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STEREOSELECTIVE SYNTHESIS OF METHYL (1R) TRANS- AND (1R) CIS-HEMICARONALDEHYDES FROM NATURAL TARTARIC ACID : APPLICATION TO THE SYNTHESIS OF S-BIOALLETHRIN AND DELTAMETHRIN INSECTICIDES §

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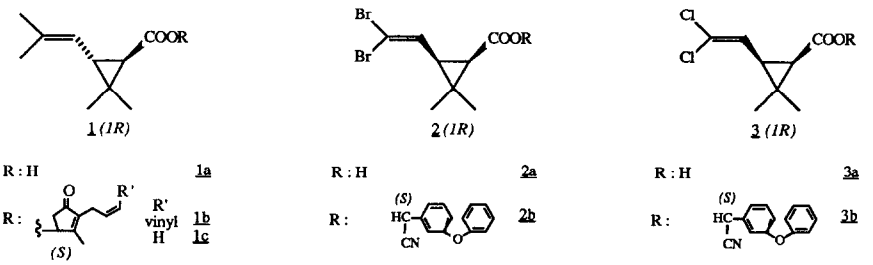
Very efficient enantioselective syntheses of (1R)-trans-and cis-hemicaronaldehydes precursors of (1R)-trans chrysanthemic acid and its (1R)-cis dibromovinyl analogue starting from natural tartaric acid or D-mannitol are described. They are based on the reaction between isopropylidenetriphenylphosphorane or isopropylidenediphenylsulfurane and chiral γ-alkoxy-α,β-unsaturated esters. The general problem of the diastereoselective addition to such esters is discussed.

Suitable esters of the trans-chrysanthemic acid 1a and of its dihalogeno-cis analogues 2a, 3a are potent insecticides, safe to mammals and biodegradable (Scheme 1). The higher biological activity and photostability of the esters 2b and 3b belonging to the unatural cis series has opened an important market in agriculture, the esters 1b, 1c derived from the natural trans series being mainly used for domestic purposes due to their valuable knock-down effect.

Although most of these pesticides are sold as a mixture of all possible stereoisomers, only the one possessing the 1R stereochemistry on the cyclopropane ring usually concentrates almost all the biological activity. Only in rare cases, such as these of S-bioallethrin 1c and deltamethrin 2b, the pure biologically active enantiomer is commercialized.

Scheme 1



1b : Pyrethrin I; 1c : S-Bioallethrin; 2b : Deltamethrin; 3b : Cypermethrin (sold as a mixture of isomers)

An increadibly large number of synthetic routes to chrysanthemic acid and analogues has been disclosed [1] often in the patent literature. Most of them lead to a cis-trans mixture of stereoisomers and only few syntheses of the biologically active enantiomers have been described. The later involve : **(i)** the transformation of chirons from the pool of chiral natural products,[2] **(ii)** asymmetric induction implying chiral inductors,[3] chiral catalysts [4] and enzymes,[5] but none of them are actually used for production in industry which prefers the separation of racemates.[1]

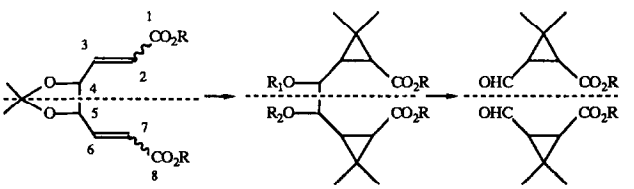
We have been involved in this field over the past fifteen years and have proposed original stereo and enantioselective syntheses of each of the two acids 1a and 2a. Most of our approaches involve the cyclopropanation of suitably functionalized α,β-unsaturated esters with reagents able to deliver an isopropylidene moiety. [2j,k,3b,f,g,6,7] Isopropylidenetriphenylphosphorane [2j,k,3b,f,g,6a-d] 4a and isopropylidenediphenylsulfurane [2k,3b,f,6e] 4b have been *inter alias* used for that purpose. The phosphorus ylide

§ Dedicated to Professor D. H. R. Barton on the occasion of his seventieth birthday.

[8a,b] offers the advantages **(i)** to be readily accessible from the corresponding phosphonium salt and n-BuLi in THF and **(ii)** to be stable for long periods of time at room temperature. The synthesis of the sulfur ylide [8a,c-f], under the conditions originally described [LDA, CH_2Cl_2, THF, -78°C] is more tedious and care must be taken since this organometallic decomposes at temperatures higher than -50°C.

In a preliminary study performed on dialkyl fumarates and maleates we found that isopropylidenetriphenylphosphorane 4a behaves differently from its sulfur analogue 4b. In the first case, the reaction proved completely stereoselective producing the corresponding trans-caronate whether the (E)-or the (Z)-olefinic compound is used,[3f,g,6b,c] whereas the second reaction is moderately stereospecific since it exclusively produces the trans-caronate from the fumarate [8d] but leads to a cis /trans (2/1) mixture of caronates when the maleate is instead used [8d]. We have also reacted [3b] both ylides with dimenthyl fumarate and found that whereas high diastereoselection can be observed with isopropylidenetriphenylphosphorane (de : 76 %), a very low one results from the reaction of its sulfur analogue. In the course of this study, we also reacted [3f,g] both ylides with 4 **(i)** menthyl 4-oxo-2(E)-butenoate, **(ii)** menthyl 4,4-dimethoxy-2(E)-butenoate, **(iii)** with the acetals derived from (2R,3R)-butanediol and methyl 4-oxo-2-butenoate and **(iv)** the oxazolidine derived from the same esters and ephedrine [3d,f,g] and observed depending upon the case a low to good diastereoselection.[3f,g] As a continuation of this work, we decided to perform the above mentioned cyclopropanation reaction on the di-unsaturated esters 5 (Scheme 2).

Scheme 2



5 R_1 R_2: $C(Me)_2$ 6 8

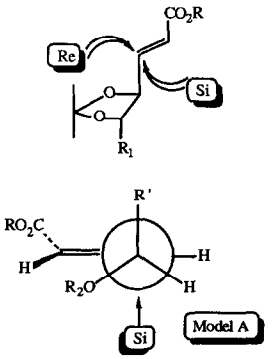
R_1, R_2: H 7

This yet unknown building block should possesses exceptional features due to the various functionalities present on each carbon and also to the chiral nature of some of its forms. It can be regarded as a masked 4-oxo-2-butenoate and possesses two asymmetric centers (C4 and C5) and two carbon-carbon double bonds which can have either the (Z)- or the (E)- stereochemistry. It can therefore exist as ten stereoisomers which include the meso derivatives (4S, 5R) with (2Z, 6Z) or (2E, 6E) C,C double bonds and the remarkable compounds which possess a C_2 axis of symmetry [(4R, 5R) derivatives with (2E, 6E) or (2Z, 6Z) stereochemistry and their (4S, 5S) enantiomers] which are susceptible to allow on further additions on the C,C bonds two consecutive asymmetric inductions leading to dicyclopropanes 6. Further hydrolysis of the dioxolane moiety and cleavage of the resulting diol 7 with sodium periodate would produce twice the corresponding hemicaronaldehyde 8. In the most favorable case, enantioselective (100 %) synthesis of 6 could be expected if the attack occurs twice from Re or from the Si faces of 5 (C_2 axis of symetry) whereas in the worst case a racemate could be produced if no facial differentiation or if complete facial differentiation working once from the Re and the other time from the Si face of 5 instead takes place. From the previous results [6c, 8d] the (E,E) diester 5a was expected to be the precursor of the trans-cyclopropane 6a whatever the phosphorus 4a or the sulfur ylide 4b is used whereas the (Z,Z) analogue 5b should produce the desired cis-cyclopropane derivative 6b but at the condition that isopropylidenediphenylsulfurane is used.[8d] At this stage, we had to decide which one of the (4R, 5R) or the (4S, 5S) stereoisomers would produce the (1R) trans-hemicaronaldehyde 8a and the (1R) cis-stereoisomer 8b precursors of the natural chrysanthemic acid [1,3b] 1a and of its dibromovinyl analogue 2a [1,3b] and therefore of the industrially important S-bioallethrin 1c and deltamethrin 2b respectively.[1]

Diasteroselective additions to allyl ethers and especially to γ-alkoxy α,β-unsaturated esters has been recently the subject of intensive work. [2h,j,k,3a,d,f,g,9] They have been used in various enantioselective syntheses, including the one of (1R) trans-chrysanthemic acid which has been achieved[2h] from the γ-alcoxy-α,β-unsaturated ester 9a derived from D-glyceraldehyde and isopropylidenetriphenylphosphorane (Scheme 3). Thus if, we could reasonably expect from the above work [2h] that (1R) trans-chrysanthemic acid 1a would be available from the (E,E) diester 5a possessing (4S, 5S) stereochemistry and 4a,we were suspicious to extend

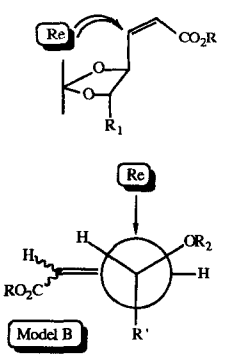
the prediction to the case of isopropylidenediphenylsulfurane 4b and the (Z,Z) diester 5b. In fact, some reagents such as 1-acetoxy-2-(trimethylsilyl)methyl-2-propene,[9c] cyclopentadiene [9d] and amines [9b] are known to lead to adducts whose stereochemistry at the β carbon is exclusively related to the one of the γ carbon on the starting γ-alkoxy-α,β-unsaturated ester (attack from the Re face on the ester possessing the (4S) stereochemistry). Osmium tetroxide [9f] and organocopper-boron trifluoride complexes [9g] behave differently since these reagents approach by the same face as above the (Z) unsaturated esters (attack from the Re face on the ester possessing the (4S) stereochemistry) but on the opposite face of its (E) stereoisomer (attack from the Si face). The former results have been rationalized by Trost [9c] who assumed that the favored approach of the reagent must take place from the less hindered side of the starting unsaturated ester adopting the conformation shown on the model B whatever is the stereochemistry of its C,C bond. A different explanation has been given by Stork [9f] for the last series of results. He suggested that the conformation shown on the model A, which results from a favorable interaction between the p orbitals of the double bond and an unshared pair of the γ oxygen is operative in the (E) series of compounds. This conformation could not be attained due to repulsive interactions in the (Z) series which now adopt the conformation shown in the model B.

