Deltamethrinic acid; Chrysanthemic acid.
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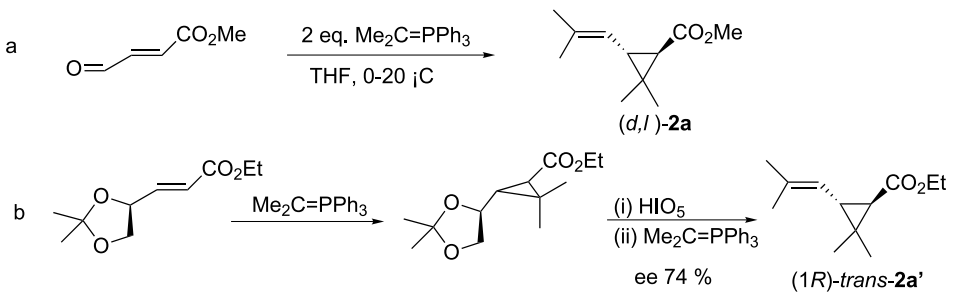
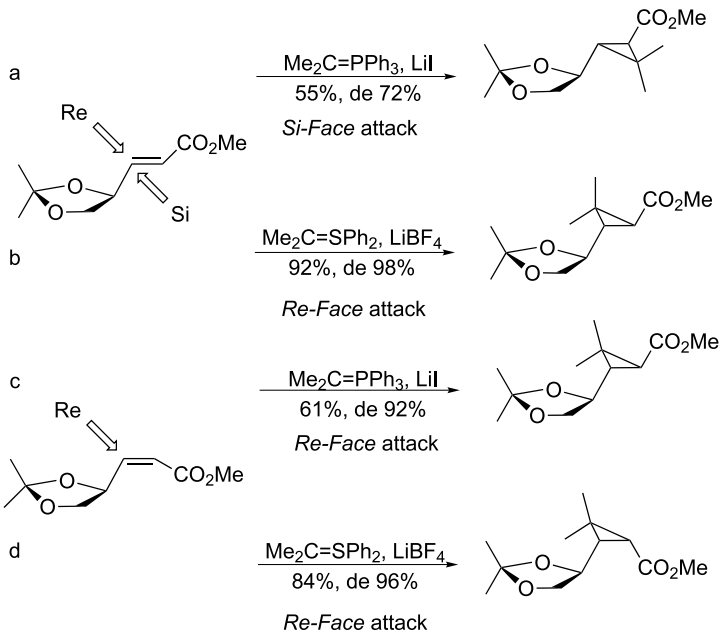
doi:10.1016/j.tet.2004.06.035



Scheme 2. Previous syntheses of *trans*-chrysanthemates.



Scheme 3. Stereocontrolled addition of P- and S-ylides to γ-alkoxy enoates.

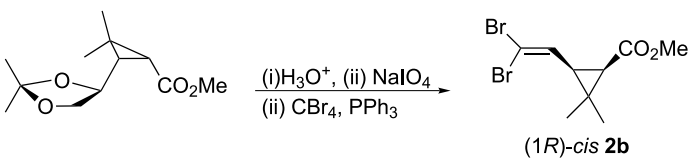
(Scheme 3; entry b) and to the *cis*-cyclopropane carboxylate from its *Z*-diastereoisomer (Scheme 3; entry d).[5b–f]

Asymmetric induction is as expected dependant on the stereochemistry of the allylic carbon to which the alkoxy group is attached. Enoates whose structures are described above belong to the (*S*)-series. Their syntheses have been selectively achieved using well established protocols from the acetonides of D-glyceraldehyde derived from (*d*)-mannitol.[1e,5a–d]

The strategy used to produce the required vinylcyclopropane carboxylates from the above mentioned adducts involves (i) acid hydrolysis of the acetal moieties, (ii) sodium periodate cleavage of the resulting diol and (iii) Wittig olefination reaction. An even shorter approach involves periodic acid which performs, in the same pot, the transformation of the acetal moiety to methyl hemicaronates.[7]

The synthesis of methyl *trans*-chrysanthemate implies isopropylidenetriphenylphosphorane ($Ph_3P{=}CMe_2$, THF, 20 °C, Scheme 2, entry b)[5c,7] whereas that of methyl deltamethrinate requires instead the use of dibromomethylenetriphenylphosphorane (CBr_4, PPh_3, THF, 20 °C, *cis*: 81% yield, Scheme 4).[5b,c]

The most important substrates are those which possess the appropriate stereochemistry to produce, without any stereochemical modification, either methyl (1*R*)-*trans*-chrysanthemate **2a** or methyl (1*R*)-*cis*-deltamethrinate **2b**. Thus starting from the (*S*)-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylate derived from D-glyceraldehyde, the *E*-α,β-unsaturated carboxylates and isopropylidenetriphenyl-



Scheme 4. Synthesis of methyl deltamethrinate.

phosphorane must be used for the synthesis of the former compound (Scheme 2, entry b; Scheme 3, entry a)[2k,3] and *Z*-α,β-unsaturated carboxylates and isopropylidene-diphenylsulfurane for the latter (Scheme 3, entry d; Scheme 4).[5a,b]

The synthesis of methyl (1*R*)-*cis*-deltamethrinate works fine.[2i,k] Not only the *cis*-content (100%) and the enantiomeric excess (98%) are excellent, but also the strategy which requires the introduction of the dibromomethylene moiety at the end of the synthesis is reasonably good. This is not the case of methyl (1*R*)-*trans*-chrysanthemate which suffers both from quite poor enantiomeric excess (74–72%) and quite lengthy functional group manipulation to produce the vinyl side chain.[5,7]

We have therefore designed two new routes to methyl (1*R*)-*trans*-chrysanthemate which use both isopropylidene-diphenylsulfurane as cyclopropanating agent (Scheme 5).[2t,u] The latter is known to provide much better asymmetric induction than the related phosphorus ylide (Scheme 3). This choice requires using as partner *E*-α,β-unsaturated carboxylates possessing the inverted (*R*)-stereochemistry on the chiral carbon bearing the alkoxy moiety.

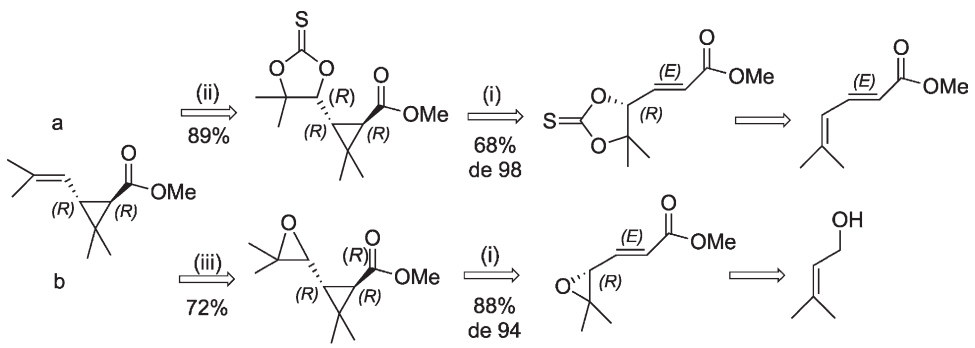
In order to increase the diastereoselection and to shorten the number of steps leading to methyl (1*R*)-*trans*-chrysanthemate, we have performed the cyclopropanation on methyl γ-alkoxy-α,β-unsaturated carboxylates whose hydrocarbon content provides, after sequential cyclopropanation ($Me_2C{=}SPh_2$–$LiBF_4$, DME, −78 °C, 2 h, −78 to 20 °C, 1 h) and reductive decomposition, directly the desired compound. Methyl (*R*)-3-(5,5-dimethyl-2-thioxo-[1,3]dioxolan-4-yl)-[5g] and (*R*)-3-(3,3-dimethyl-oxiranyl)-[5h] acrylates (Scheme 5, entries a and b, respectively) proved to be the perfect candidates: (i) they are readily prepared from methyl 5-methyl-hexa-2,4-dienoate and AD-mix β using Sharpless catalytic asymmetric dihydroxylation reaction (AD reaction, Scheme 5, entry a)[8a] and 3-methyl-but-2-en-1-ol, titanium tetraisopropoxide, *tert*-butylhydroperoxide and l-diisopropyl tartrate according to Sharpless catalytic asymmetric epoxidation of allyl alcohols (AE reaction, Scheme 5, entry b)[9] respectively, (ii) after cyclopropanation has been achieved the thionocarbonate substructure present on the former product can be efficiently reduced according to the Hopkins[10] variation of the Corey–Winter reaction ($(CH_2NMe)_2P$–Ph, neat, 40 °C, 6 h, 89%; Scheme 5, entry a)[5g] whereas the epoxy[5h] substructure present on the latter adduct has been transformed to the corresponding tri-substituted C,C double bond on reaction with P_2I_4 (CS_2, pyridine, 5 h, reflux, 72%; Scheme 5, entry b).[11]

In the examples reported above the control of the stereochemistry (1*R*)/(1*S*), *cis*/*trans* on the cyclopropane ring depends on (i) the nature of the ylide (S or P) and (ii) the stereochemistry (*R* or *S*) at [C-3] and also the stereochemistry (*Z* or *E*) of the [C,C] double bond of the γ-alkoxy-α,β-unsaturated carboxylates.[5] Therefore the stereochemistry of the [C,C] double bond has to be perfectly controlled for successful enantioselective synthesis of pyrethroic acids.

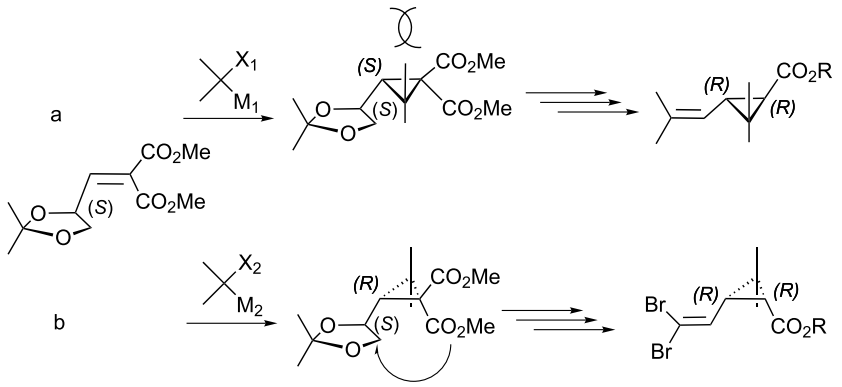
Use of γ-alkoxy-alkylidene malonates in place of the corresponding α,β-unsaturated carboxylates should avoid the latter constraint for the control of the face of attack and therefore for the control of the stereochemistry at [C-2] on the methyl chrysanthemate.[6] This strategy nevertheless introduces other constraints since the stereochemistry at [C-1] on the cyclopropane carboxylate is no longer related to the stereochemistry of the [C,C] double bond of the starting material and will be created at the time the tandem decarboxylative-dealkylation is achieved. We expected that the production of the *trans*-stereochemistry will take advantage of steric hindrance between the group at [C-2] and the carboxy group at [C-1] (Scheme 6, entry a) whereas the *cis*-stereochemistry will derive from lactone ring formation (Scheme 6, entry b).

In order to achieve the two approaches leading to each of the two epimeric cyclopropane moieties at [C-2] present in chrysanthemates **2a** and deltamethrinates **2b**, we had to find cyclopropanating agents able to react with complete stereocontrol but divergently on the same methyl γ-alkoxy-alkylidene malonate (Scheme 6).[6]

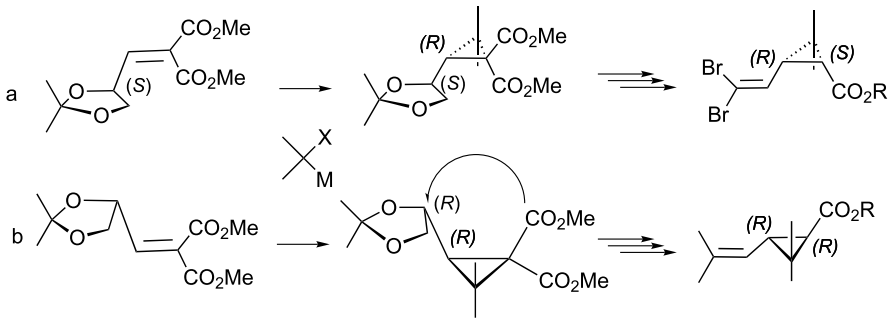
Another less constraining approach uses the same reagent but requires the synthesis of each of the two enantiomers of methyl γ-alkoxy-alkylidene malonate such as 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester (Scheme 7).



Scheme 5. Straightforward synthesis of methyl (1*R*)-*trans*-chrysanthemate.



Scheme 6. Planned enantioselective syntheses of pyrethroates using different ylides.



Scheme 7. Planned enantioselective syntheses of pyrethroates pyrethroates using different enoates.

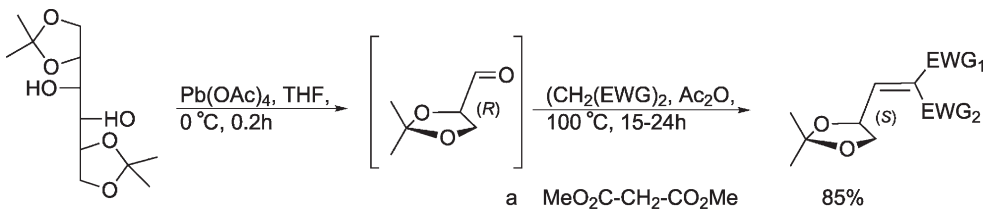
We have successfully performed each of the two approaches[6] but will present only the latter in this paper.[6a]

2. Synthesis of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid esters, related malononitriles and malonodinitrile

When we started this work 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid diethyl ester was already known. It was produced in modest yield (24–30%), via a Knoevenagel reaction[12] from (*R*)-2,2-dimethyl-[1,3]dioxolane-4-carbaldehyde (the acetonide of D-glyceraldehyde)[13] and diethyl malonate using piperidine as the catalyst (toluene, 20 °C, 1–24 h)[14] but its stereochemical integrity was not described. Piperidinium acetate which was successfully used by Tietze[12] for related cases does not lead to the desired compound using dimethyl malonate. Titanium tetrachloride in the presence of pyridine[15] proved the most suitable combination at the condition that the ingredients are mixed at low temperature (dimethyl malonate, $TiCl_4$, pyridine, THF, −78 to 20 °C, 72 h, 70% yield on 10 g scale; 20 °C, 72 h, 24–41% yield).[6a]

It was later found that even better results could be obtained if both the oxidative cleavage of central diol of the terminal diacetonide of D-mannitol ($Pb(OAc)_4$, THF, 0 °C, 0.2 h) and the Knoevenagel reaction (dimethyl malonate, acetic anhydride, reflux, 24 h, 85% yield, $[\alpha]_D^{20}=+20.1$, $c=1.05$; ee >96%, Scheme 8, entry a) were carried out in the same pot according to the procedure described for the corresponding methyl malononitrile[16] (Scheme 8, entry d).

