Tetrahedron Vol. 44, No. 23, pp. 7127 to 7144, 1988
Printed in Great Britain.

0040–4020/88 $3.00+.00

ATTEMPTED AND ACCOMPLISHED SYNTHESES OF A FEW MONOFLUORINATED CHRYSANTHEMIC ACID DERIVATIVES

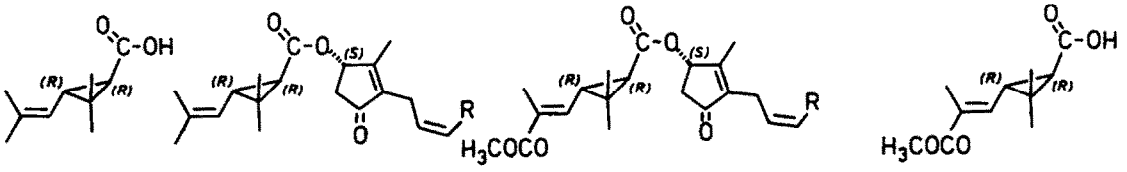
SYLVAIN COTTENS and MANFRED SCHLOSSER*

Institut de Chimie organique de l'Université
Rue de la Barre 2, CH-1005 Lausanne, Switzerland

(*Received in Germany* 10 *June* 1988)

Summary - A sulfone mediated approach presumably did produce methyl α-fluorochrysanthemate **10** but, if formed, the latter immediately underwent dehydrofluorination under the strongly basic reaction conditions. The cis- and trans-isomers of methyl β- and γ-fluorochrysanthemates **11** and **12** were concomitantly obtained by treating 3-fluoro-2,5-dimethyl-2,4-hexadiene with methyl diazoacetate in the presence of catalytic amounts of rhodium acetate. After enzymatic and chromatographic separation the four individual components were converted to the *m*-phenoxybenzyl esters (**11e** and **12e**).

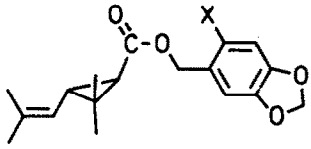
Pyrethrum [1] is a powder prepared from dried flowers of chrysanthemum species (notably *C. cinerariaefolium* in the Mediterranean area and *C. coccineum* in the Near East). Already in the middle ages it was commercialized by Caucasians as a potent insecticide. In Europe it became popular early in the 19th century. The active ingredients are esters of the chrysanthemic acid (**1**) and pyrethric acid (**2**) : cinerins (**3a** and **4a**), jasmolins (**3b** and **4b**) and pyrethins (**3c** and **4c**). The latter are not only naturally most abundant (totalling two thirds of the flower extract with nitromethane), but are also endowed with the highest insecticidal activity.



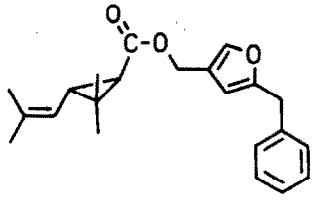
1 (Chrysanthemic acid)	**3a:** R = CH_3	(Cinerin I)	**4a:** R = CH_3	(Cinerin II)	**2** (Pyrethric acid; chrysanthemum dicarboxylic acid monomethyl ester)
	3b: R = C_2H_5	(Jasmolin I)	**4b:** R = C_2H_5	(Jasmolin II)	
	3c: R = $CH{=}CH_2$	(Pyrethrin I)	**4c:** R = $CH{=}CH_2$	(Pyrethrin II)	
	3d: R = H	(Allethrin)			

The pyrethrum constituents have the big advantage of being innocuous to mammals and birds. They suffer, however, from a serious drawback. Both, the acid and the alcohol component of the esters are extremely sensitive to photo-stimulated oxidative degradation. Thus, no agricultural application could be envisaged until structural modification provided sufficient chemical stability. First attempts were undertaken by Staudinger and Ruzicka shortly after they had completed, simultaneously with R. Yamamoto [2], the structure elucidation [3] of the chrysanthemic acid as well as a first synthesis. Unfortunately, when they replaced the cyclopentenone moiety

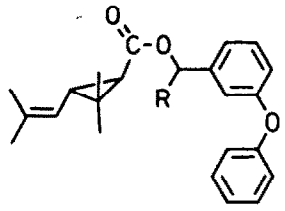
by a benzyl or *p*-anisyl group all biological activity was lost and with a piperonyl group (**5a**) it was retained only to a small extent [4]. In contrast, esterification with modified five-membered ring alcohols such as racemic allethrolone and 5-benzylfurfurol (leading to **3d** [5] and **6** [6], respectively) was rewarded with considerable success. Thus, benzyl-type substitution was neglected as a dead end until the introduction of a chlorine atom into position 6 of the piperonyl group (**5b**) [7] showed very encouraging results. Finally, the disclosure of the *m*-phenoxybenzyl and α-cyano-*m*-phenoxybenzyl chrysanthemates (**5c** [8] and **5d** [9, 10]) marked a breakthrough in the field of synthetic, photoresistant pyrethroids.



5a: X = H
5b: X = Cl (Barthrin)

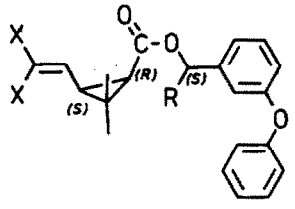


6 (Resmethrin)



5c: R = H (Phenothrin)
5d: R = CN (Cyphenothrin)

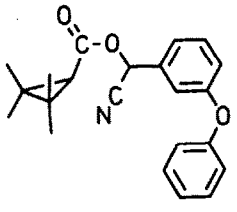
In the meantime, another important progress had been achieved as far as the acid component was concerned. When the terminal methyl groups at the side chain were replaced by electronegative substituents the metabolic or photooxidative degradation was substantially retarded if not completely prevented. In this respect the permethrinic acid, first described by Šorm et al. [11], turned out to be particularly valuable. When combined with *m*-phenoxybenzyl alcohol and α-cyano-*m*-phenoxybenzyl alcohol new esters **7a** [12, 13] and **7b** [12, 13], having most impressive properties, were obtained. Although similar in toxicity towards mammals, they outperformed the natural pyrethroids as insecticides by orders of magnitude. The dibromo analogs (such as the famous Deltamethrin **7c** [12]) showed equal or slightly enhanced activities. Amazingly, however, one stereocenter had to be inverted compared with the natural model. Halogenated synthetic pyrethroids of type **7** have little effect unless their side chain occupies a *cis* position with respect to the ester function.

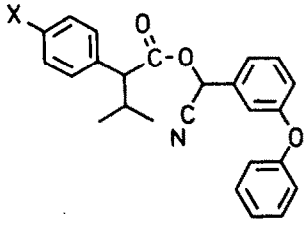


7a: X = Cl, R = H (Permethrin)
7b: X = Cl, R = CN (Cypermethrin)
7c: X = Br, R = CN (Deltamethrin)

Finally, the unsaturated side chain can be completely removed. "Primitive derivatives" of achiral cyclopropanes (such as **8**) or ring opened mimics (such as **9a** or **9b**) still conserve an exceptionally high insecticidal activity as long as they remain esterified with the (*S*)-cyanohydrin of *m*-phenoxy-benzaldehyde.

8
(Fenpropathrin)

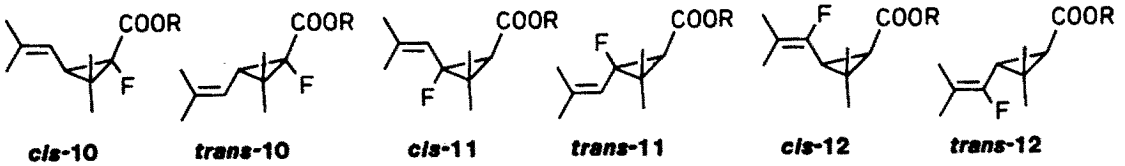




9a: X = Cl (Fenvalerate)
9b: X = F_2CHO

The standards being as high as nowadays, it should become more and more difficult to design or find pyrethroids having superior activities and selectivities. Our ambitions did not reach as far when we decided to synthesize α-, β- and γ-monofluorinated analogs **10**, **11** and **12** of the chrysanthemic acid. The aim was a modest one. We

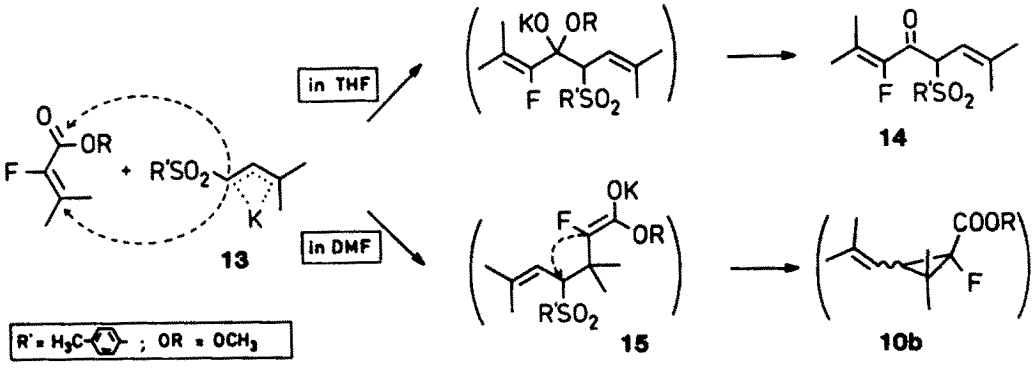
expected the fluorine substituent to exert some protective effect against photostimulated oxidation as observed previously with diene-type model compounds [14]. On the other hand, we wanted to test the rule-of-thumb [15] according to which fluorine and hydrogen atoms are nearly "isosteric". Consequently the receptor sites on nerve plasma membranes, presumably ion channels [16], should not much differentiate between the natural pyrethroid poison and its fluorinated analogs. Both assumptions proved to be correct.