Scheme 3



	OsO_4	$RCuBF_3$	$Ph_3P{=}CMe_2$
Si face de:	(E,100)	(E,38)	(E,82)
Re face de:	(Z,100)	(Z,56)	(Z,96)

	TMS, OAc		RNH_2,	$Ph_2S{=}CMe_2$
Re face de:	(E,52)	(E,20)	(E,100)	(E,98)
Re face de:	(Z,98)	(Z,70)	(Z,100)	(Z,96)

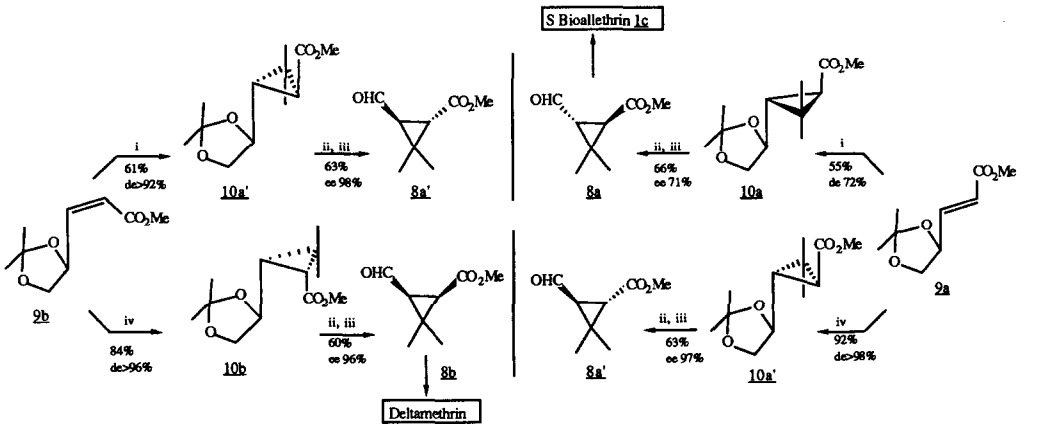


On the basis of the results discussed above, it seems reeasonable to predict that (Z) α,β-unsaturated esters will produce whatever the reagent used the compound resulting from the attack shown on the model B. We suspected that the phosphorous ylide 4a would approach the (Z) α,β-unsaturated ester 9b derived from D-glyceraldehyde from the Re face and therefore that *a reversed asymmetric* induction as the one observed by Mulzer [2h] on the (E) isomer 9a would take place. However, no prediction could reasonably be made for the reaction involving the closely related sulfur ylide 4b and the ester 9a. We therefore decided to study as a model the reaction of isopropylidenetriphenylphosphorane 4a on the (Z)-ester 9b derived from D glyceraldehyde [16a,17] and the one of isopropylidenediphenylsulfurane 4b on both the (E) and (Z)-unsaturated esters [9a,13] 9a and 9b. In a standardized procedure we have performed the reaction with 4a (THF, 0°C, 1h then 20°C, 1h) and 4b (DME, - 78°C, 0,2h, -78°C to 20°C, 1h) prepared respectively from isopropyltriphenylphosphonium iodide and n-BuLi in tetrahydrofurane (THF) [8b,6a,b] and from isopropyldiphenylsulfonium tetrafluoroborate, lithium diisopropylamide (LDA) and methylenedichloride in dimethoxyethane (DME).[8d,f] After completion of the reactions and hydrolysis, the crude mixtures have been analyzed by gas chromatography on capillary column and the ratio of the different diasterostereoisomers 10 has been determined. The mixture of diasteroisomers 10 has been freed from triphenylphosphine (preparative layer chromatograhy on SiO_2, PLC) and directly transformed to the corresponding hemicaronaldehydes 8 on sequential treatment with an aqueous solution of perchloric acid (2N, 20°C, 6h, leading to the diols) and sodium periodate (1.5 equiv., MeOH, phosphate buffer pH 7.2, 20°C, 1h) whose enantiomeric purity has been determined at this stage after PLC purification of the resulting mixture and comparison to authentic samples of (1R) trans- 8a and cis- 8b hemicaronaldehydes obtained by ozonolysis of methyl (1R) trans- and cis-chrysanthemates kindly provided by the Roussel Uclaf Company.[10]

We found that whereas the (1R) trans-hemicaronaldehyde 8a is mainly produced (55 x 66% yield, 8a/ 8a' = 86/14, 72% ee) as already described by Mulzer [2h] from the phosphorane 4a and the (E) unsaturated ester 9a, its (1S) trans-enantiomer 8a' (61 x 63% yield, 8a'/8a : 99/1, 98% ee) is almost exclusively formed from the

(Z)-unsaturated ester 9b (Scheme 4). Furthermore the (1S) trans-hemicaronaldehyde 8a' (92 x 63% yield, 8a' / 8a : 99/1, 98% ee) and the (1R) cis- hemicaronaldehyde 8b (84 x 60 % yield , 8b / 8b' : 98/2, ee : 96) are quite exclusively produced if the sulfurane 4b is instead reacted on 9a and 9b respectively (Scheme 4). Clearly the two reagents behave differently although they belong to the same family. Thus the sulfurane 4b reacts on the Re face of the unsaturated esters 9a and 9b derived from D-glyceraldehyde wathever the stereochemistry of the C,C double bond whereas the phosphorane 4a attacks the Re face of the (Z) isomer 9b and the Si face of its (E)-isomer 9a. It must be also pointed out that the cyclopropanation reaction involving the sulfur ylide is completely stereospecific (100 %) under the described conditions since the trans- and the cis-cyclopropane are formed from the (E)- and (Z)-olefin respectively whereas the one implying the phosphorane is completely stereoselective (100 %) since the trans-cyclopropane derivative is produced whether the (E)- or the (Z)-olefin is used.

Scheme 4



(i) 1.5 equiv. $Ph_3P{=}C(Me)_2$, LiI, THF, 0°C, 1h then 20°C, 1 h - (ii) 4 equiv. 2N aq. $HClO_4$, THF, 20°C, 6h - (iii) 1.5 equiv. $NaIO_4$, MeOH, Phosphate buffer pH 7.2, 20°C, 1h. (iv) 1.5 equiv. $Ph_2S{=}C(Me)_2$, DME, -78°C, 0.2 h then -78°C to -50°C, 0.7 h then -50°C to 20°C, 0.3 h.

The above experiments therefore allow the stereoselective formation of three of the four possible stereoisomers of hemicaronaldehydes 8 from D-glyceraldehyde. Furthermore, our results put some light on the intimate mechanism of the reaction of phosphorus ylides with (Z)-α,β-unsaturated esters. They unambigously show that it does not involve the prior (Z) to (E) isomerization of the C,C double bond of the enoate (which would have produced 8a instead of 8a'). Therefore, although the reaction is not concerted, the betaine is not in equilibrium with the starting material. Since (1R) trans-chrysanthemic acid 1a and its (1R) cis-dibromovinyl analogue 2a have been already stereoselectively (100 %) obtained from (1R) trans-8a and (1R) cis-8b hemicaronaldehyde [1,3b] respectively, the synthesis of the precursor of S-bioalletrhin 1c involves the D-glyceraldehyde and isopropylidenetriphenylphosphorane as already described by Mulzer, whereas deltamethrin 2b is available from the same aldehyde and isopropylidenediphenylsulfurane (Scheme 4).

Although the later transformation allows the straightforward synthesis of this particularly valuable industrial insecticide in high yield and with very high stereo- and enantioselection, it however implies the generation of the unstable isopropylidenediphenylsulfurane via a particularly lengthy procedure from isopropyl diphenylsulfonium tetrafluoroborate and dichloromethyllithium [8f] in a sequence of reactions which involve **(i)** the generation of lithium diisopropylamide from n-butyllithium and diisopropylamine and **(ii)** the metallation of dichloromethane by the resulting base. Therefore alternative syntheses of this ylide were welcomed. A simpler procedure would have involved the direct metallation of the sulfonium salt with n-butyllithium. This is not suitable since it is expected [8a,c-f] to produce appreciable amounts of butylideneisopropylphenylsulfurane which would result from **(i)** an initial attack of the reagent on the sulfur atom, **(ii)** decomposition of the σ sulfurane to butylisopropylphenylsulfonium salt and phenyllithium and **(iii)** further metallation of this salt by phenyllithium.

Use of phenyllithium in place of butyllithium should preclude the above problems since the σ sulfurane is expected to be in equilibrium with the starting materials and therefore would produce at the end the desired ylide

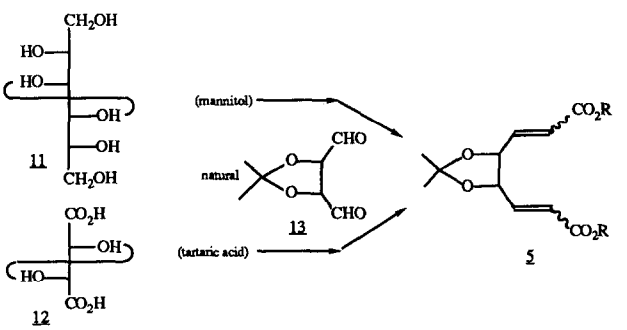
4b. In fact, phenyllithium has been once used [11] for the synthesis of isopropylidenediphenylsulfurane which was then used for the synthesis of the labelled 3T-2,3-oxidosqualene. Thus, we have reacted isopropylidenediphenylsulfurane generated from the corresponding sulfonium salt and phenyllithium in THF with the (Z) and (E) unsaturated esters 9b and 9a and found that it produces results qualitatively similar to those we reported above but in slightly lower yield (75 % yield of 10a' from 9a and 71 % yield of 10b from 9b).

An even more interesting procedure involves the in situ generation of the ylide by addition of potassium tert-butoxide on the mixture of isopropyl diphenylsulfonium tetrafluoroborate and of the unsaturated ester 9. A related procedure has been already used for the synthesis of sulfur ylides from trimethylsulfonium iodide, [8a-c,g,h] n-alkyl-diphenylsulfonium salts [8a,c,g,h] and cyclopropyldiphenylsulfonium fluoroborate [8c,i]. It has been however reported to be unsuitable [11b] for isopropyl diphenylsulfonium tetrafluoroborate. Nevertheless we have reacted potassium tert-butoxide (1.5 equiv.) on a mixture of this salt and methyl hexene-2-oate (1.5M in THF, -78°C). We did not obtain the corresponding cyclopropyl ester but we instead isolated methyl 2-isopropyl-hex-3-enoate in 28 % yield resulting from the metallation of the unsaturated ester followed by alkylation of the resulting enolate by the sulfonium salt [12].

Despite this discouraging results, we performed the same reaction with the γ-alkoxy-α,β-unsaturated ester 9b , the precursor of deltamethrin 2b, expecting that the alkoxy moiety would lower its aptitude to be metallated. We were able, to our delight, to obtain the desired cis- cyclopropyl ester 10b in reasonable yield (77 %) and with almost quantitative diastereoselection (de 98%) when the reaction is carried out at -78°C. At higher temperature the yield of 10b dramatically decreases at the expense of products resulting probably from a competing metallation reaction (35 % of 10b, when performed at -20°C, rapid addition). In these cases, a slighly better yield of 10b is observed if the tert-BuOK is added very slowly to the medium. Surprisingly the (E) unsaturated ester 9a does not produce a cyclopropyl ester 10 under these conditions. All other conditions proved unsuccessful not only with the (E) ester 9a but also with its (Z) stereoisomer 9b. For example, addition of 9b to a preformed solution of the ylide 4b (from the sulfonium salt and tert-BuOK) maintained at -78°C does not produce the cyclopropyl ester 10b in good yield due to the rapid decomposition of 4b. This decomposition is already very important after 0.2 h and almost complete if the ylide solution is stirred for 0.5 h at -78°C prior to additon of 9b. The clearcut difference of stability of the species obtained from the sulfonium salt and the lithium and potassium containing bases suggests that 4b must be viewed as an α-heterosubstituted organometallic rather than as a π- sulfurane.