The same process was successfully used for the synthesis of methyl tertiobutyl and di-tertiobutyl-alkylidene malonates ((i) $Pb(OAc)_4$, THF, 0 °C, 0.2 h, (ii) malonate, acetic anhydride, reflux, 24 h, 96 and 87% yield, respectively, Scheme 8, entries b and c). Those conditions do not work with malonodinitrile. The corresponding alkylidene malonodinitrile has been however prepared in almost

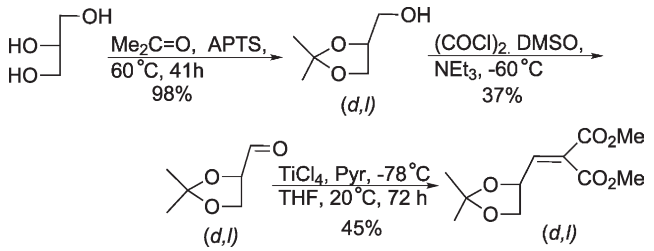


a	$MeO_2C\text{-}CH_2\text{-}CO_2Me$	85%
b	$t\text{-}BuO_2C\text{-}CH_2\text{-}CO_2Me$	96% (Z/E: 45/55)
c	$t\text{-}BuO_2C\text{-}CH_2\text{-}CO_2t\text{-}Bu$	87%
d	$MeO_2C\text{-}CH_2\text{-}CN$	77%
e	$NC\text{-}CH_2\text{-}CN$	00%

Scheme 8. Synthesis of alkylidene malonates and alkylidene malononitriles derived from (*R*)-2,2-dimethyl-[1,3]dioxolane-4-carbaldehyde.

quantitative yield, on reaction of the acetonide of D-glyceraldehyde and malonodinitrile in the presence of 4-*N*,*N*-dimethylaminopyridine (CH_2Cl_2, 0 °C, 1 h, 20 °C, quantitative yield) but its isolation from 4-*N*,*N*-dimethylaminopyridine was unsuccessful and it has been used without purification in the next step.

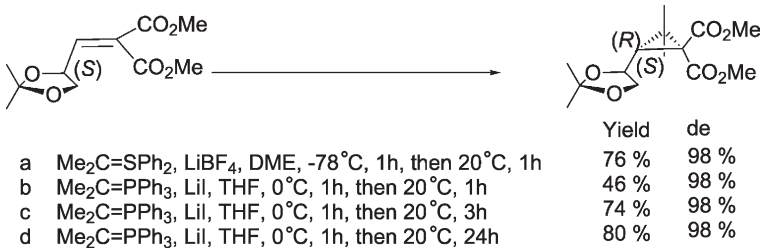
We have checked the stereochemical purity of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester just prepared by comparison on HPLC (Diacel, Chiracel, ODH, isopropanol/hexane: 3/7 (v/v) 1 ml/min; 47 bar; λ_{DET} 254 nm) of an authentic racemic sample prepared on reaction of acetonide of *rac*-glyceraldehyde, obtained from glycerol on acetalization (acetone, APTS, pentane, 60 °C, 41 h, 98%)[17] and Swern oxidation (1.2 equiv. $(COCl)_2$, 2.5 equiv. DMSO, 5 equiv. NEt_3, −60 °C, 37%),[18a] using the procedure we already disclosed ($TiCl_4$, pyridine, THF, −78 to 20 °C, 72 h, 45% yield, Scheme 9).[6a] The latter reaction does not work if PCC is used instead of Swern oxidation.[18b,c]



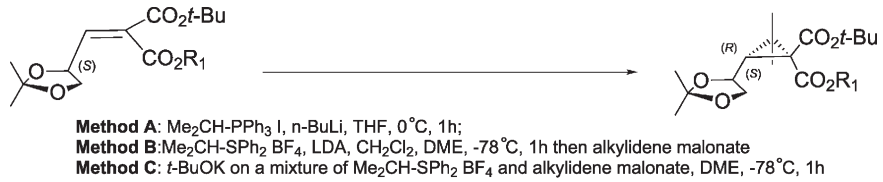
Scheme 9. Synthesis of *rac*-2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester.

3. Synthesis of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dialkyl esters, related ester, nitriles and dinitriles

Isopropylidenetriphenylphosphorane generated from the corresponding isopropyltriphenylphosphonium iodide and *n*-butyllithium (THF, 0 °C, 0.2 h)[19] and isopropylidene-diphenylsulfurane synthesized from isopropyldiphenyl-sulfonium tetrafluoroborate, LDA and dichloromethane (DME, −78 °C, 0.5 h)[20] have been successfully reacted with 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl-ene)-malonic acid dimethyl ester and provide both 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester in extremely good yield and enantioselectivity (Scheme 10).[6a] The two ylides react by the same *Re*-face of the alkylidene malonate as it has been described from the reaction of these two ylides with 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylic acid methyl ester.



Scheme 10. Cyclopropanation of-2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester.

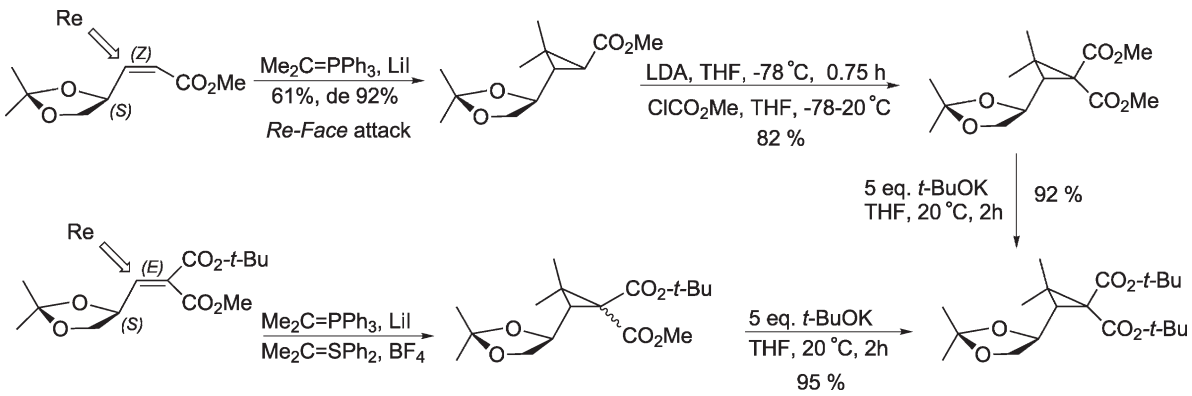


Entry	R_1	X	Method	Yield %	*Re/Si*
a	*t*-Bu	PPh_3	A	90	> 99/1
b	*t*-Bu	SPh_2	B	78	> 99/1
c	*t*-Bu	SPh_2	C	58	> 99/1
d	Me	PPh_3	A	69	> 99/1
e	Me	PPh_3	A	75	> 99/1
f	Me	PPh_3	A	84	> 99/1
g	Me	SPh_2	B	77	> 99/1

Scheme 11. Cyclopropanation of alkylidenemalonates.

Entry	X	EWG	Method	Yield %	*Re/Si*
a	PPh_3	CO_2Me	A	75	80/20
b	SPh_2	CO_2Me	B	75	80/20
c	PPh_3	CN	A	29	52/48
d	SPh_2	CN	B	33	59/41

Scheme 12. Cyclopropanation of alkylidene malononitriles.



Scheme 13. Structure determination of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester.

Isopropylidenediphenylsulfurane (DME, −78 °C, 2 h, 20 °C, 1 h, 76% yield, de 98%, Scheme 10, entry a) proved be more reactive than its phosphorus analogue (THF, 0 °C, 24 h, 80%, de 98%, Scheme 10, entry d, compare to entries b and c).[6a]

Similar results were obtained when instead the reactions are carried out on the related di-tertiobutyl malonate (Scheme 11, entries a–c) or on a 45/55 *Z*/*E* diastereomerize mixture of tertiobutyl methyl malonates (Scheme 11, entry a) in this case the reaction proceeds with complete facial control but leads to about a 45/55 mixture of *cis*/*trans* cyclopropane derivatives (Scheme 11, entries d–g).

The reaction still proceeds with complete control of the relative stereochemistry on the cyclopropane ring when instead performed on the related alkylidene malononitrile possessing the *E*-stereochemistry since the cyclopropane derivatives belong both to the *trans*-series. Reaction by the Re face is now predominant but no longer exclusive (de 60; Scheme 12, entries a and b) whatever the nature of the ylide is. And interestingly, almost no stereocontrol is found with alkylidene malonodinitrile (de 4–18%; (Scheme 12, entries c and d). In such case the reaction has been carried out on the crude mixture of the electrophilic derivative whose enantiomeric integrity has not been ascertained, just after its synthesis due to its instability.

The structure of all the cyclopropane derivatives has been ascertained by physical methods and in the case of cyclopropane dicarboxylates has been in complement achieved by comparison with authentic samples (Scheme 13). Thus 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester resulting from the reaction of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester with isopropylidenediphenylsulfurane (Scheme 13) has been compared to an authentic sample prepared in a multistep sequence from methyl 3-(2,2-dimethyl-[1,3]-dioxolan-4-yl)-acrylate and isopropylidenetriphenylphosphorane followed by a tandem metalation–carboxylation

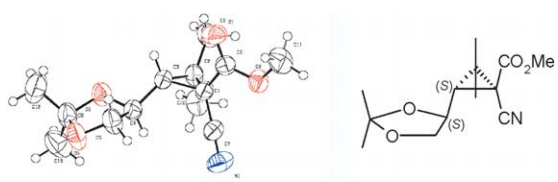
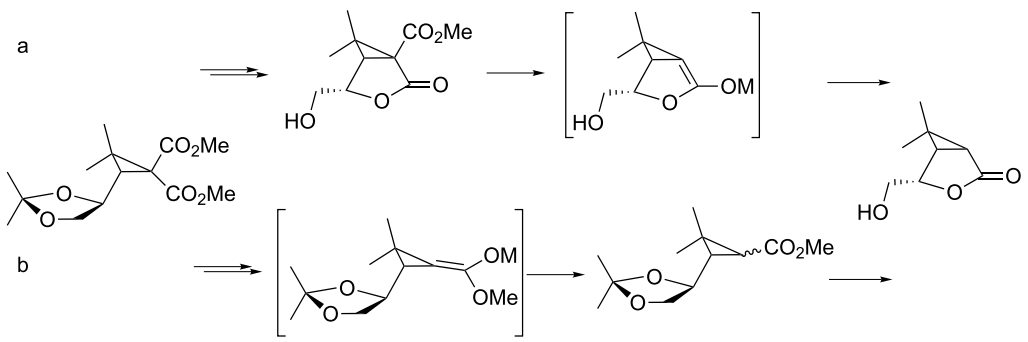


Figure 1. Structure of methyl 1-cyano-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropanecarboxylate.



Scheme 14. Strategies for deltamethrinic acid synthesis.

reaction of the resulting methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropanecarboxate ((i) LDA, THF, −78 °C, 0.75 h, (ii) $ClCO_2Me$, THF, −78 to 20 °C, Scheme 13).

Furthermore, 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester as well as the stereoisomeric mixture of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,carboxylic acid methyl ester-1-carboxylic acid tertiobutyl ester have been both transformed to the 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid ditertiobutyl ester (Scheme 13) on reaction with potassium *t*-butoxide in THF, −78 to 20 °C, 2 h, 92 and 95% yield, respectively).

Finally, the structure of the major stereoisomer of methyl 1-cyano-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropanecarboxylate has been unambiguously accessed by X-ray crystallography (Fig. 1).[6c]

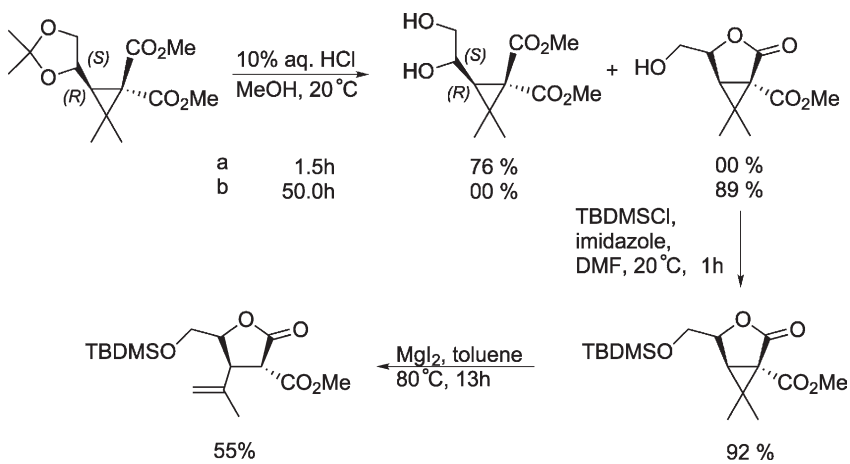
4. Synthesis of deltamethrinic acid from 3(*S*)-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester

The (3*R*) stereochemistry at [C-3] of 3(*R*)-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester suggests that it could be a valuable precursor of deltamethrinic acid. The strategy used for that purpose requires the lactone ring formation. The most suitable approach would have been ideally to generate at first the lactone ring then to perform the demethylation–decarboxylation reaction (Scheme 14, entry a). This should avoid the extra *trans*/*cis*-epimerisation which should be otherwise required (Scheme 14, entry b).

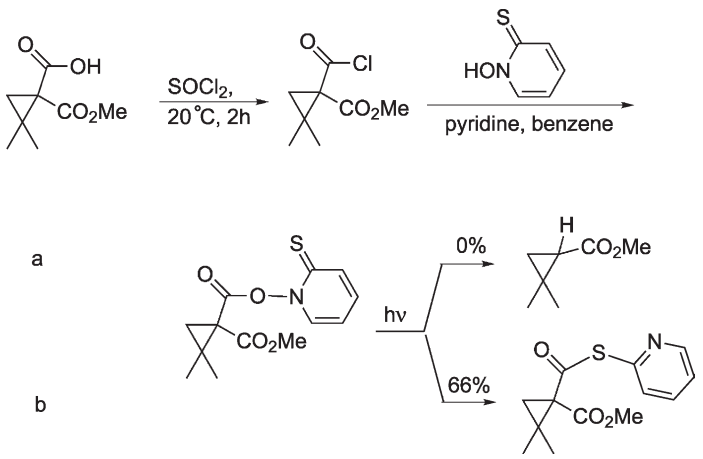
In fact the decarboxylation reaction of dimethyl cyclopropane dicarboxylates is not as easy as that of dimethyl malonates missing the cyclopropane ring probably because the enol or enolate intermediate has a lower propensity to be formed due to the extra strain induced by the three-membered ring (Scheme 14, entry b). This effect is at its paroxysm when decarboxylation is carried out on 4-hydroxymethyl-6,6-dimethyl-3-oxa-bicyclo[3.1.0]hexan-2-one because the enol or enolate intermediate is at a bridgehead position (Scheme 14, entry a).

We tried the first route because it was the most challenging one. We planned to perform the decarboxylation reaction through a Barton reaction[21] involving a radical process as it was described in a related series.[22a]

Acid catalyzed dioxolane ring opening was successfully achieved using aqueous hydrochloric acid (Scheme 16). Careful monitoring of this reaction shows however that methyl 3-(1,2-dihydroxy-ethyl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylate is efficiently obtained if the reaction is performed within a few hours (10% aq. HCl, 20 °C, 1.5 h, 76% yield, Scheme 15, entry a). Otherwise,



Scheme 15. Unsuccessful decarboxylation reaction.



Scheme 16. Radical promoted decarboxylation reaction.

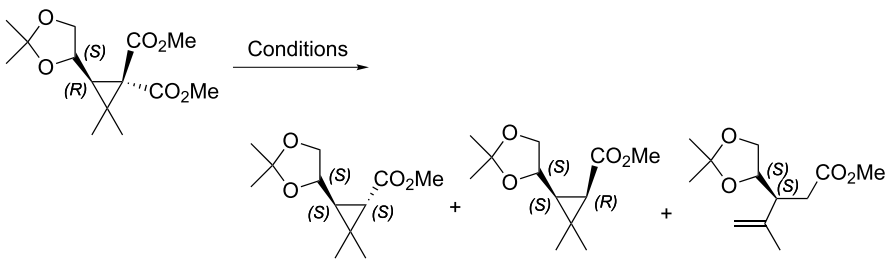
cyclization of the diol on the *cis*-carbomethoxy group takes place and leads to methyl 4-hydroxymethyl-6,6-dimethyl-2-oxo-3-oxa-bicyclo[3.1.0]hexane-1-carboxylate in very good yield (10% aq. HCl, 20 °C, 50 h, 89% yield, Scheme 16, entry b). Protection as *tert*-butyl dimethylsilylether of the hydroxyl group of the resulting lactone has been achieved on reaction with *tert*-butyl dimethylsilylchloride (TBSCl, imidazole, DMF, 20 °C, 1 h, 92%, Scheme 15, entry b). We however gave up this approach because the milder conditions used which involves magnesium diiodide,[22] as reported above, induces the cyclopropane ring opening rather than the desired dimethylation–carboxylation reaction (MgI_2, 110 °C, 10 h, 54% or 80 °C, 13 h, 55%, Scheme 15).

