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Regio- and Chemoselective Epoxidation of Fluorinated Monoterpenes and Sesquiterpenes by Dioxiranes

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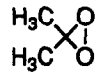
Abstract: A comparative study on chemoselectivity of dimethyldioxirane (DMD) and methyl(trifluoromethyl)dioxirane (TFMD) in the epoxidation of trisubstituted C=C bonds presenting different activation in fluorinated monoterpene and sesquiterpene derivatives has been carried out. With respect to DMD, epoxidations performed with TFMD were faster under milder conditions, although high conversion yields were obtained with both reagents. In ease of epoxidation of unsaturated moieties the trend observed was: $(CH_3)(R^1)C=CH(R^2) \cong (CH_3)(R^1)C=CH(CH_2OR) \cong (CH_3)(R^1)C=CF(R^2) >> (CH_3)(R^1)C=CH(COOR) > (CF_3)(R^1)C=CH(R^2)$. Results reported herein present the first example of direct epoxidation of a double bond bearing a CF_3 substituent by non-biochemical means.

Key words: Epoxidation. Dimethyldioxirane. Methyl(trifluoromethyl)dioxirane. Chemoselectivity. Regioselectivity. Monoterpenes. Sesquiterpenes.

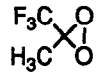
Considerable research on biorational strategies for insect pest control has been focused on juvenile hormones (JH) [1], since these compounds play a key role in the regulation of insect growth and development at both larval and adult stages. Besides the attempts carried out for suppressing JH production by inhibition of its biosynthesis [2], approaches involving the preparation of JH analogs that could interfere with the metabolic deactivation of these hormones have been also contemplated [3]. In this context, we deemed that introduction of fluorine atoms in selected segments of JH III (**5**, Scheme 1) could give rise to potential JH modulators [4]. However, the stimulatory JH activity elicited by one of the fluorinated analogs synthesized, i.e., trifluoromethyl derivative **20**, remained difficult to interpret due to the reluctance of this compound to undergo chemical or enzymatic oxidation at the terminal double bond [5]. A literature survey revealed that the only report of procedure of direct epoxidation of a carbon-carbon double bond bearing a trifluoromethyl substituent was the microbial oxidation of 3,3,3-trifluoropropene, a monosubstituted olefin [6].

In recent years, the ability shown by dioxiranes to act as powerful epoxidation reagents under mild conditions have led to a variety of synthetic applications [7]. In the field of insect chemistry, we have used dimethyldioxirane (DMD) in the first direct epoxidation of precocenes [8] and for the preparation of several JH III epoxy derivatives [9]. We now report on our results concerning the regio- and chemoselectivity exhibited by DMD and methyl(trifluoromethyl)dioxirane (TFMD) [10] in the epoxidation of trisubstituted C=C bonds having

different electronic activation. The substrates investigated were the monoterpene and sesquiterpene derivatives containing fluorinated and/or conjugated double bonds shown in Scheme 1.

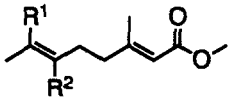


DMD

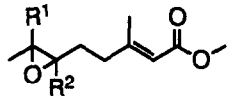


TFMD

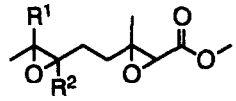
Scheme 1



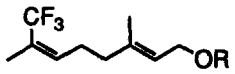
1: $R^1 = CH_3$; $R^2 = H$
8: $R^1 = CH_3$; $R^2 = F$
15: $R^1 = CF_3$; $R^2 = H$



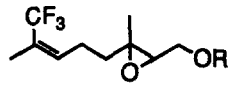
2: $R^1 = CH_3$; $R^2 = H$
9: $R^1 = CH_3$; $R^2 = F$



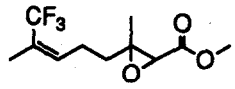
3: $R^1 = CH_3$; $R^2 = H$
10: $R^1 = CH_3$; $R^2 = F$
17: $R^1 = CF_3$; $R^2 = H$



11: R = H
13: R = THP



12: R = H
14: R = THP



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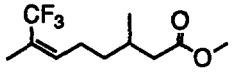

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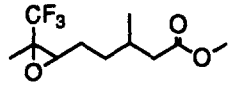

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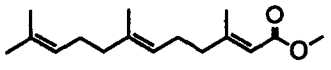

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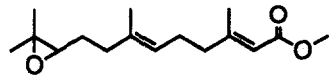

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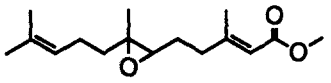

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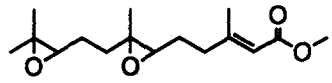

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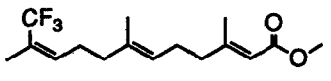

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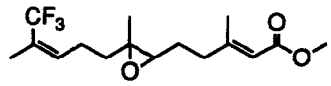

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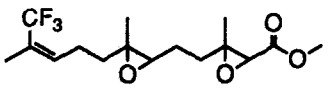

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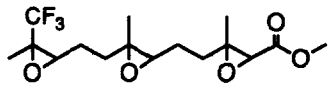

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Results and Discussion

Previously we had shown that using DMD instead of organic peroxyacids does not improve the regioselectivity in the epoxidation at the terminal double bond of methyl farnesate (**4**), which occurs preferentially at the 10,11 double bond [9]. Employing the more reactive TFMD allowed to carry out the epoxidation at temperature as low as -90 °C; however, the composition of the reaction mixture, consisting of unreacted ester, mono an diepoxy derivatives (**4**:**5**:**6**:**7** in 51:9:2:28 molar ratio, respectively) confirmed the poor regioselectivity obtained with DMD.

Table 1. Epoxidation of monoterpene and sesquiterpene derivatives with DMD and TFMD

		Reaction conditions			
Substrate	Product	Dioxirane [a]	Temp. (°C)	Reaction time	Isolated yield (%)
1	**2**	DMD	20	10 min	96
1	**2**	TFMD	-40	3 min	97
2	**3**	DMD	0	48 h	90
2	**3**	TFMD	-70	2 h	90
8	**9**	DMD	20	15 min	95
8	**9**	DMD	-40	3 min	95
8	**10**	DMD	0	8 days	90
11	**12**	DMD	20	15 min	98
11	**12**	TFMD	-15	3 min	98
13	**14**	DMD	20	15 min	98
13	**14**	TFMD	-40	3 min	99
15	**16**	DMD	0	8 days	42
15	**16**	TFMD[b]	0	3 min	85[c]
15	**17**	DMD	0	12 days	85[d]
15	**17**	TFMD[e]	0	1 h	93
18	**19**	DMD	0	16 days	93[c,f]
18	**19**	TFMD[g]	0	30 min	93
20	**21**	DMD	20	15 min	100[c]
20	**21**	TFMD	-20	3 min	85[c]
21	**22**	DMD	20	3 days	56[c]
21	**22**	TFMD	-70	1 h	85[c]
22	**23**	DMD	20	8 days	93[c]
22	**23**	TFMD	-20	1 h	94

[a] Unless noted otherwise, each substrate was reacted with one molar equivalent of dioxirane solution (see Experimental). [b] 1.4 molar equivalents. [c] Determined by GC. [d] Conversion yield was estimated as 95% (GC). [e] 2.3 molar equivalents.[f] Conversion yield was estimated as 93% (GC).[g] 2 molar equivalents.