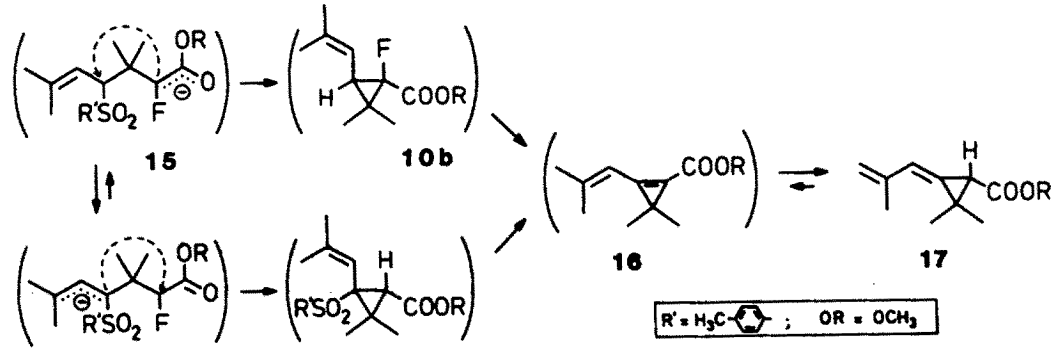
***cis*-10** ***trans*-10** ***cis*-11** ***trans*-11** ***cis*-12** ***trans*-12**

a: OR = OH **b:** OR = OCH_3 **c:** OR = OC_2H_5 **d:** OR = $OC(CH_3)_3$ **e:** OR = $OCH_2C_6H_4$-*m*-OC_6H_5

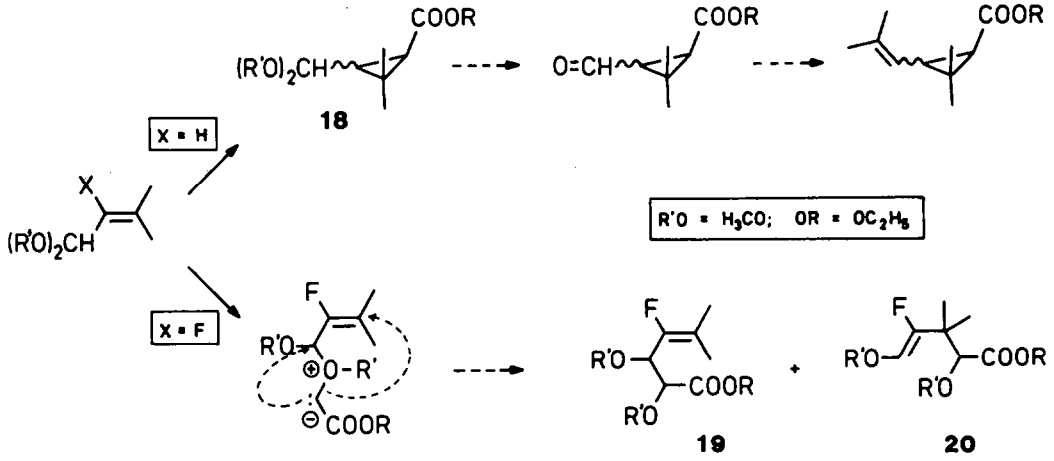
We hoped to find an easy entry to α-fluorochrysanthemates *cis*- and *trans*-**10** by merely adapting the Martel-Julia method [17]. However when a solution of 3-methyl-2-butenyl *p*-tolyl sulfone in tetrahydrofuran was consecutively treated with potassium *tert*-butoxide (generating the α-sulfonylallyl potassium species **13**) and methyl 2-fluoro-3-methyl-2-butenoate, the α-acylated sulfone **14** was isolated as the sole new product. Its formation implies a 1,2-addition, a reaction mode which had never been observed with the corresponding halogen-free and hence less electrophilic ester. In the more dissociative medium dimethylformamide, 1,4-addition did occur and possibly did produce the desired methyl α-fluorochrysanthemate **10b**.



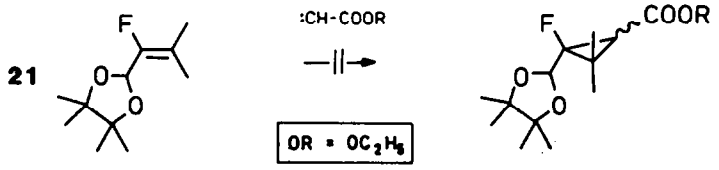
If formed, the α-fluoroester **10b** did however not persist under the reaction conditions. Base promoted elimination of hydrogen fluoride followed by base catalyzed isomerization of the cyclopropene intermediate **16** must have immediately converted it to methyl 2,2-dimethyl-3-(2-methyl-2-propenylidene)cyclopropane carboxylate (**17**) having a thermodynamically more favorable exocyclic double bond [18]. An alternative mechanism cannot be ruled out at present. Rather than to cyclize directly under sulfinate expulsion (producing **10b**), the transient enolate **15** resulting from a 1,4-addition could first tautomerize to give a new sulfonylallyl anion which then would accomplish ring closure by fluoride expulsion and after elimination of *p*-toluenesulfinate also attain the cyclopropene key intermediate **16**.



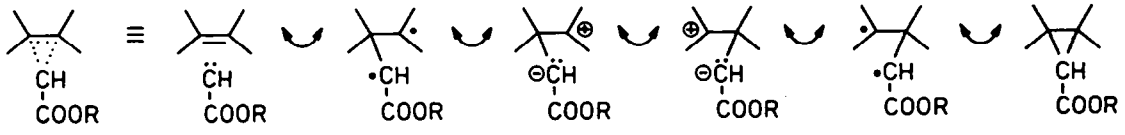
At this stage we learned that another laboratory had succeeded in the preparation of α-fluorochrysanthemic acid **10a** [19]. We abandoned our goal and focussed on the remaining two regioisomers **11** and **12**. As an access to the former, again we simply thought to modify a method which had already been elaborated for the halogen-free series and again we failed. The copper- [20], palladium- [21] or rhodium [22]-catalyzed decomposition of ethyl diazoacetate in the presence of 3-methyl-2-butenal dimethyl acetal does afford 3-methoxycarbonyl-2,2-dimethyl-cyclopropanecarbaldehyde dimethyl acetal (**18**, caronaldehyde dimethyl acetal methyl ester), although the yield is only moderate and unidentified by-products are formed. The same reaction carried out with the fluoro-analog of the acetal **18** takes a different route. Rather than to attack the olefinic double bond in a [2+1]cycloaddition mode, the ethoxycarbonylcarbene gets attached at one of the oxygen atoms. The resulting oxonia ylid immediately rearranges by 1,2- and 1,4-migrations giving ethyl 4-fluoro-2,3-dimethoxy-5-methyl-4-hexenoate (**19**, *erythro/threo* mixture) and ethyl (*Z*)-4-fluoro-2,5-dimethoxy-3,3-dimethyl-4-pentenoate (**20**).



Sterically hindered acetals such as 2-(1-fluoro-2-methyl-1-propenyl)-4,4,5,5-tetramethyl-1,3-dioxolane (**21**) do not react at all. Ethyl maleate and ethyl fumarate were the only products detected.



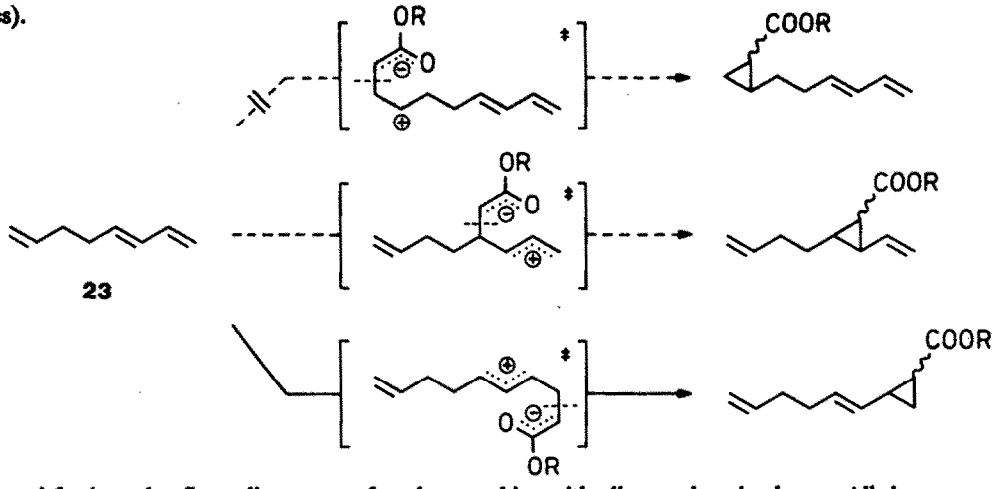
In order to understand the perturbation caused by the fluorine substituent, we may consider the cycloaddition transition state **22** as a superposition of bonding, non-bonding, biradical and zwitterionic resonance structures. We believe the latter to contribute substantially to the overall electronic situation. A fluorine atom should destabilize an adjacent positively charged center due to its inductive electron-withdrawing effect and thus retard the reaction.