We have also unsuccessfully tried to perform the decarboxylation of 2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid methyl ester as model using the Barton[21] procedure since the end-product proved to be mainly 2,2-dimethyl-1-(pyridin-2-ylsulfanylcarbonyl)-cyclopropane-carboxylic acid methyl ester (Scheme 16, entry b) instead of the expected methyl cyclopropanecarboxylate (Scheme 16, entry a).[22]

We therefore turned our attention to the second approach in which the decarboxylation of 3-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester has to be achieved first but this was not a simple task.

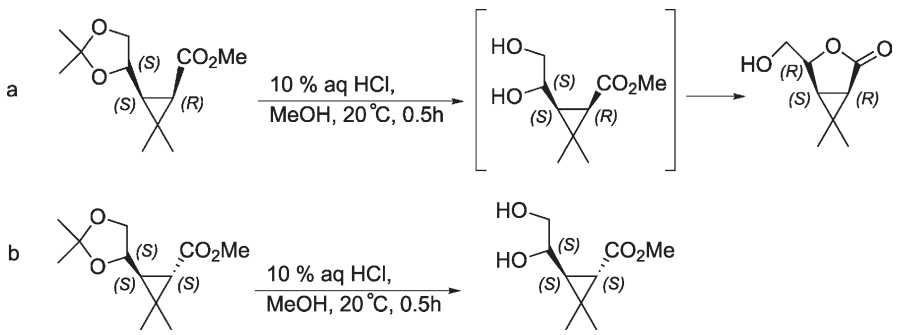
We decided not to use acidic conditions to avoid competing deacetalisation which would favor lactone ring formation and tried to use almost neutral conditions which are known for allowing a tandem dealkylation–decarboxylation by substitution at the methyl of the methoxy group of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester.

The most usual conditions which use metal halides or



Entry	Reagents	Temp (° C)	Time (h)	Yield (%)	*trans*/*cis* ring fission ratio
a	NaCl-aq. DMSO	160	6	73	27/21/52
b	1 NaCN, aq. DMF	120	48	88	50/34/16
c	*p*(H_2N)PhS Cs, DMF	90	26	68	61-39/0
d	Me_4NOAc, HMPA	95	4	90	70/30/0

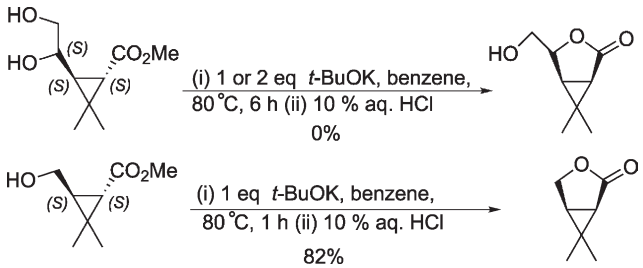
Scheme 17. Decarboxylation of alkylidene malonates.



Scheme 18. Acid catalyzed ring opening of dioxolane moiety. Potential lactone ring formation.

sodium cyanide in DMF or DMSO required too drastic conditions (160–140 °C, 6–60 h, Scheme 17, entries a and b).[4a,23] They in fact leads to the formation of substantial amount of methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)-4-methyl-pent-4-enoate resulting from cyclopropane ring opening. Other conditions which used instead metal chalcogenides in DMF[24] proceed at lower temperature but require too longer time to go to completion and methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)-2,2-dimethyl-cyclopropanecarboxylate is obtained in quite modest yields (90 °C, 26–30 h, 54–68%, Scheme 17, entry c). Tetramethyl ammonium acetate in anhydrous polar solvents, which was used by Trost,[25] proved to be the best compromise since the desired compound, methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropanecarboxylate is obtained, in extremely high yield, as a mixture of diastereoisomers, under relatively mild conditions and without competing cyclopropane ring opening (Scheme 17, entry d).

Acid hydrolysis of the 70/30 *trans*/*cis*-mixture of diastereoisomeric methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-ylmethyl)-2,2-dimethyl-cyclopropanecarboxylate (Scheme 17, entry d) leads to a 70/30 mixture of methyl *trans*-3-(2,3-dihydroxy-propyl)-2,2-dimethyl-cyclopropanecarboxylate and 4-hydroxymethyl-6,6-dimethyl-3-oxa-bicyclo[3.1.0]hexan-2-one resulting from lactonization of the *cis*-diastereoisomer (10% aq. HCl, MeOH, 20 °C, 0.5 h, $[\alpha]_D^{20}=-68.7$ ($CHCl_3$, $c=1.27$), Scheme 18).



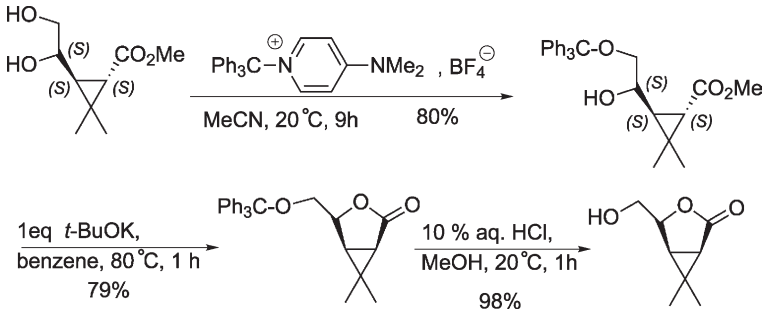
Scheme 19. Lactones synthesis by cyclization of γ-hydroxy esters.

It was also found that lactonization of methyl *cis*-3-(2,3-dihydroxy-propyl)-2,2-dimethyl-cyclopropanecarboxylate, occurs even faster than that of 3-(2,3-dihydroxy-propyl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester (compare Scheme 15 to Scheme 18, entry a).

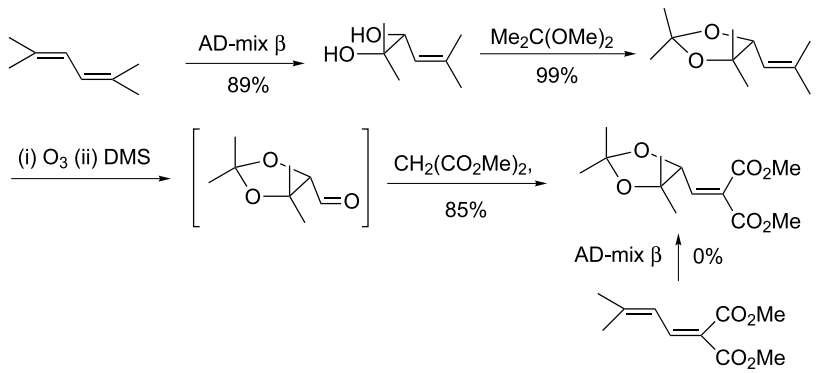
Lactonization of the remaining methyl *trans*-3-(1,2-dihydroxy-ethyl)-2,2-dimethyl-cyclopropanecarboxylate to 4-hydroxymethyl-6,6-dimethyl-3-oxa-bicyclo[3.1.0]hexan-2-one, which is required to reach the *cis*-cyclopropane derivative, was problematic. No reaction takes place under conditions which successfully allow lactonization of methyl 3-hydroxymethyl-2,2-dimethyl-cyclopropanecarboxylate[2f] (i) 1 or 2 equiv. *t*-BuOK, benzene, 80 °C, 6 h; (ii) 10% aq. HCl, Scheme 19) and other conditions which use lithium hydride to protect each of the two hydroxyl groups as their lithium alcoholates and potassium *t*-butoxide to perform the epimerization reaction fail too.

Successful contrathermodynamic *trans*/*cis*-isomerisation has been finally achieved on reaction of methyl 3-(1-hydroxy-2-trityloxy-ethyl)-2,2-dimethyl-cyclopropanecarboxylate, which possesses a trityloxy group at its terminus, with potassium *t*-butoxide in benzene (Scheme 20).

The trityl protecting group which was selectively introduced on reaction of methyl *trans*-3-(1,2-dihydroxy-ethyl)-2,2-dimethyl-cyclopropanecarboxylate with *N*,*N*-4-dimethyl-amino-*N*-triphenylmethylpyridinium chloride (prepared



Scheme 20. The lactone ring formation requires the protection of the primary hydroxyl group present on the diol, as a trityl ether.



Scheme 21. AD-mix is able to oxidize 2,5-dimethyl-hexadiene but not 2-(3-methyl-but-2-enylidene)-malonic acid dimethyl ester.

from dimethylaminopyridine and triphenylmethyl-chloride)[26] was then easily removed from 6,6-dimethyl-4-trityloxymethyl-3-oxa-bicyclo[3.1.0]hexan-2-one on acid hydrolysis (10% aq. HCl, MeOH, 20 °C, 1 h, Scheme 20).[27] The synthesis of deltamethrinic acid from this compound has been already disclosed.[28]

5. Synthesis of methyl *trans*-chrysanthemate from 3(*R*)-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester

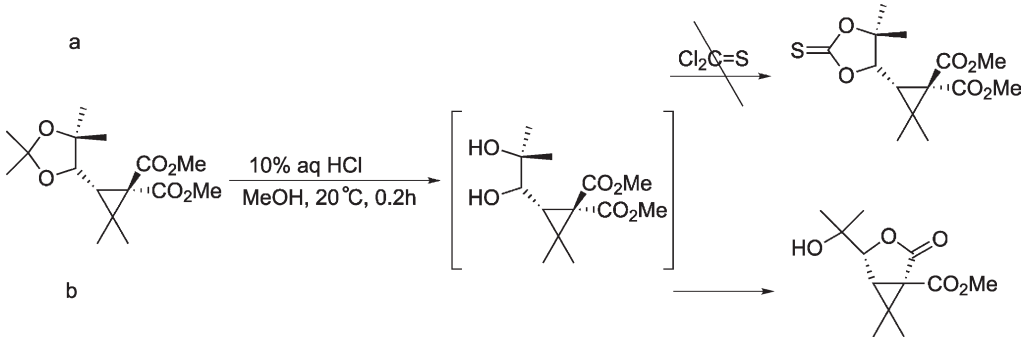
The synthesis of methyl *trans*-chrysanthemate has been performed, as outlined in Schemes 23 and 24 from 2,5-dimethyl-hexadiene using Sharpless AD reaction[8a] (AD-mix β, $K_2OsO_2(OH)_4$, DHQD, $K_3Fe(CN)_6$, K_2CO_3, *t*-BuOH–H_2O (1:1), $MeSO_2NH_2$, 20 °C, 2 h, 89% yield). Protection of the resulting diol ($Me_2C(OMe)_2$, acetone, *p*TSA, 99% yield) leads to 2,2,4,4-tetramethyl-5-(2-methyl-propenyl)-[1,3]dioxolane. Its ozonolysis followed by reduction of the resulting ozonide ((i) O_3, CH_2Cl_2, −78 °C, 2 h (ii) DMS, 20 °C, 12 h) leads to 2,2,5,5-tetramethyl-[1,3]dioxolane-4-carbaldehyde which has been subjected without purification to the Knoevenagel reaction ($CH_2(CO_2Me)_2$, $TiCl_4$, pyridine, THF, −78 to 20 °C, 72 h, 85%, Scheme 23).

A much straightforward approach to 2-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester which instead would have implied 2-(3-methyl-but-2-enylidene)-malonic acid dimethyl ester and AD-mix β proved to be unsuccessful (20 °C, 140 h, 0% yield, Scheme 21).

Cyclopropanation of 2-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester using isopropylidenetriphenylphosphorane or isopropylidene-diphenylsulfurane proved to be excellent ($Me_2C{=}PPh_3$, LiI, 0 °C, 1 h then 20 °C, 24 h; 82% yield, de 90%, Scheme 22, entry a; $Me_2C{=}SPh_2$, BF_4, −78 °C, 2 h, 20 °C, 1 h, 76%, de 98%, Scheme 22, entry b).

We have been unable to produce alkyl *trans*-chrysanthemates from 2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropane-1,1-dicarboxylic acid dimethyl ester by the route disclosed in Scheme 23, entry a which involves acetonide deprotection and thionocarbonate reduction. We have been unable to isolate the expected

Scheme 22. Cyclopropanation of 2-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester.



Scheme 23. Unsuccessful deoxygenation of a diol moiety.

3-(1,2-dihydroxy-2-methyl-propyl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester due to the extreme ease with which it cyclizes to 4-(1-hydroxy-1-methyl-ethyl)-6,6-dimethyl-2-oxo-3-oxa-bicyclo[3.1.0]-hexane-1-carboxylic acid methyl ester (Scheme 23, entry b).

It is interesting to compare the ease of that lactone ring formation (Scheme 25, entry b) to that of the related desdimethylated analogue disclosed in Scheme 15 or the *cis*-cyclopropanecarboxylate disclosed in Scheme 19, entry a) which all possess the same relative diastereoisomeric relationship around the stereogenic centers.

In order to achieve the desired transformation leading to (1*R*)-*trans*-chrysanthemic we used a more lengthy route which requires to perform at first the decarboxylation of 2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropane-1,1-dicarboxylic acid dimethyl ester and to effect the deoxygenation of the side chain at the end of the sequence (Scheme 24). Almost all the reactions which have been used for such purpose have already used but in another order for the synthesis of deltamethrin acid disclosed above.

6. Conclusion

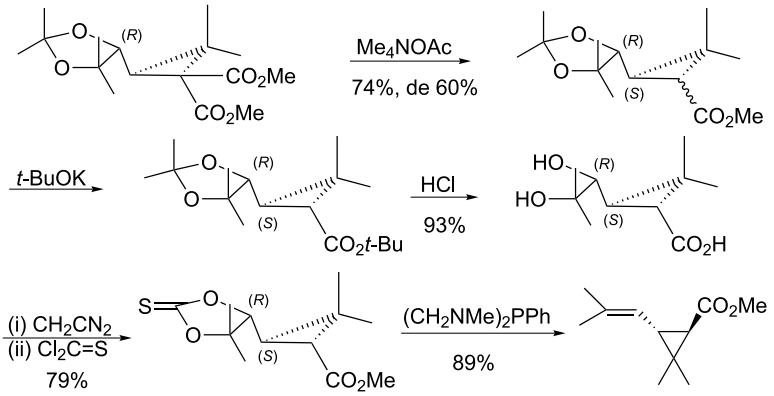
Addition of various reagents to alicyclic electrophilic olefins bearing an alkoxy group in γ-position has been the subject of intensive work over the last twenty years.[29] Most of these reactions involve γ-alkoxy-α,β-unsaturated esters whose C,C double bond is either *E* or *Z* and γ-alkoxy-malonates possessing a stereogenic centre at C-γ. Those can be attacked either by one or the other face producing compounds possessing the *syn*- or *anti*-stereochemistry between Cβ and C-γ (Scheme 25).

These belong to different class of 'reagents' and are involved in a large variety of organic reaction implying polar or radical type of additions, concerted and non concerted cycloadditions and performed under different conditions, for example, in different solvents.[5c,7,29–48] Although several explanations and calculations,[36,46b,c,49] often based on the Felkin–Anh model[50–55] have been disclosed, till now there is no model which explain all these results and it is therefore impossible to predict, unless very closely related examples are available, the stereochemical course of addition reaction to *E*-γ-alkoxy-α,β-unsaturated esters, their *Z*-stereoisomers and related γ-alkoxy-alkylidene malonates. We are working towards this end.

