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gem-DIFLUOROCYCLOPROPANES CARRYING OXYGEN-FUNCTIONAL SUBSTITUENTS

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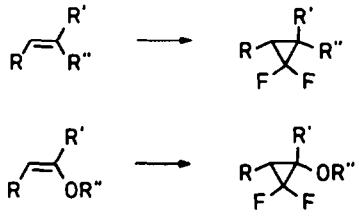
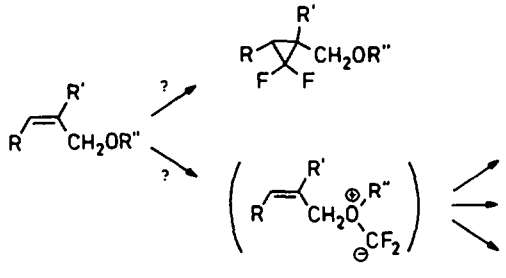
Summary : Protection of allyl alcohols as acetals, addition of difluorocarbene and deprotection lead to *gem*-difluoro(hydroxymethyl)cyclopropanes (**3** and **11**). These can be converted to potential insecticides of the pyrethroid type (**5, 6, 7** and **12**).

As reported in the preceding article [1], alkenes add difluorocarbene to give *gem*-difluorocyclopropanes. Enethers react with particular ease. Once again the superior electron releasing capacity of resonance active alkoxy groups proves to be superior to alkyl groups which only operate through a simple inductive effect.

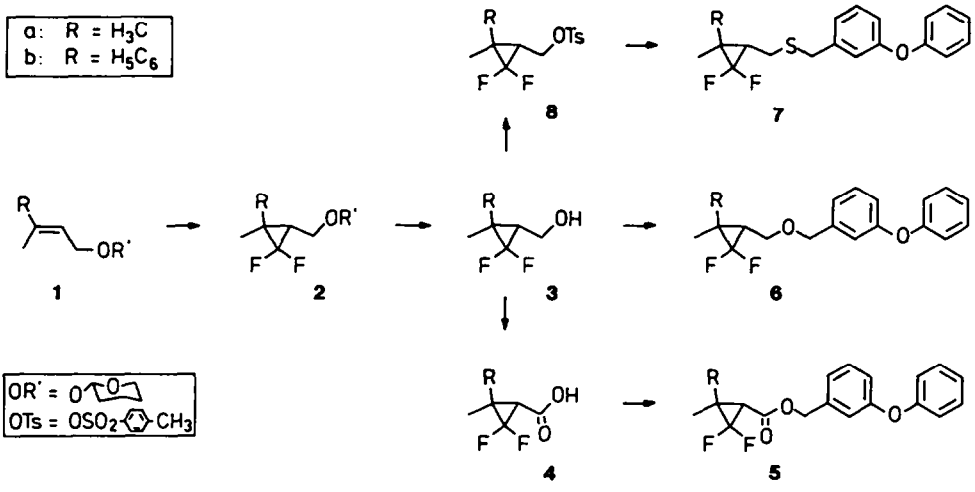


R,R' = H, alkyl; R" = alkyl

We wondered how allyl ethers would behave in this respect. Being no longer in conjugation with an unsaturated moiety, the oxygen atom should primarily act as an electronegative center and hence tend to retard the attack of carbenes or other electrophiles at the neighboring double bond. Moreover, the difluorocarbene could get attached to the hetero atom and produce a transient allyl oxonia ylid [2] which subsequently would get stabilized by insertion or rearrangement reactions.