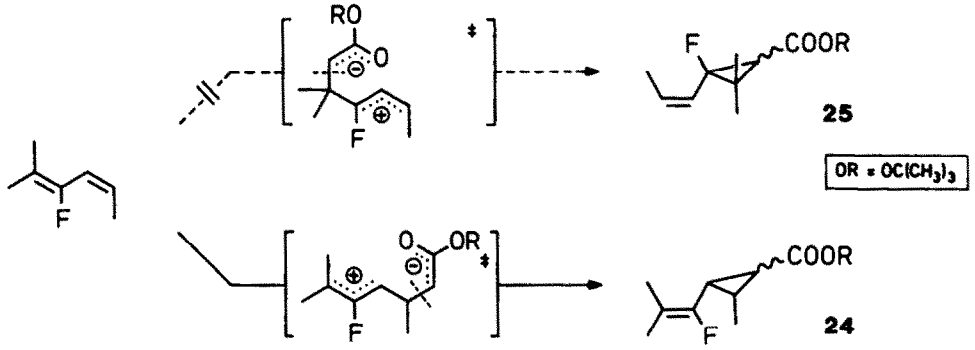
22

This model of a polar state predicts an enhanced reactivity of dienes compared with simple olefins. This expectation is nicely corroborated by an intramolecular competition experiment: 1,3,7-octatriene **23** adds ethoxy-

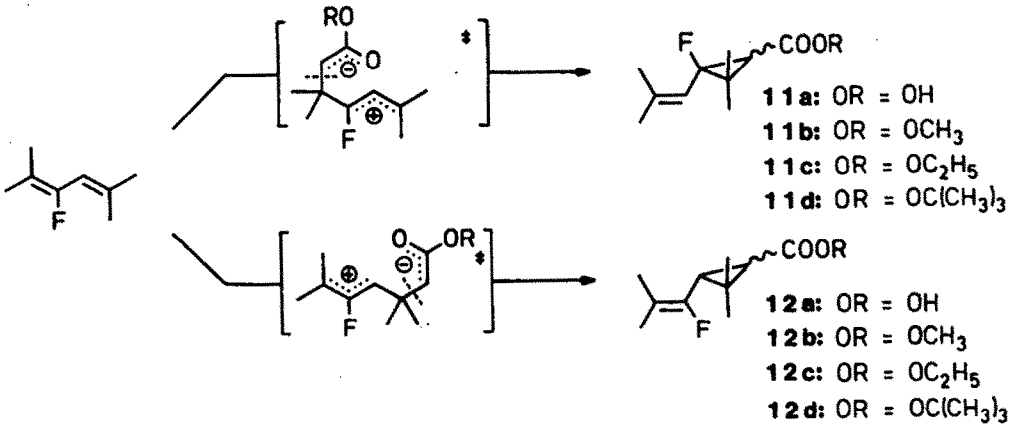
carbonylmethylene not at the isolated double bond [23] but preferentially at the terminal diene double bond, taking advantage of the most favorable transition state (only the best polar resonance structure shown in the schemes).



To our satisfaction, also fluorodienes were found to combine with alkoxycarbonylcarbenes. Alkyl groups, which can lower the free energy of the transition state, play a crucial role and dictate the site at which the cycloaddition process occurs. The rhodium acetate-catalyzed decomposition of *tert*-butyl diazoacetate in the presence of *cis*-3-fluoro-2-methyl-2,4-hexadiene [24,25] only gave rise to a pair of diastereomers **24** (*syn*/*anti*-ratio [26] 1 : 1). No regioisomer **25** having the geminal methyl groups attached to the three-membered ring was detected. In other words, the charge stabilizing inductive effect of a methyl group outweighs the donor capacity of a fluorine atom.

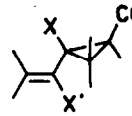


With 3-fluoro-2,5-dimethyl-2,4-hexadiene [25] as the substrate and ethyl diazoacetate as the carbene source both regioisomers, **11c** (38%) and **12c** (30%), were formed in roughly equal quantities. The replacement of the diazo compound by the corresponding methyl or *tert*-butyl ester did not alter these proportions very much (39% **11b** + 28% **12b** and 25% **11d** + 29% **12d**, respectively).

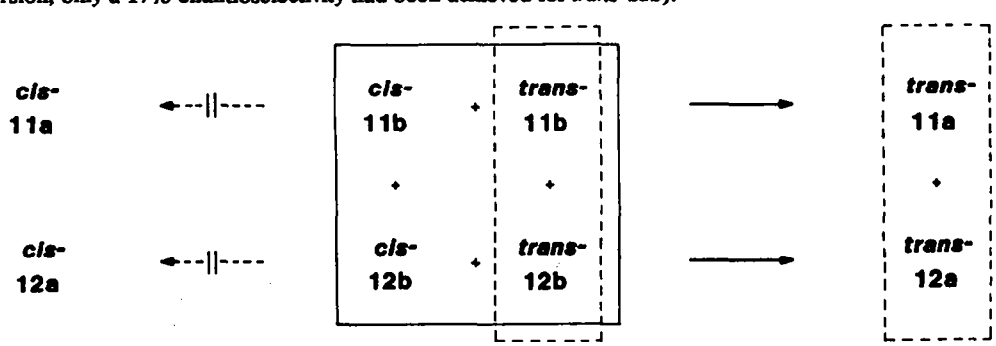


In a competition experiment methyl diazoacetate was allowed to decompose in the presence of an equimolar mixture of 3-fluoro-2,5-dimethyl-2,4-hexadiene and its halogen-free analog. After statistical correction (two identical double bonds in 2,5-dimethyl-2,4-hexadiene !) the product composition allows to calculate partial rate factors (see table). As these reveal, the fluorine deactivates both double bonds. However, the closer one, to which the heteroatom is directly attached, is less affected. Apparently, the corresponding transition state offers to the fluorine substituent the possibility to compensate its adverse electron withdrawing inductive effect, to some extent at least, by a mesomeric electron releasing effect [27]. The *cis/trans* ratios approximate 2 : 3 for the halogen-free chrysanthemate standard as well as for its γ-fluorinated derivative, but are reversed for the β-fluorinated isomer. The opposite stereoselectivity may reflect an electrostatic repulsion of the halogen and the neighboring ester function in the *trans*-isomer of **11b**. (To facilitate the comparison with the structural analogs **10** and **12**, also in the case of compounds **11** "*cis*" and "*trans*" continue to denote the position of the isobutenyl chain relative to the ester function regardless of the ordinary sequence priority of fluorine over carbon in nomenclature.)

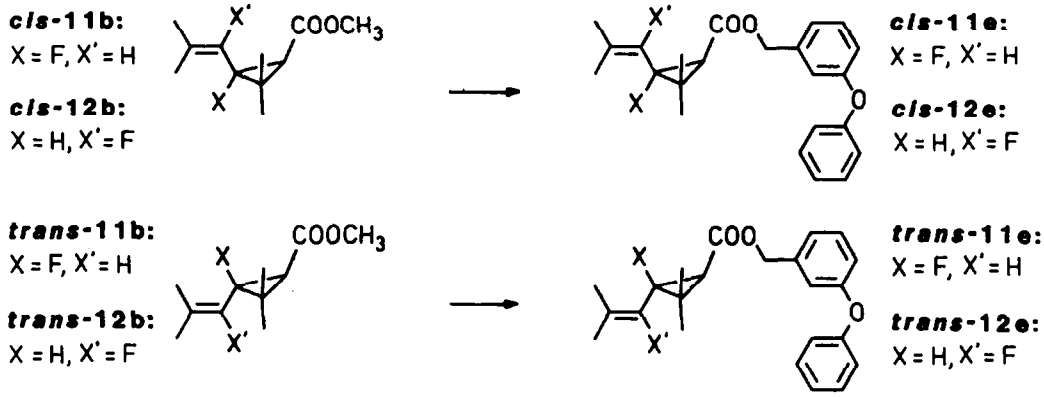
Table. Cycloaddition of methoxycarbonylmethylene to 2,5-dimethyl-2,4-hexadiene and its 3-fluoro derivative giving *cis*- and *trans*-diastereomers : relative reactivity of the three different double bonds.

			under $CuSO_4$ catalysis		under $Rh(OCOCH_3)_2$ catalysis	
compound	X	X'	*cis*	*trans*	*cis*	*trans*
methyl chrysanthemate	H	H	0.66	≡ 1.00	0.63	≡ 1.00
11b	F	H	0.36	0.17	0.25	0.25
12b	H	F	0.11	0.20	0.11	0.15

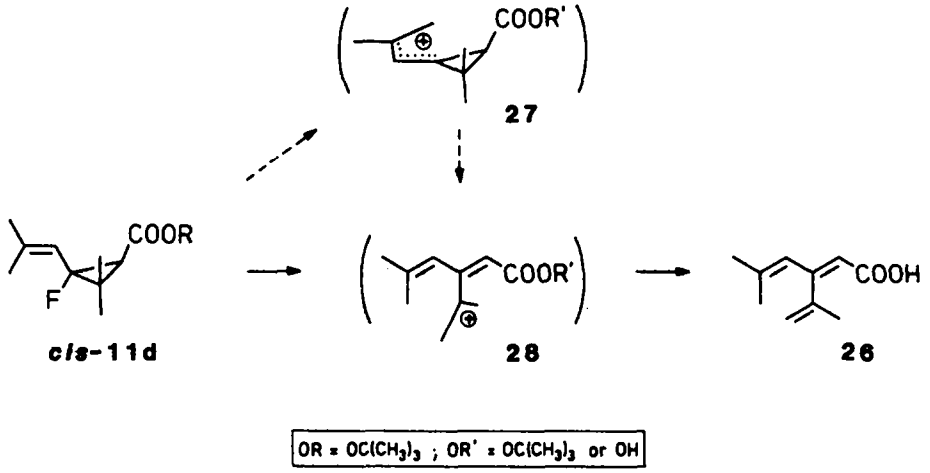
To obtain four desired products in a single, one-stage reaction looks quite attractive provided the components can afterwards be readily separated. We had to proceed stepwise. As described for the non-fluorinated methyl chrysanthemate [28], pig liver esterase promoted the complete hydrolysis of the *trans*-isomers **11b** and **12b** while the *cis*-isomers remained unchanged. (By the way, when the enzymatic hydrolysis was interrupted after 50% conversion, only a 17% enantioselectivity had been achieved for *trans*-**11b**).



After their alkaline extraction the acids *trans*-**11a** and *trans*-**12a** were neutralized and reesterified with diazomethane. Then the two pairs of regioisomers, *cis*-**11b** + *cis*-**12b** and *trans*-**11b** + *trans*-**12b**, were split into the individual components by preparative gas chromatography. Finally each of the pure methyl esters was treated with lithium *m*-phenoxybenzyl alcoholate to give the fluoro-analogs (**11e** and **12e**) of "phenothrin" (**5c**).