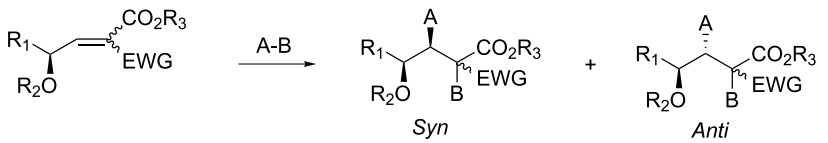
7. Experimental

7.1. General

NMR spectra were recorded on a JEOL JNM EX-400 (400 and 100.6 MHz, for ^{1}H and ^{13}C, respectively) or JEOL JNM EX-90 (90 and 22.5 MHz, for ^{1}H and ^{13}C, respectively). All spectra were carried out in $CDCl_3$ unless otherwise stated using TMS as internal standard. IR spectra reported in cm^{-1} were recorded on a BIO-RAD FTS-165 spectrometer. Melting points were recorded on a Tottoli–Büchi apparatus and are uncorrected. Optical rotations were measured on a Helwett–Packard digital polarimeter, the concentration being expressed as *c*: g/100 ml. Mass spectra were recorded on a HP 5989B spectrometer. Elemental analyses were performed by the Service d'Analyse de l'Université Pierre et Marie Curie, 75252 Paris Cedex 05, France. X-ray diffraction measurements were carried out at the 'Laboratoire de Chimie Moléculaire Structurale des FUNDP-Namur-Belgium'. |GC^2| were recorded on a HP 5890A chromatograph using a capillary SE30 column (25 m×0.25 mm×0.2 μm) in the following standard conditions: T detector: 250 °C, T injector: 250 °C, He pressure (1 ml/min). The oven temperatures were, respectively: program A (heating from 100 to 220 °C with a temperature increase of 10 °C/min), program B (heating from 60 to 220 °C with a temperature increase of 10 °C/min). Enantio-



Scheme 24. Synthesis of 2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropane-1,1-dicarboxylic acid dimethyl ester.



Scheme 25. *syn*- or *anti*-adducts produced on addition of various reagents to γ-alkoxy-α,β-unsaturated esters.

meric excess (e.e.) were determined by |GC²| using a chiral capillary β-cyclodextrine column (Diacel, Chiracel, ODH, 25 m×0.25 mm×0.2 μm) in the following standard conditions: T detector: 250 °C, T injector: 250 °C, He pressure (1 ml/min).TLC was performed on pre-made commercial glass-backed plate SiO_2 (Merck 5719, 250 mesh) $60PF_{254}$ as fluorescent indicator. Compounds were visualized by UV illumination (254 nm) and by heating to 150 °C after spraying 20% phosphomolybdic acid in ethanol. Preparative layer chromatography (PLC) was performed on SiO_2 plates from silica gel $60PF_{254}$ (Merck 5719) All reactions were carried under Ar, unless stated otherwise. Solvents were freshly distilled from Na/benzophenone (THF, Et_2O), Na (toluene), $LiAlH_4$ (DME), Calcium hydride (DMSO, HMPA) or P_2O_5 (CH_2Cl_2). Column chromatography was performed using silica gel 60 under usual techniques. 1,2-5,6-Diisopropylidene-D-mannitol,[55] 2,3-*O*-isopropylidene-D-glyceraldehyde,[55] and 3,4-isopropylidene-D-mannitol[12c] were prepared following the procedures described in the literature.

7.1.1. Synthesis of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester. *Procedure A*. Titanium (IV) chloride (140 mmol, 26.6 g) was added dropwise under an atmosphere of argon, to 420 ml of anhydrous THF maintained at −78 °C. The resulting yellow suspension was kept at this temperature for 0.25 h. A mixture of dimethyl malonate (200 mmol, 26.1 g), 2,3-*O*-isopropylidene-D-glyceraldehyde (70 mmol, 9.1 g) and pyridine (280 mmol, 22.1 g) was then added dropwise to the yellow suspension. The resulting mixture was stirred at 20 °C for 120 h before the reaction was quenched with a saturated ammonium chloride solution (200 ml). The aqueous phase was extracted with ether (7×100 ml). The combined organic layers were washed with brine (100 ml), dried ($MgSO_4$) and the solvents were removed under reduced pressure to give 33.5 g of brown oil. The crude product (33.3 g) was purified by distillation (bp 95 °C, 0.2 mm Hg) to yield the pure alkylidene malonate (12.0 g, 70%) as a yellow oil.

Procedure B. Lead tetracetate (12.4 mmol, 5.5 g) was added under an atmosphere of argon, in small portions to a solution of 1,2-5,6-diisopropylidene-D-mannitol (11.4 mmol, 3.0 g) in anhydrous THF (200 ml) maintained at 0 °C. The mixture was stirred at 0 °C for 10 min and dimethyl malonate (30 mmol, 3.96 g) and freshly distilled acetic anhydride (4.65 ml) were added. The resulting mixture was then heated under reflux for 24 h. After cooling, the solution was filtered and the solvents eliminated under reduced pressure. The residue was dissolved in dichloromethane (100 ml), washed with a saturated aqueous sodium bicarbonate solution (1×20 ml) and brine (1×20 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give an orange oil which was purified by distillation (bp 95 °C, 0.2 mm Hg) to yield the pure alkylidene malonate (4.73 g, 85%) as a yellow oil. $[\alpha]_D^{20}$=+20.4 (*c* 1.0, $CHCl_3$); TLC, SiO_2: R_f 0.5 (pentane/ether: 70/30). |GC²|, program A, 5.3 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 7.02 (d, 1H, *J*=6.9 Hz, C*H*=C(CO_2-Me)$_2$), 4.90 (m, 1H, C*H*−O), 4.27 (m, 1H, C*H*−O), 3.83 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.72 (m, 3H, C*H*−O), 1.44 (s, 3H, CH_3), 1.38 (s, 3H, CH_3). ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 164.6, 163.6, 148.4, 128.1, 110.3, 73.1, 68.8, 52.4, 52.3, 26.1, 25.3; IR (film, KBr) 2989, 2956, 2883, 1733, 1655, 1438, 1373, 1258, 1224, 1155, 1060, 1033, 986, 942, 840, 794, 765, 647 cm^{-1}; GC/MS *m/z* 244 (M^+), 229, 214, 182, 169, 156, 138, 123, 85, 59. Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found C, 53.96; H, 6.62.

7.1.2. Synthesis of (2,2-dimethyl-[1,3]dioxolan-4-yl)-methanol. Glycerol (109 mmol, 10.0 g), acetone (ACS reagent, 30 ml), pentane (30 ml) and *p*-toluenesulfonic acid (1.57 mmol, 300 mg) were successively introduced into a vessel fitted with a Dean−Stark. The mixture was then stirred at reflux for 41 h. After cooling, sodium acetate (1.83 mmol, 150 mg) was added. The mixture was filtered and the solvents were evaporated under reduced pressure to give the pure alcohol (14.1 g, 98%) as alight yellow oil. |GC²|, program B, 2.5 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.28−3.57 (br, 3H, C*H*−OH+C*H*−O), 2.6 (br, 3H, CH_2−OH+O*H*), 1.45 (s, 3H, CH_3), 1.39 (s, 3H, CH_3); IR (film, KBr) 3435, 2988, 2937, 1458, 1381, 1372, 1257, 1214, 1157, 1118, 1074, 1053, 971, 845, 793 cm^{-1}. Spectral and analytical data are in agreement with the reported data.[17a]

7.1.3. Synthesis of 2,3-*O*-isopropylidene-(*d,l*)-glyceraldehyde. Freshly distilled DMSO (48 mmol, 3.75 g), diluted in 5 ml of anhydrous dichloromethane, was added dropwise to a well stirred solution of oxalyl chloride (22 mmol, 2.79 g) in anhydrous dichloromethane (50 ml) maintained at −60 °C. The mixture became yellow and (2,2-dimethyl-[1,3]dioxolan-4-yl)-methanol (20 mmol, 2.64 g), diluted with 10 ml of anhydrous dichloromethane, was introduced dropwise to the solution which was then stirred for 15 min. Triethylamine (100 mmol, 10.1 g) was added dropwise and the mixture was then heated to room temperature. Water (50 ml) and dichloromethane (50 ml) were added. Organic layer was washed with water (25 ml) and the combined aqueous layers were extracted with dichloromethane (3×50 ml). Organic layers were dried ($MgSO_4$) and the solvents were evaporated under reduced pressure to give 1.60 g of crude material which was rapidly purified by distillation (40 °C, 20 mm Hg) to yield the aldehyde (893 mg, 37%) as colorless oil. |GC²|, program A, 1.6 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 9.71 (d, 1H, *J*=2.2 Hz, C*H*=O), 4.61−3.91 (br, 3H, 3C*H*−OH), 1.49 (s, 3H, CH_3), 1.44 (s, 3H, CH_3); IR (film, KBr) 3423, 2989, 2938, 2893, 1737, 1457, 1375, 1256, 1217, 1154, 1154, 1074, 848 cm^{-1}. Spectral data are in agreement with those from the enantiopure 2,3-*O*-isopropylidene-(*d*)-glyceraldehyde.[55]

7.1.4. Synthesis of (*d,l*) 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester. Has been achieved on 2,3-*O*-isopropylidene-(*d,l*)-glyceraldehyde (10 mmol, 1.30 g) according to the procedure described for 2,3-*O*-isopropylidene-D-glyceraldehyde (see above).

7.1.5. Synthesis of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene) malonic di-*tert*-butyl ester. It has been performed according to the Procedure B described above for the related dimethyl ester using lead tetracetate (18.6 mmol, 8.4 g) and di-*tert*-butyl malonate (45 mmol, 9.6 g) to yield pure alkylidene malonate (10.7 g, 96%) as a colorless oil.

$[\alpha]_D^{20}$=+15.8 (*c* 2.37, $CHCl_3$); TLC, SiO_2: R_f 0.7 (pentane/ether: 90/10). |GC²|, program A, 10.9 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 6.76 (d, 1H, *J*=7.5 Hz, C*H*=C(CO_2-*t*Bu)$_2$), 4.88 (m, 1H, C*H*–O–), 4.26 (m, 1H, C*H*–O–), 3.72 (m, 1H, C*H*–O–), 1.53 (s, 9H, C(CH_3)$_3$), 1.51 (s, 9H, C(CH_3)$_3$), 1.46 (s, 3H, CH_3), 1.40 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 164.0, 162.8, 144.3, 139.0, 132.3, 110.2, 82.3, 82.0, 73.1, 72.3, 68.9, 27.7, 26.3, 25.5; IR (film, KBr) 2982, 2937, 2877, 1725, 1654, 1479, 1457, 1393, 1371, 1273, 1251, 1162, 1063, 1024, 904, 851, 787 cm^{-1}; GC/MS *m/z* 328 (M^+), 273, 217, 199, 187, 159, 138, 123, 85, 59. Anal. Calcd for $C_{17}H_{28}O_6$: C, 62.18; H, 8.59. Found C, 62.15; H, 8.67.

7.1.6. Synthesis of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid *tert*-butyl ester methyl ester. It has been performed according to the Procedure B described above for the related dimethyl ester using lead tetracetate (18.6 mmol, 8.4 g) and *tert*-butyl-methyl malonate (45 mmol, 7.8 g) to give an orange oil (16.3 g) which was purified by column chromatography (pentane/ether: 70/30 (v/v)) to yield pure alkylidene malonate (8.5 g, 87%) as a colorless oil (45/55 mixture of two isomers); TLC, SiO_2: R_f 0.63 (pentane/ether: 70/30). |GC²|, program A, 9.2 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 6.90 (d, *J*=7.1 Hz, C*H*=C(CO_2R)$_2$ *E*), 6.88 (d, *J*=7.0 Hz, C*H*=C(CO_2R)$_2$ *Z*), 4.91 (m, C*H*–O *E*), 4.87 (m, C*H*–O *Z*), 4.26 (br, C*H*–O *Z*+*E*), 3.82 (s, OCH_3 *Z*), 3.80 (s, OCH_3 *E*), 3.75–3.70 (br, C*H*–O *Z*+*E*), 1.53 (s, C(CH_3)$_3$ *E*), 1.50 (s, C(CH_3)$_3$ *Z*), 1.45 (s, CH_3 *Z*+*E*), 1.40 (s, CH_3 *E*), 1.39 (s, CH_3 *Z*); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 165.4, 164.7, 163.6, 162.5, 146.3, 140.4, 139.8, 130.5, 130.3, 110.5, 82.9, 82.5, 79.4, 76.4, 73.3, 73.2, 72.4, 69.0, 66.3, 52.4, 52.3, 27.9, 27.4, 26.7, 26.4, 25.8, 25.5; IR (film, KBr) 2986, 2955, 2939, 2881, 1731, 1656, 1478, 1457, 1438, 1372, 1329, 1256, 1225, 1160, 1062, 1032, 967, 905, 847, 754, 645 cm^{-1}; GC/MS *m/z* 287 (M^++1), 244, 229, 215, 201, 177, 169, 143, 115, 101, 85, 72, 59. Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.72; 7.74. Found C, 58.65; H, 7.79.

7.1.7. Synthesis of 2-cyano-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)acrylic acid methyl ester. It has been performed according to the Procedure B described above for the related dimethyl ester using lead tetracetate (12.4 mmol, 5.5 g) and methyl cyanoacetate (30 mmol, 2.97 g). It give an orange oil (6.9 g) which was rapidly purified by column chromatography (pentane/ethyl acetate: 85/15 (v/v)) to yield the pure alkylidene malonate (3.49 g, 74%) as a light yellow oil. $[\alpha]_D^{20}$=+17.0 (*c* 1.88, $CHCl_3$); TLC, SiO_2: R_f 0.51 (pentane/ether: 70/30). |GC²|, program A, 6.8 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 7.58 (d, 1H, *J*=7.6 Hz, C*H*=C(CO_2Me)(CN)), 5.07 (m, C*H*–O), 4.34 (m, 1H, C*H*–O), 3.90 (s, 3H, OCH_3), 3.80 (m, 1H, C*H*–O), 1.50 (s, 3H, CH_3), 1.43 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 161.0, 159.7, 112.7, 111.5, 109.9, 73.6, 68.2, 53.5, 26.3, 25.3 IR (film, KBr) 2992, 2959, 2889, 2235, 1740, 1637, 1439, 1376, 1329, 1309, 1261, 1225, 1151, 1060, 1034, 963, 921, 843, 762, 513 cm^{-1}; GC/MS *m/z* 212 (M^++1), 196, 181, 154, 136, 123, 108, 94, 72, 59, 52. The analytical data are in agreement with that reported in the literature.[16]

7.1.8. Synthesis of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malononitrile. Malononitrile (5.5 mmol, 360 mg) was added under an atmosphere of argon, to a solution of 4-*N*,*N*-dimethylaminopyridine (0.5 mmol, 60 mg) and 2,3-*O*-isopropylidene-D-glyceraldehyde (5 mmol, 655 mg) in anhydrous dichloromethane (10 ml) maintained at 0 °C. The orange mixture was then stirred at 0 °C for 1 h and at 20 °C for 2 h. The solvents were then evaporated under reduced pressure to give the crude compound (1.11 g), as an orange glue which could not be purified and was used directly in the next reactions. This compound decomposes rapidly on alumina, silica gel and by heating. ^{1}H NMR δ (400 MHz, $CDCl_3$) 7.26 (d, 1H, *J*=7.6 Hz, C*H*=C(CN)$_2$), 5.34 (m, 1H, C*H*–O), 4.35 (m, 1H, C*H*–O), 3.86 (m, 1H, C*H*–O), 1.51 (s, 3H, CH_3), 1.43 (s, 3H, CH_3); IR (film, KBr) 3348, 3332, 3055, 2992, 2941, 2899, 2241, 2202, 2169, 2112, 1757, 1720, 1650, 1617, 1570, 1481, 1457, 1379, 1345, 1264, 1217, 1153, 1122, 1064, 966, 919, 840, 738 cm^{-1}.