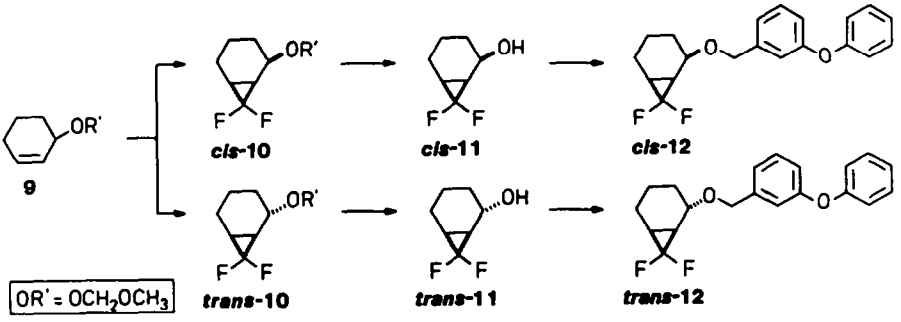


All these worries, however, proved to be unjustified. The *O*-2-tetrahydropyranyl protected derivatives of 3-methyl-2-buten-1-ol ["prenol", **1a**] and (*E*)-3-phenyl-2-buten-1-ol ["3-methylcinnamyl alcohol", **1b**] produced the *gem*-difluorocyclopropanes **2a** and **2b** with quite satisfactory purities and yields (90% and 76%). Acid hydrolysis afforded (2,2-difluoro-3,3-dimethyl-1-cyclopropyl)methanol (**3a**) and (2,2-difluoro-*cis*-3-methyl-*trans*-3-phenyl-1-cyclopropyl)methanol (**3b**) almost quantitatively.



Permanganat oxidation of alcohols **3** gave the carboxylic acids **4** which, to some extent, ressemble the structure of chrysanthemic acid. Therefore, they were converted to the corresponding *m*-phenoxybenzyl esters **5** which were then tested for their insecticidal properties. The carbonyl-free analog **6** was prepared too since ethers are known to be metabolically much more stable than esters [3]. Finally, the thioethers **7** were found to be readily accessible through the *p*-toluenesulfonate **8**.

As expected [1] the acetal **9** derived from 2-cyclohexenol reacted more sluggishly than the open-chain and branched analogs **1**. The (methoxymethoxy)difluoronorcaranes **10** were obtained in only poor yield (15%) and with a *cis/trans* ratio of 1 : 9. The acetals were hydrolyzed to give the alcohols **11** and the latter were converted to the *m*-phenoxybenzyl ethers **12**.



EXPERIMENTAL PART

Generalities : see preceding article [1].

1. Acetals Derived from Allyl Alcohols

3-Methyl-1-(2-tetrahydropyranyloxy)-2-butene (1a) [4] : 3-Methyl-2-buten-1-ol (51 mL, 43 g, 0.50 mol) and 3,4-dihydro-2*H*-pyran (68 mL, 63 g, 0.75 mol) were added to a solution of pyridinium *p*-toluenesulfonate (12.6 g, 50 mmol) in dichloromethane (200 mL). After 4 h at 25°C, the mixture was washed with a saturated aqueous solution (100 mL) of sodium hydrogen carbonate. Evaporation and distillation afforded 78 g (92%) of **1a**; bp 90 - 91°C/11 mmHg; n_D^{20} 1.4580. - ^{1}H-NMR ($CDCl_3$) : 5.36 (1 H, symm. m), 4.64 (1 H, dd, *J* ~4, ~3), 4.23 (1 H, dd, *J* 11.5, 6.5), 4.00 (1 H, dd, *J* 11.5, 7.5), 3.9 (1 H, m), 3.5 (1 H, m), 1.77 (3 H, s, broad), 1.7 (6 H, m), 1.70 (3 H, s, broad). - MS : 170 (1%, M^+), 85 (100%), 69 (94%).

(*E*)-3-Phenyl-1-(2-tetrahydropyranyloxy)-2-butene (1b) : In the same way, (*E*)-3-phenyl-2-buten-1-ol [5] (15 g, 0.10 mol [prepared from (*E*)-3-phenyl-2-butenoic acid [6] by reduction with lithium aluminum hydride [5]]) was converted to **1b**. After evaporation of the solvent, the remaining crude liquid was purified by elution with a 9 : 1 (v/v) pentane/diethyl ether mixture from a silica gel column; 18 g (91%); n_D^{20} 1.5398. - ^{1}H-NMR ($CDCl_3$) : 7.3 (5 H, m), 5.97 (1 H, ddq, *J* 7.5, 6.3, 1.2), 4.71 (1 H, dd, *J* 3.8, 2.8), 4.45 (1 H, ddd, *J* 13.0, 6.0, 0.8), 4.26 (1 H, ddd, *J* 13.0, 6.0, 0.8), 3.95 (1 H, symm. m), 3.56 (1 H, symm. m), 2.11 (3 H, d, *J* 1.3), 1.9 (1 H, m), 1.8 (1 H, m), 1.6 (4 H, m). - MS : 232 (0.3%, M^+), 131 (50%), 91 (25%), 85 (100%). - Analysis : calc. for $C_{15}H_{20}O_2$ (232.32) C 77.55, H 8.68; found C 77.36, H 8.91%.