Under proton catalysis the γ-fluorochrysanthemates **12b**, **12c** and **12d** can be readily hydrolyzed to afford the free acids **12a**. In contrast, the β-fluorinated derivatives **11b**, **11c** and **11d** prove to be very fragile in acidic medium. The three-membered ring breaks up and under loss of fluorine the triply unsaturated 5-methyl-3-(1-methylethenyl)-2,4-hexadienoic acid (**26**) is formed. The *cis*-isomers, for example *cis*-**11d**, are cleaved considerably faster than the *trans*-isomers. This difference in reactivity advocates against a common intermediate such as the allylic cation **27**. Presumably the proton assisted departure of the fluoride ion and the rupture of the carbon-carbon bond across the ring occur simultaneously generating immediately the tertiary carbenium ion **28**.



The new compounds **11e** and **12e** were submitted to ten standard biological tests. As expected, the *cis*-isomers were more or less ineffective while the *trans*-isomers showed a similar activity profile as the corresponding halogen-free parent compound **5c** ("phenothrin").

EXPERIMENTAL PART

1. General remarks

Starting materials have been purchased from Fluka AG, Buchs, Aldrich-Chemie, Steinheim, or Merck-Schuchardt, Darmstadt, unless literature sources or details for the preparation are given. All commercial reagents were used without further purification.

Butyllithium was supplied by CheMetall, Frankfurt. *Air and moisture sensitive compounds* were stored in Schlenk tubes or Schlenk burettes. They were protected by and handled under an atmosphere of 99.995% pure nitrogen. *Anhydrous diethyl ether* and *tetrahydrofuran* were obtained by distillation after the characteristic blue color of in situ generated sodium diphenylketyl [20] was found to persist.

Ethereal extracts were dried with sodium sulfate. Before distillation of compounds prone to radical polymerisation or sensitive to acids a spatula tip of *hydroquinone* or, respectively, *potassium carbonate* was added.

The temperature of dry ice-methanol baths is consistently indicated as -75°C, "room temperature" (22 - 26°C) as 25°C. *Melting ranges* (mp) are reproducible after resolidification, unless otherwise stated ("dec."), and are corrected using a calibration curve which was established with authentic standards.

Whenever reaction products were not isolated, their yields were determined by *gas chromatography* comparing their peak areas with that of an internal standard and correcting the ratios by calibration factors. The purity of distilled compounds was checked on at least two columns loaded with stationary phases of different polarity. Chromosorb G-AW of 80 - 100 and, respectively, 60 - 80 mesh particle size were chosen as the support for packed analytical or preparative columns (2 or 3 m long, 2 mm inner diameter and 3 or 6 m long, 1 cm inner diameter, respectively). All packed columns were made of glass, while quartz was chosen as the material for coated, GROB-type capillary columns (≥ 10 m long). The type of the stationary phase used is abbreviated as SE-30 (silicone rubber), DEGS (diethylene glycol succinate polyester), and C-20M (polyethylene glycol).

Infrared spectra were recorded of films if the sample was liquid at room temperature, while solid substances were embedded in potassium bromide pellets. The intensities of absorption bands are abbreviated as s (strong), m (moderate), w (weak) and b (broad).

Nuclear magnetic resonance spectra of hydrogen nuclei were recorded in the 360 MHz field, of carbon-13 nuclei in the 90.6 MHz field (either under broad band or gated decoupling) and of fluorine-19 nuclei in the 188 MHz field. Unless otherwise stated, deuterochloroform was used as the solvent. Chemical shifts refer to the signal of tetramethylsilane (δ = 0 ppm), which served as an internal standard for ^{1}H and ^{13}C spectra and of α,α,α-trifluorotoluene for ^{19}F spectra. Coupling constants (J) are measured in Hz. Coupling patterns are described by abbreviations : *s* (singulet), *d* (doublet), *t* (triplet), *q* (quadruplet), *pent* (pentuplet), *hept* (heptuplet), *oct* (octuplet), *td* (triplet of a doublet) and *m* (multiplet).

In general, *mass spectra* were obtained at a 70 eV ionization potential. Whenever no molecular peak was observed under standard conditions, chemical ionization ("c.i.") in an ammonia atmosphere was applied.

2. Starting materials

2-Fluoro-3-methyl-2-butenal dimethyl acetal

A mixture of 1-chloro-1-fluoro-3-methoxy-2,2-dimethylcyclopropane [29] (9.0 g, 66 mmol) and triethylamine (9.6 mL, 7.0 g, 69 mmol) in methanol (50 mL) were heated 14 h to reflux. After dilution with a saturated aqueous solution of sodium bicarbonate (25 mL) the product was extracted with pentane (3 x 50 mL) and distilled; 7.8 g (80%), bp 49 - 51°C/10 mmHg (lit. [30] bp 54°C/17 mmHg).

2-(1-Fluoro-2-methyl-1-propenyl)-4,4,5,5-tetramethyl-1,3-dioxolane (21)

A mixture of 1-chloro-1-fluoro-3-methoxy-2,2-dimethylcyclopropane [29] (7.2 g, 53 mmol), triethylamine (7.7 mL, 5.6 g, 55 mmol) and pinacol (2,3-dimethyl-2,3-butandiol, 24.0 g, 200 mmol) were heated 4 h to 110°C. Extraction and distillation afforded a colorless liquid; 7.7 g (72%), bp 90 - 92°C/10 mmHg, n_D^{20} 1.4452.

^{1}H-NMR (80 MHz): 5.76 (1 H, *d*, *J* 22), 1.73 (3 H, *d*, *J* 2), 1.68 (3 H, *d*, *J* 2), 1.26 (6 H, *s*), 1.24 (6 H, *s*).

^{19}F-NMR: -72 (*dm*, *J* 23).

MS: 202 (1%, M^+), 187 (77%), 101 (86%), 85 (100%).

Analysis: calc. for $C_{11}H_{19}FO_2$ (202.27) C 65.32%, H 9.47%; found C 65.17%, H 9.15%.

Methyl 2-fluoro-3-methyl-2-butenoate

A mixture prepared of 2-fluoro-3-methyl-2-butenal (45 g, 0.44 mol), potassium cyanide (65 g, 1.00 mmol), acetic acid (57 mL, 60 g, 1.00 mol) and manganese dioxide (0.5 kg, 6 mol) in methanol (0.8 L) was stirred 24 h at 25°C. The suspension was filtered and the insoluble material washed with methanol (2 x 0.1 L). The combined solutions were diluted with water (0.5 L) and extracted with pentane (4 x 0.2 L). A colorless liquid was collected upon distillation under reduced pressure; 41 g (71%), bp 78 - 80°C/70 mmHg.

IR: 1730 (*s*, ν[C=O]), 1300 (*s*, ν[C-O]), 1240 (*s*, ν[C-O]), 1150 (*s*, ν[C-O]).

^{1}H-NMR (80 MHz): 3.68 (3 H, *s*), 2.11 (3 H, *d*, *J* 4), 1.88 (3 H, *d*, *J* 4).

^{19}F-NMR: -66 (*hept*, *J* 4).

Analysis: calc. for $C_6H_9FO_2$ (132.13) C 54.54%, H 6.86%; found C 54.88%, H 7.09%.

3-Fluoro-2-methyl-2,4-hexadiene

At -75°C, 2-fluoro-3-methyl-2-butenal (10.2 g, 100 mmol) was added dropwise to a solution of (triphenylphosphonio)ethanide (100 mmol, prepared by the "instant ylid" technique [31]) in diethyl ether (200 mL). As soon as the mixture had reached 25°C, the solvent was evaporated and the product distilled; 9.0 g (79%), bp 50 - 53°C/ 65 mmHg.

MS: 114 (16%, M^+), 99 (59%), 79 (100%).

Analysis: calc. for $C_7H_{11}F$ (114.16) C 73.65%, H 9.71%; found C 73.56%, H 10.18%.

The product consisted of two stereoisomers in the approximate *cis/trans* ratio of 90 : 10. They were separated by preparative gas chromatography (3 m, 10% SE-30, 90°C).

(*Z*)-Isomer:

^{1}H-NMR: 5.96 (1 H, *dd*, *J* 29.0, 11.2), 5.55 (1 H, *dq*, *J* 11.2, 7.0), 1.90 (3 H, *d*, *J* 7.0), 1.76 (3 H, *dd*, *J* 3.0, 1.5), 1.69 (3 H, *d*, *J* 3.0).

^{19}F-NMR: -53 (*doct*, *J* 28.5, 3.0).

(*E*)-Isomer:

^{1}H-NMR: 6.13 (1 H, *ddq*, *J* 27.0, 15.5, 1.5), 5.91 (1 H, *dq*, *J* 15.5, 6.0), 1.83 (3 H, *dq*, *J* 6.0, 1.0), 1.75 (3 H, *d*, *J* 3.0), 1.71 (3 H, *d*, *J* 3.0).

^{19}F-NMR: -62 (*dm*, *J* 26.5).

3-Fluoro-2,5-dimethyl-2,4-hexadiene

An analogous reaction with 2-triphenylphosphonio-2-propanide (100 mmol, "instant ylid" [31] preparation) gave 8.4 g (66%) of the corresponding fluorodiene; bp 64 - 65°C/65 mmHg.

^{1}H-NMR (80 MHz): 5.68 (1 H, *d*, *J* 22), 1.78 (6 H, *s*), 1.67 (3 H, *d*, *J* 3), 1.59 (3 H, *d*, *J* 2).

^{19}F-NMR: -51 (*d*, *J* 22.0).

MS: 128 (100%, M^+), 113 (97%), 93 (74%).

Analysis: calc. for $C_8H_{13}F$ (128.19) C 74.96%, H 10.22%; found C 75.22%, H 9.96%.

3. Attempted synthesis of methyl α-fluorochrysanthemate

3-Fluoro-2,7-dimethyl-5-*p*-tolylsulfonyl-2,6-octadien-4-one

Under nitrogen atmosphere, potassium *tert*-butoxide (0.45 g, 4.0 mmol) was added to a solution of 3-methyl-2-butenyl *p*-tolyl sulfone (0.90 g, 4.0 mmol) in tetrahydrofuran (20 mL). An orange color and, 5 min later, a precipitate appeared. After 15 min methyl 2-fluoro-3-methyl-2-butenoate (0.53 g, 4.0 mmol) was added under stirring. The reaction mixture rapidly turned brown and became homogeneous, but a short while later a new precipitate had formed. After 2 h the mixture was poured into water (50 mL) and extracted with diethyl ether (3 x 20 mL). When the solvent was dried and evaporated, a solid residue (1.1 g) remained. Elution from a silica gel (60 g) column with ethyl acetate-hexane (1 : 10 v/v) gave 0.6 g (15%) of 14 (followed by 0.4 g of the sulfone starting material); mp 90 - 91°C (after recrystallization from isopropanol and sublimation).