7.1.9. Synthesis of 2,4-dimethyl-hex-4-ene-2,3-(*R*)-diol. AD-mix β (15 g) was added in small portions to a well stirred mixture of water (50 ml) and *tert*-butanol (50 ml) at 20 °C. Methane sulfonamide (10 mmol, 950 mg) was added and the mixture was stirred at 20 °C for 10 min. 2,5-Dimethyl-2,4-hexadiene (10 mmol, 1.1 g) was added dropwise to the solution and the mixture was stirred vigorously at 20 °C for 2 h. Sodium bisulfite (15 g) was added in small portions and the resulting grey mixture was kept at room temperature for 1 h, extracted with ethyl acetate (3×70 ml). Organic layers were washed with brine (2×10 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 2.3 g of crude material which was purified by column chromatography (pentane/ether: 0/100 (v/v)) to yield the pure 2,4-dimethyl-hex-4-ene-2,3-(*R*)-diol (1.17 g, 89%) as a colorless oil. $[\alpha]_D^{20}$=+9.57 (*c* 0.94, $CHCl_3$); TLC, SiO_2: R_f 0.61 (pentane/ethyl acetate: 0/100). |GC²|, program A, 3.2 min; chiral |GC²| (β-Dextrine column, 110 °C isotherm) 13,2 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 5.22 (d, 1H, *J*=9.2 Hz, C*H*=CMe_2), 4.16 (d, 1H, *J*=9.3 Hz, C*H*–O), 2.19 (br, 2H, 2O*H*), 1.79 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.16 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 137.1, 123.6, 74.9, 73.4, 26.0, 25.9, 23.1, 18.4; IR (film, KBr) 3399, 2977, 2933, 2917, 1677, 1449, 1379, 1303, 1265, 1222, 1160, 1116, 1040, 1027, 989, 963, 898, 849, 775, 733 cm^{-1}; GC/MS *m/z* 144 (M^+), 127, 111, 97, 93, 86, 77, 71, 59, 55. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found C, 66.38; H, 11.39.

7.1.10. Synthesis of 2,2-dimethyl-4-(2-methyl-propenyl)-[1,3]dioxolane. *p*-Toluenesulfonic acid (50 mg) and 2,2-dimethoxypropane (50 ml) were added under an atmosphere of argon to a solution of 2,4-dimethyl-hex-4-ene-2,3-(*R*)-diol (12 mmol, 1.74 g) in acetone (A.C.S reagent, 50 ml) maintained at 20 °C. The mixture was stirred at 20 °C for 12 h. A saturated sodium bicarbonate solution (5 ml) was then added and the mixture was extracted with diethyl ether (3×70 ml). Organic layers were dried ($MgSO_4$) and the solvents were removed under reduced pressure to give the pure acetonide (2.2 g, 99%) as a colorless oil. $[\alpha]_D^{20}$=−3.14 (*c* 2.96, $CHCl_3$); TLC, SiO_2: R_f 0.33 (pentane/ether: 90/10). |GC²|, program A, 3.3 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 5.21 (d, 1H, *J*=8.8 Hz, C*H*=CMe_2), 4.50 (d, 1H, *J*=8.9 Hz, C*H*–O), 1.80 (s, 3H, CH_3), 1.76 (s, 3H, CH_3), 1.46 (s, 3H,

CH_3), 1.39 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.13 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 139.0, 119.4, 80.9, 80.0, 28.3, 26.8, 26.0, 25.5, 23.2, 18.3; IR (film, KBr) 2982, 2935, 2889, 1779, 1679, 1454, 1376, 1372, 1311, 1266, 1234, 1217, 1202, 1145, 1121, 1048, 1035, 995, 962, 933, 916, 866, 829, 806, 654 cm^{-1}; GC/MS *m/z* 169 (M^+-CH_3), 126, 111, 109, 97, 84, 67, 59, 51. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found C, 71.56; H, 11.14.

7.1.11. Synthesis of 2,2-5,5-tetramethyl-[1,3]dioxolane-4-carbaldehyde. 2,2-Dimethyl-4-(2-methyl-propenyl)-[1,3]-dioxolane (9.8 mmol, 1.8 g) was dissolved in anhydrous dichloromethane (40 ml) and the mixture was cooled to −78 °C. Ozone was then bubbled for 1 h in the solution. Methyl sulfide (4 ml) was then added, the mixture was stirred at room temperature overnight and the solvents were removed under reduced pressure to give aldehyde (2.34 g) as a light yellow oil. This product was used directly without purification in the Knoevenagel condensation with dimethyl malonate. ^1H NMR δ (400 MHz, $CDCl_3$) 9.70 (d, 1H, *J*=2.11 Hz, C*H*=O), 4.10 (d, 1H, *J*=2.03 Hz, C*H*–O), 1.57 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.21 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 200.3, 102.1, 86.6, 80.8, 40.4, 27.9, 27.0, 26.7, 23.6; IR (film, KBr) 3268, 2985, 2938, 2882, 2731, 2593, 1735, 1465, 1438, 1406, 1374, 1313, 1259, 1233, 1221, 1198, 1130, 1071, 1025, 1004, 953, 916, 893, 862, 828, 813, 735, 701, 666 cm^{-1}; GC/MS *m/z* 143 (M^+-CH_3), 129, 110, 95, 85, 59, 55.

7.1.12. Synthesis of 2-(2,2-5,5-tetramethyl-[1,3]dioxolane-4-ylmethylene)-malonic acid dimethyl ester. Titanium (IV) chloride (18 mmol, 2.03 g) was added dropwise under an atmosphere of argon, to anhydrous THF (57 ml) maintained at −78 °C. The resulting yellow suspension was kept at this temperature for 0.25 h. A mixture of dimethyl malonate (27 mmol, 3.6 g), 2,2-5,5-tetramethyl-[1,3]dioxolane-4-carbaldehyde (9 mmol, 2.3 g) and pyridine (36 mmol, 2.85 ml) was then added dropwise to the yellow suspension. The resulting orange mixture was stirred at 20 °C for 48 h before the reaction was quenched with a saturated ammonium chloride solution (50 ml). The aqueous phase was extracted with diethyl ether (3×80 ml). The combined organic layers were washed with brine (20 ml), dried ($MgSO_4$) and the solvents were removed under reduced pressure to give 5.11 g of brown oil. The crude product (4.98 g) was purified by distillation (bp 110 °C, 0.1 mm Hg) to yield the pure alkylidene malonate (2.11 g, 88%) as a yellow oil. $[\alpha]_D^{20}=-2.66$ (*c* 1.43, $CHCl_3$); TLC, SiO_2: R_f 0.43 (pentane/ether: 80/20). |GC^2|, program A, 8.3 min; ^1H NMR δ (400 MHz, $CDCl_3$) 6.89 (d, 1H, *J*=6.6 Hz, C*H*=C(CO_2Me)$_2$), 4.56 (d, 1H, *J*=6.7 Hz, C*H*–O), 3.84 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 1.47 (s, 3H, CH_3), 1.37 (m, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.17 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 165.4, 163.7, 142.0, 129.5, 109.0, 82.0, 80.7, 52.6, 52.3, 28.1, 27.0, 26.1, 23.9; IR (film, KBr) 2985, 2957, 2850, 1735, 1659, 1559, 1438, 1372, 1338, 1252, 1224, 1199, 1147, 1119, 1075, 1040, 1017, 1001, 944, 904, 862, 672 cm^{-1}; GC/MS *m/z* 257 (M^+-CH_3), 225, 214, 197, 183, 156, 139, 125, 110, 95, 73, 59, 53. Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found C, 56.55; H, 7.38.

7.1.13. Cyclopropanation of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester. *Typical procedure C, using isopropylidene triphenylphosphorane*. To a well stirred suspension of isopropyltriphenylphosphonium iodide (3.6 mmol, 1.55 g) in anhydrous THF (8 ml) was added under an atmosphere of argon, dropwise *n*-butyllithium (1.6 N in hexane, 3.0 mmol, 1.84 ml) maintained at 0 °C. The dark red mixture was then stirred at room temperature for 0.25 h before addition of the alkylidene malonate (2.0 mmol, 488 mg) to the solution at 0 °C. After stirring at this temperature for 1 h, the mixture was stirred at 20 °C for 24 h. Water was added and the mixture was extracted with diethyl ether (3×50 ml), washed with water (1×10 ml), with brine (1×10 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give orange oil (1.16 g). The crude material (1.09 g) was purified by column chromatography (pentane/ether: 70/30 (v/v)) to yield the pure cyclopropane-1,1-dicarboxylate (432 mg, 80%) as a colorless oil.

Typical procedure D, using isopropylidene diphenylsulfurane. A solution of LDA 0.55 N (2.10 ml) was added dropwise under an atmosphere of argon, to a well stirred mixture of isopropyldiphenylsulfonium tetrafluoroborate (1.2 mmol, 380 mg) and freshly distilled dichloromethane (1.2 mmol, 102 mg) in anhydrous DME (7 ml) maintained at −78 °C. The yellow solution was then stirred for 0.3 h at −78 °C. The alkylidene malonate (1.0 mmol, 244 mg), diluted in DME (1 ml), was added. After stirring for 2 h at −78 °C and 1 h at 20 °C, the mixture was hydrolyzed by the addition of a saturated aqueous ammonium chloride solution (5 ml), extracted with diethyl ether (3×50 ml), washed with brine (1×10 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give an orange oil (442 mg). The crude material (370 mg) was purified by column chromatography (pentane/ether: 70/30 (v/v)) to yield the pure cyclopropane-1,1-dicarboxylate (180 mg, 76%) as a colorless oil. $[\alpha]_D^{20}=+0.93$ (*c* 1.01, $CHCl_3$); TLC, SiO_2: R_f 0.6 (pentane/ether: 70/30). |GC^2|, program A, 6.3 min; ^1H NMR δ (400 MHz, $CDCl_3$) 4.16 (m, 1H, C*H*–O), 3.98 (m, 1H, C*H*–O), 3.79 (m, 1H, C*H*–O), 3.73 (s, 6H, 2OCH_3), 1.81 (d, 1H, *J*=9.8 Hz, *H* cyclopropane), 1.45 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 168.7, 167.6, 109.2, 73.3, 69.1, 52.6, 52.3, 38.8, 30.9, 26.9, 25.5, 22.0, 18.0; IR (film, KBr) 2998, 2956, 2878, 1733, 1437, 1380, 1291, 1250, 1159, 1123, 1112, 1067, 1032, 996, 947, 917, 852, 823, 791, 735, 649 cm^{-1}; GC/MS *m/z* 271 (M^+-CH_3), 211, 185, 153, 125, 101, 59. Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.74. Found C, 58.62; H, 7.97.

7.1.14. Cyclopropanation of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid di-*tert*-butyl ester. *According to procedure C*. Using isopropyltriphenylphosphonium iodide (3.6 mmol, 1.55 g) and the alkylidene malonate (2.0 mmol, 656 mg), gives an orange oil (1.56 g) purified by column chromatography (pentane/ether: 70/30 (v/v)) to yield the pure cyclopropane-1,1-dicarboxylate (638 mg, 90%).

According to procedure D. Using isopropyldiphenylsulfonium tetrafluoroborate (1.2 mmol, 380 mg). The alkylidene malonate (1.0 mmol, 328 mg) to give an orange oil

(629 mg) purified by column chromatography (pentane/ether: 90/10 (v/v)) to yield the pure cyclopropane-1,1-dicarboxylate (261 mg, 78%) as a colorless oil.

According to procedure E. A solution of potassium *tert*-butoxide (0.7 mmol, 79 mg) in anhydrous THF was added dropwise under an atmosphere of argon, to a well stirred mixture of isopropyldiphenylsulfonium tetrafluoroborate (0.75 mmol, 237 mg) and alkylidene malonate (0.5 mmol, 164 mg) in anhydrous THF maintained at −78 °C. After stirring the light yellow solution for 1 h at −78 °C and 1 h at 20 °C, the mixture was hydrolyzed by the addition of water (10 ml), extracted with diethyl ether (3×30 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give orange oil (308 mg). The crude material (272 mg) was purified by column chromatography (pentane/ether: 85/15 (v/v)) to yield the pure cyclopropane-1,1-dicarboxylate (96 mg, 58%) as a colorless oil. $[\alpha]_D^{20}=+3.00$ (*c* 1.40, $CHCl_3$); TLC, SiO_2: R_f 0.42 (pentane/ether: 80/20). |GC^2|, program A, 11.4 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.15 (m, 1H, C*H*–O), 3.95 (m, 1H, C*H*–O), 3.80 (m, 1H, C*H*–O), 1.68 (d, 1H, *J*=9.8 Hz, *H* cyclopropane), 1.46 (s, 18H, 2O(CH_3)$_3$), 1.45 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.24 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 167.7, 166.6, 109.1, 81.7, 81.4, 73.7, 69.3, 37.2, 29.6, 28.0, 27.0, 26.9, 25.6, 22.1, 17.8; IR (film, KBr) 2994, 2978, 2939, 2873, 2362, 1726, 1464, 1395, 1370, 1338, 1291, 1258, 1218, 1156, 1129, 1113, 1066, 1018, 978, 947, 921, 909, 859, 815, 790, 737, 667 cm^{-1}; GC/MS *m*/*z* 339, 315, 299, 287, 259, 229, 215, 201, 183, 165, 157. Anal. Calcd for $C_{20}H_{34}O_6$: C, 64.84; H, 9.25. Found C, 64.83; H, 9.19.

7.1.15. Cyclopropanation of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid *tert*-butyl ester dimethyl ester. *According to procedure C*. Using isopropyltriphenylphosphonium iodide (2.7 mmol, 1.17 g) and the alkylidene malonate (1.5 mmol, 429 mg) to give orange oil (923 mg). The crude material (867 mg) was purified by column chromatography (pentane/ether: 70/30 (v/v)) to yield a intractable 59/41 mixture of cyclopropane-1,1-dicarboxylates (388 mg, 84%) as a colorless oil.

According to procedure D. Using isopropyldiphenylsulfonium tetrafluoroborate (1.2 mmol, 380 mg) and the alkylidene malonate (1.0 mmol, 286 mg), gives an orange oil (627 mg). The crude material (583 mg) purified by column chromatography (pentane/ether: 80/20 (v/v)) to yield a intractable 55/45 mixture of cyclopropane-1,1-dicarboxylates (235 mg, 77%) as a colorless oil. TLC, SiO_2: R_f 0.8 (pentane/ether: 80/20). |GC^2|, program A, 9.8 and 9.9 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.21–4.14 (m, C*H*–O *Z*+*E*), 4.02–3.94 (m, C*H*–O *Z*+*E*), 3.84–2.78 (m, C*H*–O *Z*+*E*), 3.73 (s, OCH_3 *E*), 3.72 (s, OCH_3 *Z*), 1.79–1.74 (d, *J*=9, 4, 9.0 Hz, *H* cyclopropane *Z*+*E*), 1.47 (s, OC(CH_3)$_3$ *E*), 1.46 (s, 2CH_3), 1.45 (s, OC(CH_3)$_3$ *Z*), 1.36 (s, CH_3), 1.35 (s, 2CH_3), 1.34 (s, CH_3), 1.30 (s, CH_3), 1.28 (s, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 169.4, 168.3, 167.3, 166.2, 109.2, 81.9, 81.8, 73.6, 73.4, 69, 3, 69.2, 52.4, 52.1, 42.7, 30.3, 30.2, 27.9, 27.8, 27.0, 26.9, 25.5, 22.1, 22.0, 18.1, 17.8; IR (film, KBr) 2985, 2956, 2937, 2877, 1347, 1731, 1458, 1437, 1393, 1371, 1291, 1253, 1222, 1209, 1160, 1125, 1112, 1067, 997, 949, 917, 849, 809, 791, 740, 588, 515 cm^{-1}; GC/MS *m*/*z* 313 (M^+-CH_3), 257, 227, 215, 197, 171, 153, 139, 101, 93, 73, 57. Anal. Calcd for $C_{17}H_{28}O_6$: C, 62.18; H, 8.60. Found C, 62.24; H, 8.56.