Results obtained in the epoxidation of substrates **1, 2, 8, 11, 13, 15, 18, 20, 21** and **22** with DMD and TFMD are shown in Table 1. The epoxidation of dienoate **1** with DMD to give monoepoxide **2** was highly chemoselective; this is expected in view of the poor reactivity of α,β-unsaturated carbonyls towards electrophilic epoxidation. However, employing TFMD allows one to reduce considerably the reaction time for the further oxidation of **2** to the diepoxy derivative **3** [11]. Actually, the remarkable reactivity displayed by TFMD for the epoxidation of even poorly α,β-unsaturated ester moieties requires careful control of reaction conditions if one wishes to obtain just monoepoxide **2**. The same precautions need to be applied in the monoepoxidation of fluorinated trienoate **20** to yield **21** (see below).

The reactivity exhibited by monofluoro dienoate **8** was comparable to that observed for its non-fluorinated analog. In fact, a rapid epoxidation of non-conjugated double bond took place by using either DMD or TFMD; this is akin to what observed employing peroxyacids [4b]. However, use of dioxiranes has the advantage of ease of product isolation under conditions close to neutrality; this is valuable, given the high tendency of these fluoroepoxy derivatives to rearrange into the corresponding ketones in the presence traces of acid.

Epoxidation of trifluoromethyl dienoates **11** and **13** with either DMD or TFMD afforded the corresponding monoepoxides in near quantitative yields. It is worth of note that in these substrates the reaction occurred chemoselectively at the allylic double bond bearing a hydroxy group or a tetrahydropyranyl substituent. This is remarkable since it has been reported that dioxiranes efficiently afford conversion of alcohols into carbonyls [12] or cleavage of acetals through α-CH oxygen insertions [13].

Trifluoromethyl enoate **18** was chosen as model in order to assay epoxidation of an isolated double bond bearing a CF_3 substituent [14]. As mentioned above, these moieties are strongly resistant to electrophilic oxidations and remain unaffected after reaction with peroxyacids. However, treatment of ester **18** with DMD afforded the corresponding epoxide **19** in high yields. The reaction was slow, requiring 16 days for completion, and further addition of equimolecular amounts of dioxirane every 24 h [15]. By contrast, 2 molar equivalents of oxidant at 0 °C were sufficient for a complete consumption of **18** when TFMD was used as epoxidation agent. To our knowledge, this constitutes the first example of direct epoxidation of a C=C bond bearing a CF_3 group by non-biochemical means. It should be mentioned that compounds resulting from hydroxylation reactions were not detected; this is relevant since TFMD is capable of attacking unactivated C-H bonds [10].

When two double bonds bearing deactivating substituents such as CF_3 and CO_2Me are present in the same substrate, i.e. ester **15**, the results (Table 1) witness a higher reactivity of the α,β-unsaturated carbonyl double bond with respect to with the double bond bearing a CF_3 group. In this case, however, regioselectivity exhibited by DMD was poor. In fact attempts to obtain monoepoxide **16** using DMD resulted in a mixture of compound **16** and diepoxy derivative **17**, in 42 and 38% yields, respectively [16]. Conversely, employing TFMD resulted in higher regioselectivity affording monoepoxide **16** in 85% yield (accompanied by diepoxide **17**). When 2.3 molar equivalents of TFMD were used, ester **15** gave the diepoxy derivative **17** in high yield (Table 1).

With this background, we turned to the epoxidation of the JH III fluorinated analog **20**. As already mentioned, good yields of monoepoxide **21** could be obtained using both dioxiranes; however, overepoxidation to the diepoxide is easily avoided employing DMD. On the other hand, TFMD appears to be the reagent of choice for the synthesis of either diepoxide **22** or triepoxide **23**. Thus, these compounds could be obtained in excellent yields under very mild conditions (Table 1).

As for the ease of epoxidation by dioxiranes displayed by the various unsaturated moieties, data in Table 1 allow one to discern the following trend:

$$(CH_3)(R^1)C{=}CH(R^2) \cong (CH_3)(R^1)C{=}CH(CH_2OR) \cong (CH_3)(R^1)C{=}CF(R^2) >>$$
$$(CH_3)(R^1)C{=}CH(COOR) > (CF_3)(R^1)C{=}CH(R^2)$$

Thus, the less powerful DMD (a relatively cheap reagent) is quite appropriate for the epoxidation of ordinary or moderately deactivated C=C moieties. In addition, DMD offers the additional advantage that it could be thoroughly dried without significant decomposition [17]. On the other hand, the outstanding reactivity of TFMD makes this reagent the eminently suited for the epoxidation of deactivated double bonds. Moreover, this dioxirane is chemoselective in epoxidizing $(CH_3)(R^1)C{=}CH(COOR)$ moieties in the presence of $(CF_3)(R^1)C{=}CH(R^2)$ groups; it also shows preference for the epoxidation of trisubstituted C=C bonds in front of the hydroxylation of hydroxylation of C-H bonds of hydrocarbons or acetals. Finally, TFMD also allows epoxidation of isolated C=C bonds carrying CF_3, as demonstrated by transformations of **18** into **19** and **22** into **23** (Table 1). The availability of these epoxides will make possible the study of such compounds as epoxyhydrase effectors. Research along this line is now in progress.

Experimental Section

The NMR spectra (^1H, ^{13}C and ^{19}F NMR) were recorded on a Varian Gemini 200 or a Varian Unity 300 spectrometer. All NMR spectra were performed in neutralized $CDCl_3$ solutions; chemical shifts are given in ppm using tetramethylsilane as internal reference. The GC-MS-EI spectra (70 eV) were obtained using a Hewlett Packard 5995 C system equipped with a 25 m OV-101 capillary column . The GC-MS-CI spectra were obtained using a Hewlett Packard 5988 system, methane as ionization gas and 30 m HP-5 bonded phase capillary column (0.25 mm i.d.). The MS with direct probe and high resolution MS were obtained using a AEI MS 902 S apparatus. Elemental analyses were performed on a Carlo Erba 1108 instrument (Microanalysis Service, CID).