IR: 1700 (*m*, ν[C=O]), 1630 (s, ν[C=C]), 1320 (*s*, ν[S=O]), 1150 (*s*, ν[S=O]).

^{1}H-NMR: 7.73 (2 H, *d*, *J* 8), 7.40 (2 H, *d*, *J* 8), 5.6 (1 H, *m*), 5.2 (1 H, *m*), 2.45 (3 H, *s*), 2.10 (3 H, *d*, *J* 3), 1.86 (3 H, *d*, *J* 4), 1.76 (3 H, *s*), 1.54 (3 H, *s*).

^{19}F-NMR: -63 (*s*, broad).

MS: 324 (14%, M^+), 169 (100%), 141 (24%, 91 (45%).

Analysis: calc. for $C_{17}H_{21}FO_3S$ (324.41) C 62.94%, H 6.52%; found C 62.95%, H 6.68%.

Methyl 2,2-dimethyl 3-(2-methyl-2-propenylidene)cyclopropanecarboxylate (17)

An otherwise identical reaction was carried out in anhydrous dimethylformamide (20 mL) rather than in tetrahydrofuran. When, after evaporation of the solvents, the extract was distilled under reduced pressure (10 mmHg), 0.35 g of a colorless liquid was collected which contained 0.18 g (25%) of 17 while 0.40 g (44%) of the starting material 3-methyl-2-butenyl *p*-tolyl sulfone remained as a residue. The ester 17 was purified by preparative gas chromatography (3 m, 10% SE-30, 140 → 180°C [10°C/min]).

IR: 1725 (*s*, ν[C=O]), 1618 (*m*, ν[C=C]), 1310 (*s*, ν[C-O]).

^{1}H-NMR (80 MHz): 6.43 (1 H, *s*), 4.99 (2 H, *s*), 3.68 (3 H, *s*), 2.19 (1 H, *s*), 1.88 (3 H, *s*), 1.36 (6 H, *s*).

^{13}C-NMR: 171.6 (*s*), 141.6 (*s*), 134.3 (*s*), 123.6 (*d*, *J* 158.6), 116.4 (*t*, *J* 158.6), 51.5 (*q*, *J* 143.5), 28.9 (*d*, *J* 172.1), 27.5 (*s*), 26.7 (*q*, *J* 128.3), 19.5 (*q*, *J* 123.8), 19.4 (*q*, *J* 123.8).

With excess potassium *tert*-butoxide (8.0 rather than 4.0 mmol) only little sulfone starting material (22%) was recovered and the yield of ester 17 raised to 49%.

4. Decomposition of diazoacetates in the presence of fluoroolefins

Ethyl 4-fluoro-2,3-dimethoxy-5-methyl-4-hexenoate (19) and
Ethyl 4-fluoro-2,5-dimethoxy-3,3-dimethyl-4-pentenoate (20)

Ethyl diazoacetate (2.1 mL, 2.3 g, 20 mmol) in diethyl ether (8 mL) was added, in the course of 2 h and under vigorous stirring to 2-fluoro-3-methyl-2-butenal dimethyl acetal (3.0 g, 20 mmol), in which copper powder (0.05 g, 0.8 mmol) was suspended and which was kept at 125°C (the solvent being continuously removed). Distillation under reduced pressure (bp 73 - 78°C/1 mmHg) afforded a colorless liquid composed of equal amounts an *erythro/threo*-mixture (again 1 : 1) of 19 (1.2 g, 25%) and of (*Z*)-20 (1.2 g, 25%). Consecutive preparative gas chromatography allowed first to separate the pair of regioisomers (3 m, 10% SE-30, 150°C) and next the pair of diastereoisomers (3 m 20% C-20M, 175°C).

19 : The configurational assignment relies on the arguable generalization that the geminal coupling constant of a *threo*-compound is larger than that of the corresponding *erythro*-isomer [33]. The combustion analysis has been executed with the diastereomeric mixture.

erythro-19 :

IR : 1750 (*s*, ν[C=O]), 1115 (*s*, ν[C-O]).
^{1}H-NMR : 4.31 (1 H, *dd*, *J* 26.0, 7.5), 4.2 (2 H, *m*), 3.99 (1 H, *dd*, *J* 7.5, 0.9), 3.45 (3 H, *s*), 3.36 (3 H, *s*), 1.70 (3 H, *d*, *J* 3.5), 1.66 (3 H, *d*, *J* 3.0), 1.26 (3 H, *t*, *J* 7.0).
^{19}F-NMR : -64 (*dhept*, *J* 26.0, 3.3).
MS : 161 (2%), 117 (100%).
Analysis : Calc. for $C_{11}H_{19}FO_4$ (234.27) C 56.40%, H 8.17%; found C 56.37%, H 8.09%.

threo-19 :

IR : 1745 (*s*, ν[C=O]), 1125 (*s*, ν[C-O]), 1095 (*s*, ν[C-O]).
^{1}H-NMR : 4.3 (3 H, *m*), 3.88 (1 H, *d*, *J* 8.7), 3.36 (3 H, *s*), 3.26 (3 H, *s*), 1.76 (3 H, *d*, *J* 3.5), 1.73 (3 H, *d*, *J* 3.0), 1.45 (3 H, *t*, *J* 7.2).
^{19}F-NMR : -68 (*dhept*, *J* 27.0, 3.3).
MS : 234 (0.3%, M^+), 161 (3%), 117 (100%).

20 : The (*Z*)-configuration of the double bond was assigned on the basis of the J_{HF}-coupling constant [32].

IR : 1750 (*s*, ν[C=O]), 1130 (*m*, ν[C-O]), 1110 (*s*, ν[C-O]).
^{1}H-NMR (80 MHz) : 5.52 (1 H, *d*, *J* 22), 4.22 (2 H, *q*, *J* 7), 3.75 (1 H, *s*), 3.63 (3 H, *s*), 3.35 (3 H, *s*), 1.29 (3 H, *t*, *J* 7), 1.14 (3 H, *s*), 1.10 (3 H, *s*).
^{13}C-NMR : 170.8 (*s*), 149.9 (*d*, *J* 250.0), 129.3 (*dd*, *J* 171.9, 10.0), 84.3 (*d*, *J* 144.8), 60.6 (*t*, *J* 147.5), 60.4 (*q*, *J* 143.3), 58.6 (*q*, *J* 141.7), 40.5 (*d*, *J* 20.0), 21.3 (*q*, *J* 128.3), 20.5 (*q*, *J* 128.3), 14.3 (*q*, *J* 128.2).
^{19}F-NMR : -80 (*d*, *J* 23.0).
MS : 234 (2%, M^+), 161 (9%), 117 (100%).
Analysis : calc. for $C_{11}H_{19}FO_4$ (234.27) C 56.40%, H 8.17%; found C 56.18%, H 8.14%.

tert-Butyl 3-(1-fluoro-2-methyl-1-propenyl)-2-methylcyclopropanecarboxylate (24)

In the course of 1 h, *tert*-butyl diazoacetate [34] (0.71 g, 5.0 mmol) in diethyl ether (1 mL) was added to the vigorously stirred suspension of rhodium diacetate (6 mg, 0.03 mmol) in *cis*-3-fluoro-2-methyl-2,4-hexadiene

(1.1 g, 10 mmol). Upon distillation under reduced pressure a 1 : 1 mixture of isomers of **24** was collected (gas chromatography : 3 m, 5% SE-30, 145 → 190°C [10°C/min]; 3 m, 5% C-20M, 145 → 190°C [10°C/min]); 0.90 g (79%); bp 64 - 68°C/1 mmHg.

Analysis : calc. for $C_{13}H_{21}FO_2$ (228.31) C 68.39%, H 9.27%; found C 68.42%, H 9.11%.

After separation by preparative gas chromatography (3 m, 20% C-20M, 175 → 190°C) they were identified, in the order of their elution, as ***tert*-butyl *t*-3-(1-fluoro-2-methyl-1-propenyl)-*t*-2-methyl-*r*-1-cyclopropanecarboxylate** ("*trans*-**24**") and ***tert*-butyl *c*-3-(1-fluoro-2-methyl-1-propenyl)-*c*-2-methyl-*r*-1-cyclopropanecarboxylate** ("*cis*-**24**").

cis-**24**: n_D^{20} 1.4508.

IR : 1730 (*s*, ν[C=O]), 1145 (*s*, ν[C-O]).

^{1}H-NMR : 2.07 (1 H, *tm*, *J* 9), 1.81 (1 H, *dt*, *J* 8.5, 2.2), 1.68 (3 H, *dd*, *J* 3.0, 2.0), 1.60 (3 H, *dd*, *J* 3.0, 1.1), 1.5 (1 H, *m*), 1.44 (9 H, *s*), 1.34 (3 H, *dd*, *J* 6.5, 1.2).

^{19}F-NMR : -45 (*s*, broad).

MS : 172 (26%), 127 (45%), 57 (100%).

trans-**24** : n_D^{20} 1.4479.

IR : 1730 (*s*, ν[C=O]), 1155 (*s*, ν[C-O]).

^{1}H-NMR : 2.20 (1 H, *ddd*, *J* 17.0, 9.0, 4.5), 1.66 (6 H, *d*, *J* 3.0), 1.6 (2 H, *m*), 1.45 (9 H, *s*), 1.11 (3 H, *dd*, *J* 6.2, 1.8).

^{19}F-NMR : -48 (*dm*, *J* 17).

MS : 228 (1%, M^+), 172 (11%), 127 (23%), 57 (100%).