3-(Methoxymethoxy)cyclohexene (9) : 2-Cyclohexen-1-ol (25 g, 0.25 mol [prepared by isomerization of 1,2-epoxycyclohexane using lithium diisopropylamide and potassium *tert*-butoxide [7]]), chloromethyl methyl ether [8] (20 mL, 21 g, 0.26 mol) and *N,N*-diisopropylethylamine (35 mL, 25 g, 0.25 mol) were dissolved in hexane (0.10 L). After 12 h at 25 °C, the mixture was centrifuged and the supernatant liquid decanted. Distillation afforded 28.8 g (81%) of **9** as a colorless oil; bp 64 - 65 °C/16 mmHg; n_D^{20} 1.4534. - ^{1}H-NMR ($CDCl_3$) : 5.87 (1 H, dtd, *J* 10.0, 3.4, 1.3), 5.76 (1 H, ddt, *J* 10.0, 3.5, 2.0), 4.74 (1 H, d, *J* 6.8), 4.71 (1 H, d, *J* 6.8), 4.10 (1 H, symm. m), 3.39 (3 H, s), 2.0 (5 H, m), 1.6 (1 H, m). - MS : 142 (0.2%, M^+), 84 (23%), 45 (100%). - Analysis : calc. for $C_8H_{14}O_2$ (142.20) C 67.57, H 9.92; found C 67.72, H 9.83%.

2. *gem*-Difluorocyclopropanes Carrying an Acetal Functional Group

1,1-Difluoro-2,2-dimethyl-3-(2-tetrahydropyranyloxymethyl)-cyclopropane (2a) : As previously described [1], 3-methyl-1-(2-tetrahydropyranyloxy)-2-butene (**1a**, 7.8 mL, 8.5 g, 50 mmol) was treated with dibromodifluoromethane, triphenylphosphine and potassium fluoride in the presence of 1,4,7,10,13,16-hexaoxacyclooctadecane ("18-crown-6"). The product (**2a**) was isolated by distillation; 9.9 g (90%); bp 40 - 41°C/0.1 mmHg; n_D^{20} 1.4293. - ^{1}H-NMR ($CDCl_3$) : 4.61 (0.5 × 1 H, dd, *J* 4.5, 2.5), 4.59 (0.5 × 1 H, dd, *J* 4.5, 2.5), 3.8 (2 H, m), 3.5 (2 H, m), 1.7 (7 H, m), 1.23 (3 H, dd, *J* 3.0, 1.5), 1.15 (0.5 × 3 H, dd, *J* 3.0, 1.5), 1.14 (0.5 × 3 H, dd, *J* 3.0, 1.5). - ^{19}F-NMR (C_6D_6) : -85.4 (0.5 × 1 F, d, broad, *J* 160), -84.9 (0.5 × 1 F, d, broad, *J* 157), -74.1 (1 F, dd, broad, *J* 156, 14). - MS : 220 (0.1%, M^+), 118 (16%), 85 (100%). - Analysis : calc. for $C_{11}H_{18}F_2O_2$ (220.26) C 59.98, H 8.24; found C 60.18, 8.06%.