7.1.16. Cyclopropanation of 2-cyano-3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-acrylic acid methyl ester. *According to procedure C*. Using isopropyltriphenylphosphonium iodide (2.7 mmol, 1.17 g) and the α-cyanoacrylate (1.5 mmol, 317 mg) gives an orange oil (721 mg). The crude material (704 mg) purified by column chromatography (pentane/ether: 80/20 (v/v)) yields two pure cyclopropane derivatives: *Re* compound (colorless oil, 240 mg, 67%) and *Si* compound (white solid, 29 mg, 8%). Overall yield: 75%.

According to procedure D. Using isopropyldiphenylsulfonium tetrafluoroborate (1.2 mmol, 380 mg) and the α-cyanoacrylate (1.0 mmol, 211 mg), gives an orange oil (612 mg). The crude material (582 mg) was purified by column chromatography (pentane/ether: 70/30 (v/v)) to yield two pure cyclopropane derivatives. *Re compound* (colorless oil, 161 mg, 67%) and *Si* compound (white solid, 19 mg, 8%). Overall yield: 75%. *Re compound*: $[\alpha]_D^{20}=+11.13$ (*c* 0.72, $CHCl_3$); TLC, SiO_2: R_f 0.33 (pentane/ether: 80/20). |GC^2|, program A, 8.0 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.23 (m, 1H, C*H*–O), 4.05 (m, 1H, C*H*–O), 3.83 (s, 1H, OCH_3), 3.81 (m, 1H, C*H*–O), 2.12 (d, 1H, *J*=10.4 Hz, *H* cyclopropane), 1.54 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.35 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 165.8, 115.9, 109.8, 72.8, 68.3, 53.2, 39.9, 36.4, 27.8, 26.6, 25.2, 20.2, 18.4; IR (film, KBr) 2982, 2938, 2865, 2245, 1740, 1460, 1436, 1295, 1233, 1167, 1113, 1073, 1046, 999, 936, 915, 871, 844, 786, 689, 613, 552 cm^{-1}; GC/MS *m*/*z* 238 (M^+-CH_3), 196, 178, 164, 152, 137, 120, 101, 93, 73, 59, 53. Anal. Calcd for $C_{13}H_{19}O_4N$: C, 61.,64; H, 7.56; N, 5.53. Found C, 61.64; H, 7.58; N, 5.55. *Si compound*: $[\alpha]_D^{20}=-12.13$ (*c* 0.80, $CHCl_3$); TLC, SiO_2: R_f 0.19 (pentane/ether: 80/20). |GC^2|, program A, 8.1 min; mp 97 °C. ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.13 (m, 1H, C*H*–O), 4.07 (m, 1H, C*H*–O), 3.82 (s, 1H, OCH_3), 3.74 (m, 1H, C*H*–O), 2.16 (d, 1H, *J*=9.6 Hz, *H* cyclopropane), 1.46 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.32 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 166.2, 116.1, 110.0, 73.1, 68.2, 53.4, 41.0, 35.2, 29.6, 26.7, 25.4, 20.5, 19.2; IR (film, KBr) 3034, 2998, 2982, 2938, 2865, 2369, 2345, 2245, 1740, 1460, 1436, 1380, 1375, 1325, 1294, 1233, 1167, 1113, 1073, 1046, 999, 936, 915, 871, 844, 786, 689, 613, 552 cm^{-1}; *GC/MS m*/*z* 238 (M^+-CH_3), 196, 178, 164, 152, 137, 120, 101, 93, 72, 59, 53. Anal. Calcd for $C_{13}H_{19}O_4N$: C, 61.64; H, 7.56; N, 5.53. Found C, 61.60; H, 7.75; N, 5.49.

7.1.17. Cyclopropanation of 2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethylene)-malononitrile. *According to procedure C*. Using isopropyltriphenylphosphonium iodide (18.0 mmol, 7.8 g) and the alkylidene malononitrile (prepared just before as previously described from 10.0 mmol of 2,3-*O*-isopropylidene-D-glyceraldehyde, gives an brown oil (3.2 g). The crude material was purified by column chromatography (pentane/ether: 70/30 (v/v)) to yield two pure cyclopropane derivatives as white solids. *Re* compound (246 mg, 11%) and *Si* compound (396 mg, 18%). Overall yield over two steps: 29%.

According to procedure D. Using isopropyldiphenylsulfonium tetrafluoroborate (6.0 mmol, 1.9 g) and the alkylidene malononitrile (prepared just before as previously described from 5.0 mmol of 2,3-*O*-isopropylidene-D-glyceraldehyde, gives an brown oil (1.31 g). The crude material was purified by column chromatography (pentane/ether: 70/30 (v/v)) to yield two pure cyclopropane derivatives as white solids: *Re* compound (145 mg, 13%) and the *Si* compound (218 mg, 20%). Overall yield over two steps: 33%. *Re compound*: $[\alpha]_D^{20}=-7.75$ (*c* 0.96, $CHCl_3$); TLC, SiO_2: R_f 0.38 (pentane/ether: 50/50). |GC^2|, program A, 7.5 min; mp 118 °C. ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.15 (m, 1H, C*H*–O), 3.99 (m, 1H, C*H*–O), 3.77 (m, 1H, C*H*–O), 1.90 (d, 1H, *J*=9.7 Hz, *H* cyclopropane), 1.51 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.40 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 114.1, 112.5, 110.5, 72.3, 67.8, 43.3, 33.8, 26.7, 25.2, 24.1, 17.4, 14.9; IR (film, KBr) 2997, 2943, 2904, 2870, 2243, 1477, 1457, 1421, 1383, 1338, 1263, 1226, 1210, 1153, 1113, 1063, 1048, 1003, 978, 916, 839, 791, 638 cm^{-1}; GC/MS *m/z* 221 (M^++1), 205, 190, 175, 163, 145, 120, 118, 73, 59, 53. Anal. Calcd for $C_{12}H_{16}O_2N_2$: C, 65.43; H, 7.32; N, 12.72. Found C, 65.33; H, 7.47; N, 12.53. *Si compound*: $[\alpha]_D^{20}=+6.9$ (*c* 0.81, $CHCl_3$); TLC, SiO_2: R_f 0.4 (pentane/ether: 50/50). |GC^2|, program A, 6.5 min; mp 117 °C. ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.22 (m, 1H, C*H*–O), 3.93–3.86 (m, 2H, 2C*H*–O), 1.82 (d, 1H, *J*=9.3 Hz, *H* cyclopropane), 1.46 (s, 6H, 2CH_3), 1.40 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 113.9, 112.6, 110.5, 72.5, 68.3, 42.5, 35.2, 26.9, 25.2, 24.0, 17.0, 13.2; IR (film, KBr) 3034, 2986, 2937, 2884, 2244, 1481, 1456, 1378, 1260, 1222, 1164, 1075, 1055, 992, 974, 931, 858, 834, 793, 720, 691, 649 cm^{-1}; *GC/MS m/z* 205, 190, 175, 163, 145, 128, 118, 101, 73, 59, 53. Anal. Calcd for $C_{12}H_{16}O_2N_2$: C, 65.43; H, 7.32; N, 12.72. Found C, 65.93; H, 7.52; N, 12.11.

7.1.18. Cyclopropanation of 2-(2,2-5,5-tetramethyl-[1,3]dioxolan-4-ylmethylene)-malonic acid dimethyl ester. *According to procedure C*. Using isopropyltriphenylphosphonium iodide (1.94 mmol, 838 mg) and the alkylidene malonate (1.08 mmol, 293 mg), gives yellow oil (1.41 g). The crude material (1.37 g) was purified by column chromatography (pentane/ether: 70/30 (v/v)) to yield a mixture of cyclopropane-1,1-dicarboxylates (269 mg, 82%) as a colorless oil (95/5 *Si*/*Re* compounds).

According to procedure D. Using isopropyldiphenylsulfonium tetrafluoroborate (1.2 mmol, 380 mg) and the alkylidene malonate, gives brown oil (639 mg). The crude material (602 mg) was purified by column chromatography (pentane/ether: 80/20 (v/v)) to yield the pure *Si* compound (224 mg, 76%) as a colorless oil. *Si compound*: $[\alpha]_D^{20}=+23.90$ (*c* 0.70, $CHCl_3$); TLC, SiO_2: R_f 0.47 (pentane/ether: 80/20). |GC^2|, program A, 9.3 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 3.88 (d, 1H, *J*=10.2 Hz, C*H*–O), 3.74 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 1.84 (d, 1H, *J*=10.4 Hz, *H* cyclopropane), 1.44 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.22 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 169.2, 168.2, 79.1, 52.6, 52.2, 35.1, 30.6, 28.9, 27.2, 26.4, 23.8, 23.7, 16.7; IR (film, KBr) 2982, 2956, 2938, 2878, 1733, 1461, 1437, 1377, 1346, 1291, 1250, 1216, 1201, 1169, 1126, 1109, 1077, 1052, 1032, 1001, 962, 937, 912, 891, 861, 824, 800, 753 cm^{-1}; GC/MS *m/z* 299 (M^+-CH_3), 256, 225, 185, 153, 139, 73, 59. Anal. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34. Found C, 60.97; H, 8.54. *Re compound*: $[\alpha]_D^{20}=-9.05$ (*c* 1.21, $CHCl_3$); TLC, SiO_2: R_f 0.48 (pentane/ether: 80/20). |GC^2|, program A, 9.1 min; mp 56 °C. ^{1}H NMR δ (400 MHz, $CDCl_3$) 3.82 (d, 1H, *J*=9.5 Hz, C*H*–O), 3.76 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 1.89 (d, 1H, *J*=9.7 Hz, *H* cyclopropane), 1.46 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.21 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 169.1, 80.2, 79.2, 52.6, 52.2, 35.6, 30.3, 28.5, 26.8, 26.5, 23.7, 23.5, 18.2; IR (film, KBr) 2985, 2957, 2938, 1729, 1462, 1440, 1429, 1380, 1370, 1350, 1301, 1246, 1215, 1192, 1109, 1182, 1168, 992, 962, 935, 914, 889, 861, 828, 815, 752 cm^{-1}; GC/MS *m/z* 299 (M^+-CH_3), 225, 185, 153, 139, 100, 73, 59. Anal. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34. Found C, 60.98; H, 8.37.

7.1.19. Synthesis of the authentic sample of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester from methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1-carboxylate.[5c] To a well stirred solution of diisopropylamine (1.5 mmol, 151 mg) in anhydrous tetrahydrofuran (2 ml) was added under an atmosphere of argon, *n*-butyllithium (1.6 N in hexane, 1.2 mmol, 0.75 ml) maintained at 0 °C. The mixture was stirred at 0 °C for 15 min and then cooled to −78 °C before addition of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1-methylcarboxylate (1.0 mmol, 228 mg) previously prepared as the well known procedure.[5c] The yellow solution was stirred at −78 °C for 45 min and methyl chloro formate (1.5 mmol, 142 mg) was then added dropwise. After stirring at this temperature for 2 h, the mixture was hydrolyzed by addition of water (5 ml), extracted with diethyl ether (4×20 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 313 mg of crude material. 173 mg were purified by column chromatography (pentane/ether: 80/20) to yield the pure 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester (131 mg, 82%). Spectral and analytical data are in agreement with the authentic sample previously described in this paper.

7.1.20. Transesterification of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid *tert*-butyl ester methyl ester with potassium *tert*-butoxide. To a well stirred solution of potassium *tert*-butoxide (2.8 mmol, 314 mg) in anhydrous THF (3.7 ml) was added under an atmosphere of argon, the 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester (0.91 mmol, 300 mg) maintained at 20 °C. The mixture was then stirred 2 h at room temperature. Water was added (5 ml) and the mixture was extracted with diethyl ether (3×30 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 392 mg of crude material. 337 mg were purified by thin layer chromatography (pentane/ether: 90/10) to yield the pure 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid di-*tert*-butyl ester (274 mg, 95%). Spectral and analytical

data are in agreement with the authentic sample previously described in this paper.

7.1.21. Bis-transesterification of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester with potassium *tert*-butoxide. To a well stirred solution of potassium *tert*-butoxide (20.0 mmol, 2.24 g) in anhydrous THF (16 ml) was added under an atmosphere of argon, 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid *tert*-butyl ester methyl ester (4 mmol, 1.15 g) maintained at 20 °C. The mixture was then stirred for 1.5 h at room temperature. Water was added (7 ml) and the mixture was extracted with diethyl ether (3×50 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 1.52 g of crude material. 1.47 g were purified by column chromatography (pentane/ether: 90/10) to yield the pure 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid di-*tert*-butyl ester (1.21 g, 92%). Spectral and analytical data are in agreement with the authentic sample previously described in this paper. Acid cleavage of the dioxolane ring of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester: (HCl 10%) which exist at the smaller/MeOH, 1.5 h at 20 °C. 10% Aqueous hydrochloric acid (3.0 ml) was added to a solution of cyclopropane-1,1-dicarboxylate (2.0 mmol, 572 mg) in methanol (10 ml). The mixture was then stirred for 1.5 h at room temperature and the solvents were rapidly removed under reduced pressure. The residue was then solved with ethyl acetate (100 ml) and the solution was filtered through a mixture of sodium bicarbonate and magnesium sulfate. The solvents were removed under reduced pressure to give 556 mg of crude material. 433 mg were purified by column chromatography (ethyl acetate) to yield the pure methyl 3-(1,2-dihydroxy-ethyl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylate (291 mg, 76%) as a colorless oil. $[\alpha]_D^{20}=-14.2$ (*c* 2.43, $CHCl_3$); TLC, SiO_2: R_f 0.25 (pentane/ether: 0/100). ^{1}H NMR δ (400 MHz, $CDCl_3$) 3.73 (s, 6H, 2OCH_3), 3.84–3.63 (br, 3H, 3CH–O), 1.79 (d, 1H, *J*=9.8 Hz, *H* cyclopropane), 1.37 (s, 3H, CH_3), 1.27 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 169.0, 168.0, 69.3, 66.1, 52.8, 52.5, 37.6, 30.5, 22.7, 17.8; IR (film, KBr) 3404, 2956, 2882, 1728, 1438, 1382, 1298, 1256, 1201, 114, 1120, 1033, 993, 950, 923, 874, 823, 804, 747, 722, 695, 600 cm^{-1}; GC/MS *m*/*z* 247 (M^+ +1), 229, 215, 199, 185, 179, 153, 137, 122, 109, 95, 73, 67, 55. Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.70; H, 7.04. Found C, 53.46; H, 7.15.

7.1.22. Acid cleavage of dioxolane ring of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester. 10% HCl/MeOH, 50 h at 20 °C. 10% Aqueous hydrochloric acid (3.0 ml) was added to a solution of cyclopropane 1,1-dicarboxylate (2.0 mmol, 572 mg) in methanol (10 ml). The mixture was then stirred for 50 h at room temperature and the solvents were rapidly removed under reduced pressure. The residue was then solved with ethyl acetate (100 ml) and the solution was filtered through a mixture of sodium bicarbonate and magnesium sulfate. The solvents were removed under reduced pressure to give 463 mg of crude material. 382 mg were purified by column chromatography (ethyl acetate) to yield the pure methyl 4-hydroxymethyl-6,6-dimethyl-2-oxo-3-oxa-bicyclo[3.1.0]hexane-1-carboxylate (316 mg, 89%) as a colorless oil. $[\alpha]_D^{20}=-21.86$ (*c* 2.20, $CHCl_3$); TLC, SiO_2: R_f 0.51 (pentane/ether: 0/100). $|GC^2|$, program A, 6.1 min; δ_H (400 MHz, $CDCl_3$) 4.81 (m, 1H, CH–O), 3.98–3.73 (br, 2H, 2CH–OH), 3.82 (s, 3H, OCH_3), 2.52 (d, *J*=4.4 Hz, 1H, *H* cyclopropane), 2.40 (br, 1H, O*H*), 1.41 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 169.4, 166.0, 79.5, 61.4, 52.8, 42.1, 36.1, 33.4, 22.0, 19.5; IR (film, KBr) 3440, 2999, 2958, 2883, 1770, 1730, 1639, 1441, 1320, 1233, 1196, 936, 897, 871, 804, 730, 638 cm^{-1}; GC/MS *m*/*z* 215 (M^++1), 199, 197, 183, 165, 153, 151. Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found C, 55.03; H, 6.87.