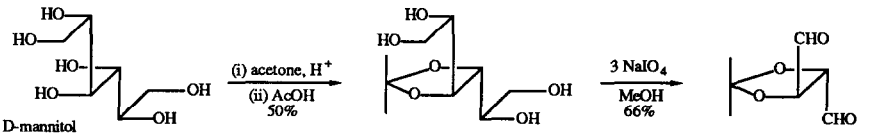
With all these informations in hand, we then studied the more complex case of the di-unsaturated esters 5. From the previous results, the (1R) trans-chrysanthemic acid 1a is expected to be produced from isopropylidenetriphenylphosphorane 4a and the (2E, 6E) - (4S, 5S) di-unsaturated ester 5a or from isopropylidenediphenylsulfurane 4b and its (2E, 6E) - (4R, 5R) stereoisomer 5a' whereas the synthesis of deltamethrin 2b should involve the sulfur ylide 4b and the (2Z, 6Z) - (4S, 5S) stereoisomer 5b. These yet unknown chiral building blocks were expected to be produced from 2,3-isopropylidene tartraldehydes 13 and Wittig ($Ph_3P{=}CHCO_2Me$, MeOH) or Wittig-Horner [$(EtO)_2P(O)CHNaCO_2Me$, DME) reagents which are known to allow the stereoselective synthesis of the (Z) and (E) unsaturated esters respectively from aldehydes [9a,13] Moreover, the 2, 3-isopropylidene tartraldehydes 13 should be, in principle, easily derived from natural products, D-mannitol 11 or tataric acid 12 (Scheme 5).

Scheme 5



Surprisingly, 2,3-isopropylidene tartraldehydes 13 were quite unknown when we started this work. The (2S, 3S) stereoisomer however had been transiently obtained by Fisher [14] during the assignement of the stereochemistry of D-mannitol 11 and was immediately reduced to the corresponding diol. We readily achieved the synthesis of this dialdehyde from the tetrol 14 [14] derived from D-mannitol 11 and sodium periodate (3 equiv., MeOH, phosphate buffer pH 7.2, 0°C, 0.5 h, 66 % yield) [15] (Scheme 6) but its isolation from the reaction medium was extremely difficult due to its exceedingly high solubility in hydroxylic solvents (especially water) in which it forms at least in part hemiacetals or hydrates. Moreover, although D-mannitol is readily available and cheap, its L-enantiomer, the expected precursors of the (4S, 5S) stereoisomers 5a and 5b, is very expensive.

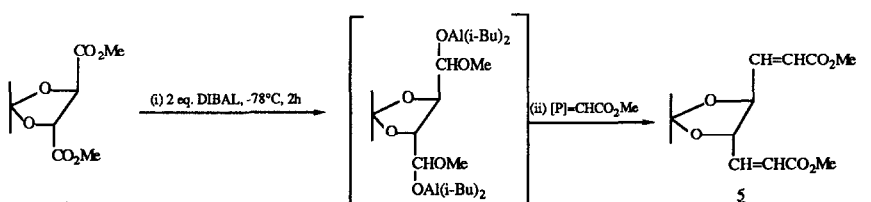
Scheme 6



11 14 13

Tartaric acid was the next potential precursor we chose. It is commercially available [16a] both as the (R, R) 12 and as the (S, S) 12' forms which are both cheap and are therefore expected to be precursors of each of the desired diesters 5a, 5b and 5a', 5b'. Surprisingly, although tartaric acid has been already transformed to valuable ligands [16b-e] and building blocks, [16a,f-m] it has never been reduced to our knowledge to the desired dialdehyde 13. We found that this reduction can be readily achieved by reaction of dimethyl 2,3-O-isopropylidene tartrate 15 [17] with diisobutyl aluminium hydride (2 equiv., 1.5 N toluene, solution, -78°C, 2h). Again, the separation of the reduced compound from the inorganic salts required tedious manipulations. These can be however avoided since we found (Scheme 7) that the Wittig and Wittig Horner reactions can be directly performed on the dialuminate 16 [2.5 equiv. Ph_3PCHCO_2Me, MeOH, -78°C, 20°C, 3h, 83 % yield as 1/30/19 mixture of (E,E) / (Z,Z) / (E,Z) stereoisomers or 2.5 equiv. $(EtO)_2P(O)CH(Na)CO_2Me$, DME, -78°C, 0.1h then 20°C, 4 h, 60 % yield as a 96/4 mixture of the (E,E) / (E,Z) stereoisomers] and produce respectively after purification by preparative layer chromatography the (2Z, 6Z) - (4S, 5S) stereoisomer 5b in 55 % overall yield and the (2E, 6E) - (4S, 5S) stereoisomer 5a in 51 % overall yield from dimethyl (2R, 3R)-O-isopropylidene tartrate 15 (Scheme 7). These transformations are remarkable since they involve each a four steps one pot process, each step occurring in more than 80 % yield. It is by far more efficient that the two pots sequence which requires the isolation of the dialdehyde 13 derived from mannitol and its further reaction with sodio carbomethoxy methyl diethylphosphonate (2.2 equiv., DME, 22 % overall yield in the (2E, 6E) - (4R, 5R) stereoisomer 5a' containing 8 % of its (E, Z) stereoisomer).

Scheme 7



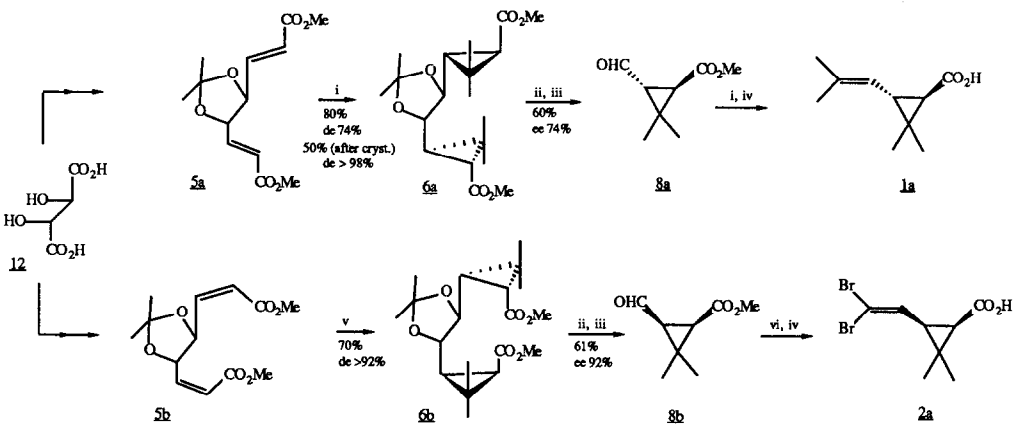
15 16 5

		E, E	Z, Z	Z, E
2.5 eq. $(EtO)_2P(O)CH(Na)CO_2Me$/DME -78°C, 0.1h; 20°C, 4h	60%	96		4
2.5 eq. Ph_3PCHCO_2Me/MeOH -78°C to 20°C, 3h	83%	2	60	38

The cyclopropanation of the (E, E) isomer 5a derived from (2R, 3R) tartaric acid 12 with isopropylidene-triphenylphosphorane (2.5 equiv. from isopropyl triphenylphosphonium iodide and n-BuLi, 0°C; then addition of 5a and reaction at 0°C for 1h., then at 20°C for 1h.) leads to a 87/13 mixture of the trans trans 6a/6a'

stereoisomers from which the major one 6a (mp 127°C, cyclohexane) is isolated in 50 % overall yield after one crystallization [15] (Scheme 8). The experimental conditions described above for the cyclopropanation reaction are crucial for its success since for example a mixture of monoadducts and diadducts in which the 6a/6a' ratio decreases, is produced if the cyclopropanation reaction is carried out between -78°C and 20°C instead of between 0°C and 20°C.

Scheme 8



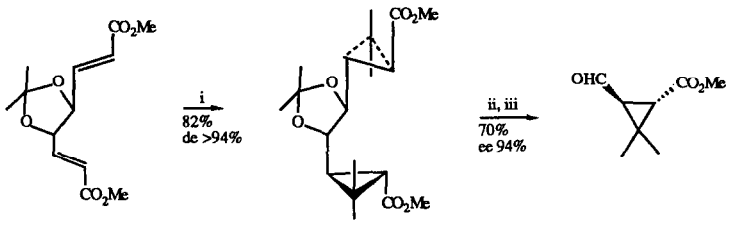
(i) 2.5 equiv. $Ph_3P{=}C(Me)_2$, LiI, THF, 0°C, 1h then 20°C, 1h - (ii) 4 equiv. 2N aq. $HClO_4$, THF, 20°C, 6h - (iii) 1.5 equiv. $NaIO_4$, MeOH, Phosphate buffer pH 7.2, 20°C, 1h - (iv) KOH, MeOH then aq. HCl - (v) 2.5 equiv. $Ph_2S{=}C(Me)_2$, DME, -78°C, 0.2h. then -78°C to -50°C, 0.7h. then -50°C to 20°C, 0.3h. - (vi) CBr_4, PPh_3.

On the other part, the (2Z, 6Z) - (4S, 5S) stereoisomer 5b was reacted with isopropylidenediphenylsulfurane (3 equiv. of isopropyldiphenylsulfonium fluoroborate and 3 equiv. LDA and CH_2Cl_2 in DME, -78°C, then addition of 5b, and reaction in the following conditions : -78°C, 0.3 h, then -50°C, 0.7 h, then -50°C to 20°C or from 3 equiv. of isopropyl diphenylsulfonium fluoroborate, 2.8 equiv. PhLi, -78°C, 0.5 h, then addition of 5b, and same conditions as above) and delivers the cis,cis-diadduct 6b in good yield (70 % and 60 % respectively) with very high diastereoselection (de > 92 %) (Scheme 8). The compound 6b is the precursor of (1R) cis- dibromovinyl chrysanthemic acid and of deltamethrin. The cyclopropanation reaction of this (Z, Z) diester was also carried out by *in situ* generation of the isopropylidenediphenylsulfurane. Thus addition of tert-BuOK (3 mmol.) on the mixture of 5b (1 mmol.) and the sulfonium salt (3 mmol.) (THF, -78°C, 2h) leads to a mixture of the diadduct 6b and of a monocyclopropane 18 in the 1/1 ratio. Use of a larger excess of the reagents (sulfonium salt and ter-BuOK : 4 mmol.) gives a 8/2 mixture of 6b/21 from which 6b can be separated by PLC (6b, 60 % yield, 21 15% yield). It is produced with very high asymmetric induction (de : 96 %). Clearly the monoadduct is far less reactive than the starting material.

Both the trans, trans 6a and the cis, cis 6b diadducts have been successfully transformed to (1R) -trans- and (1R) -cis- hemicaronaldehyde 8a and 8b precursors of S-Bioallethrin and deltamethrin using the conditions already described for 10 (2N aq.$HClO_4$, THF, 20°C, 6h, diols 7a or 7b, 98 % yield; 1.5 equiv. $NaIO_4$, MeOH, phosphate buffer pH 7.2, 20°C, 1h, 8a, 68 % yield, ee : 98 %, 8b, 63 % yield; ee : 92 %) respectively from the reaction involving phosphorus ylide after crystallisation of 6a from the diastereoisomeric mixture (see above) and from the reaction involving the sulfur ylide.