Methyl (2*E*,6*Z*)-8,8,8-trifluoro-3,7-dimethyl-2,6-octadienoate (15).

Following the general procedure described by Corey et al. [18], NaCN (3.4 g, 69 mmol), activated MnO_2 (22.8 g, 262 mmol) and glacial acetic acid (1.3 mL, 23 mmol) were added to a soln. of (2*E*,6*Z*)-8,8,8-trifluorogeranial [4b] (2.56 g, 12.4 mmol, prepared from ether **13** [19]) in MeOH (100 mL), maintained at 0 °C and the mixture was stirred for 20 h at 25 °C. The crude reaction mixture was filtered, concentrated, poured into $NaHCO_3$ satd. soln. (500 mL) and extracted with pentane (6 x 50 mL). The combined organic extracts were washed with water (3 x 50 mL) and dried over $MgSO_4$. After evaporation of solvent, the residue was purified by column chromatography (silica gel, hexane:^{t}-BuOMe 99:1) yielding 1.09 g of unreacted aldehyde, 0.45 g of ester with 2*Z* configuration and 0.55 g (36%) of the expected ester **15**. IR (film) 1725, 1650, 1225, 1150 cm^{-1}; ^1H NMR δ 6.05 (t, 1 H, J = 7.5 Hz, H-6, *E* isomer), 5.67 (q, 1 H, J = 1.5 Hz, H-2), 5.63 (t, 1 H, J = 7 Hz, H-6, *Z* isomer), 3.68 (s, 3 H), 2.48-2.36 (2 H, H-5), 2.28-2.16 (2 H, H-4), 2.15 (q, 3 H, J = 1.5 Hz, CH_3 at C-3), 1.84 (q, 3 H, J = 1.5 Hz, CH_3 at C-7); ^{13}C NMR δ 167.0 (C-1), 158.4 (C-3), 135.0 (d, J = 3 Hz, C-6), 126.2 (q, J = 29 Hz, C-7), 124.2 (q, J = 274 Hz, C-8), 115.9 (C-2), 50.9 (OCH_3), 40.2 (C-4), 25.8 (d, J = 1.5 Hz, C-5), 18.5 (CH_3 at C-3), 18.4 (q, J = 2.5 Hz, CH_3 at C-7); ^{19}F NMR δ 15.6 (s, integral 9, *Z* isomer), 7.8 (s, integral 1, *E* isomer), ; MS (EI), m/z 236 (M^+), 216, 205, 196, 185, 177, 157, 137 (base peak). Anal. Calcd. for $C_{11}H_{15}F_3O_2$: C, 55.93; H, 6.40. Found: C, 55.86; H, 6.37.

Methyl (6*Z*)-8,8,8-trifluoro-3,7-dimethyl-2,6-octenoate (18).

Following the general procedure reported by Semmelhack et al. [20], Red-Al® (1.1 mL, 3.7 mmol) was added to a suspension of CuBr (0.50 g, 3.5 mmol) in THF (12 mL), maintained at 0 °C. The suspension was

stirred for 30 min; then the temperatue was lowered to -70 °C, and 2-butanol (0.034 g, 0.46 mmol) and a soln. of the ester **15** (0.11g, 0.45 mmol) in THF (3 mL) were subsequently added to the reaction flask. The reaction mixture was stirred for 1 h at -20 °C (GC monitoring). The crude reaction mixture was quenched with water (5 mL), poured into NH_4Cl satd. sol. (60 mL) and extracted with pentane (2 x 50 mL). The combined organic extracts were washed with 0.5N HCl (2 x 100 mL), $NaHCO_3$ satd. sol. (2 x 100 mL), water (2 x 100 mL) and brine (2 x 100 mL) and dried with $MgSO_4$. Evaporation of solvent afforded the expected ester **18** (0.083 g, 77% yield, over 95% pure by ^1H NMR). IR (film) 1740, 1160, 1120 cm^{-1}; ^1H NMR δ 6.05 (t, 1 H, J = 7.5 Hz, H-6, *E* isomer), 5.67 (t, 1 H, J = 7 Hz, H-6, *Z* isomer), 3.67 (s, 3 H), 2.35-2.15 (2 H, H-5), 2.31 (dd, 1 H, J_1 = 6.5 Hz, J_2 = 15 Hz, H-2a), 2.15 (dd, 1 H, J_1 = 8 Hz, J_2 = 15 Hz, H-2b), 2.04-1.91 (m, 1 H, H-3), 1.84 (q, 3 H, J = 1.5 Hz, CH_3 at C-7), 1.50-1.36 (1 H, H-4a), 1.35-1.21 (1 H, H-4b), 0.95 (d, 3 H, J = 6.5 Hz, CH_3 at C-3) ; ^{13}C NMR δ 173.4 (C-1), 136.7 (q, J = 3.5 Hz, C-6), 127.1 (q, J = 275 Hz, C-8), 125.8 (q, J = 29 Hz, C-7), 51.4 (OCH_3), 41.4 (C-2), 36.1 (C-4), 29.9 (C-3), 25.6 (C-5), 19.4 (CH_3 at C-3), 18.4 (d, J = 2.5 Hz, CH_3 at C-7); ^{19}F NMR δ 14.2 (s, integral 9, *Z* isomer), 6.3 (s, integral 1, *E* isomer); MS (CI), m/z 267 (M^+ + 29), 239 (M^++1), 219 (base peak), 187. Anal. Calcd. for $C_{11}H_{17}F_3O_2$: C, 55.45; H, 7.19. Found: C, 55.23; H, 7.09.

Epoxidations. General procedure: An aliquot of standarized soln. of DMD (0.08 M in acetone) [21] or of TFMD (0.7 M in 1,1,1-trifluoroacetone)[10] was added quickly to a soln. of the substrate in the corresponding solvent kept at the given temperature. Eventually, careful concentration of the crude reaction mixture and addition of further dioxirane aliquots were required to reach a suitable conversion of deactivated substrates. After reaction was completed (GC and TLC monitoring), products isolation was achieved by removal of the solvents in vacuo or, when necessary, by column chromatography as indicated.

Epoxidation of ester 4 with TFMD.

A soln. of methyl farnesate (**5**, 0.029 g, 0.12 mmol) in dichloromethane (1 mL) was treated with an equimolecular amount of TFMD at -90 °C and the formation of the reaction products (epoxides **5** and **6**, and diepoxide **7**)[9] was followed by GC (see Results and Discussion).