1,1-Difluoro-*cis*-2-methyl-*trans*-2-phenyl-*r*-3-(2-tetrahydropyranyloxymethyl)cyclopropane (2b) : The standard procedure [1] was modified in the sense that (*E*)-3-phenyl-1-(2-tetrahydropyranyloxy)-2-butene (**1b**, 5.2 mL, 5.8 g, 25 mmol) was treated with a threefold, rather than twofold, excess of (bromodifluoromethyl)triphenylphosphonium bromide (75 mmol), three equal portions of which were introduced in 4 h intervals. After a total of 10 h reaction time, the product (**2b**) was purified by elution with a 9 : 1 (v/v) mixture of pentane and diethyl ether from a chromatography column filled with silica gel (100 g); 5.4 g (76%); n_D^{20} 1.4919. - ^{1}H-NMR ($CDCl_3$) : 7.3 (5 H, m), 4.72 (0.5 × 1 H, t, *J* 3.5), 4.68 (0.5 × 1 H, t, *J* 3.5), 4.07 (0.5 × 1 H, ddd, *J* 10.8, 7.0, 1.3), 3.94 (0.5 × 3 H, symm. m), 3.77 (0.5 × 1 H, ddd, *J* 10.8, 7.0, 1.3), 3.65 (0.5 × 1 H, symm. m), 3.56 (1 H, symm. m), 2.14 (1 H,

symm. m), 1.8 (6 H, m), 1.49 (0.5 × 3 H, dd, *J* 2.6, 1.5), 1.46 (0.5 × 3 H, dd, *J* 2.6, 1.5). - ^{19}F-NMR (C_6D_6) : -82.6 (0.5 × 1 F, symm. dm, *J* 152), -82.1 (0.5 × F, symm. dm, *J* 152), -65.5 (0.5 × 1 F, symm. ddm, *J* 152, 15), -65.7 (0.5 × 1 F, symm. ddm, *J* 152, 15). - MS (c.i.) : 300 (10%, $M^+ + NH_4$), 180 (22%), 118 (5%), 85 (100%). - Analysis : calc. for $C_{16}H_{20}F_2O_2$ (282.33) C 68.07, H 7.14; found C 67.92, H 7.36%.

7,7-Difluoro-2-(methoxymethoxy)bicyclo[4.1.0]heptane (10) : In deviation from the standard procedure [1], 3-(methoxymethoxy)cyclohexene (7.1 g, 50 mmol) was treated with a sixfold, rather than twofold, excess of (bromodifluoromethyl)triphenylphosphonium bromide (300 mmol), six equal portions of which were introduced in 7 h intervals. After a total of 48 h reaction time, the reaction mixture was centrifuged. The organic layer was thoroughly washed with a 2% aqueous solution of sodium hydroxide (3 × 0.5 L) before being dried and evaporated. Carcful distillation gave 1.4 g (15%) of a colorless liquid; bp 72 - 74 °C/11 mmHg; n_D^{20} 1.4280. - Analysis: calc. for $C_9H_{14}F_2O_2$ (192.21) C 56.24, H 7.34; found C 56.37, H 7.04%. - According to gas chromatography (30 m, DB-WAX, 150 °C; 30 m, DB-1, 150 °C) the product consisted of two stereoisomers in the ratio of 8 : 92. The major component carried the acetal function in the *trans* position (see below). Both isomers were separated and isolated by preparative gas chromatography (3 m, 8% C-20M, 120 °C). - *cis*-Isomer : ^{1}H-NMR ($CDCl_3$) : 4.80 (1 H, d, *J* 7.2), 4.76 (1 H, d, *J* 7.2), 4.00 (1 H, symm. m), 3.43 (3 H, s), 1.9 (4 H, m), 1.6 (2 H, m), 1.2 (2 H, m). - ^{19}F-NMR ($CDCl_3$) : -85.4 (d, *J* 160), -60.2 (dt, *J* 160, 15). - MS (c.i.) : 210 (100%, $M^+ + NH_4$), 189 (26%), 130 (40%). - *trans*-Isomer : ^{1}H-NMR ($CDCl_3$) : 4.70 (2 H, s), 3.92 (1 H, t-like m, *J* ~ 5), 3.40 (3 H, s), 1.8 (1 H, m), 1.7 (3 H, m), 1.5 (3 H, m), 1.2 (1 H, m). - ^{19}F-NMR ($CDCl_3$) : -86.8 (d, *J* 161), -63.0 (dt, *J* 161, 15). - MS (c.i.) : 210 (100%, $M^+ + NH_4$), 142 (53%), 130 (21%). - Analysis : calc. for $C_9H_{14}F_2O_2$ (192.21) C 56.24, H 7.34; found C. 56.42, H 7.18%.