During this work, we have also reacted isopropylidenediphenylsulfurane with the (E,E) diester 5a and isopropylidenetriphenylphosphorane with the (Z,Z) diester 5b. The first reaction proceeds as expected from the corresponding model involving ester 9a and leads to the trans, trans diadduct 6a' in very good yield (82 %) and with almost complete diastereoselection (de : 94 % 6a'/6a : 97/3) whether the ylide is generated from dichlormethyl- or from phenyllithium (Scheme 9). However, as already mentioned, from 9a the cyclopropanation reaction does not occur on 5a if the ylide is prepared in situ using potassium tert-butoxide as the base.

Scheme 9

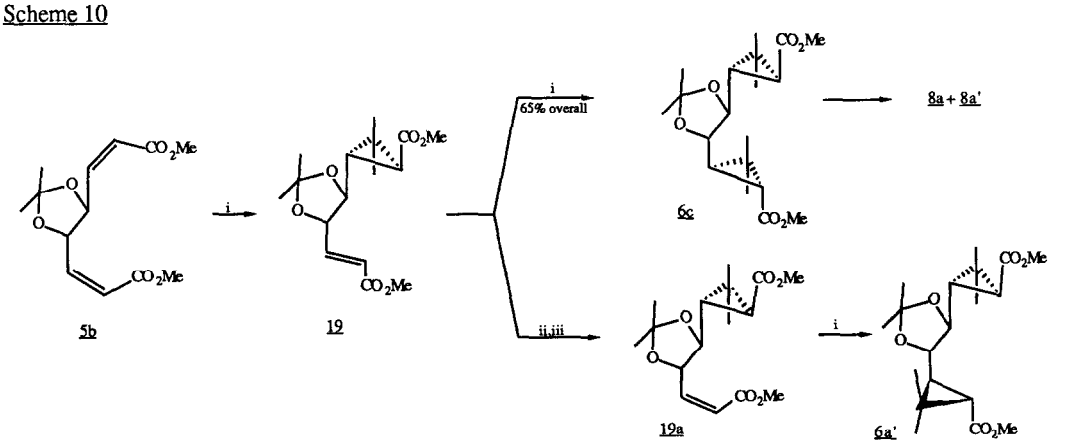


5a 6a' 8a'

(i) 2.5 equiv. $Ph_2S{=}C(Me)_2$, DME, -78°C, 0.2h then -78°C to -50°C, 0.7h then -50°C to 20°C, 0.3h - (ii) 4 equiv. 2N aq.$HClO_4$, THF, 20°C, 6h. - (iii) 1.5 equiv. $NaIO_4$, MeOH, Phosphate buffer pH 7.2, 20°C, 1h.

The reaction of the (Z,Z) stereoisomer 5b with isopropylidenetriphenylphosphorane gave an unexpected result since the diadduct 6c, produced in 65 % yield led to trans hemicaronaldehyde 8 whose composition is close to a racemate. Therefore, two asymmetric inductions working in opposite directions are operative. From our previous results involving 9b and 9a we assumed that a (Z) to (E) isomerisation leading to 19 has taken place. We proved that it is indeed the case. Thus, we performed the reaction between 5b and only one equivalent of 4a. We obtained besides the unreacted starting material 5b and the diadduct 6c the monoadduct 19 possessing the (1S,3S) cis- cyclopropyl ester moiety but an (E) instead of (Z) stereochemistry (5b/19/6c ratio = 1/1/1). We have transformed this monoadduct to its (Z) stereoisomer 19a by a sequence of reactions involving (i) ozonolysis of the reaction mixture containing the monoadduct 19, (ii) reaction of the resulting aldehyde 20 with methyl triphenylphosphoranilidene acetate yielding a mixture of 19a and 19 in the 67/33 ratio, (iii) difficult fractionnation of these mixture to afford relatively pure 19a (19a/19 : 9/1). The monoadduct 19a submitted to the sequence of reaction described in scheme 10 led to (1S, 3S) -trans hemicaronaldehyde 8a'. This observation led us to assume that the isomerisation has taken place via an unknown mechanism on the betaine resulting from the first addition of the ylide on 5b and not on the starting material 5b (which was recovered unchanged in the experiment previously described) nor on the monoadduct 19a on which, as we have proved, cyclopropanation occurs from the Re face.

Scheme 10



5b 19

(i) $Ph_3P{=}C(Me)_2$, LiI, THF, 0°C, 1h then 20°C, 1h - (ii) O_3, CH_2Cl_2, -78°C then Me_2S, -78°C to +20°C - (iii) Ph_3PCHCO_2Me, MeOH, 0°C, 2h then 20°C 1h

In conclusion, the transformations we have described can be efficiently used for the enantioselective synthesis of (1R) -trans chrysanthemic acid and its (1R)-cis dibromovinyl analogue from natural tartaric acid. The last sequence is particularly valuable since not only it can be performed from cheap and readily available

isopropyl diphenylsulfonium fluoroborate [18] and potassium tert-butoxide but also since fair amount of deltametrin (70 g) can be formally produced [19] from 1 mole (150 g) of tartaric acid.

We have also found that both ylides 4a and 4b behave similarly on the (Z) α,β-unsaturated esters but differently on the (E) stereoisomer. As it has been discussed, the reaction involving various reagents and γ-alkoxy α,β-unsaturated ester still remains unpredictable and therefore much experimental and theoretical work is required before it can be properly understood and predicted. We are currently working on this problem.

Experimental

General : ^1H NMR spectra have been measured in CCl_4 with TMS as an internal standard (δ : 0.00) on JEOL JNM60 Si (60 MHz) and FX 90Q (90 MHz) spectrometers. IR spectra reported in cm^{-1} were performed on neat liquids (unless otherwise stated) using a Perkin-Elmer model 337 spectrophotometer. Mass spectra were obtained on a HP 5995A GC/MS spectrometer. In the discussion M refers to $M^{+\cdot}$. Optical rotatory powers were measured on a Perkin-Elmer 241 MC polarimeter in the ORSY laboratory (UCL, Louvain-la-Neuve), the concentration being expressed as c : mg / ml. | GC^2| were recorded on a HP 5890 chromatograph using a capillary SE30 column (l 25 m, Ø 0.2 mm) in the following standard conditions : T detector : 250°C, T injector : 250°C, He pressure : 1.6 kg/cm^2). The oven temperatures were respectively : 1) conditions A : 140°C for 10 min then heating to 220°C with a temperature increase of 10°C/min; 2) conditions B : heating from 180°C to 220°C with a temperature increase of 10°C/min, then 220°C for 20 min; 3) conditions C : heating from 100°C to 220°C with a temperature increase of 10°C min. In all the cases of reactions implying asymetric induction, the purified products were compared to the crude mixture by |GC^2| (in some cases by |GC^2|-MS in order to ensure that the purification method was not responsible for a significant modification of the diastereoisomers composition. Layer chromatography : Analytical thin-layer chromatography (TLC) was performed on premade, glass-backed plate SiO_2, $60PF_{254}$, 250 microns (Merck 5719). Compounds were visualized by UV illumination and by heating to 150°C after spraying phosphomolybdic acid in ethanol. Preparative layer chromatography (PLC) was performed on SiO_2 plates prepared from silica gel, 60 PF_{254} (Merck 7747).

Synthesis of methyl (E)-(S)-4,5-O-isopropylidene-pent-2-enoate 9a. To 0.3g of sodium hydride (80 % in mineral oil) in anhydrous DME (5 ml) were added, at 0°C, 2.1 g (10 mmol) of methyl diethylphosphonoacetate in DME (15 ml) and the mixture was stirred for 0.5 h at 20°C. The resulting solution was cooled at -78°C and 0.95 g (7.3 mmol) of (R)-2,3-O-isopropylidene glyceraldehyde [9a] in DME (5 ml) were slowly added and the mixture was stirred for 1 h while heating from -78°C to 20°C. Water (5 ml) was then added. The mixture was extracted with ether (3x50 ml) and the organic layers were combined, washed with water (2x5 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vacuo afforded 1.25 g of crude mixture which was fractionnated by column chromatography on silicagel (eluent : pentane/ether : 8/2) to give 0.84 g of the (E) αβ unsaturated ester 9a (64 % yield) and 0.02 g of the (Z) isomer 9b (1.5 % yield). The analytical data for compound 9a are in agreement with the data of the literature [2h] : Tlc, Rf 0.3 (ether/pentane, 8/2). $[\alpha]^{20}_D$ + 44.3° (c : 13.7, $CHCl_3$). ^1H NMR δ : 1.33 and 1.38 (2s, 6H, $(CH_3)_2C$), 3.5 (d.d with s at 3.7, 4H, CO_2CH_3 and one H of CH_2O), 4.07 (dd, 1H, one H of CH_2O), 4.55 (m, 1H, CHO), 5.95 (dd, 1H, $=CH_A\text{-}CO_2CH_3$, J_{AB} : 16 Hz), 6.75 (dd, 1H, $CH\text{-}CH_B=$, J_{BA} = 16 Hz). IR : 1728 ($\nu_{C=O}$), 1663 cm^{-1} ($\nu_{C=C}$)

Synthesis of methyl (Z)-(S)-4,5-O-isopropylidene-pent-2-enoate 9b. To a solution of 0.95 g (7.3 mmol) of (R)-2,3-O-isopropylidene glyceraldehyde in anhydrous methanol (20 ml), was rapidly added , at 0°C, 3.34 g (10 mmol) of methyl triphenylphosphoranilidene acetate. The mixture was stirred for 3h at 0°C then hydrolyzed (5 ml of water). The methanol was evaporated under vaccuo and the resulting mixture was extracted with ether (3x50 ml). The organic layers were combined , washed with water (2x5 ml) and dried over magnesium sulfate. After filtration and removal of the solvents under vaccuo, the mixture was stirred with pentane (30 ml) and the triphenylphosphine oxide was filtered off. The filtrate was concentrated under vaccuo affording 1.15g of crude mixture which was fractionnated by column chromatography on silicagel (eluent : pentane/ether : 8/2) to give 0.95 g of the (Z) αβ unsaturated ester 9b (73 % yield) and 0.1 g of the (E) isomer 9a (8 % yield). The analytical data for compound 9b are in agreement with the data of the litterature [13b]: Tlc, Rf 0.5 (ether/pentane, 8/2). $[\alpha]^{20}_D$ +127.25° (c : 13.5, $CHCl_3$). ^1H NMR δ : 1.30 and 1.35(2s, 6H, $(CH_3)_2$ C), 3.45 (dd, 1H, one H of CH_2O), 3.65 (s, 3H, CO_2CH_3), 4.25 (dd, 1H, one H of CH_2O), 5.30 (m, 1H, CHO), 5.7 (dd, 1H, $=CH_A\text{-}CO_2CH_3$) J_{AB} : 12 Hz), 6.30 (dd, 1H, $CH\text{-}CH_B=$ J_{BA} : 12 Hz). IR : 1723 ($\nu_{C=O}$), 1645 cm^{-1} ($\nu_{C=C}$).