Methyl (2*E*)-6,7-Epoxy-3,7-dimethyl-2-octenoate (2).

This compound was obtained from ester **1**[22] (0.041 g, 0.23 mmol, prepared from geranial as described above for ester **15**) and DMD (3 mL, 10 min at 20 °C, 96% yield) or TFMD (0.34 mL, 3 min at -40 °C, 97% yield). **2**[23]: IR (film) 1725, 1655, 1225, 1155 cm^{-1}; ^1H NMR δ 5.70 (q, 1 H, J = 1.5 Hz, H-2), 3.67 (s, 3 H), 2.70 (t, 1 H, J = 6.0 Hz, H-6), 2.4-2.1 (br, 2 H, H-4), 2.17 (d, 3 H, J = 1.5 Hz, CH_3 at C-3), 1.8-1.6 (br, 2 H, H-5), 1.25 and 1.29 (s, 6 H, C-8, CH_3 at C-7) ppm.

Methyl (2R*,3S*)-2,3,6,7-Diepoxy-3,7-dimethyloctanoate (3).

This compound was obtained as a diastereomeric mixture by reaction of ester **2** (0.080 g, 0.40 mmol) with DMD (two 5 mL portions added in a 24 h interval, 90% yield), or with TFMD (0.65 mL, 2 h at -70 °C, 90% yield). **3** (diastereomeric mixture): IR (film) 1755, 1205 cm^{-1}; ^1H NMR δ 3.79 (s, 3 H), 3.38 and 3.36 (s, 1 H, H-2, two diast.), 2.72 (m, 1 H, H-6), 1.92-1.56 (br, 4 H, H-4, H-5), 1.38 and 1.37 (s, 3 H, CH_3 at C-3 for the two diast.), 1.32 (s, 3 H, CH_3), 1.28 i 1.27 (s, 3 H, CH_3, two diast.); ^{13}C NMR δ 168.8 and 168.7 (C-1, two diast.), 63.5 and 63.4 (C-6, two diast.), 62.3 and 62.1 (C-3, two diast.), 58.6 and 58.2 (C-2, two diast.), 58.5 (C-7), 52.3 (OMe), 34.7 and 34.4 (C-4, two diast.), 24.8 (CH_3), 24.5 and 24.3 (C-5, two diast.), 18.7 and 18.6 (CH_3, two diast.), 16.3 and 16.1 (CH_3 at C-3, two diast.); MS (CI), m/z 215 (M^++ H), 197 (M^+-H_2O), 155 (M^+- CO_2CH_3), 127 (12), 71 (base peak).Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.70; H, 8.41.

Methyl (2*E*)-6,7-Epoxy-6-fluoro-3,7-dimethyl-2-octenoate (9).

This compound was obtained by reaction of ester **8**[4b] (0.096 g, 0.48 mmol) with DMD (6 mL, 15 min, 95% yield), or with TFMD (0.7 mL, 3 min at -40 °C, 95% yield). **4** : IR (film) 1725 , 1645, 1225, 1150 cm^{-1}; ^1H NMR δ 5.71 (q, 1 H, J = 1 Hz, H-2), 3.68 (s, 3 H), 2.43 (t, 2 H, J = 8 Hz, H-4), 2.18 (d, 3 H, J = 1 Hz, CH_3 at C-3), 2.16-1.90 (2 H, H-5), 1.43 (d, 3 H, J = 1 Hz, CH_3 *trans* to fluorine), 1.28 (d, 3H, J = 2.5 Hz,

CH_3 *cis* to fluorine); ^{13}C NMR δ 166.9 (C-1), 158.0 (C-3), 116.0 (C-2), 100.9 (d, J = 263.0 Hz, C-6), 64.3 (d, J = 20.0 Hz, C-7), 50.8 (OMe), 34.5 (C-4), 28.5 (d, J = 31.0 Hz, C-5), 20.0 (d, J = 2.0 Hz, C-8), 19.0 (CH_3 at C-3), 18.8 (d, J = 4.0 Hz, CH_3); ^{19}F NMR δ -60.9 (br.t, J = 18.0 Hz); MS (EI, direct probe), m/z: 216 (M^+), 196 (M^+- HF), 185 (M^+- OMe), 155, 137, 127, 95 (base peak). Anal. Calcd. for $C_{11}H_{17}FO_3$: C, 61.10; H, 7.92. Found: C, 61.24; H, 8.01.

Methyl (2R*,3S*)-2,3,6,7-Diepoxy-6-fluoro-3,7-dimethyloctanoate (10).

This compound was obtained as a diastereomeric mixture by reaction of ester **8** (0.018 g, 0.09 mmol) with DMD (1 mL portion added in a 24 h interval during 8 days, 0 °C, 90% yield). **10** (diastereomeric mixture): IR (film) 1755, 1160 and 1095 cm^{-1}; ^1H NMR δ 3.73 (s, 3 H), 3.34 and 3.32 (s, 1 H, H-2, two diast.), 2.01-1.83 (4 H, H-4, H-5), 1.39 (3 H, CH_3), 1.33 and 1.325 (s, 3 H, CH_3 at C-3, two diast.), 1.26 (t, 3 H, J = 2.5 Hz, 3 H, CH_3); ^{13}C NMR δ 168.6 (C-1), 101.0 (d, J = 261.0 Hz, C-6), 64.5 (d, J = 30.0 Hz, C-7), 61.9 and 61.8 (C-3, two diast.), 58.5 and 58.3 (C-2, two diast.), 52.25 (OMe), 31.7 and 31.5 (C-4, two diast.), 25.7 and 25.6 (d, J = 32.0 Hz, C-5 two diast.), 19.9 (d, J = 3.0 Hz, CH_3), 19.0 (CH_3), 16.3 and 16.1 (CH_3 at C-3, two diast.) ppm; ^{19}F NMR δ -60.3 (m, one diast.) and -60.63 (br.t., J = 17.5 Hz, one diast.); MS (EI, direct probe), m/z 232 (M^+), 173 (M^+-CO_2CH_3), 154 , 126, 58 (base peak). Anal. Calcd. for $C_{11}H_{17}FO_4$: C, 56.89; H, 7.38. Found: C, 57.03; H, 7.47.

(2R*,3S*)-(6Z)-2,3-Epoxy-8,8,8-trifluoro-3,7-dimethyl-6-octenol (12).