For comparison, **7,7-difluoro-3-(methoxymethoxy)bicyclo[4.1.0]heptane** was prepared in an analogous fashion. The required starting material was obtained by treatment of 3-cyclohexen-1-ol with chloromethyl methyl ether in the presence of *N,N*-diisopropylethylamine (see Section 1, compound 9); 60%; bp 67 - 68 °C/14 mmHg; n_D^{20} 1.4514. - ^{1}H-NMR ($CDCl_3$) : 5.7 (1 H, m), 5.6 (1 H, m), 4.73 (1 H, d, *J* 6.9), 4.69 (1 H, d, *J* 6.9), 3.83 (1 H, symm. m), 3.37 (3 H, s), 2.4 (1 H, m), 2.1 (3 H, m), 1.9 (1 H, m), 1.6 (1 H, m). - MS (c.i.) : 160 (47%, $M^+ + NH_4$), 142 (0.2%), 128 (15%), 110 (30%), 81 (100%). - Analysis : calc. for $C_8H_{14}O_2$ (142.20) C 67.57, H 9.92; found C 67.51, H 9.85%. - This product was found to form the *gem*-difluorocyclopropane more readily than its previously described (see above) regioisomer (3 times faster, according to a competition experiment) and gave rise to a 45 : 55 stereoisomeric mixture (by gas chromatography : 3 m, C-20M, 150 °C; 10 m, SE-54, 120 °C). The two components were separated by preparative gas chromatography (3 m, 8% C-20M, 120 °C). - *cis*-Isomer : bp 203 - 204 °C; n_D^{20} 1.4294. - ^{1}H-NMR ($CDCl_3$) : 4.69 (1 H, d, *J* 7.0), 4.64 (1 H, d, *J* 7.0), 3.45 (1 H, symm. m), 3.37 (3 H, s), 2.26 (1 H, symm. m), 2.08 (1 H, symm. m), 1.90 (1 H, symm. m), 1.7 (4 H, m), 1.28 (1 H, symm. m). - ^{19}F-NMR ($CDCl_3$) : -87.0 (d, *J* 156), -63.4 (dt, *J* 156, 14). - MS (c.i.) : 210 (100%, $M^+ + NH_4$), 192 (0.1%), 128 (6%). - Analysis : calc. for $C_9H_{14}F_2O_2$ (192.21) C 56.24, H 7.34; found C 56.33, H 7.21%. - *trans*-Isomer : bp 195 - 196 °C; n_D^{20} 1.4289. - ^{1}H-NMR ($CDCl_3$) : 4.67 (2 H, s), 3.63 (1 H, symm. m), 3.37 (3 H, s), 2.03 (1 H, symm. m), 1.9 (2 H, m), 1.6 (5 H, m). - ^{19}F-NMR ($CDCl_3$) : -87.3 (d, *J* 155), -64.1 (dt, *J* 155, 14). - MS (c.i.) : 210 (100%, $M^+ + NH_4$), 192 (8%), 162 (52%). - Analysis : calc. for $C_9H_{14}F_2O_2$ (192.21) C 56.24, H 7.34; found C 56.15, H 7.25%.

3. Hydroxy Substituted *gem*-Difluorocyclopropanes

1,1-Difluoro-3-hydroxymethyl-2,2-dimethylcyclopropane (3a) : A vigorously stirred mixture of 1,1-difluoro-2,2-dimethyl-3-(2-tetrahydropyranyloxymethyl)cyclopropane (**2a**, 5.5 g, 25 mmol) *p*-toluenesulfonic acid (0.05 g, 0.3 mmol) glycerine (36 mL, 48 g, 0.50 mL), was heated during 4 h to 100°C. Upon distillation, the product was collected as a colorless liquid; 2.8 g (82%); bp 61 - 63°C/10 mmHg; n_D^{20} 1.4025. - ^{1}H-NMR ($CDCl_3$) : 3.76 (2 H, symm. m), 2.14 (1 H, s), 1.46 (1 H, dtd, *J* 15.5, 7.8, 1.2), 1.24 (3 H, dd, *J* 3.0, 1.5), 1.18 (3 H, dd, *J* 3.0, 1.5). - ^{19}F-NMR ($CDCl_3$) : -86.1 (d, *J* 157), -74.4 (dd, *J* 157, 14). - MS : 118 (2%, M^+ - 18), 105 (100%), 77 (65%). - Analysis : calc. for $C_6H_{10}F_2O$ (136.14) C 52.93, H 7.40; found C 52.93, H 7.56%.