7.1.23. Protection as *tert*-butyl dimethylsilylether of the hydroxyl group of methyl 4-hydroxymethyl-6,6-dimethyl-2-oxo-3-oxa-bicyclo[3.1.0]hexane-1-carboxylate. Imidazole (18.0 mmol, 1.21 g) was added under an atmosphere of argon, to a solution of 4-hydroxymethyl-6,6-dimethyl-2-oxo-3-oxa-bicyclo[3.1.0]hexane-1-carboxylate (7.2 mmol, 1.55 mg) in anhydrous DMF (10 ml) maintained at room temperature. The mixture was then stirred for 1 h at room temperature. Water (10 ml) was added and the mixture was extracted with ethyl acetate (3×30 ml). Organic layer was dried ($MgSO_4$) and the solvents were removed under reduced pressure to give 2.6 g of crude material which were purified by thin layer chromatography (pentane/ether: 70/30 (v/v)) to yield the pure lactone (2.2 g, 92%) as a colorless oil. TLC, SiO_2: R_f 0.48 (pentane/ether: 70/30). $|GC^2|$, program A, 13.5 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.81 (m, 1H, CH–O), 3.98–3.73 (br, 2H, 2CH–OTBS), 3.82 (s, 3H, OCH_3), 2.49 (d, 1H, *J*=4.4 Hz, *H* cyclopropane), 1.36 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 0.86 (s, 9H, SiC(CH_3)$_3$), 0.05 (s, 3H, SiCH_3), 0.04 (s, 3H, SiCH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 169.4, 166.3, 78.6, 61.5, 52.8, 41.8, 36.4, 33.3, 25.7, 25.6, 21.9, 19.1, 18.1, −5.2, −5.6; IR (film, KBr) 2955, 2932, 2886, 2858, 2363, 1786, 1731, 1464, 1439, 1407, 1391, 1363, 1318, 1276, 1256, 1229, 1195, 1106, 1078, 1051, 1020, 991, 960, 939, 902, 840, 780, 713, 666 cm^{-1}; GC/MS *m*/*z* 329 (M^++1), 313, 297, 271, 253, 239, 225, 197, 179, 159, 153. Anal. Calcd for $C_{16}H_{28}O_5Si$: C, 58.50; H, 8.59. Found C, 58.44; H, 8.64.

7.1.24. Attempted demethoxycarbonylation of methyl 4-*tert*-butyl-dimethylsilyloxymethyl-6,6-dimethyl-2-oxo-3-oxa-bicyclo[3.1.0]hexane-1-carboxylate with magnesium iodide. To a mixture of magnesium turnings (0.67 mmol, 16 mg) in anhydrous diethyl ether (3 ml) was added under an atmosphere of argon, portion wise iodine (0.54 mmol, 138 mg) maintained at room temperature. When the color of the iodine disappeared, the ether was evaporated, the residue was dissolved in anhydrous toluene (3 ml) and the lactone (0.54 mmol, 176 mg) was added. After 13 h at 80 °C, the mixture was cooled at room temperature, a saturated aqueous bicarbonate solution (10 ml) was added and the layers were separated. The aqueous layer was acidified with 10% aqueous HCl and was extracted with diethyl ether (3×30 ml). Organic layers were dried ($MgSO_4$) and the solvents were removed under reduced pressure to give cyclopropane ring opening compound (93 mg, 55%) as a brown solid (purity ~90%). ^{1}H NMR δ (400 MHz, $CDCl_3$) 5.11 (s, *H* olefinic), 4.96 (s, *H* olefinic), 4.69 (m, *H* vinylic), 4.11 (d, 1H, *J*=13 Hz,

C*H*(CO_2H) cyclopropane), 3.86–3.69 (br, 3H, 2C*H*–OTBS+C*H*–O), 1.87 (s, 3H, CH_3), 0.89 (s, 9H, SiC(CH_3)$_3$). 0.08 (s, 3H, SiCH_3), 0.05 (s, 3H, SiCH_3); IR (film, KBr) 2957, 2932, 2860, 1720, 1655, 1390, 1335, 1256, 1161, 1112, 1061, 1037, 1006, 997, 911, 868, 837, 808, 781, 734 cm^{-1}.

7.1.25. Decarboxylation of 2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid methyl ester using the Barton procedure. Thionyl chloride (1 ml) was added dropwise under an atmosphere of argon, to a well stirred solution of carboxylic acid[X] (1.37 mmol, 250 mg) in benzene (1 ml) maintained at 0 °C. One drop of anhydrous DMF was added and the mixture was stirred at room temperature for 2 h. The solvents were removed under reduced pressure. The residue (in 5 ml of benzene) was then added to a solution of thione[21a] (1.51 mmol, 189 mg) in benzene (4 ml) before introduction of pyridine (0.12 ml). The resulting mixture, sheltered from sunlight, was stirred at room temperature for 2 h at room temperature, was filtered and the solvents were removed under reduced pressure. After exposition to sunlight, the mixture was purified by thin layer chromatography (pentane/ether: 60/40) to yield 169 mg of the pure 2,2-dimethyl-1-(pyridine-2-ylsulfanylcarbonyl)-cyclopropanecarboxylic acid methyl ester (169 mg, 66%) as a colorless liquid. TLC, SiO_2: R_f 0.93 (pentane/ether: 60/40). |GC^2|, program A, 9.8 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 8.41 (m, *H* aromatic), 7.55 (m, *H* aromatic), 7.30 (s, *H* aromatic), 7.01 (m, *H* aromatic), 3.71 (s, 3H, OCH_3), 2.05 (d, 1H, *J*=4.77 Hz, *H* cyclopropane), 1.48 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.07 (d, 1H, *J*=5.34 Hz, *H* cyclopropane); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 160.7, 149.2, 136.7, 120.9, 119.5, 52.8, 36.0, 30.1, 22.9, 21.1, −0.1; IR (film, KBr) 3047, 2990, 2953, 2931, 2877, 1723, 1605, 1576, 1561, 1452, 1435, 1419, 1377, 1329, 1283, 1243, 1191, 1149, 1128, 1106, 1046, 1017, 998, 986, 966, 944, 874, 854, 759, 726, 667, 619 cm^{-1}; GC/MS *m/z* 237 (M$^+$), 222, 205, 204, 178, 162, 151, 136, 122, 111, 99, 78, 67, 5. Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90. Found C, 60.57; H, 6.59; N, 5.78.

7.1.26. Demethoxycarbonylation of 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1,1-dicarboxylic acid dimethyl ester. (i) *Using NaCl in wet DMSO at 180 °C*. A mixture of sodium chloride (4.0 mmol, 236 mg), water (6.0 mmol, 108 mg) and cyclopropane-1,1-dicarboxylate (3.0 mmol, 858 mg) in DMSO (3 ml) was stirred at 180 °C for 6 h. After cooling to room temperature, the mixture was hydrolyzed with water (10 ml) and extracted with diethyl ether (4×25 ml). Organic layers were washed with water (10 ml), with brine (10 ml), dried ($MgSO_4$) and the solvents were removed under reduced pressure to give 591 mg of crude material. 522 mg were purified by column (pentane/ether: 70/30 (v/v)) to yield a mixture (449 mg, 73%) of three compounds (*trans*/*cis*/*open*: 27/21/52) as a colorless oil.

trans-Cyclopropane carboxylate. $[\alpha]_D^{20}$=−17.8 (*c* 0.91, $CHCl_3$); TLC, SiO_2: R_f 0.78 (pentane/ether: 70/30). |GC^2|, program A, 4.1 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.55 (m, 1H, C*H*–O), 4.05 (m, 1H, C*H*–O), 3.66–3.60 (s+m, 4H, OCH_3+C*H*–O), 1.56 (d, *J*=8.8 Hz, 1H, C*H*(CO_2Me), 1.45 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.24 (s+m, 4H, CH_3+*H* cyclopropane); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 172.0, 109.2, 72.4, 69.2, 68.0, 66.4, 51.5, 35.2, 29.3, 28.2, 27.2, 25.7; IR (film, KBr) 2988, 2955, 2872, 1728, 1458, 1440, 1378, 1320, 1236, 1205, 1149, 1124, 1097, 1060, 1012, 938, 855, 790, 742 cm^{-1}; GC/MS *m/z* 213 (M$^+$−CH_3), 153, 139, 127, 111, 101, 72, 71, 55. Spectral and analytical data are in agreement with those reported.[5]

cis-Cyclopropyl ester. $[\alpha]_D^{20}$=+32.6 (*c* 12.0, $CHCl_3$); TLC, SiO_2: R_f 0.68 (pentane/ether: 70/30). |GC^2|, program A, 3.6 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.06 (m, 1H, C*H*–O), 3.76–3.68 (br, 2H, 2C*H*–O), 3.67 (s, 3H, OCH_3), 1.55 (m, 1H, *H* cyclopropane), 1.45 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.27 (2s, 4H, CH_3+C*H*(CO_2Me)), 1.26 (s, 3H, CH_3); IR (film, KBr) 2987, 2954, 2876, 1730, 1449, 1377, 1349, 1284, 1234, 1214, 1175, 1117, 1067, 999, 941, 909, 852, 792, 736, 646 cm^{-1}; GC/MS *m/z* 213 (M$^+$−CH_3), 197, 127, 93, 59. Spectral and analytical data are in agreement with that reported.[5c]

Opened form. TLC, SiO_2: R_f 0.78 (pentane/ether: 70/30). |GC^2|, program A, 3.9 min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.91 (s, 1H, *H* olefinic), 4.81 (s, 1H, *H* olefinic), 4.20 (m, 1H, C*H*–O), 3.97 (m, 1H, C*H*–O), 3.83 (s, 3H, OCH_3), 3.80 (m, 1H, C*H*–O), 2.82 (br, 1H, *H* vinylic), 2.46 (m, 2H, CH_2(CO_2Me), 1.80 (s, 3H, CH_3 olefinic), 1.45 (s, 3H, CH_3), 1.36 (s, 3H, CH_3); IR (film, KBr) 2988, 2952, 2937, 2876, 1727, 1660, 1503, 1384, 1256, 1234, 1213, 1175, 1155, 1093, 1063, 1001, 939, 908, 854, 792, 736, 659 cm^{-1}; GC/MS *m/z* 228 (M$^+$), 213, 197 (M$^+$−OCH_3), 169, 127, 95, 59. Spectral and analytical data are in agreement with those reported.

(ii) *Using PATP in DMF with a catalytic amount of cesium carbonate*. A solution of PATP (2.0 mmol, 250 mg), cyclopropane-1,1-dicarboxylate (1.0 mmol, 286 mg) and cesium carbonate (0.32 mmol, 105 mg) in anhydrous DMF (9 ml) was stirred under an atmosphere of argon, maintained at 90 °C for 26 h, then cooled, hydrolyzed with water (10 ml), extracted with diethyl ether (3×20 ml), washed with water (10 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 910 mg of crude material which were purified by column chromatography (pentane/ether: 80/20 (v/v)) to yield a mixture (155 mg, 68%) of the two desired cyclopropyl carboxylates (*trans*/*cis*: 61/39).

(iii) *Using Me_4NOAc in DMPU*. Tetramethylammonium acetate (1.1 g) was added under an atmosphere of argon, to a solution of the cyclopropane-1,1-dicarboxylate (1.0 mmol, 286 mg) in anhydrous DMPU (9 ml) maintained at 20 °C. The mixture was then stirred for 6 h at 95 °C, cooled, hydrolyzed with water (10 ml), extracted with diethyl ether (3×20 ml), washed with water (10 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 850 mg of crude material which were purified by column chromatography (pentane/ether: 80/20 (v/v)) to yield a mixture (180 mg, 79%) of the two desired cyclopropyl carboxylates (*trans*/*cis*: 68/32).

7.1.27. Acidic cleavage of dioxolane ring of methyl 3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-cyclopropane-1-carboxylate. *cis-Compound*. 10% aqueous

hydrochloric acid (3 ml) was added to a solution of cyclopropane (2.41 mmol, 456 mg) in methanol (10 ml). The mixture was then stirred for 30 min at room temperature and the solvents were rapidly removed under reduced pressure. The residue was then solved with ethyl acetate (50 ml) and the solution was filtered through a mixture of sodium bicarbonate and magnesium sulfate. The solvents were removed under reduced pressure to give 503 mg of crude material. 481 mg were purified by column chromatography (pentane/ether: 0/100 (v/v)) to yield the pure lactone (257 mg, 89%) as a colorless oil. $[\alpha]_D^{20}=-68.7$ (*c* 1.27, $CHCl_3$). ^{1}H NMR δ (400 MHz, $CDCl_3$) 4.78 (m, 1H, C*H*–O), 3.98 (m, 1H, CH_2–OH), 3.77 (m, 1H, CH_2-OH), 2.07 (d, 1H, *J*=5.4 Hz, C*H*–C=O), 1.97 (m, 1H, *H* cyclopropane), 1.75 (s, 1H, O*H*), 1.32 (s, 3H, CH_3), 1.17 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 172.2, 68.0, 66.3, 51.4, 33.9, 29.1, 28.6, 25.1; IR (film, KBr) 3421, 2960, 1755, 1648, 1456, 1383, 1353, 1313, 1291, 1201, 1119, 1086, 1050, 990, 940, 883, 845, 784 cm^{-1}; GC/MS *m*/*z* 152, 139, 126, 115, 111, 97, 93, 81, 69, 67, 55. The spectral and analytical data agree with those previously reported.[28]

trans-Compound. 10% aqueous hydrochloric acid (3 ml) was added to a solution of cyclopropane (2.41 mmol, 456 mg) in methanol (12 ml). The mixture was then stirred for 30 min at room temperature and the solvents were rapidly removed under reduced pressure. The residue was then solved with ethyl acetate (50 ml) and the solution was filtered through a mixture of sodium bicarbonate and magnesium sulfate. The solvents were removed under reduced pressure to give 491 mg of crude material which was purified by column chromatography (ethyl acetate) to yield the pure diol (417 mg, 92%) as colorless oil. $[\alpha]_D^{20}=+45.0$ (*c* 2.91, $CHCl_3$). ^{1}H NMR δ (400 MHz, $CDCl_3$) 3.67 (s, 3H, OCH_3), 3.74–3.57 (br, 2H, 2C*H*–O), 3.40 (m, 1H, C*H*–O), 2.69 (br, 2H, 2O*H*), 1.51 (m, 1H, *H* cyclopropane), 1.40 (d, 1H, *J*=9.7 Hz, C*H*(CO_2Me)), 1.30 (s, 3H, CH_3), 1.25 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 172.5, 72.4, 66.2, 51.7, 34.2, 30.9, 26.7, 21.2, 20.7; IR (film, KBr) 3407, 2954, 2932, 2877, 2745, 1731, 1449, 1381, 1357, 1288, 1214, 1171, 1117, 1090, 1039, 1014, 998, 969, 938, 909, 874, 843, 778, 733, 653 cm^{-1}; GC/MS *m*/*z* 127, 97, 95, 79, 73, 67, 59, 51. Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found C, 56.53; H, 8.76.