This compound was obtained as a diastereomeric mixture by reaction of alcohol **11**[4c] (0.021 g, 0.10 mmol) with DMD (1.5 mL, 15 min, 98% yield), or with TFMD (0.02 mL, 3 min at -15 °C, 98% yield). **12**: IR (film) 3600-3200, 1675, 1160 and 1120 cm^{-1}; ^1H NMR δ 6.05 (br. t., 1 H, J = 7.0 Hz, 1 H, H-6 *E* isomer), 5.69 (br. t., 1 H, J = 7.0 Hz, H-6 *Z* isomer), 3.84 (dd, 1 H, J_1 = 12.0 Hz, J_2 = 4.0 Hz, 1 H, CH_2OH), 3.69 (dd, 1 H, J_1 = 12.0 Hz, J_2 = 6.5 Hz, CH_2OH), 2.97 (dd, 1 H, J_1 = 4.0 Hz, J_2 = 6.5 Hz, H-2), 2.35 (q, 2 H, J = 8.0 Hz, H-5), 1.85 (q, 3 H, J = 1.5 Hz, CH_3 at C-7), 1.80-1.52 (2 H, H-4), 1.31 (s, 3 H, CH_3 at C-3); ^{13}C NMR δ 135.7 (q, J = 3.5 Hz, C-6), 125.9 (q, J = 29.0 Hz, C-7), 124.3 (q, J = 274.0 Hz, C-8), 62.7 (C-2), 61.3 (C-1), 60.7 (C-3), 38.0 (d, J = 1.0 Hz, C-4), 24.0 (d, J = 2.0 Hz, C-5), 18.4 (q, J = 2.5 Hz, CH_3 at C-7), 16.6 (CH_3 at C-3); ^{19}F NMR δ 14.09 (s, integral 9, 6*Z* isomer), 6.15 (s, integral 1, 6*E* isomer); MS (EI), m/z 193 (M^+-CH_3O), 123, 117, 58, 43 (base peak). Anal. Calcd. for $C_{10}H_{15}F_3O_2$: C, 53.57; H, 6.74. Found: C, 53.52; H, 6.77.

(2R*,3S*,2'R*)-(6Z)-2,3-Epoxy-2-tetrahydropyranyloxy-8,8,8-trifluoro-3,7-dimethyloct-6-ene (14).

This compound was obtained as a diastereomeric mixture by reaction of ether **13**[4c] (0.029 g, 0.10 mmol) with DMD (1.3 mL, 15 min, 98% yield), or with TFMD (0.15 mL, 3 min at -40 °C, 99% yield). **14** (diastereomeric mixture): IR (film) 1675, 1160, 1120, 1075, 1060 and 1030 cm^{-1}; ^1H NMR δ 6.05 (br.t., 1 H, J = 7.0 Hz,H-6 *E* isomer), 5.70 (br. t., 1 H, J = 7.5 Hz, H-6 *Z* isomer), 4.65 (m, 1 H, H-2'), 3.88 (dd, 1 H, J_1 = 11.5 Hz, J_2 = 4.5 Hz, H-1a one diast.) and 3.80 (dd, 1 H, J_1 = 11.5 Hz, J_2 = 6.0 Hz, H-1a one diast.), 3.60 (dd, 1 H, J_1 = 11.5 Hz, J_2 = 5.0 Hz, H-1b one diast.) and 3.54 (dd, 1 H, J_1 = 11.5 Hz, J_2 = 6.5 Hz, H-1b one diast.), 3.93-3.48 (2 H, H-6'), 3.00 (dd, 1 H, J_1 = 5.0 Hz, J_2 = 6.0 Hz, H-2), 2.35 (2 H, H-5), 1.84 (q, 3 H, J = 1.5 Hz, CH_3 at C-7), 1.90-1.48 (8 H, H-3, H-4, H-4', H-5'), 1.29 (s, 3 H, CH_3 at C-3); ^{13}C NMR δ 135.9 (q, J = 3.5 Hz, C-6), 125.8 (q, J = 29.0 Hz, C-7), 124.4 (q, J = 274.0 Hz, C-8), 99.3 and 98.6 (C-2', two diast.), 66.3 and 65.7 (C-6', two diast.), 62.4 and 61.9 (C-1, two diast.), 61.3 and 60.9 (C-2, two diast.), 59.9 and 59.7 (C-3, two diast.), 37.9 (C-4), 30.6 and 30.5 (C-3', two diast.), 25.4 and 25.35 (C-5', two diast.), 23.9 (t, J = 1.5 Hz, C-5), 19.4 and 19.1 (C-4', two diast.), 18.5 (q, J = 2.5 Hz, CH_3 at C-7), 16.7 and 16.6 (CH_3 at C-3, two diast.); ^{19}F NMR δ 14.08 (s, integral 9, 6*Z* isomer), 6.18 (s, integral 1, 6*E* isomer); MS (EI), m/z 223 (M^+- THP), 207 (M^+- OTHP), 101 (OTHP), 85 (THP, base peak). Anal. Calcd. for $C_{15}H_{23}F_3O_3$: C, 58.43; H, 7.52. Found: C, 58.57; H, 7.54.

Methyl (2R*,3S*)-(6*Z*)-2,3-Epoxy-8,8,8-trifluoro-3,7-dimethyl-6-octenoate (16).