Synthesis of (E,E)-(4S,5S)-α,β-unsaturated diester 5a. To a cooled (-78°C) solution of 4.36 g (20 mmol) of dimethyl-2,3-O-isopropylidene-(2R,3R)-(-)-tartrate 15 (prepared according to known procedure [17] from natural (2R,3R)-(+)-tartaric acid) in anhydrous toluene (60 ml) was added diisobutylaluminum hydride (40.10^{-3} m, 27 ml of a 1.5 M solution in toluene). The mixture was stirred for 2 h at -78°C. Then, was added at -78°C a solution of sodio methyl diethylphosphonacetate (obtained by adding, at 0°C, 10.5 g (50 mmol) of methyl diethylphosphonoacetate in anhydrous DME (50 ml) to 1.6 g of sodium hydride (80 % in mineral oil) suspended in anhydrous DME (20 ml) and stirring the mixture for 0.25 h at 20°C). The cooling bath was removed after 0.1 h and the resulting mixture stirred for 4 h. Water (50 ml) was then added and the mixture was poured into ether (0.5 l). The organic layer was separated, washed with water (4x50 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo afforded 4.8 g of crude mixture which was fractionnated by column chromotography on silicagel (eluent :

hexane/ethyl acetate : 9/1) to give 2.8 g of a mixture of the (E,E) 5a and (Z,E) 5c diesters in the 96/4 ratio (determined by IGCI[2] analysis) (51 % yield). Analytical data for the (E,E) diester 5a : Tlc, Rf 0.5 (ether/pentane : 3/7). IGCI[2], conditions B, RT : 4.8 min. $[\alpha]^{20}_D$ -70.2 (c : 6, $CHCl_3$). ^1H NMR δ : 1.45 (s.6H, $(CH_3)_2C$), 3.70 (s, 6H, CO_2CH_3), 4.15-4.30 (m, 2H, CHO), 6.03 (d, 2H, $=CH_ACO_2CH_3$, J_{AB} : 15 Hz), 6.55-6.75 and 6.85-7.00 (2m, 2H, $CH\text{-}CH_B=$). IR : 1720 ($\nu_{C=O}$), 1660 cm^1 ($\nu_{C=C}$). IGCI[2] MS : m/e 255 ($M\text{-}CH_3$). Anal. Calcd. for $C_{13}H_{17}O_6$: C, 57.80; H, 6.70. Found : C, 57,81 ; H, 6.67.

Synthesis of (Z,Z)-(4S,5S) and (Z,E)-(4S,5S)-α,β-unsaturated diesters 5b and 5c. To a cooled solution of 2.18 g (10 mmol) of dimethyl-2,3-O-isopropylidene-(2R,3R)-(-) tartrate 15 in anhydrous toluene (50 ml) was added diisobutylaluminum hydride (20.10^{-3} m, 13.5 ml of a 1.5 M solution in toluene). The mixture was stirred from 2 h at -78°C. Then, was added a solution of 8.35 g (25 mmol) of methyl triphenylphosphoranilidene acetate in anhydrous methanol (150 ml). The cooling bath was removed after 0.1 h and the resulting mixture stirred for 3 h, then hydrolyzed (50 ml of water). The methanol was evaporated under vaccuo and the resulting mixture was extracted with ether (3x100 ml). The organic layers were combined, washed with water (2x50 ml) and dried over magnesium sulfate. After filtration and removal of the solvents under vaccuo, the mixture was stirred with pentane (200 ml) and the triphenylphosphine oxide was filtered off affording 2.5 g of crude mixture which was fractionnated by column chromatography on silicagel (eluent : pentane/ether : 7/3) to give 1.5 g pure (Z,Z) αβ unsaturated diester 5b (55 % yield) and 1.03 g of a mixture of the (Z,E) and (E,E) isomers 5c and 5a in the 90/10 ratio (38 % yield). Analytical data for the (Z,Z) diester 5b : Tlc, Rf 0.55 (ether/pentane : 7/3). IGCI[2], conditions B, 3.7 min. $[\alpha]^{20}_D$ +307.7 (c : 12, $CHCl_3$). Mp : 51-52°C. ^1H NMR δ : 1.45 (s, 6H, $(CH_3)_2C$), 3.60 (s, 6H, CO_2CH_3), 5.30 (dd, 2H, CHO), 5.75 (d, 2H, $=CH_ACO_2CH_3$, J_{AB} : 12 Hz), 6.25 (ddd, 2H, $CH\text{-}CH_B=$, J_{BA} : 12 Hz). Calcd. for $C_{13}H_{18}O_6$: C, 57.80; H, 6.70. Found : C, 57.95; H, 6.70. Characteristics of the mixture of (Z,E) and (E,E) isomers 5c and 5a. Tlc, one spot, Rf 0.43 (ether/pentane : 3/7).IGCI[2], conditions B, RT for the (Z,E) isomer 5c 4.2 min and for the (E,E) isomer 5a, 4.7 min. $[\alpha]^{20}_D$ + 57.7 (c : 12,2, $CHCl_3$). ^1H NMR of the major compound 5c, δ : 1.50 (s, 6H, $(CH_3)_2C$), 3.75 (s, 6H, CO_2CH_3), 4.0-4.35 (m, 1H, CH_3O next to the E C=C bond), 5.30 (C, 1H, CHO next to the Z C=C bond), 5.75-6.40 (m, 3H , (E)- $R(H_1)C=C(H_2)CO_2CH_3$ and (Z)-$R(H_5)C=C(H_6)CO_2CH_3$), 6.90 (dd, 1H, (E)-$R(H_1)C=C(H_2)CO_2CH_3$, $J_{1,2}$: 16 Hz, $J_{1,3}$: 5 Hz). IR : 1731 ($\nu_{C=O}$), 1662 cm^{-1} ($\nu_{C=C}$) IGCI[2] MS : m/e 255 ($M\text{-}CH_3$) on both peaks (RT 4.2 and 4.7 min). Anal. Calcd. for $C_{13}H_{18}O_6$: C, 57.80; H, 6.70. Found : C, 57.92; H, 6.65.

Synthesis of (E,E)-(4R,5R)-α,β-unsaturated ester 5a' from 3,4-O-isopropylidene-D-Mannitol 14. (a) To a solution of 1g (4.5 mmol) of 3,4-O-isopropylidene-D-Mannitol 14 (prepared according to known procedures) [17b-d] in methanol (75 ml) and phosphate buffer (pH 7.13, 75 ml), was added, at 0°C, in small portions, 2.9 g (13.5 mmol) of sodium periodate. The mixture was then stirred for 0.5 h at 0°C and 0.5 h at 20°C. The precipitate was filtered off and washed with methanol. The filtrate was evaporated under vaccuo (0.1 mmHg) leaving a white solid which was extracted with hot THF (5x50 ml). The organic extracts were combined, filtered, and dried over magnesium sulfate. After filtration and removal of the solvents under vaccuo, the residue was dried over phosphorus pentoxide to give 0.47 g of a white solid. The spectroscopic data for this compound sustained the presence of an aldehyde moiety. ^1H NMR δ : 9.6 (d, CH = O). IR : 1730 cm^{-1}($\nu_{C=O}$). Although complete data are not compatible with the structure of pure isopropylidene tartraldehyde 13, this compound was used for the next step without further purification. (b) To a suspension of 0.435 g (14.5 mmol) of sodium hydride (80 % in mineral oil) in anhydrous DME (10 ml) was added, at 0°C, 3.05g (14.5 mmol of methyl diethylphosphonoacetate in anhydrous DME (10 ml). The mixture was stirred for 0.25h at 0°C, then cooled to -78°C and 0.47 g of the "dialdehyde"13 (obtained as described above) in anhydrous DME (10 ml) was slowly added. The cooling bath was immediately removed and the mixture stirred for 1h. Water (5 ml) was then added and the mixture was poured into ether (100 ml). The organic layer was separated, washed with water (4x5 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo afforded 1.03 g of crude mixture which was fractionnated by preparative layer chromatography (ether-pentane, 4/6) to give 0.3 g of a mixture of the (E,E) and (Z,E) diester 5a' and 5c' and I' in the 90/10 ratio (determined by IGCI[2] analysis (22 % total yield from 3,4-O-isopropylidene-D-Mannitol). $[\alpha]^{20}_D$ +68,5 (c : 13,5, $CHCl_3$). All the other analytical data are the same as described for the corresponding (4S,5S) (E,E) and (Z,E) enantiomers 5a and 5c.

Reaction of methyl (S)-4,5-O-isopropylidene-pent-2-enoates 9 with isopropylidenetriphenylphosphorane. To 0.65 g (1.5 mmol) of isopropyl triphenylphosphonium iodide in anhydrous THF (5 ml) was added, at 0°C, n butyllithium (1 ml) and the mixture was stirred for 0.25 h at 20°C, then cooled at 0°C and 0.186 g (1 mmol) of αβ unsaturated ester 9 in anhydrous THF (4 ml) was slowly introduced. After stirring for 1h at 0°C and 1h at 20°C, water (5 ml) was added. The resulting mixture was extracted with ether (3x25 ml) and the organic layers were combined, washed with water (2x5 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo afforded a crude mixture which was fractionnated by preparative layer chromatography on silicagel (eluent : ether/pentane : 2/8). **From the (E)-α,β-unsaturated ester 9a**, 0.125 g (55 % yield) of a mixture of the diastereoisomers 10a and 10'a in the 86/14 ratio (determined by IGCI[2] analysis was obtained $[\alpha]^{20}_D$ - 10.9 (c : 10.8; $CHCl_3$). Analytical data for the major diasteroisomer 10a : IGCI[2], conditions A, RT : 6.7 min. ^1H NMR δ : 0.95-1.70 (m, 14 H, CH_3 and cyclopropanic H), 3.50-4,10 (m with s at 3.65, 6H, CO_2CH_3, CHO and CH_2O). IR : 1731 cm^{-1}/ νC = O). MS : m/e 213 ($M\text{-}CH_3$). These data are in agreement with that of the litterature[2h]. **From the (Z)-α,β-unsaturated ester 9b**, 0.14 g (61 % yield) of a mixture of the diastereoisomers 10a' and 10a in the 96/4 ratio (determined by IGCI[2] analysis was obtained, $[\alpha]^{20}_D$ +33 (c : 12.2, $CHCl_3$). Analytical data for the major diastereoisomer 10a' : IGCI[2], conditions

A, RT : 6.4 min. ^{1}H NMR δ : 0.95-1.70 (m with 2s at 1.20 and 1.35, 14H, CH_3 and cyclopropanic H), 3.80-4.25 (m with s at 3.80, 6H, CO_2CH_3, CHO and CH_2O). IR : 1751 cm^{-1}($\nu_{C=O}$). MS : m/e 213 (M-CH_3). Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.20 ; H, 8.80. Found : C, 63.29; H, 8.75.