1,1-Difluoro-*r*-3-hydroxymethyl-*cis*-2-methyl-*trans*-2-phenylcyclopropane (3b) : In an analogous reaction, the acetal 1,1-difluoro-*cis*-2-methyl-*trans*-2-phenyl-*r*-3-(2-tetrahydropyranyloxymethyl)cyclopropane (**2b**, 4.2 g, 15 mmol) was deprotected to give the free alcohol **3b**, which was isolated by column chromatography on silica gel (50 g) using a 3 : 1 (v/v) mixture of pentane and diethyl ether as the eluent; 2.5 g (85%); n_D^{20} 1.4995. - ^{1}H-NMR

($CDCl_3$) : 7.3 (5 H, m), 4.0 (1 H, m), 3.9 (1 H, m), 2.10 (1 H, dddd, *J* 14.5, 8.7, 7.5, 1.4), 1.89 (1 H, s, broad), 1.48 (3 H, dd, *J* 2.5, 1.8). - ^{19}F-NMR ($CDCl_3$) : -82.7 (symm. dm, *J* 154), -65.5 (symm. ddm, *J* 154, 15). - MS : 198 (1%, M^+), 180 (12%), 167 (90%), 147 (100%), 127 (63%). - Analysis : calc. for $C_{11}H_{12}F_2O$ (198.21) C 66.66, H 6.10; found C 66.54, H 6.20%.

7,7-Difluoro-*trans*-2-(hydroxymethyl)bicyclo[4.1.0]heptane (*trans*-11) : A solution of acetal *trans*-**10** (2.9 g, 15 mmol) in methanol (20 mL) containing a trace amount (0.1 mL) of concentrated hydrochloric acid was heated 2 h under reflux. The mixture was neutralized with potassium hydroxide pellets over night, filtered and evaporated. Upon distillation under reduced pressure 2.0 g (91%) of *trans*-**11** were collected; bp 74 - 76 °C/10 mmHg, n_D^{20} 1.4442. - ^{1}H-NMR ($CDCl_3$) : 4.08 (1 H, s, broad, t-like), 1.7 (7 H, m), 1.38 (1 H, symm. m), 1.3 (1 H, m). - ^{19}F-NMR ($CDCl_3$) : -86.6 (d, *J* 161), -62.5 (dt, *J* 161, 15). - MS (c.i.) : 166 (100%, $M^+ + NH_4$), 130 (18%), 99 (13%), 90(17%), 81 (51%). - Analysis : calc. for $C_7H_{10}F_2O$ (148.15) C 56.75, H 6.80; found C 56.98, H 7.06%.

4. *m*-Phenoxybenzyloxy Substituted *gem*-Difluorocyclopropanes

1,1-Difluoro-2,2-dimethyl-3-([3'-phenoxy]benzyloxymethyl)cyclopropane (6a) : 1,1-Difluoro-3-hydroxymethyl-2,2-dimethylcyclopropane (**3a**, 4.8 g, 35 mmol) and, 1 h later, 3-phenoxybenzyl bromide [9, 10] (8.9 g, 34 mmol) were added to a vigorously stirred suspension of potassium hydride (1.6 g, 40 mmol). After an additional period of 1 h the mixture was absorbed on silica gel (10 g). The dry powder was poured on top of a column filled with fresh silica gel (70 g) and eluted with a 9 : 1 (v/v) mixture of pentane and diethyl ether. After evaporation of the solvent, 10.3 g (95%) of a colorless liquid were left behind; n_D^{20} 1.5270. - ^{1}H-NMR ($CDCl_3$) : 7.4 (3 H, m), 7.0 (6 H, m), 4.55 (1 H, d, *J* 12.0), 4.45 (1 H, d, *J* 12.0), 3.6 (2 H, m), 1.48 (1 H, symm. m), 1.26 (3 H, dd, *J* 2.7, 1.8), 1.15 (3 H, dd, *J* 3.0, 1.9). - ^{19}F-NMR (C_6D_6) : -83.6 (d, *J* 154), -73.0 (dd, *J* 154, 14). - MS : 318 (7%, M^+), 225 (27%), 197 (23%), 183 (100%), 105 (19%). - Analysis : calc. for $C_{19}H_{20}F_2O_2$ (318.37) C 71.68, H 6.33; found C 71.54, H 6.39%.