This compound was obtained by reaction of ester **15** (0.106 g, 0.45 mmol) with: a) DMD (6.7 mL portions added at 24 h intervals during 8 days, at 0 °C) to give a mixture of the starting substrate, the corresponding monoepoxide and the diepoxide in a 2:55:42 equimolecular ratio (GC monitoring). The crude reaction mixture was purified by chromatography on silica gel (hexane:^{t}BuOMe 99:1) to afford 47 mg of the monoepoxide **16** with a 1:1 *Z:E* isomeric ratio (^{19}F-NMR monitoring) in 42% yield and 45 mg of the diepoxide **17** (see below, 38% yield). b) TFMD (1.4:1 TFMD:substrate molecular ratio, 3 min at 0 °C) to give a mixture of compounds **16:17** in 85:15 molecular ratio (GC monitoring, 9:1 *Z:E* isomeric ratio, ^{19}F NMR). **16**: IR (film) 1760, 1730, 1200, 1180, 1160, 1125 cm^{-1}; ^{1}H NMR δ 6.05 (br.s, 1 H, H-6 *E* isomer), 5.67 (br.t., 1 H, J = 8.0 Hz, H-6 *Z* isomer), 3.80 (s, 3 H, *E* isomer), 3.78 (s, 3 H, *Z* isomer), 3.36 (s, 1 H, H-2 *E* isomer), 3.33 (s, 1 H, H-2 *Z* isomer), 2.37 (m, 2 H, H-5 *Z* isomer), 2.25 (m, 2 H, H-5 *E* isomer), 1.84 (q, 3 H, J = 1.5 Hz, CH_3 at C-7), 1.79-1.60 (2 H, H-4), 1.38 (s, 3 H, CH_3 at C-3, *E* isomer), 1.36 (s, 3 H, CH_3 at C-3, *Z* isomer); ^{13}C NMR δ 168.7 (C-1, *E* isomer), 168.6 (C-1, *Z* isomer), 135.0 (q, J = 3.5 Hz, C-6 *Z* isomer), 131.3 (q, J = 6.0 Hz, C-6 *E* isomer), 126.3 (q, J = 29.0 Hz, C-7), 124.2 (q, J = 274.0 Hz, C-8), 62.1 (C-3, *E* isomer), 62.0 (C-3, *Z* isomer), 58.4 (C-2, *E* isomer), 58.3 (C-2, *Z* isomer), 52.3 (OMe, *E* isomer), 52.2 (OMe, *Z* isomer), 37.3 (q, J = 1.0 Hz, C-4, *Z* isomer), 36.4 (q, J = 1.0 Hz, C-4, *E* isomer), 23.8 (q, J = 2.0 Hz, C-5, *E* isomer), 23.8 (q, J = 2.0 Hz, C-5, *Z* isomer), 18.4 (q, J = 2.5 Hz, CH_3 at C-7, *E* isomer), 18.4 (q, J = 3.0 Hz, CH_3 at C-7, *Z* isomer), 16.2 (CH_3 at C-3, *E* isomer), 16.0 (CH_3 at C-3, *Z* isomer); ^{19}F NMR δ 13.98 (s, integral 1, *Z* isomer), 6.02 (s, integral 1, *E* isomer); MS (CI), m/z 253 (M^++ H), 235 (16), 193 (M^+- CO_2CH_3), 165, 117 (base peak). Anal. Calcd. for $C_{11}H_{15}F_3O_3$: C, 52.38; H, 5.99. Found: C, 52.19; H, 6.02.

Methyl (2R*,3S*,6R*,7R*)-Diepoxy-8,8,8-trifluoro-3,7-dimethyloctanoate (17).

This compound was obtained by reaction of ester **15** (0.080 g, 0.34 mmol) with: a) DMD (4.3 mL portions added at 24 h intervals during 12 days, at 0 °C) to give a mixture of compounds **16:17** in 5:95 molecular ratio (GC mointoring). The crude reaction mixture was purified by chromatography on silica gel (hexane:^{t}BuOMe 99:1) to afford 5 mg of the monoepoxide **16** (6*E* isomer, 6% yield) and 77 mg of the diepoxide **17** (diastereomeric mixture, 85% yield). b) TFMD (2.3:1 TFMD:substrate molecular ratio, 1 h at 0 °C) to give the diepoxide **17** (diastereomeric mixture, 93% yield, 9:1 *cis:trans* isomeric ratio). **17**: IR (film) 1760, 1735, 1185, 1150 and 1135 cm^{-1}; ^{1}H NMR δ 3 .80 (s, 3 H), 3.38 and 3.37 (s, 1 H, H-2, two diast.), 2.93 (m, 1 H, H-6), 1.94-1.78 (4 H, H-4, H-5), 1.49 (br. s, 3 H, CH_3 at C-7), 1.39 and 1.38 (s, 3 H, CH_3 at C-3, two diast.); ^{13}C NMR δ 168.6 and 168.5 (C-1, two diast.), 124.3 (q, J = 279.0 Hz, C-8), 62.9 (C-6), 62.0 and 61.7 (C-3, two diast.), 58.7 and 58.6 (q, J = 36 Hz, C-7, two diast.), 58.5 and 58.2 (C-2, two diast.), 52.3 (OMe), 34.7 and 34.4 (C-4, two diast.), 22.9 and 22.8 (q, J-= 2.5 Hz, C-5, two diast.), 16.7 (q, J = 1.5 Hz, CH_3 at C-7), 16.1 and 16.0 (CH_3 at C-3, two diast.); ^{19}F NMR δ 5.16 (s, integral 9, *cis* epoxide), -2.46 (s, integral 1, *trans* epoxide); MS (CI), m/z 269 (M^++ H), 268 (M^+), 251, 237, 209 (M^+- CO_2CH_3, base peak), 191, 181. Anal. Calcd. for $C_{11}H_{15}F_3O_4$: C, 49.24; H, 5.64. Found: C, 48.97; H, 5.63.

Methyl (3R*,6R*,7S*)-Epoxy-8,8,8-trifluoro-3,7-dimethyloctanoate (19).

This compound was obtained by reaction of ester **18** (0.019 g, 0.08 mmol) with: a) DMD (1.1 mL portions added at 24 h intervals during 16 days, at 0 °C) to give a mixture of compounds **18:19**(*cis*):**19**(*trans*) in a 6:80:13 molecular ratio (^{19}F NMR). b) TFMD (two 0.1 mL portions, 30 min at 0 °C, 2.3:1 TFMD:substrate molecular ratio, 1 h at 0 °C, 93% yield, 9:1 *cis:trans* isomeric ratio). **19**: IR (film) 1740, 1185 and 1150 cm^{-1}; ^{1}H NMR δ 3.68 (s, 3 H), 2.88 (m, 1 H, H-6), 2.37-2.14 (2 H, H-2), 2.06-1.98 (br., 1 H, H-3), 1.48 (br.s, 3 H, CH_3 at C-7), 1.82-1.24 (4 H, H-4, H-5), 0.99 and 0.97 (d, 3 H, J = 1.0 Hz, 3 H, CH_3 at C-3, two diast. *trans*), 0.98 and 0.96 (d, 3 H, J = 1.0 Hz, CH_3 at C-3 two diast. *cis*); ^{13}C NMR δ 173.2 (C-1), 124.4 (q, J = 277 Hz, C-8), 63.8 and 63.8 (C-6, two diast.), 58.5 and 58.4 (q, J = 36 Hz, C-7, two diast.) 51.4 (OMe), 41.4 and 41.1 (C-2, two diast.), 33.4 (C-4), 30.0 and 29.9 (C-3, two diast.), 24.7 and 24.7 (q, J = 2.5 Hz, C-5, two diast.), 19.6 and 19.3 (CH_3 at C-3, two diast.), 16.8 (q, J = 1.5 Hz, CH_3 at C-7, two diast.); ^{19}F NMR δ 5.06 (s, integral 9, *cis*), -2.47 (s, integral 1.5, *trans*) ppm; MS (CI), m/z 283 (M^++ CH_2CH_3), 255 (M^++ H), 237 , 235 (M^+- F), 223 (M^+- OMe, base peak), 217, 203.