Reactions of (4S, 5S)-α,β-unsaturated diesters 5 with a 2.5 equimolar amount of isopropylidenetriphenyl phosphorane To a cooled (0° C) solution of 0.27 g (1 mmol) of α,β–unsaturated diesters 5 in anhydrous THF (5 ml) was slowly added a solution of isopropylidenetriphenylphosphorane (obtained by adding, at 0° C, n-butyllithium (2.5 mmol, 1.56 ml) to 1.08 g (2.5 mmol) of isopropyl triphenylphosphonium iodide in anhydrous THF (5 ml) and stirring the mixture for 0.25 h at 0° C). The mixture was stirred for 1 h at 0°C and 1 h at 20° C, then hydrolyzed (5 ml of water), and extracted with ether (3x25 ml). The organic layers were combined, washed with water (2x5 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo afforded a crude mixture which was fractionnated by preparative layer chromatography on silicagel (eluent : pentane-ether : 7/3). **From the (E,E)-α,β-unsaturated diester 5a**, 0.28 g (80 % yield) of a mixture of the diastereoisomers 6a and 6a' in the 87/13 ratio (determined by IGC[2] analysis) was obtained. This mixture was fractionnated by cristallization in cyclohexane to give 0.17 g (50 % yield) of the pure dicyclopropane 6a. Analytical data for 6a : Tlc, RF 0.5 (ether-pentane, 3/7). IGC[2], conditions B, RT : 6.20 min. $[\alpha]^{20}_D$ -55.1 (c : 19.7, $CHCl_3$) Mp : 127-8°C. ^{1}H NMR δ : 1.10-1.70 (m with s at 1.25 and 1.3, 22H, CH_3 and cyclopropanic H), 3.45-3.65 (m with s at 3.65, 8H, CO_2CH_3 and CHO). IR (KBr) : 1724 cm^{-1} ($\nu_{C=O}$). MS : m/e 279 (M-$C_3H_7O_2$). Anal. Calcd. for $C_{19}H_{30}O_6$: C, 64.40; H, 8.50. Found : C, 64.36 ; H, 8.50. **From the (E,E)-(4R,5R)-α,β–unsaturated diester 5a'**. The reaction has been carried out, following the same procedure, to afford 0.175 g (51 % yield) of the enantiomeric dicyclopropane 6d. $[\alpha]^{20}_D$: +54.5 (c : 18.2, $CHCl_3$). All the other analytical data are the same as described above for the dicyclopropane 6a. **From the (Z,Z)-α,β–unsaturated diester 5b.**The reaction has been carried out, following the same procedure, to afford 0.23 g (65 %) yield of the dicylopropane 6c was obtained. Analytical data for 6c : Tlc, Rf 0.55 (ether/pentane, 3/7). IGC[2], conditions B, RT : 5.8 min. $[\alpha]^{20}_D$ -41.9 (c : 19.2, $CHCl_3$). ^{1}H NMR δ : 0.85-1.70 (m, 22H, CH_3 and cyclopropanic H), 3.10-3.65 (m with s at 3.65, 8H, CO_2CH_3 and CHO). MS : m/e 279 (M-$C_3H_7O_2$). Anal. Calcd. for $C_{19}H_{30}O_6$: C, 64.40; H, 8.50. Found : C, 64.61; H, 8.49.

Reaction of (Z,Z) - (4S,5S)-α,β-unsaturated diester 5b with an equimolar amount of isopropylidenetriphenylphosphorane. To a cooled (0°C) solution of 0.54g (2 mmol) of (Z,Z)-α,β-unsaturated diester 5b in anhydrous THF (8 ml), was slowly added a solution of isopropylidenetriphenylphosphorane (obtained by adding, at 0°C, n butyllithium (1.30 ml, 2 mmol) to 0.92 g (0.2 mmol) of isopropyl triphenylphosphoniumiodide in anhydrous THF (8 ml) and stirring the mixture for 0.25 h at 0°C). The mixture was stirred for 1h at 0°C and 1h at 20°C, then hydrolyzed (5 ml of water) and extracted with ether (3 x 25 ml). The organic layers were combined, washed with water (2 x 10 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo afforded 1.05 g of crude mixture which was fractionnated by preparative layer chromatography (ether/pentane : 3/7) to give 0.41 g of a mixture containing the dicyclopropane 6c and a monocyclopropane derivative 19 in the 45/55 ratio IGC[2]I analysis, conditions B, respective RT : 5.8 min and 5.1 min). ^{1}H NMR analysis of the mixture clearly establishes that the monocyclopropane 19 possesses a trans C=C bond, δ : 5.95 (d, (E)-R(H_1)C=C(H_2)CO_2CH_3, $J_{2,1}$: 16Hz), 6.7 (dd, (E)-R(H_1)C=C(H_2)CO_2CH_3, $J_{1,2}$: 16 Hz, $J_{1,3}$: 8 Hz).

Treatment of the mixture containing the monocyclopropane 19 by an excess of isopropylidenetriphenylphosphorane Reaction of 0.11g of the mixture containing 19 and 6c (55/45 ratio, see above) with 0.8 mmol of isopropylidenetriphenylphosphorane, in the conditions described above, gave, after usual work-up, 0.26 g of crude mixture which was fractionnated by preparative layer chromatography (ether/pentane : 3/7) to afford 0.11 g of pure dicyclopropane 6c. Analytical data of this compound are described above. Estimated yield for the cyclopropanation of the monocylopropane 19 : 80-90 %.

Ozonolysis of the mixture containing the monocyclopropane 19. 0.14 g of the mixture containing 19 and 6c (55/45 ratio, see above) was dissolved in dichloromethane and cooled to -78°C. Ozone was then slowly bubbled into the solution untill a blue colour was observed. The excess of ozone was eliminated by passing a stream of argon and dimethylsulfide was added (2 ml). The mixture was then stirred for 20 h at 20°C, diluted in ether (20 ml), washed with water (2 x 5 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo afforded 0.13 g of crude mixture which was fractionnated by preparative layer chromatography (ether/pentane : 6/4) to give 0.055 g of the aldehyde 20 (estimated yield : 90 %). Analytical data for compound 20 : ^{1}H NMR δ : 1.15-1.65 (m, 14H, $(CH_3)_2C$ and cyclopropanic H), 3.5-3.8 (m with s at 3.65, 4H, CO_2CH_3 and OC$\underline{H}$-C_3 ring); 4.1 (dd, 1H, C$\underline{H}$-CH=O), 9.7 (d, 1H, CH=O). IR : 1730 cm^{-1}. ($\nu_{C=O}$).

Reaction of the aldehyde 20 with methyl triphenylphosphoranilidene acetate. To a solution of 0.055 g (0.25 mmol) of aldehyde 20 in methanol (5 ml), was added, at 0°C, 0.17 g (0.5 mmol) of methyl triphenylphosphoranilidene acetate and the mixture was stirred for 0.25h at 0°C and 2h at 20°C. Methanol was then removed under vaccuo and the residual mixture was dissolved in ether (25 ml), washed with water (2x5 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo gave 0.21 g of crude mixture which was fractionnated by preparative layer chromatography to afford 0.05 g of a mixture of monocyclopropane derivatives 19a and 19 (67/33 ratio determined by IGC[2] analysis, conditions B, respective RT : 5/2

min and 4.8 min). Total yield of the olefination reaction : 75 %. A second fractionnation by preparative layer chromatography (benzene/ethyl acetate : 9/1, four runs) gave 0.03 g of a mixture of the compound 19 and 19a in the 10/90 ratio (determined by $IGCI^2$ analysis). ^{1}H NMR analysis of the mixture clearly establishes that the main compound 19a possesses a cis C=C bond, δ : 5.8 (d, (Z)-R(H_1)C=C($\underline{H_2}$)CO_2CH_3, $J_{2,1}$: 12 Hz), 6.2 (dd, (Z)-R($\underline{H_1}$)C=C(H_2)CO_2CH_3, $J_{1,2}$: 12 Hz).

Treatment of the mixture containing the monocyclopropane 19a by an excess of isopropylidenetriphenylphosphorane. Reaction of 0.03 g of the mixture containing 19a and 19 (90/10 ratio see above) with 0.3 mmol of isopropylidene triphenylphosphorane in the conditions described above, gave, after usual work-up, 0.15 g of crude mixture which was fractionnated by preparative layer chromatography (ether/pentane : 3/7) to afford 0.028 g of a mixture of the dicyclopropanes 6c and 6a' (15/85 ratio, determined by $IGCI^2$ and $IGCI^2$ MS comparisons with authentic samples prepared as described elsewhere and whose complete analytical data are given.

Reaction of methyl (S)-4,5-O-isopropylidene-pent-2-enoates 9 with isopropylidenediphenylsulfurane. Method A : To a cooled (-78°C) solution of 0.574 g (1.5 mmol) of isopropyl diphenylsulfonium tetrafluoroborate and 0.13 g (1.5 mmol) of anhydrous dichloromethane in anhydrous DME (12 ml) was slowly added a solution of lithium diisopropylamide (obtained by adding n butyllithium (1.05 ml) to a cooled (-78°C) solution of 0.172 g (1.6 mmol) of diisopropylamine in anhydrous DME (5 ml) and stirring the mixture for 0.25 h at -78°C). The mixture was then stirred for 0.25h at -78°C and a solution of 0.186 g (1 mmol) of the αβ unsaturated ester 9 in anhydrous DME (2 ml) was slowly added. The resulting mixture was stirred for 0.25 h at -78°C, for 0.75h between -65°C and -50°C and finally for 0.25h without external cooling. Then, water (5 ml) was added and the mixture was extracted with ether (3x25 ml). The organic layers were combined, washed with water (2x5 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo afforded 0.4 g of crude mixture which was fractionnated by preparative layer chromatography on silicagel (eluent : pentane/ether : 75/25). **Method B:** To a cooled solution (-78°C) of 0.574 g (1.5 mmol) of isopropyl diphenylsulfonium tetrafluoroborate in anhydrous THF (10 ml) was added phenyllithium (1.3 ml, 1.5 mmol). The mixture was then stirred at -78°C for 0.25h and a solution of 0.186 g (1 mmol) of the αβ unsaturated ester 9 in anhydrous THF (2 ml) was slowly added. The procedure described in method A was then followed. **From the (E)-α,β-unsaturated ester 9a :** Following method A, 0.21 g (92 % yield) of a mixture of the diasteroisomer 10a' and 10a in the 99/1 ratio (determined by $IGCI^2$ analysis, conditions A, respective RT : 6.4 min and 6/7 min) was obtained ; Following method B, 0.175 g (75 % yield) of a mixture of the diasteroisomer 10a' and 10a in the 98/2 ratio (see above) was obtained. Analytical data for 10'a and 10a were previously described. **From the (Z)-α,β-unsaturated ester 9b :** Methods A and B afforded respectively 0.192 g (84 % yield) and 0.162 g (71 % yield) of pure diastereoisomer 10b. Analytical data for compound 10b : Tlc, Rf 0.45 (ether/pentane : 2/8). IGC^2I, conditions A, RT : 5.7 min $[\alpha]^{20}_D$ -15.04 (c : 18.7, $CHCl_3$). ^{1}H NMR δ : 0.90-1.80 (m, 14H, $(CH_3)_2$ C and cyclopropanic H), 3.20-3.65 (m with s at 3.6, 4H, CO_2CH_3 and one H of the CH_2O group), 3.95 (dd, 1H, one H of the CH_2O group), 4.25-4.66 (m, 1H, CHO). IR : 1729 cm^{-1} ($\nu_{C=O}$). MS : m/e 213 (M-CH_3). Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.20 ; H, 8.80. Found : C, 63.93; H, 9.03.