Fluoro-substituted methyl chrysanthemates (11b and 12b)

In the course of 10 h, methyl diazoacetate [34] (6.0 g, 60 mmol) in diethyl ether (5 mL) was added to the vigorously stirred suspension of rhodium diacetate (0.06 g, 0.3 mmol) in 3-fluoro-2,5-dimethyl-2,4-hexadiene (14.1 g, 110 mmol). Distillation allowed to recover unconsumed fluorodiene (7.3 g) and to isolate a mixture consisting of methyl ***c*-3-fluoro-2,2-dimethyl-*t*-3-(2-methyl-1-propenyl)cyclopropanecarboxylate** (*trans*-**11b**), ***t*-3-fluoro-2,2-dimethyl-*c*-3-(2-methyl-1-propenyl)cyclopropanecarboxylate** (*cis*-**11b**), **methyl *c*-3-(1-fluoro-2-methyl-1-propenyl)-2,2-dimethylcyclopropanecarboxylate** (*cis*-**12b**) and ***t*-3-(1-fluoro-2-methyl-1-propenyl)-2,2-dimethyl-cyclopropanecarboxylate** (*trans*-**12b**) in the approximate ratio of 1.0 : 2.1 : 1.1 : 1.3 (according to gas chromatography : 3 m, 5% SE-30 or C-20M, 120 → 190°C [10°C/min]); 8.0 g (67%), bp 58 - 62°C/1 mmHg.

Analysis : calc. for $C_{11}H_{17}FO_2$ (200.25) C 65.98%, H 8.56%; found C 66.05%, H 8.63%.

The four components were separated by preparative gas chromatography first pairwise into regioisomers (3 m, 10% SE-30, 135°C) and then, in a second run (3 m, 10% C-20M, 135°C) into individual stereoisomers.

cis-**11b** : n_D^{20} 1.4498.

IR : 1740 (*s*, ν[C=O]), 1205 (*m*, ν[C-O]), 1160 (*s*, ν[C-O]).

^{1}H-NMR : 5.56 (1 H, *d*, *J* 8.8), 3.65 (3 H, *s*), 1.91 (1 H, *d*, *J* 19.5), 1.84 (3 H, *dd*, *J* 6.0, 1.2), 1.76 (3 H, *dd*, *J* 4.5, 0.8), 1.38 (3 H, *d*, *J* 1.5), 1.18 (3 H, *d*, *J* 1.9).

^{19}F-NMR : -98 (*m*).

MS : 200 (7%, M^+), 185 (14%), 165 (21%), 141 (100%).

trans-**11b** : n_D^{20} 1.4551.

IR : 1750 (*s*, ν[C=O]), 1200 (*m*, ν[C-O]), 1150 (*m*, ν[C-O]).

^{1}H-NMR : 5.43 (1 H, *d*, *J* 7.0), 3.69 (3 H, *s*), 1.82 (3 H, *d*, *J* 4.0), 1.80 (3 H, *dd*, *J* 6.0, 1.0), 1.48 (1 H, *d*, *J* 5.5), 1.46 (3 H, *d*, *J* 1.5), 1.10 (3 H, *d*, *J* 2.2).

^{19}F-NMR : -117 (*m*).

MS : 200 (3%, M^+), 185 (9%), 165 (11%), 141 (100%).

cis-**12b** : n_D^{20} 1.4543.

^{1}H-NMR : 3.64 (3 H, *s*), 1.96 (1 H, *dm*, *J* 9.0), 1.74 (1 H, *dd*, *J* 9.0, 1.9), 1.66 (3 H, *t*, *J* 2.0), 1.55 (3 H, *dd*, *J* 2.7, 1.3), 1.35 (3 H, *d*, *J* 1.2), 1.22 (3 H, *s*).

^{19}F-NMR : -45 (*s*, broad).

MS : 200 (17%, M^+), 141 (100%), 121 (41%).

trans-**12b** : n_D^{20} 1.4485.

IR : 1740 (*s*, ν[C=O]), 1235 (*m*, ν[C-O]), 1170 (*s*, ν[C-O]).

^{1}H-NMR : 3.70 (3 H, *s*), 2.21 (1 H, *dd*, *J* 11.0, 5.8), 1.89 (1 H, *d*, *J* 5.8), 1.65 (3 H, *d*, *J* 3.5), 1.62 (3 H, *d*, *J* 3.0), 1.27 (3 H, *s*), 1.15 (3 H, *d*, *J* 1.1).

^{19}F-NMR : -48 (*d*, broad, *J* 10).

MS : 200 (26%, M^+), 141 (100%), 121 (36%).

The same molar quantities were used and the same work-up conditions applied when the diazo decomposition was catalyzed with anhydrous copper sulfate. The reaction conditions were modified in one respect : a temperature of 80°C, rather than 25°C, was chosen. The reaction mixture rapidly turned black.

Fluoro-substituted ethyl chrysanthemates (11c and 12c)

From the crude reaction mixture obtained after rhodium catalyzed decomposition of ethyl diazoacetate only two components were obtained as pure isomers by preparative gas chromatography (3 m, 10% SE-30, 140°C).

cis-**11c** :

^{1}H-NMR : 5.59 (1 H, *dm*, *J* 9.3), 4.1 (2 H, *m*), 1.90 (1 H, *d*, *J* 20.3), 1.82 (3 H, *dd*, *J* 6.2, 1.2), 1.76 (3 H, *dd*, *J* 4.6, 1.1), 1.39 (3 H, *d*, *J* 1.4), 1.26 (3 H, *t*, *J* 7.3), 1.18 (3 H, *d*, *J* 2.1).

^{19}F-NMR : -98 (*m*).

MS : 214 (3%, M^+), 199 (5%), 141 (100%).

trans-**12c** :

^{1}H-NMR : 4.2 (2 H, *m*), 2.21 (1 H, *dd*, *J* 11.4, 5.8), 1.89 (1 H, *d*, *J* 5.8), 1.66 (3 H, *d*, *J* 2.6), 1.63 (3 H, *d*, *J* 2.9), 1.28 (3 H, *t*, *J* 7.3), 1.26 (3 H, *s*), 1.15 (3 H, *d*, *J* 1.1).

^{19}F-NMR : -48 (*m*).

MS : 214 (42%, M^+), 199 (1%), 141 (93%), 61 (100%).

Fluoro-substituted *tert*-butyl chrysanthemates (11d and 12d)

The rhodium-catalyzed decomposition of *tert*-butyl diazoacetate [34] in the presence of 3-fluoro-2,5-dimethyl-2,4-hexadiene gave a mixture containing four components, 54%, bp 57 - 60°C/0.5 mmHg. It was first split by prepa-

rative gas chromatography (3 m, 15% DEGS, 135°C) into two-component mixtures and subsequently into individual isomers (6 m, 10% SE-30, 150°C for the pair *cis*-**11d** and *trans*-**12d**; 3 m, 15% DEGS, 130°C for the pair *trans*-**11d** and *cis*-**12d**).

cis-**11d** :

IR : 1730 (*s*, ν[C=O]), 1150 (*s*, ν[C-O]).

^{1}H-NMR : 5.59 (1 H, *dm*, *J* 8.9), 1.83 (3 H, *dd*, *J* 6.0, 1.5), 1.81 (1 H, *d*, *J* 20.0), 1.78 (3 H, *dd*, *J* 4.5, 1.0), 1.43 (9 H, *s*), 1.36 (3 H, *d*, *J* 2.5), 1.16 (3 H, *d*, *J* 2.0).

^{19}F-NMR : -98 (*m*).

MS : 186 (16%), 141 (93%), 121 (39%), 57 (100%).

Analysis : calc. for $C_{14}H_{23}FO_2$ (242.33) C 69.39%, H 9.57%; found C 69.23%, H 9.73%.

trans-**11d** :

IR : 1760 (s, ν[C=O]), 1165 (*s*, ν[C-O]).

^{1}H-NMR : 5.46 (1 H, *dm*, *J* 7.5), 1.85 (3 H, *dd*, *J* 4.3, 0.9), 1.80 (3 H, *dd*, *J* 6.0, 1.1), 1.47 (9 H, *s*), 1.43 (3 H, *d*, *J* 1.8), 1.38 (1 H, *d*, *J* 6.0), 1.07 (3 H, *d*, *J* 1.2).

^{19}F-NMR : -118 (*m*).

MS : 186 (11%), 141 (91%), 121 (20%), 57 (100%).

Analysis : calc. for $C_{14}H_{23}FO_2$ (242.33) C 69.39%, H 9.57%; found C 69.38%, H 9.90%.

cis-**12d** :

IR : 1735 (*s*, ν[C=O]), 1140 (*s*, ν[C-O]).

^{1}H-NMR : 1.9 (1 H, *m*), 1.66 (3 H, *t*, *J* 2.5), 1.63 (1 H, *dd*, *J*9.0, 2.2), 1.56 (3 H, *dd*, *J* 2.5, 1.5), 1.43 (9 H, *s*), 1.33 (3 H, *d*, *J* 1.3), 1.20 (3 H, *s*).

^{19}F-NMR : -44 (*s*).

MS : 242 (1%, M^+), 186 (16%), 141 (72%), 57 (100%).

Analysis : calc. for $C_{14}H_{23}FO_2$ (242.33) C 69.39%, H 9.57%; found C 69.28%, H 9.78%.

trans-**12d** :

IR : 1730 (*s*, ν[C=O]), 1150 (*s*, ν[C-O]).

^{1}H-NMR : 2.13 (1 H, *dd*, *J* 11.7, 5.8), 1.81 (1 H, *d*, *J* 5.8), 1.66 (3 H, *d*, *J* 3.0), 1.63 (3 H, *d*, *J* 3.0), 1.46 (9 H, *s*), 1.25 (3 H, *s*), 1.13 (3 H, *d*, *J* 1.2).

^{19}F-NMR : -48 (*dm*, *J* 10).

MS : 242 (1%, M^+), 186 (10%), 141 (64%), 57 (100%).

Analysis : calc. for $C_{14}H_{23}FO_2$ (242.33) C 69.39%, H 9.57%; found C 69.16%, H 9.74%.