1,1-Difluoro-*cis*-2-methyl-*r*-3-([3'-phenoxy]benzyloxymethyl)-*trans*-2-phenylcyclopropane (6b) : In the same way, 1,1-difluoro-*r*-3-hydroxymethyl-*cis*-2-methyl-*trans*-2-phenylcyclopropane (**3b**) was converted to the ether **6b**; 93%; n_D^{20} 1.5600. - ^{1}H-NMR ($CDCl_3$) : 7.2 (14 H, m), 4.61 (1 H, d, *J* 12.0), 4.50 (1 H, d, *J* 12.0), 3.80 (1 H, ddd, *J* 10.5, 6.7, 1.3), 3.7 (1 H, m), 2.10 (1 H, dddd, *J* 15.0, 8.2, 6.7, 1.4), 1.40 (3 H, dd, *J* 2.6, 1.5). - ^{19}F-NMR ($CDCl_3$) : -82.0 (symm. dm, *J* 153), -65.8 (symm. ddm, *J* 153, 15). - MS : 380 (15%, M^+), 183 (100%), 167 (52%). - Analysis : calc. for $C_{24}H_{22}F_2O_2$ (380.44) C 75.77, H 5.83; found C 75.82, H 6.05%.

7,7-Difluoro-*trans*-2-([3'-phenoxy]benzyloxy)bicyclo[4.1.0]heptane (*trans*-12) : As described for compound **6a** (first paragraph of this Section), 7,7-difluoro-*trans*-2-(hydroxymethyl)bicyclo[4.1.0]heptane (*trans*-**11**, 0.74 g, 5.0 mmol) were reacted with 3-(phenoxy)benzyl bromide to give, after column chromatography using a 19 : 1 (v/v) mixture of pentane and diethyl ether as the eluent, 1.6 g (96%) of the colorless ether *trans*-**12**; mp -43 to -40 °C; n_D^{20} 1.5468. - ^{1}H-NMR ($CDCl_3$) : 7.2 (9 H, m), 4.56 (2 H, s), 3.70 (1 H, t, broad, *J* ~ 5) 1.7 (7 H, m), 1.2 (1 H, m). - ^{19}F-NMR ($CDCl_3$) : -86.2 (d, *J* 161), -62.7 (dt, *J* 161, 15). - MS : 330 (7%, M^+), 200 (8%), 184 (100%). - Analysis : calc. for $C_{20}H_{20}F_2O_2$ (330.38) C 72.71, H 6.10; found C 72.76, H 5.97%.