Reactions of αβ-unsaturated diesters 5 with isopropylidenediphenylsulfurane. Method A : To a cooled (-78°C) solution of 0.915 g (3 mmol) of isopropyl diphenylsulfonium tetrafluoroborate and 0.255 g (3 mmol) of anhydrous dichloromethane in anhydrous DME (12 ml) was slowly added a solution of lithium diisopropylamide (obtained by adding n butyllithium (3 mmol, 2 ml) to a cooled (-78°C) solution of 0.325 g (3.2 mmol) of diisopropylamine in anhydrous DME (5 ml) and stirring the mixture for 0.25 h at -78°C). The mixture was then stirred for 0.25 h at -78°C and a solution of 0.27 g (1 mmol) of the αβ unsaturated diester 5 in anhydrous DME (4 ml) was slowly added. The resulting mixture was stirred for 0.25 h at -78°C, for 0.75 h between -65°C and -50°C and finally for 0.25 h without external cooling. Then, water (5 ml) was added and the mixture was extracted with ether (3x25 ml). The organic layers were combined, washed with water (2x5 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo afforded ca. 0.8 g of crude mixture which was fractionnated by preparative layer chromatography on silicagel (eluent : pentane/ether : 7/3). **Method B :** To a cooled (-78°C) solution of 0.915g (3 mmol) of isopropyl diphenylsulfonium tetrafluoroborate in anhydrous THF (15 ml), was added phenyllithium (2.6 ml, 3 mmol). The mixture was then stirred at -78°C for 0.25 h and a solution of 0.27 g (1 mmol) of the αβ unsaturated diester 5 in anhydrous THF (4 ml) was slowly added. The procedure described in method A was then followed. **From the (E,E)-α,β-unsaturated diester 5a.** Methods A and B afforded respectively 0.29 g (82 % yield) and 0.175 g (50 % yield) of the pure diasteroisomer 6a' . Analytical data for compound 6a' : Tlc, Rf 0.37 (ether/pentane : 2/8). $IGCI^2$, conditions B, RT : 6.3 min. MP : 136 -137°C (crystallized from pentane). $[\alpha]^{20}_D$ -24.7 (c : 16.6, $CHCl_3$). ^{1}H NMR δ : 1.0-1.60 (m, with 3 s at 1.2, 1.24 and 1.35, 22H, $(CH_3)_2$ C and cyclopropanic H), 3.20-3.44 (m, 2H, CHO), 3.6 (s, 6H, CO_2CH_3). IR (KBr) : 1732 and 1715 cm^{-1} ($\nu_{C=O}$). MS : m/e 339 (M-CH_3). Anal. Calcd. for $C_{19}H_{30}O_6$: C, 64.40; H, 8.50. Found : C, 64.29; H, 8.69. **From the (Z,Z)-α,β-unsaturated diester 5b.** Methods A and B afforded respectively 0.24 g (70 % yield) and 0.2 g (60 % yield) of the pure diasteroisomer 6b. Analytical data for compound 6b : Tlc, Rf 0.62 (ether/pentane : 2/8). IGC^2I, conditions B, RT : 5.04 min. MP : 97-98°C (crystallized from pentane). $[\alpha]^{20}_D$ - 10.1 (c : 5.6, $CHCl_3$). ^{1}H NMR δ : 0.9-1.6 (m with 3s at 1.16, 1.25 and 1.36, 22H, $(CH_3)_2$ C and cyclopropanic H), 3.56 (s, 6H, CO_2CH_3), 4.1-4.35 (m, 2H, CHO). IR (KBr) : 1726 cm^{-1} ($\nu_{C=O}$). MS : m/e 339 (M-CH_3). Anal. Calcd for $C_{19}H_{30}O_6$: C 64.40; H, 8.50. Found : C, 64.14; H, 8.76.

Cyclopropanation of (Z)-(S)-4,5-O-isopropylidene-pent-2-enoate 9b with isopropylidenediphenylsulfurane generated "in situ". To a cooled (-78°C) of 0.372 g (2 mmol) of the (Z)-(S) ester 9b and 0.915 g (3 mmol) of isopropyl diphenylsulfonium tetrafluoroborate in anhydrous THF (8 ml), was slowly added 0.34 g (3 mmol) of potassium tert-butoxide in anhydrous THF (5 ml). The mixture was stirred for 2h at -78°C, hydrolyzed (5 ml of water) and extracted with ether (3x25 ml). The organic layers were combined, washed with water (2x5 ml) and dried over magnesium sulfate. Filtration and removal of the solvents under vaccuo afforded 1.01 g of a mixture which was fractionnated by preparative layer chromatography (ether-pentane : 3/7) to give 0.35 g (77 % yield) of pure diastereoisomer 10b whose analytical data are described above.
When applied to the corresponding (E)-(S) ester 9a, the same procedure led to a complex mixture which on IGC^2I analysis showed only traces of the expected monocyclopropane 10.

Cyclopropanation of (Z,Z) - (4S,5S)-α,β-unsaturated diester 5b with isopropylidenediphenylsulfurane generated "in situ". To a cooled (-78°C) mixture of 0.27 g (1 mmol) of the (Z,Z) diester 5b and 1.22 g (4 mmol) of isopropyl diphenylsulfonium tetrafluoroborate in anhydrous THF (8 ml), was slowly added 0.45 g (4 mmol) of potassium tert-butoxide in anhydrous THF (5 ml). Then the same procedure as above was followed. After several successive fractionnations by preparative layer chromatography (ether/pentane : 2/8) the pure dicyclopropane derivative 6b was obtained (0.21 g, 60 % yield) as well as a monocyclopropane derivative 18 which has not yet been fully characterized (15 % yield). The analytical data of the compound 6b were described above.

General procedure for the transformation of the various cyclopropane derivatives into hemicaronaldehyde 8 : (a) 1 mmol of the cyclopropane derivative containing an isopropylidene moiety was dissolved in THF (8 ml) and stirred at 20°C for 3-6h (Tlc monitoring of the reaction) in the presence of 2.5 molar aqueous perchloric acid (6 ml). After completion of the reaction, solid sodium hydrogenocarbonate was slowly added untill obtention of a basic medium, water (5 ml) was added and the medium was carefully extracted with ether (6x20 ml). The combined organic layers were washed with water (2 ml), dried over magnesium sulfate and evaporated leaving nearly pure diol which was used in the next step without further purification (nearly quantitative yield). (b) The crude diol (± 1 mmol) was dissolved in a mixture of methanol (8 ml) and phosphate buffer (pH 7) (4 ml) and stirred at 20°C for 0.5 to 1h (Tlc monitoring of the reaction) in the presence of 0.32 g (1.5 mmol) of sodium periodate. After completion of the reaction, the precipitate was filtered off and washed with ether. The organic layer was washed with water, dried over magnesium sulfate and cautiously evaporated under vaccuo. The crude mixture was analyzed by $IGCI^2$, then fractionnated by preparative layer chromatography (ether/pentane : 2/8) giving the pure hemicaronaldehyde 8 (60-70 % yield) whose stereochemistry and optical purity were determined by comparison with authentic samples obtained by ozonolysis of optically pure cis- and trans chrysanthemic acids kindly provided by the Roussel-Uclaf Company. The results are gathered in the following table.
Analytical data for pure (1R, 3R)-hemicaronaldehyde 8a : Tlc, Rf 0.6 (ether/pentane : 3/7). IGC^2I, conditions C, RT : 3.8 min. $[\alpha]^{20}_D$ +19.2 (c : 18.4, acetone). ^1H NMR δ : 1.25 and 1.33 (2s, 6H, $(CH_3)_2C$), 2.36 (m, 2H, cyclopropanic H), 3.56 (s, 3H, CO_2CH_3), 9.6 (d, 1H, CH=O). IR : 1720 cm^{-1} (νC = O). Analytical data for pure (1R, 3S)-hemicaronaldehyde 8b : Tlc, Rf 0.6 (ether/pentane : 3/7). IGC^2I, conditions C, RT : 4.3 min. $[\alpha]^{20}_D$ -79,6 (C : 17.1, acetone). ^1H NMR δ : 1.3 and 1.55 (2S, 6H, $(CH_3)_2C$), 1.65-2.10 (m, 2H, cyclopropanic H), 3.67 (s, 3H, CO_2CH_3), 9.6 (d, 1H, CH=O). IR : 1728 and 1703 cm^{-1} ($\nu_{C=O}$).

	Cyclopropane derivatives		Hemicaronaldehyde		
Entries	Method of synthesis from αβ unsaturated esters	Composition	Stereochemistry of the major enantiomer	$[\alpha]^{20}_D$ Exp. value in acetone	% ee
1	(E)-(S) monoester 9a + Ph_3PCMe_2	10a/10a' (86/14 ratio)	Trans (1R, 3R) 8a	+13.6 (c : 12.6)	71
2	(Z)-(S) monoester 9b + Ph_3PCMe_2	10a'/10a (96/4 ratio)	Trans (1S, 3S) 8a'	-18.8 (c : 13.2)	98
3	(E)-(S) monoester 9a+ Ph_2SMe_2 (method A)	10a'/10a (99/1 ratio)	Trans (1S, 3S) 8a'	-18.6 (c : 14.1)	97
4	(Z)-(S) monoester 9b + Ph_2SMe_2 (method A)	Pure 10b	Cis (1R, 3S) 8b	-76.4 (c : 16.9)	96
5	(E,E)-(4S,5S) diester 5a + Ph_3PCMe_2	6a/6a' (87/13 ratio)	Trans (1R,3R) 8a	+14.3 (c : 18.5)	74
6	(E,E)-(4S,5S) diester 5a + Ph_3PCMe_2	Pure 6a (crist.)	Trans (1R, 3R) 8a	+18.85 (c : 18.2)	98
7	(E,E)-(4R,5R) diester 5a' + Ph_3PCMe_2	6d/6d' (90/10) ratio	Trans (1S, 3S) 8a'	-14 (c : 12.5)	72
8	(Z,Z)-(4S,5S) diester 5b + Ph_3PCMe_2	Pure 6c	Trans (1R, 3R) 8a	+0.5 (c : 17.2)	2.5
9	(Z)-(4S,5S) monocyclopropane 19a + Ph_3PCMe_2	6c/6a' (15/85 ratio)	Trans (1S, 3S) 8a'	-14.45 (c : 15.9)	75
10	(E,E)-(4S,5S) diester 5a + Ph_2SCMe_2 (method A)	Pure 6a'	Trans (1S, 3S) 8a'	-18.1 (c : 17.5)	94
11	(Z,Z)-(4S,5S) diester 5b + Ph_2SCMe_2 (method A)	Pure 6b	Cis (1R, 3S) 8b	-73.2 (c : 15.6)	92

REFERENCES

1 a) J.E. Casida Ed. "Pyrethrum - The Natural Insecticide, Acad., Press, New York (1973). b) M Elliot and N.F. Janes, Chem. Soc. Rev., 1978, 7, 473. c) D. Arlt, M. Jautelat and R. Lantzsch, Angew. Chem. Int. Ed. 1981, 20, 703. d) K. Naumann, Chemie der synthetischen Pyrethroid-Insektizide, Chemie der Pfanzenschutz und Schädlingsbekämpfungsmittel, Vol. 7, Springer Verlag, Berlin, 1981. e) Deltamethrine monographie, Roussel-Uclaf 1982, ISBN 2-904-125-00-0.f)

Tessier, Chem. Ind. (London), 1984, 199. **g)** E.J. Ariëns, J.J.S. van Rensen and W. Welling, Stereoselectivity of Pesticides, Biological and Chemical Problems, Elsevier, Amsterdam, 1988.