Competition experiment

In the course of 10 min methyl diazoacetate [34] was added to the vigorously stirred slurry of rhodium diacetate (0.08 g, 0.4 mmol) or cupric sulfate (3 mg, 0.02 mmol) in a 1 : 1 mixture of 2,5-dimethyl-2,4-hexadiene and its 3-fluoro analog (both 2.0 mmol) containing some decane (0.07 g) as an internal reference ("standard"). Before and after the reaction, a sample was taken and the relative amounts of the fluorinated and halogen-free diene determined by gas chromatographic comparison of peak areas (3 m, 1% $AgNO_3$ + 30% diethylene glycol, 60°C). Insertion into the well-known logarithmic expression [35] gave the total conversion rate of the fluorinated diene relative to that of the halogen-free diene. The knowledge of product compositions, as determined by gas

chromatographic analysis, allowed finally to calculate the partial rates for all reaction channels leading to individual regio- and stereoisomers.

5. Hydrolysis and transesterifications of fluorochrysanthemates

Acid cleavage of the *tert*-butyl β-fluorochrysanthemates 11d

A solution of the *cis*-isomer ***cis*-11d** (0.27 g, 1.1 mmol) and *p*-toluenesulfonic acid (30 mg, 0.16 mmol) in benzene (10 mL) was heated 1 h under reflux. After dilution with diethyl ether (10 mL), extraction with a 2% aqueous solution of sodium bicarbonate (3 x 10 mL), reacidification (pH 1), new extraction with diethyl ether (3 x 10 mL), washing, drying and evaporation, **5-methyl-3-(1-methylethenyl)-2,4-hexadienoic acid** (**26**, 0.13 g, 71%) was left as an oily residue.

^{1}H-NMR : 6.06 (1 H, *s*, broadened), 5.88 (1 H, *d*, *J* 1.0), 5.39 (1 H, *d*, *J* 1.0), 5.26 (1 H, *d*, *J* 1.2, broadened), 1.95 (3 H, *d*, *J* 1.1), 1.86 (3 H, *d*, *J* 1.5), 1.55 (3 H, *s*, broadened).

Treatment with etheral diazomethane led to the corresponding methyl ester.

MS : 180 (9%, M^+), 165 (28%), 121 (62%), 105 (100%).

Under identical conditions the *trans*-isomer ***trans*-11d** gave a 1:1 mixture of 5-methyl-3-(1-methylethenyl)-2,4-hexadienoic acid (**26**) and ***c*-3-fluoro-2,2-dimethyl-*t*-3-(2-methyl-1-propenyl)cyclopropanecarboxylic acid** (***trans*-11a**).

^{1}H-NMR: 5.45 (1 H, *dm*, *J* 6.8), 1.84 (3 H, *dd*, *J* 4.0, 1.0), 1.81 (3 H, *dd*, *J* 6.0, 1.2), 1.49 (1 H, *d*, *J* 5.5), 1.46 (3 H, *d*, *J* 1.8), 1.12 (3 H, *d*, *J* 1.2).

Esterification with diazomethane converted it to the methyl β-fluorochrysanthemate ***trans*-11b** (identified by gaschromatographic comparison with authentic material : 3 m, 5% SE-30, 165°C; 3 m, 5% C-20M, 170°C).

Acid cleavage of the *tert*-butyl γ-fluorochrysanthemates 12d

The ester ***cis*-12d** (0.50 g, 2.1 mmol) and *p*-toluenesulfonic acid (0.06 g, 0.3 mmol) were dissolved in benzene (20 mL). After 90 min of heating to reflux temperature, the mixture was diluted with diethyl ether (10 mL) and extracted with 2% aqueous sodium bicarbonate (3 x 15 mL). The combined aqueous layers were acidified to pH 1 and rapidly extracted with diethyl ether (3 x 10 mL). Upon evaporation of the dried solution the ***c*-3-(1-fluoro-2-methyl-1-propenyl)-2,2-dimethylcyclopropanecarboxylic acid** (***cis*-12a**) was collected as a solid residue; 0.26 g (66%), mp 91 - 92°C (after recrystallization from a 1 : 1 mixture of diethyl ether and hexane).

^{1}H-NMR : 2.03 (1 H, *dm*, *J* 9.0), 1.74 (1 H, *dd*, *J* 9.0, 2.2), 1.65 (3 H, *dd*, *J* 3.0, 2.0), 1.56 (3 H, *dd*, *J* 3.0, 1.2), 1.35 (3 H, *d*, *J* 1.2), 1.23 (3 H, *s*).

In the same way, the ***t*-3-(1-fluoro-2-methyl-1-propenyl)-2,2-dimethylcyclopropanecarboxylic acid** (***trans*-12a**) was obtained, 0.28 g (71%), mp 56 - 58°C.

^{1}H-NMR : (80 MHz) 9.1 (1 H, s, broad), 2.23 (1 H, *dd*, *J* 10, 6), 1.89 (1 H, *d*, *J* 6), 1.6 (6 H, *m*), 1.31 (3 H, *s*), 1.18 (3 H, *s*).

Treatment of the acids ***cis*-12a** and ***trans*-12a** with an ethereal solution of diazomethane converted them quantitatively to the methyl esters ***cis*-12b** and ***trans*-12b** as evidenced by gas chromatographic comparison with authentic samples.

Enzymatic hydrolysis of the methyl fluorochrysanthemates *trans*-11b and *trans*-12b

A suspension of a 2 : 1 : 1 : 1 mixture of the methyl fluorochrysanthemates *cis*-11b, *trans*-11b, *cis*-12b and *trans*-12b (1.80 g, 8.9 mmol) and pig liver esterase [36] (0.01 g in 1.0 mL of water) in a buffer solution (15 mL), 0.2 M in both phosphoric acid and sodium phosphate, was stirred at 25°C while an automatic device (Metrohm, Herisau) kept the pH constant at 8.0 by feeding in 1 N aqueous sodium hydroxide. After 24 h a new portion (0.5 mL) of the enzyme solution was added and the stirring continued for another period of 24 h. Extraction with diethyl ether (3 x 20 mL), followed by washing of the combined organic layers with 2% aqueous sodium bicarbonate (3 x 20 mL), drying and evaporation allowed to recover the methyl esters *cis*-11b and *cis*-12b almost quantitatively (1.0 g, 93%). They were readily separated by preparative gas chromatography (3 m, 10% SE-30, 135°C).

The combined aqueous layers were acidified to pH 1 and extracted with diethyl ether (3 x 20 mL). After drying and evaporation a 1 : 1 mixture of the acids *trans*-11a and *trans*-12a was obtained, 0.44 g (61%). Reesterification converted them to a mixture of methyl fluorochrysanthemates *trans*-11b and *trans*-12b which was again separated by preparative gas chromatography (3 m, 10% C-20M, 135°C).

In a parallel run the reaction was stopped after 50% hydrolysis of the β-fluorochrysanthemate *trans*-11b. An nmr analysis by means of the chiral shift reagent Eu(hfc)$_3$, tris-[*O,O'*-3-(2,2,3,3,4,4,4-heptafluoro-1-oxobutyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-onato]europium, allowed to determine the enantiomeric excess in the recovered esters. It was found to be fairly weak, approximately 17% in the case of ester *trans*-11b.

Preparation of the *m*-phenoxybenzylfluorochrysanthemates 11e and 12e

Butyllithium (0.8 L, 1.2 mmol, 1.5 M in hexane) and methyl fluorochrysanthemate *cis*-11b (0.20 g, 1.0 mmol) were added in consecutive order to a solution of *m*-phenoxybenzyl alcohol (2.0 g, 10 mmol) in diethyl ether (1.5 mL). After 36 h at 25°C the mixture (containing about 80% of crude product) was concentrated and separated by chromatography on silica gel (using a type B "Lobar" column of Merck GmbH and UV detection). Elution (flow rate 450 mL/h) with a 1 : 50 (v/v) mixture of ethyl acetate and hexane afforded the pure ester *cis*-11e (0.16 g, 43%). In the same way the isomers *trans*-11e (0.20 g, 54%), *cis*-12e (0.17 g, 46%) and *trans*-12e (0.19 g, 52%) were obtained.

cis-11e : n_D^{20} 1.5386.

IR : 1740 (*s*, ν[C=O]), 1260 (*s*, ν[C-O]), 1150 (*s*, ν[C-O]).

^{1}H-NMR : 7.3 (4 H, *m*), 7.1 (2 H, *m*), 7.0 (2 H, *m*), 6.9 (1 H, *m*), 5.54 (1 H, *dm*, *J* 8.5), 5.06 (1 H, *d*, *J* 12.8), 5.04 (1 H, *d*, *J* 12.8), 1.96 1 H, *d*, *J* 19.5), 1.80 (3 H, *dd*, *J* 6.0, 1.1), 1.74 (3 H, *dd*, *J* 4.5, 1.0), 1.37 (3 H, *d*, *J* 1.5), 1.17 (3 H, *d*, *J* 1.5).

^{19}F-NMR : -98 (*m*).

MS : 368 (16%, M^+), 348 (11%), 183 (100%), 141 (90%).

Analysis : calc. for $C_{23}H_{25}FO_3$ (368.45) C 74.98%, H 6.84%; found C 74.91%, H 7.06%.

trans-11e : n_D^{20} 1.5378.

IR : 1740 (*s* ν[C=O]), 1260 (*s*, ν[C-O]), 1140 (*s*, ν[C-O]).

^{1}H-NMR : 7.3 (4 H, *m*), 7.1 (2 H, *m*), 7.0 (2 H, *m*), 6.9 (1 H, *m*), 5.43 (1 H, *dm*, *J* 7.0), 5.11 (1 H, *d*, *J* 13.0), 5.09 (1 H, *d*, *J* 13.0), 1.79 (6 H, *m*), 1.53 (1 H, *d*, *J* 5.5), 1.45 (3 H, *d*, *J* 2.0), 1.09 (3 H, *d*, *J* 1.2).

^{19}F-NMR : -116 (*m*).

MS : 368 (24%, M^+), 183 (100%), 141 (282%).

cis-12e : n_D^{20} 1.5403.