7.1.28. Selective tritylation of the primary hydroxyl group of methyl *trans*-3-(2,3-dihydroxy-propyl)-2,2-dimethyl-cyclopropanecarboxylate. *N*,*N*-4-dimethyl-amino-*N*-triphenylmethylpyridinium chloride[26] (1.28 mmol, 512 mg) was added under an atmosphere of argon, to a solution of the diol (1.06 mmol, 200 mg) in anhydrous CH_2Cl_2 (6 ml) maintained at 20 °C. The mixture was then stirred for 22 h at reflux, cooled, hydrolyzed with water (5 ml), extracted with dichloromethane (3×20 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 821 mg of crude material which were purified by column chromatography (pentane/ethyl acetate: 80/20 (v/v)) to yield the pure tritylether (405 mg, 89%) as a white solid. TLC, SiO_2: R_f 0.85 (pentane/ethyl acetate: 80/20). Mp 61 °C. ^{1}H NMR δ (400 MHz, $CDCl_3$) 7.46–7.24 (br, 15H, OC(C_6H_5)$_3$), 3.64 (s, H, OCH_3), 3.31–3.26 (br, 3H, 3C*H*–O), 2.27 (br, 1H, O*H*), 1.50 (m, 1H, *H* cyclopropane), 1.27 (d, 1H, *J*=5.5 Hz, C*H*(CO_2Me)), 1.23 (2s, 6H, 2CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 172.3, 143.8, 128.7, 128.0, 127.1, 87.0, 71.0, 67.3, 51.5, 34.6, 30.9, 26.6, 21.2, 20.7; IR (film, KBr) 3468, 3088, 3060, 3027, 2982, 2952, 2928, 2874, 2742, 2081, 1963, 1893, 1816, 1731, 1716, 1598, 1492, 1448, 1375, 1244, 1213, 1171, 1115, 1048, 986, 944, 903, 845, 766, 748, 707, 647, 633, 608 cm^{-1}; GC/MS *m*/*z* 258, 243, 229, 215, 183, 165, 152, 127, 105, 77, 67, 55. Anal. Calcd for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found C, 78.00; H, 7.16.

7.1.29. Contrathermodynamic lactonisation of methyl *trans*-3-(1-hydroxy-2-trityloxy-ethyl)-2,2-dimethyl-cyclopropanecarboxylate using potassium *tert*-butoxide in benzene. Potassium *tert*-butoxide (0.44 mmol, 51 mg) was added under an atmosphere of argon, to a solution of methyl *trans*-3-(1-hydroxy-2-trityloxy-ethyl)-2,2-dimethyl-cyclopropanecarboxylate (0.44 mmol, 169 mg) in anhydrous benzene (2 ml) maintained at 20 °C. The resulting yellow mixture was then stirred for 6 h at 80 °C, cooled and dichloromethane was added (10 ml). The solution was hydrolyzed with a saturated aqueous ammonium chloride solution (5 ml), extracted with dichloromethane (2×10 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 181 mg of crude material. 152 mg were purified by thin layer chromatography (pentane/ether: 60/40 (v/v)) to yield the pure 6,6-dimethyl-4-trityloxy-methyl-3-oxa-bicyclo[3.1.0]hexan-2-one (138 mg, 79%) as a white solid. $[\alpha]_D^{20}=-57.3$ (*c* 1.24, $CHCl_3$); TLC, SiO_2: R_f 0.40 (pentane/ether: 70/30). |GC^2|, program A, 13.7; mp 101 °C; min; ^{1}H NMR δ (400 MHz, $CDCl_3$) 7.49–7.25 (m, 15H, OC(C_6H_5)$_3$), 4.84 (m, H, C*H*–O), 3.50 (m, 1H, C*H*–O), 3.50 (m, 1H, C*H*–O), 2.27 (br, 1H, O*H*), 2.00 (br, 2H, 2*H* cyclopropane), 1.11 (s, 3H, CH_3), 1.03 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 174.4, 143.6, 128.7, 128.0, 127.3, 86.8, 78.9, 62.4, 31.4, 30.9, 26.0, 24.1, 17.4; IR (film, KBr) 3087, 3058, 3031, 2997, 2982, 2960, 2928, 2901, 2873, 1966, 1921, 1875, 1766, 1596, 1561, 1446, 1399, 1380, 1366, 1348, 1314, 1290, 1253, 1217, 1189, 1155, 1134, 1117, 1076, 1028, 991, 937, 899, 864, 848, 820, 771, 755, 703, 647, 631 cm^{-1}; GC/MS *m*/*z* 253, 251, 235, 233. Anal. Calcd for $C_{27}H_{26}O_3$: C, 81.38; H, 6.58. Found C, 81.33; H, 6.61.

7.1.30. Removal of trityl group from 6,6-dimethyl-4-trityloxymethyl-3-oxa-bicyclo[3.1.0]hexan-2-one. 10% Aqueous hydrochloric acid (0.5 ml) was added to a solution of lactone (0.25 mmol, 100 mg) in methanol (2 ml). The mixture was then stirred for 50 min at room temperature, extracted with diethyl ether (3×10 ml), dried ($MgSO_4$). The solvents were removed under reduced pressure to yield the pure lactone (39 mg, 98%) as a colorless oil. Spectral and analytical data are in agreement with the product synthesized previously and the reported data.[28]

7.1.31. Acid cleavage of dioxolane ring of 2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropane-1,1-dicarboxylic acid dimethyl ester. 10% Aqueous hydrochloric acid (3 ml) was added to a solution of cyclopropane (2 mmol, 628 mg) in methanol (10 ml). The mixture was then stirred for 15 min at room temperature and the solvents were rapidly removed under reduced pressure. The residue was then solved with ethyl acetate (30 ml) and the solution was filtered through a mixture of sodium

bicarbonate and magnesium sulfate. The solvents were removed under reduced pressure to give 589 mg of crude material which was purified by column chromatography (pentane/ether: 0/100 (v/v)) to yield pure 4-(1-hydroxy-1-methyl-ethyl)-6,6-dimethyl-2-oxo-3-oxa-bicyclo[3.1.0]hexane-1-carboxylic acid methyl ester (393 mg, 81%) as a glue. $[\alpha]_D^{20}=-25.7$ (*c* 1.43, $CHCl_3$); TLC, SiO_2: R_f 0.59 (pentane/ether: 0/100). |GC[2]|, program A, 9.9 min; ^1H NMR δ (400 MHz, $CDCl_3$) 4.00 (s, 1H, C*H*–O), 3.82 (s, 3H, OCH_3), 2.50 (s, 1H, *H* cyclopropane), 1.82 (br, 1H, O*H*), 1.32 (s, 3H, CH_3), 1.30 (s, 6H, 2CH_3), 1.29 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 169.7, 166.2, 100.6, 81.8, 71.6, 52.9, 36.5, 31.8, 25.0, 23.9, 21.2, 16.2; IR (film, KBr) 3500, 3066, 2979, 2936, 2885, 2750, 2106, 1770, 1731, 1646, 1440, 1383, 1334, 1306, 1278, 1234, 1179, 1126, 1106, 1086, 1056, 1027, 1000, 967, 932, 913, 885, 829, 800, 775, 731 cm^{-1}; *GC/MS m/z* 243 (M^++1), 225, 211 (M^+−OCH_3), 185, 169, 153, 137, 125, 95, 84, 59, 55. Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found C, 57.88, H, 7.69.

7.1.32. Demethoxycarbonylation of 2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropane-1,1-dicarboxylic acid dimethyl ester. Tetramethylammonium acetate (1.6 g) was added under an atmosphere of argon, to a solution of the 2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropane-1,1-dicarboxylic acid dimethyl ester (1.6 mmol, 502 mg) in anhydrous HMPA (14 ml) maintained at 20 °C. The mixture was then stirred for 6 h at 95 °C, cooled, hydrolyzed with water (10 ml), extracted with diethyl ether (4×30 ml). Organic layers were washed with water (2×10 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 655 mg of crude material. 612 mg were purified by column chromatography (pentane/ether: 80/20 (v/v)) to yield a mixture of the desired cyclopropyl carboxylates (81/19 *trans*/*cis*, 301 mg, 74%) as a colorless oil. $[\alpha]_D^{20}=-25.7$ (*c* 1.43, $CHCl_3$); TLC, SiO_2: R_f 0.51 and 0.47 (pentane/ether: 0/100). |GC[2]|, program A, 6.6 and 6.7 min; ^1H NMR δ (400 MHz, $CDCl_3$) 4.30 (s, C*H*–O *cis*), 3.70 (s, OCH_3 *trans*), 3.68 (s, OCH_3 *trans*), 3.56 (d, *J*=5.2 Hz, C*H*–O *trans*), 1.72 (d, *J*=8.8 Hz, C*H*(CO_2Me) *cis*), 1.70 (d, *J*=5.2 Hz, C*H*(CO_2Me) *trans*), 1.51 (mult, *H* cyclopropane *trans*), 1.44–1.21 (br, 4CH_3 *trans*+4 CH_3 *cis*+*H* cyclopropane *trans*); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 98.1, 89.1, 82.3, 51.6, 51.3, 31.9, 31.7, 30.8, 28.9, 28.7, 28.5, 27.0, 26.7, 26.3, 26.2, 23.8, 23.6, 22.1, 20.7; IR (film, KBr) 2979, 2933, 2871, 1722, 1445, 1433, 1377, 1314, 1268, 1230, 1220, 1190, 1151, 1129, 1118, 1095, 1070, 1039, 1006, 934, 729 cm^{-1}; GC/MS *m/z* 241, 198, 181, 149, 139, 100, 84, 59. Anal. Calcd for $C_{14}H_{25}O_4$: C, 65.60; H, 9.44. Found C, 65.52; H, 9.61.

7.1.33. Synthesis of *tert*-butyl *trans*-2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropanecarboxylate. To a well stirred solution of potassium *tert*-butoxide (1.6 mmol, 180 mg) in anhydrous THF (4 ml) was added under an atmosphere of argon, the mixture of cyclopropanes and (0.8 mmol, 204 mg) maintained at 20 °C. The mixture was then stirred for 2 h at room temperature. Water was added (5 ml) and the mixture was extracted with diethyl ether (3×30 ml), washed with water (10 ml) and dried ($MgSO_4$). The solvents were removed under reduced pressure to give 394 mg of crude material which is purified by column chromatography (pentane/ether: 90/10) to yield the pure *tert*-butyl *trans*-2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropanecarboxylate (222 mg, 93%) as a white solid. $[\alpha]_D^{20}=+15.3$ (*c* 0.51, $CHCl_3$); TLC, SiO_2: R_f 0.65 (pentane/ether: 90/10). |GC[2]|, program A, 8.0 min; mp 66 °C. ^1H NMR δ (400 MHz, $CDCl_3$) 3.56 (d, 1H, *J*=7.1 Hz, C*H*–O), 1.62 (d, 1H, *J*=5.8 Hz, C*H*–O). 1.46 (s, 9H, O(CH_3)$_3$), 1.43 (s, 3H, OCH_3), 1.40 (m, 1H, *H* cyclopropane), 1.33 (s, 1H, CH_3), 1.29 (s, 1H, CH_3), 1.23 (s, 1H, CH_3), 1.22 (s, 1H, CH_3), 1.21 (s, 1H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 220.4, 82.0, 31.8, 31.0, 29.6, 28.5, 28.2, 27.1, 26.3, 25.8, 23.5, 22.1, 20.6; IR (film, KBr) 2981, 2935, 2871, 1719, 1460, 1368, 1289, 1268, 1234, 1219, 1201, 1151, 1117, 1067, 1041, 1019, 1002, 917, 844, 772 cm^{-1}; GC/MS *m/z* 283 (M^+−CH_3), 242, 225, 184, 149, 139, 123, 100, 83, 59.57. Anal. Calcd for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found C, 67.55; H, 10.15.

7.1.34. Synthesis of thionocarbonate from *tert*-butyl *trans*-2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropanecarboxylate. 10% Aqueous hydrochloric acid (2 ml) was added to a solution of *tert*-butyl *trans*-2,2-dimethyl-3-(2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl)-cyclopropanecarboxylate (0.54 mmol, 166 mg) in THF (3 ml). The mixture was then stirred 4 h at room temperature and extracted with diethyl ether (4×10 ml). Organic layers were dried ($MgSO_4$) and the solvents were removed under reduced pressure to give 178 mg of crude diol as a white solid (115 °C). The diol (0.4 mmol, 81 mg) was dissolved in anhydrous diethyl ether (2 ml). Diazomethane, freshly prepared, was then added dropwise to the solution of until disappearance of the yellow color. The mixture was stirred for 1 h at 20 °C and the solvents were then removed under reduced pressure to give 98 mg of crude ester which is used directly in the next step. *N*,*N*-Dimethylaminopyridine (0.41 mmol, 50 mg) and the previous synthesized ester (0.34 mmol, 74 mg) were dissolved under an atmosphere of argon, in anhydrous dichloromethane (2 ml) maintained at 0 °C. Thiophosgene (0.82 mmol, 94 mg), diluted by 1 ml of dichloromethane, was added dropwise to the solution and the orange mixture was stirred at 0 °C for 12 h. Silicagel (2 g) was added to the solution and the solvents were removed under reduced pressure. The resulting solid was placed on a silicagel column and eluted with a mixture of pentane/ether (2/8 (v/v)) to give 69 mg of pure thionocarbonate (69 mg, 79% over three steps) as a white solid. $[\alpha]_D^{20}=+33.5$ (*c* 0.90, $CHCl_3$); TLC, SiO_2: R_f 0.40 (pentane/ether: 60/40). Mp 108 °C; ^1H NMR δ (400 MHz, $CDCl_3$) 4.10 (d, 1H, *J*=10.7 Hz, C*H*–O), 3.73 (s, 3H, OCH_3); 1.71 (m, 1H, *H* cyclopropane); 1.57 (s, 3H, CH_3); 1.50 (s, 3H, CH_3); 1.48 (d, 1H, *J*=5.6 Hz, C*H*(CO_2Me)); 1.32 (s, 3H, CH_3), 1.29 (s, 3H, CH_3); ^{13}C NMR δ (100.4 MHz, $CDCl_3$) 190.1, 170.7, 89.3, 89.0, 52.1, 30.6, 28.9, 26.3, 21.6, 21.1, 19.6; IR (film, KBr) 2989, 2963, 2932, 1733, 1465, 1385, 1326, 1299, 1275, 1251, 1221, 1196, 1180, 1113, 1003, 975, 934, 914, 865, 842, 807, 774, 735, 664 cm^{-1}; GC/MS *m/z* 127, 121, 105, 99, 91, 85, 79, 73, 67. Anal. Calcd for $C_{12}H_{18}O_4S$: C, 55.79; H, 7.02. Found C, 55.72; H, 7.13.

7.1.35. Synthesis of (1*R*) *trans*-chrysanthemate by reduction of thionocarbonate. Thionocarbonate (0.027 mmol, 69 mg) was heated for 6 h at 40 °C in the presence of diazaphospholidine (0.80 mmol, 155 mg). After cooling to room temperature, the crude mixture was purified by thin layer chromatography (pentane/ether: 90/10 (v/v)) to yield the pure methyl chrysanthemate (44 mg, 89%) as colorless liquid. $[\alpha]_D^{20}$=+19.7 (*c* 1.12, $CHCl_3$) ($[\alpha]_{D\,lit}^{20}$=+20.7 (*c* 1.1, $CHCl_3$)); TLC, SiO_2: R_f 0.80 (pentane/ether: 95/05); |GC[2]|, program A, 4.4 min; ^1H NMR δ (400 MHz, $CDCl_3$) 4.90 (d, 1H, *J*=4.8 Hz, *H* olefinic), 3.69 (s, 3H, OCH_3); 2.07 (m, 1H, *H* cyclopropane); 1.72 (s, 3H, CH_3 olefinic); 1.71 (s, 3H, CH_3 olefinic); 1.40 (d, 1H, *J*=5.4 Hz, $CH(CO_2Me)$); 1.28 (s, 3H, CH_3), 1.15 (s, 3H, CH_3); IR (film, KBr) 2952, 2926, 2881, 1730, 1440, 1411, 1379, 1322, 1285, 1235, 1198, 1165, 1142, 1117, 1083, 1065, 995, 919, 854, 782, 729 cm^{-1}. Spectral and analytical data are in agreement with the published data.[56]

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