Methyl (6R*,7R*)-(2*E*,10*Z*)-6,7-Epoxy-12,12,12-trifluoro-3,7,11-trimethyldodeca-2,10-dienoate (21).

This compound was obtained by reaction of ester **20**[4c] (0.081 g, 0.27 mmol) with: a) DMD (3.4 mL, 15 min, 100% conversion yield) to give epoxide **21**. b) TFMD (0.46 mL, 3 min at -20 °C) to give a mixture of compounds **21**:**22** in a 85:15 ratio (GC and ^{1}H NMR) in 92 % yield. **21**: IR (film) 1720, 1650, 1226, 1153 and 1118 cm^{-1}; ^{1}H NMR δ 6 .03 (t, 1 H, J = 7.0 Hz, H-10, *E* isomer), 5.70 (q, 1 H, J = 1.0 Hz, H-2), 5.66 (t, 1 H, J = 7.5 Hz, 1 H, H-10, *Z* isomer), 3.68 (s, 3 H), 2.68 (t, 1 H, J = 6.0 Hz , H-6), 2.40-2.20 (4 H, H-4, H-9), 2.17 (d, 3 H, J = 1.0 Hz, CH_3 at C-3), 1.83 (q, 3 H, J = 1.5 Hz, 3 H, CH_3 at C-10), 1.78-1.6 (4 H, H-5, H-8), 1.25 (s, 3 H, CH_3 at C-7); ^{13}C NMR δ 167.0 (C-1), 158.7 (C-3), 135.9 (d, J = 4 Hz, C-10), 125.7 (q, J = 29 Hz, C-11), 124.3 (q, J = 274 Hz, C-12), 115.7 (C-2), 62.4 (C-6), 60.4 (C-7), 50.9 (OMe), 38.1 (C-8), 37.5 (C-4), 26.6 (C-5), 24.0 (C-9), 18.7 (CH_3 at C-3), 18.4 (q, J = 3 Hz, CH_3 at C-11), 16.3 (CH_3 at C-7); ^{19}F NMR δ 14.1 (s, integral 12, 6*E* isomer), 6.2 (s, integral 1, 6*Z* isomer); MS (EI), m/z 289 (M^+-OCH_3), 263 (M^+-CO_2CH_3), 207, 69, 59, 43 (base peak). Anal. Calcd. for $C_{16}H_{23}F_3O_3$: C, 59.99; H, 7.24. Found: C, 60.03; H, 7.25.

Methyl (2R*,3S*,6R*,7R*)-(10*Z*)-2,3,6,7-Diepoxy-12,12,12-trifluoro-3,7,11-trimethyldodeca-10-enoate (22).

This compound was obtained by reaction of epoxide **21** (0.075 g, 0.23 mmol) with: a) DMD (2.9 mL portions added in a 24 h interval during 3 days at 20 °C) to give a mixture of compounds **22** and **23** in a 56:44 molecular ratio (GC monitoring, 100% conversion yield). b) TFMD (0.33 mL, 1 h at -70 °C) to give a mixture of compounds **22** and **23** in a 90:10 molecular ratio (GC, NMR monitoring) in 93% yield. A portion of this crude reaction mixture was purified by chromatography on silica gel to yield pure diepoxide **22**. **22** (diastereomeric mixture): IR (film) 1755, 1674, 1205, 1157 and 1116 cm^{-1}; ^{1}H NMR δ 6.03 (br. t, 1 H, J = 7.0 Hz, H-10, *E* isomer), 5.66 (br. t, 1 H, J = 8.0 Hz, 1 H, H-10, *Z* isomer), 3.79 (s, 3 H), 3.38 and 3.36 (s, 1 H, H-2 two diast.), 2.75-2.65 (H-6, two diast.), 2.38-2.26 (2 H, H-9), 1.83 (q, 3 H, J = 1.5 Hz, 3 H, CH_3 at C-10), 1.78-1.60 (6 H, H-4, H-5, H-8), 1.38 and 1.37 (s, 3 H, CH_3 at C-10, two diast.), 1.26 and 1.25 (s, 3 H, CH_3 at C-7, two diast.); ^{13}C NMR δ 168.7 and 168.7 (C-1, two diast.), 135.9 (d, J =3 Hz, C-10), 125.7 (q, J = 29 Hz, C-11), 124.3 (q, J = 274 Hz, C-12), 62.4 and 62.3 (C-6 two diast.), 62.2 and 62.0 (C-3 two diast.), 60.5 and 60.4 (C-7 two diast.), 58.5 and 58.2 (C-2 two diast.), 52.3 (OMe), 38.1 (C-8), 34.5 and 34.3 (C-4 two diast.), 24.3 and 24.1 (C-5 two diast.), 24.0 (C-9), 18.4 (q, J = 3 Hz, CH_3 at C-11), 16.3 (CH_3 at C-7), 16.3 and 16.1 (CH_3 at C-3, two diast.); ^{19}F NMR δ 14.1 (s, integral 9, *E* isomer), 6.2 (s, integral 1, *Z* isomer); MS (EI), m/z 259 (M^+-77), 247, 69, 59, 43 (base peak). Anal. Calcd. for $C_{16}H_{23}F_3O_4$: C, 57.14; H, 6.89. Found: C, 57.20; H, 6.99.

Methyl (2R*,3S*,6R*,7R*,10R*,11R*)-2,3,6,7,10,11-Triepoxy-12,12,12-trifluoro-3,7,11-trimethyldodecanoate (23).