IR : 1740 (*s*, ν[C=O]), 1260 (*s*, ν[C-O]), 1145 (*s*, ν[C-O]).

^{1}H-NMR : 7.3 (4 H, *m*), 7.1 (2 H, *m*), 7.0 (2 H, *m*), 6.9 (1 H, *m*), 5.05 (2 H, *s*), 1.97 (1 H, *dm*, *J* 9.0), 1.79 (1 H, *dd*, *J* 9.0, 2.0), 1.64 (3 H, *dd*, *J* 2.8, 2.0), 1.51 (3 H, *dd*, *J* 3.0, 1.1), 1.34 (3 H, *d*, *J* 1.2), 1.21 (3 H, *s*).

^{19}F-NMR : -45 (*s*).

MS : 368 (24%, M^+), 183 (100%), 141 (54%).

trans-12e : n_D^{20} 1.5368.

IR : 1730 (*s*, ν[C=O]), 1260 (*s*, ν[C-O]), 1165 (*s*, ν[C-O]).

^{1}H-NMR : 7.3 (4 H, *m*), 7.1 (2 H, *m*), 7.0 (2 H, *m*), 6.9 (1 H, *m*), 5.08 (2 H, *s*), 2.23 (1 H, *dd*, *J* 11.0, 5.5), 1.65 (3 H, *d*, *J* 2.5), 1.61 (3 H, *d*, *J* 2.8), 1.25 (3 H, *s*), 1.14 (3 H, *d*, *J* 1.1).

^{19}F-NMR : -48 (*m*).

MS : 368 (20%, M^+), 183 (95%), 141 (100%).

The transesterification requires less than 1 h if the *m*-phenoxybenzyl alcoholate is generated with potassium hydride rather than butyllithium.

Acknowledgment. The authors wish to thank Drs. D. Bellus, L. Gsell, K. Gubler and O. Rohr (all Ciba-Geigy AG, Basle) for valuable comments, support and access to testing facilities. They are grateful for a research grant (no 2.446-0.84) allocated by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung, Bern.

REFERENCES

[1] K. Naumann, *Chemie der synthetischen Pyrethroid-Insektizide*, Vol. 7 of the series *Chemie der Pflanzenschutz- und Schädlingsbekämpfungsmittel* (editor : R. Wegler), Springer-Verlag, Berlin, 1981.

[2] R. Yamamoto, *J. Chem. Soc. Japan* **44** (1923), 311.

[3] H. Staudinger, L. Ruzicka, *Helv. Chim. Acta* **7** (1924), 201.

[4] H. Staudinger, L. Ruzicka, *Helv. Chim. Acta* **7** (1924), 448, spec. 456.

[5] M.S. Schechter, R.B. LaForge, N. Greene, *J. Am. Chem. Soc.* **71** (1940), 3165.

[6] M. Elliott, A.W. Farnham, N.F. Janes, P.H. Needham, B.C. Pearson, *Nature* **213** (1967), 493.

[7] US-Patent 2'886'485(applic. 12 Sept. 1957, issued 12 May 1959) to Boyce-Thomson Institute (inventor : W.F. Barthel, B.H. Alexander, J.B. Gahan, P.G. Piquett); *Chem. Abstr.* **53** (1959), 12'922d.

[8] Ger. Offen. 1'926'433 (disclosed 4 Dec. 1969; Japan. Applic. filed 31 May/17 June 1968) to Sumitomo Chem. Co (inventors : N. Itaya, K. Kamoshita, S. Kitamura, Y. Okuno, T. Mizutani, S. Nakai, N. Kameda, K. Fujimoto); *Chem. Abstr.* **72** (1970), 66'647j; see also : K. Fujimoto, N. Itaya, Y. Okuno, T. Kadota, T. Yamaguchi, *Agr. Biol. Chem.* **37** (1973), 2'681; *Chem. Abstr.* **80** (1974), 36'807j.

[9] Ger. offen. 2'231'312 (filed 26 June 1972, discl. 11 Jan. 1973) to Sumitomo Chem. Co (inventors : T. Matsuo, N. Itaya, Y. Okuno, T. Mizutani, N. Ohno). *Chem. Abstr.* **78** (1973), 84'072w; T. Matsuo, N. Itaya, T. Mizutani, N. Ohno, K. Fujimoto, Y. Okuno, H. Yoshioka, *Agr. Biol. Chem.* **40** (1976), 247; *Chem. Abstr.* **84** (1976), 135'838j.

[10] Ger. Offen. 2'651'341 (discl. 26 May 19877; Brit. Applic. filed 12 Nov. 1975) to Shell Int. Res. Maatsch. (inventor : D.A. Wood); *Chem. Abstr.* **87** (1977), 134'690e.

[11] J. Farkaš, P. Kourim, F. Šorm, *Collect. Czech. Chem. Commun.* **24** (1959), 2230.

[12] Brit. Patent 1'413'491 (filed 25 May 1972/15 Aug. 1973, issued 23 March 1977) to Nat. Research Dev. Corp. (inventors : M. Elliott, N.F. Janes, D.A. Pulman); *Chem. Abstr.* **80** (1974), 132'901f; M. Elliott, A. W. Farnham, N.F. Janes, P.H. Needham, D.A. Pulman, *Nature* **248** (1974), 710.

[13] Commercialized as a mixture of stereoisomers.

[14] S. Cottens, thèse de doctorat, Ecole Polytechnique Fédérale de Lausanne, 1985, p. 20 - 21.

[15] M. Schlosser, *Tetrahedron* **34** (1978), 3.

[16] T. Narahashi, *Pestic. Sci.* **7** (1976), 267; *Chem. Abstr.* **85** (1976), 172'703c; *Insect. Biochem. Physiol.* (Editor : C.F. Wilkinson), Plenum Press, New York 1976, p. 327; *Chem. Abstr.* **86** (1977), 51'386p.

[17] J. Martel, C. Huynh, *Bull. Soc. Chim. Fr.* **1967**, 985; M. Julia, A. Guy-Rouault, *Bull. Soc. Chim. Fr.* **1967**, 1411; P.F. Schatz, *J. Chem. Educ.* **55** (1978), 468.

[18] Analogies : W.E. Billups, T.C. Shields, W.Y. Chow, N.C. Deno, *J. Org. Chem.* **37** (1972), 3676.

[19] J.-L. Brayer (Roussel-Uclaf, Romainville), private communication (May 1985).

[20] I.G.M. Campbell, S.H. Harper, *J. Chem. Soc.* **1945**, 283; T. Aratani, Y. Yoneyoshi, T. Nagase, *Tetrahedron Lett.* **23** (1982), 685.

[21] R. Paulissen, A.J. Hubert, P. Teyssié, *Tetrahedron Lett.* **13** (1972), 1465; U. Mende, B. Radüchel, W. Skuballa, H. Vorbrüggen, *Tetrahedron Lett.* **13** (1972), 1465.

[22] A.J. Hubert, A.F. Noels, A.J. Anciaux, P. Teyssié, *Synthesis* **1976**, 600; M.P. Doyle, J.H. Griffin. M.S. Chinn, D. van Leusen, *J. Org. Chem.* **49** (1984), 1917; H.J. Callot, F. Metz, *Tetrahedron* **41** (1985), 4495.

[23] A.J. Anciaux, A. Demonceau, A.F. Noels, R. Warin, A.J. Hubert, P. Teyssié, *Tetrahedron* **39** (1983), 2169.

[24] B. Spahić, M. Schlosser, *Helv. Chim. Acta* **63** (1980), 1242.

[25] K. Kondo, S. Cottens, M. Schlosser, *Chem. Lett.* **1984**, 1470.

[26] M. Schlosser, G. Heinz, Le Van Chau, *Chem. Ber.* **104** (1971), 1921.

[27] See, *e.g.*, H.G. Kuivila, A.R. Hendrickson, *J. Am. Chem. Soc.* **74** (1952), 5068; G. Illuminati, G. Marino, *J. Am. Chem. Soc.* **78** (1956), 4975; L.M. Stock, H.C. Brown, *Adv. Phys. Org. Chem.* **1** (1963), 35, spec. 74; G.A. Olah, Y.K. Mo, Y. Halpern, *J. Chem.* Soc. **94** (1972), 3551; H. Volz, W.D. Mayer, *Liebigs Ann. Chem.* **1975**, 835; H. Volz, H.J. Streicher, *Tetrahedron* **33** (1977), 3133.

[28] M. Schneider, N. Engel, H. Boensmann, *Angew. Chem.* **96** (1984), 52; *Angew. Chem. Int. Ed. Engl.* **23** (1984), 64.

[29] Y. Bessière, Dang Ngoc-Huê Savary, M. Schlosser, *Helv. Chim. Acta* **60** (1977), 1739.

[30] F. Camps, J. Coll, A. Messeguer, M.A. Pericás, *J. Heterocycl. Chem.* **17** (1980), 1377.

[31] M. Schlosser, B. Schaub, *Chimia* **46** (1982), 396.

[32] For comparison, see : R.E.A. Dear, *J. Org. Chem.* **35** (1970), 1703; J.W. Emsley, L. Phillips, V. Wray, *Progress in Nuclear Magnetic Resonance Spectroscopy* (editors : J.W. Emsley, J. Feeney, L.H. Sutcliffe), Vol. 10, p. 109, Pergamon Press, Oxford, 1977.

[33] See, *e.g.*, C.A. Kingsbury, W. B. Thornton, *J. Org. Chem.* **31** (1966), 1000; M. Schlosser, K.F. Christmann, *Liebigs Ann. Chem.* **708** (1967), 1.

[34] M. Regitz, J. Hocker, A.M. Liedheger, *Org. Prep. Proced.* **1** (1969), 99; *Chem. Abstr.* **71** (1969), 60'640j.

[35] R. Huisgen, in : *Methoden der organischen Chemie* (editor : E. Müller), Vol. 3/1, p. 99 - 162, spec. 144, G. Thieme Verlag, Stuttgart 1955; M. Schlosser, V. Ladenberger, Chem. Ber. **100** (1967), 3901.

[36] Supplied by Boehringer GmbH, D-68 Mannheim.