2 a) M. Matsui, H. Yoshioka, Y. Yamada, H. Sakamoto and T. Kitahara, Agric. Biol. Chem., 1965, **29**, 784 - from Δ^3 carene. **b)**A.K. Mandal, D.P. Borude, R. Armugasamy, N.R. Soni, D.G. Jawalkar, S.W. Mahajan, K.R. Ratnam and A.D. Gogahre, Tetrahedron, 1986, **42**, 5715 - Δ^3 carene. **c)** R.B. Mitra and A.S. Khanra, Synth. Commun. 1977, **7**, 245 - from α-pinene. **d)** B.J. Fitzsimmons and B. Fraser-Reid, J. Am. Chem. Soc., 1979, **101**, 6123 -from a sugar derivative. **e)** T. Matsuo, K. Mori, M. Matsui, Tetrahedron Lett. 1976, 1979 - from Pantolactone. **f)** T.L. Ho and Z.U. Din, Synth. Commun, 1982, **12**, 257 - from carvone. **g)** S. Torii, T. Inokuchi and R. Oi, J. Org. Chem. 1983, **48**, 1944 - from pulegone. **h)** J. Mulzer and M. Kappert, Angew. Chem. Int. Ed. 1983, **22**, 63 - from D. Mannitol via D glyceraldehyde. **i)** A. Krief, W. Dumont and P. Pasau, Tetrahedron Lett., 1988, **29**, 1079 - from mannitol and L-tartaric acid. **j)** A. Krief and W. Dumont, Tetrahedron Letters, 1988, **29**, 1083 - from D-mannitol and L-tartaric acid.

3 a) J. Martel, J. Tessier and J.P. Demoute, Eur. Pat. Appl. 1980, 0023454. **b)** M.J. Devos and A. Krief, Tetrahedron Lett., 1983, **24** , 103. **c)** W.A. Kleschick, M.W. Reed and J. Bordner, J. Org. Chem., 1987, **52**, 3168. **d)** H. Abdallah ,These de doctorat , Université de Rennes I, 23 Juillet 1983. **e)** H. Abdallah, R. Gree and R. Carrié, Tetrahedron Lett., 1982, **23**, 503. **f)** M.J. Devos, Ph.D. Thesis, Faculté N.D. de la Paix 1980. **g)** A. Krief, 28th Congress IUPAC, Vancouver (Canada), August 16-21 1981, EUCHEM Conference "Methods in Organic Synthesis" Louvain-la-Neuve (Belgium), July 5-9 1982. **h)** A. Monpert, J. Martelli, R. Gree and R. Carrié, Nouv. J. Chem., 1983, **7**, 345. **i)** M. Franck-Neumann, D. Martina and M.P.Heitz, Tetrahedron Lett., 1982, **23**, 3493. **j)** M. Franck-Neumann, M. Sedrati, J.-P. Vigneron and V. Bloy, Angew. Chem. Int. Ed., 1985, **24**, 996.

4 a) T. Aratani, Y. Yoneyoshi and T. Nagase, Tetrahedron Lett., 1975, 2599. **b)** T. Aratani, Y. Yoneyoshi and T. Nagase, Tetrahedron Lett. 1975, 1707.

5 a) I.J. Jakovac, H.B. Goodbrand, K.P. Lok and J.B. Jones, J. Am. Chem. Soc., 1982, **104**, 2244. **b)** P. Mohr, N. Waespe-Sarcevic, C. Tamm, K. Gawronska and J. Gawronski, Helv. Chim. Acta, 1983, **66**, 85. **c)** M. Schneider, N. Engel, P. Hönicke, G. Heinemann and H. Görisch, Angew. Chem. Int. Ed., 1984, **23**, 67. **d)** J. d'Angelo, G. Revial, R. Azerad and D. Buisson, J. Org. Chem., 1986, **51**, 40.

6 a) M.J. Devos, L. Hevesi, P. Bayet and A. Krief, Tetrahedron Lett., 1976, 3911. **b)** M.J. Devos and A. Krief, Tetrahedron Lett. 1979, 1511 and 1515. **c)** M.J. Devos, J.N. Denis and A. Krief, Tetrahedron Lett. 1978, 1847 and ref. cited. **d)** M.J. Devos and A. Krief, J. Am. Chem. Soc. 1982, **104**, 4282. **e)** M. Sevrin, L. Hevesi and A. Krief, Tetrahedron Lett. 1976, 3915.

7 a) M.J. Devos, L. Hevesi, P. Mathy, M. Sevrin, G. Chaboteaux and A. Krief in "Organic Synthesis : an Interdisciplinary Challenge", J. Streith, H. Prinzbach and G. Schill, Ed., Blackwell Ed. 1985, 123, Proceedings of the 5th IUPAC Symposium, Freiburg 1984. **g)** J.H. Babler and K.P. Spina, Tetrahedron Lett., 1985, **26**, 1923. **b)** A. Krief, L. Hevesi, G. Chaboteaux, P. Mathy, M. Sevrin and M.J. Devos, J. Chem. Soc. Chem. Commun., 1985, 1693 and references cited.

8 a) A.W. Johnson, Ylide Chemistry, Organic Chemistry a series of monographs, Academic Press (1966). **b)** P.A. Gricco and R.S. Finkelhor, Tetrahedron Lett. 1972, 3781. **c)** E. Block, Reactions of organosulfur compounds, Organic chemistry a series of monographs, Academic Press (1978). **d)** E.J. Corey and M. Jautelat, J. Am. Chem. Soc., 1967, **89**, 3912. **e)** E.J. Corey, M. Jautelat and W. Oppolzer, Tetrahedron Lett., 1967, 2325. **f)** E.J. Corey and W. Oppolzer, J. Am. Chem. Soc., 1964, **86**, 1899. **g)** V. Franzen and H.E. Driessen, Tetrahedron Lett. 1962, 661. **h)** V. Franzen and H.E. Driessen, Chem. Ber. 1963, **96**, 1881. **i)** B.M. Trost and M.J. Bodganowicz, J. Am. Chem. Soc. 1973, **95**, 5311.

9 a) J. Jurczak, S. Pikul and T. Bauer, Tetrahedron, 1986, **42**, 447. **b)** H. Matsunaga, T. Sakamakjei, H. Nagoka and Y. Yamada, Tetrahedron Lett., 1983, **24**, 3009. **c)** B.M. Trost and S.M. Mignani, Tetrahedron Lett., 1986, **27**, 4137. **d)** J. Mulzer and M. Kappert, Tetrahedron Lett. 1985, **26**, 1631. **e)** T. Katsuki, A.W.M. Lee, P. Ma, V.S. Martin, S. Masamune, K.B. Sharpless, D. Tuddenham and F.J. Walker, J. Org. Chem., 1982, **47**, 1378. **f)** G. Stork and M. Kahn, Tetrahedron Lett., 1983, **24**, 3951. **g)** Y. Yamamoto, S. Nishii and T. Ibuka, J.C.S. Chem. Commun., 1987, 464. **h)** W.R. Roush and B.M. Lesur, Tetrahedron Lett., 1983, **23**, 2231.

10 The authors thank the Roussel Uclaf Company for the gift of this sample.

11 a) R.G. Nadeau and R.P. Hanzlik, Methods Enzymol., 1969, **15**, 346. **b)** See the reference 17 cited in our ref. 11a.

12 See for example : **a)** R.J. Grawford, J. Org. Chem., 1983, **48**, 1362. **b)** B. Badet, M. Julia and M. Ramirez-Munoz, Synthesis, 1980, 926.

13 a) W.S. Wadsworth, Organic Reactions, 1977, **25**, 73. **b)** N. Minami, S.S. Ko and Y. Kishi, J. Am. Chem. Soc., 1982, **104**, 1109.

14 L.J. Rubin, H.A. Lardy and H.O.L. Fischer, J. Am. Chem. Soc., 1952, **74**, 425.

15 P. Pasau, mémoire de licence, Facultés Universitaires N.D. de la Paix, June 1986.

16 a) Merck Schuchardt MS INFO 85-8. **b)** S. Hanessian, Total Synthesis of Natural Products : The Chiron Approach, Vol. 3, Organic Chemistry Series, J.E. Baldwin in Ed. Pergamon Press 1983. **c)** H.B. Kagan and T.P. Dang, J. Am. Soc. 1972, **94**, 6429. **c)** T. Katsuki and K.B. Sharpless, J. Am. Chem. Soc., 1980, **102**, 5974. **d)** K.B. Sharpless, S.S. Woodward, M.G. Finn, Pure and Appl. Chem., 1983, **55**, 1823. **e)** L.D.-L. Lu, R.A. Johnson, M.G. Finn and K.B. Sharpless, J. Org. Chem., 1984, **49**, 728. **f)** P.W. Feit, J. Med. Chem., 1964, **7**, 14. **g)** G. Stork, Y. Nakahara, W.J. Greenlee, J. Am. Chem. Soc., 1978, **100**, 7775. **h)** K. Mori, T. Takigawa and T. Matsuo, Tetrahedron, 1979, **35**, 933. **i)** D. Seebach and E. Hungerbühler, E. Scheffold Ed. "Modern Synthetic Methods", Otto Salle Verlag, Frankfurt/Main 1980. **j)** A.I. Meyers and R.A. Amos, J. Am. Chem. Soc., 1980, **102**, 870. **k)** E. Hungerbühler and D. Seebach, Helv. Chim. Acta, 1981, **64**, 687. **l)** R. Naef and D. Seebach, Angew. Chem. Int. ed., 1981, **20**, 1030. **m)** E.J. Corey, A. Marfat and D.J. Hoover, Tetrahedron Lett., 1981, **22**, 1587.

17 a) M. Carmack and C.J. Kelly, J. Org. Chem., 1968, **33**, 2171. **b)** L.F. Wiggins, J. Chem. Soc., 1946, 13. **c)** E. Fischer, Ber., 1895, **28**, 1167. **d)** E. Fischer, Ber., 1915, **48**, 226.

18 B. Badet and M. Julia Tetrahedron Lett. 1979, 1101

19 From the unoptimized results described in this paper on small scale experiments and those obtained by the Roussel-Uclaf company from 8b to 2b on optimized large scale process.