This compound was obtained by reaction of diepoxide **22** (0.051 g, 0.15 mmol) with: a) DMD (1.9 mL portions added in a 24 h interval during 8 days at 20 °C) to give a mixture of compounds **22** and **23** in a 5:95 molecular ratio (GC monitoring, 93% yield). b) TFMD (0.25 mL, 1 h at -20 °C) to give triepoxide **23** in 94 % yield. **23**: 1755, 1205, 1180, 1147 and 1137 cm^{-1}; ^{1}H NMR δ 3.77 (s, 3 H), 3.37, 3.37, 3.36 and 3.35 (s, 1 H, H-2 four diast.), 2.88 (br., 1 H, H-10), 2.73 (br., 1 H, H-6), 1.90-1.52 (8 H, H-4, H-5, H-8, H-9), 1.45 (s, 3 H, CH_3 at C-11), 1.36 and 1.35 (s, 3 H, CH_3 at C-3), 1.29, 1.28 and 1.26 (s, 3 H, CH_3 at C-7, diast.); ^{13}C NMR δ 168.7, 168.7, 168.6 (C-1 diast.), 124.3 and 124.3 (q, J = 277 Hz, C-12), 63.4 and 63.3 (C-10), 62.7, 62.5, 62.2 and 62.1 (C-6 diast.), 62.2, 62.1, 62.0 and 62.0 (C-3 diast.), 60.3, 60.3, 60.2 and 60.1 (C-7 diast.), 58.5 and 58.4 (q, J = 36 Hz, C-11 diast.), 58.5, 58.5, 58.3 and 58.2 (C-2 diast.), 52.2 (OMe), 35.6 and 35.1 (C-8 diast.), 34.5, 34.5, 34.3 and 34.2 (C-4 diast.), 24.3, 24.2, 24.1 and 24.0 (C-5 diast.), 23.0 and 22.9 (q, J = 2.5 Hz, C-9 diast.), 16.7 (q, J = 1 Hz, CH_3 at C-11), 16.4 and 16.2 (CH_3 at C-3, diast.), 16.3, 16.2, 16.0 and 16.0 (CH_3 at C-7, diast.); ^{19}F NMR δ 5.1 (s, integral 88, *cis*), -4.3 (s, integral 7, *trans*); MS (EI), m/z 352 (M^+), 293, 209, 197 69, 59, 43 (base peak).

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Notes and References.

1. Schooley, D. A.; Baker, F. C. in *Comprehensive Insect Physiology, Biochemistry and Pharmacology*, Kerkut, G. A. and Gilbert, L. I. eds., Pergamon Press, Oxford, **1985**, Vol. 7, pp 363-389.
2. Staal, G. B. *Ann. Rev. Entomol.* **1986**, *31*, 391.
3. a) Szekacs, A.; Hammock, B. D.; Abdel-Aal, Y. A. I.; Halarnkar, P. P.; Philpott, M.; Matolcsy, G. *Pest. Biochem. Physiol.* **1989**, *33*, 112 and references therein. b) Casas, J.; Harshman, L.G.; Hammock, B.D. *Insect Biochem.* **1991**, *21*, 17.
4. a) Camps, F.; Canela, R.; Coll, J.; Messeguer, A.; Roca, A.*Tetrahedron*, **1979**, *34*, 2179. b) Camps, F.; Messeguer, A.; Sánchez-Baeza, F. *Tetrahedron* **1988**, *44*, 5161. c) Camps, F.; Sánchez-Baeza, F.; Messeguer, A. *Synthesis* **1988**, 823.
5. Belles, X.; Camps, F.; Casas, J.; Mauchamp, B.; Piulachs, M. D.; Messeguer, A. *Arch. Insect Biochem. Physiol.* **1989**, *11*, 257.
6. Takahashi, O.; Furuhashi, K.; Fukumasa, M.; Hirai, T. *Tetrahedron Lett.* **1990**, *31*, 7031.
7. For reviews on these reagents, see a) Adam.; Hadjiarapoglou, L. P.; Curci, R.; Mello, R. in *Organic Peroxides*; Ando, W., Ed.; Wiley: New York; Chapter 4, pp 195-219. b) Curci, R., en "Advances in Oxygenated Processes", A.L. Baumstark, ed., JAI Press Inc., London, 1990, pp 1-60. c) Murray, R.W. *Chem. Rev.* **1989**, *89*, 1187-1201. d) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205-211.
8. Bujons, J.; Camps, F.; Messeguer, A. *Tetrahedron Lett.* **1990**, *31*, 5235.
9. Messeguer, A; Sánchez-Baeza, F.; Casas, J.; Hammock, B. D. *Tetrahedron* **1991**, *47*, 1291. For a recent report on the epoxidation of trisubstituted C=C bonds, see also Ebenezer, W.; Pattenden, G. *Tetrahedron Lett.* **1992**, *33*, 4053.
10. Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749.
11. In this sense, it is known that epoxidation of α,β-unsaturated carbonyl compounds with DMD requires long reaction times (Adam W.; Hadjiarapoglou, L.; Nestler, B. *Tetrahedron Lett.* **1990**, *31*, 331).
12. Mello, R.; Cassidei. L.; Fiorentino, M.; Fusco, C.; Hümmer, W.; Jäger, V.; Curci, R. *J. Am. Chem. Soc.* **1991**, *113*, 2205.
13. Curci, R.; D'Accolti, L.; Fiorentino, M.; Fusco, C.; Adam W.; Gonzalez-Nuñez, M.E.; Mello, R. *Tetrahedron Lett.* **1992**, *33*,, 4225.
14. The CF_3 moiety was introduced into the starting terpene derivatives through a Wittig condensation with 1,1,1-trifluoroacetone (see ref. 4c), leading to mixtures with a *Z:E* 9:1 isomeric ratio which could not be separated. Hence, unless stated otherwise, all trifluoromethyl olefins and epoxides described heretofore contained a 10% of the corresponding configuration isomer.
15. At the end of the process, the analysis of the reaction crude revealed the presence, in addition to the expected ester **19**, of a small amount of unreacted ester **18** with *E* configuration (cf. ref. 14), which suggests a preference for the epoxidation of the double bond with *Z* configuration.
16. In this case, **16** was a 1:1 *Z:E* isomeric mixture whereas **17** contained the fluorinated epoxide with the (6R*,7R*) configuration (i.e., resulting from the epoxidation of the isomer with *Z* configuration), which confirms the observations mentioned in the precedent note.
17. Although it has been reported that DMD decomposes in the presence of molecular sieves at room temperature (Singh, M.; Murray, R. W. *J. Org. Chem.* **1992**, *57*, 4263), we have observed that DMD solutions could be dried and stored at -20 °C under molecular sieves without significant decomposition.
18. Corey, E. J.; Gilman, N. W.; Ganem, B. E. *J. Am. Chem. Soc.* **1968**, *90*, 5616.
19. Arbonés, C.; Sánchez, F. J.; Marco, M. P.; Camps, F.; Messeguer, A. *Heterocycles* **1990**, *31*, 67.
20. Semmelhack, M. F.; Stauffer, R. D.; Yamashita, A. *J. Org. Chem.* **1977**, *42*, 3180.
21. Murray, R. W.; Jerayaman, R.; *J. Org. Chem.* **1985**, *50*, 2847.
22. Burrel, J. W.; Garwood, R.; Jackman, L. M.; Oskay, E.; Weedon, B. C. *J. Chem. Soc (C)* **1966**, 2145.
23. Henrick, C. A.; Schaub, F.; Siddall, J. B. *J. Am. Chem. Soc.* **1972**, *94*, 5374.