5. *m*-Phenoxybenzylthio Substituted *gem*-Difluorocyclopropanes

(2,2-Difluoro-3,3-dimethyl-1-cyclopropyl)methyl *p*-toluenesulfonate (8a) : A mixture of 1,1-difluoro-3-hydroxymethyl-2,2-dimethyl-1-cyclopropane (**3a**, 19 g, 0.14 mol) and *p*-toluenesulfonyl chloride (29 g, 0.15 mol) in pyridine (0.15 L, 0.15 kg) was kept 6 h at 0°C before being poured into ice-water (0.15 L). The precipitate was filtered, washed with ice-water and dried; 33.2 g (82%) **8a**; mp 67 - 68°C (after recrystallization from hexane). - ^{1}H-NMR ($CDCl_3$) : 7.78 (2 H, dd, *J* 8.0, 1.3), 7.36 (2 H, d, broad, *J* 7.9), 4.23 (1 H, dd, broad *J* 11.2, 6.7), 4.04 (1 H, ddt, *J* 11.4, 9.2, 1.6), 2.46 (3 H, s), 1.48 (1 H, ddd, *J* 13.5, 9.4, 7.0), 1.17 (3 H, dd, *J* 2.5, 1.5), 1.08 (3 H, dd, *J* 3.0, 1.5). - ^{1}H-NMR (C_6D_6) : 7.70 (2 H, dt, *J* 8.1, 1.3), 6.65 (2 H, d, *J* 8.0), 3.9 (2 H, m), 1.79 (3 H, s), 1.12 (1 H, ddd, *J* 13.5, 8.5, 7.5), 0.7 (6 H, m). - ^{19}F-NMR ($CDCl_3$) : -84.1 (d, broad, *J* 158), -73.6 (dd, broad, *J* 159, 14). - MS : 290 (0.2, M^+), 155 (39%), 118 (90%), 91 (100%). - Analysis : calc. for $C_{13}H_{16}F_2O_3S$ (290.33) C 53.78, H 5.56; found C 54.16, H 5.81%.

1,1-Difluoro-2,2-dimethyl-3-([3-phenoxy]benzylthiomethyl)cyclopropane (7a) : 3-Phenoxy-α-toluenethiol [11, 12] (4.3 g, 20 mmol) was dissolved in a vigorously stirred suspension of sodium hydride (0.60 g, 25 mmol) in tetrahydrofuran (75 mL). After 1 h, (2,2-difluoro-3,3-dimethyl-1-cyclopropyl)methyl *p*-toluenesulfonate (**8a**, 5.8 g, 20 mmol) was added and the mixture was kept 2 h at 25°C. The thio ether **7a** was purified by column chromatography using silica gel as the support and a 19 : 1 (v/v) mixture of pentane and diethyl ether as the eluent; 5.9 g (88%); n_D^{20} 1.5548. - ^{1}H-NMR (C_6D_6) : 7.0 (9 H, m), 3.34 (2 H, s), 2.3 (1 H, m), 2.2 (1 H, m), 1.1 (1 H, m), 0.88 (3 H, dd, *J* 2.5, 1.8), 0.79 (3 H, dd, *J* 3.0, 1.7). - ^{19}F-NMR ($CDCl_3$) : -84.3 (d, *J* 152), -73.5 (dd, *J* 152, 14). - MS : 334 (7%, M^+), 241 (13%), 183 (100%). - Analysis : calc. for $C_{19}H_{20}F_2OS$ (334.43) C 68.24, H 6.03; found C 68.31, H 6.00%.

(2,2-Difluoro-*cis*-3-methyl-*trans*-3-phenyl-*r*-1-cyclopropyl)methyl *p*-toluenesulfonate (8b) : A mixture of 1,1-difluoro-*r*-3-hydroxymethyl-*cis*-2-methyl-*trans*-2-phenylcyclopropane (**3b**, 5.9 g, 30 mmol) and *p*-toluenesulfonyle chloride (6.7 g, 35 mmol) in pyridine (23 mL, 23 g) was kept 6 h at 0 °C. Ice-water (50 mL) was added and the yellowish-white precipitate filtered and dried; 8.7 g, 82%; mp 103 - 104 °C (after recrystallization from hexane). - ^{1}H-NMR ($CDCl_3$) : 7.87 (2 H, dt, *J* 8.5, 1.3), 7.41 (2 H, d, broad, *J* 8.3), 7.3 (5 H, m), 4.45 (1 H, dd, broad, *J* 11.2, 6.3), 4.20 (1 H, ddt, *J* 11.5, 10.4, 1.4), 2.48 (3 H, s), 2.16 (1 H, ddd, *J* 14.1, 9.8, 6.5), 1.39 (3 H, dd, *J* 2.8, 1.6). - ^{19}F-NMR ($CDCl_3$) : -81.9 (d, *J* 151), -66.2 (dd, *J* 151, 14). - MS (c.i.) : 370 (100%, $M^+ + NH_4$), 224 (5%), 190 (14%), 180 (48%). - Analysis : calc. for $C_{18}H_{18}F_2O_3S$ (352.40) C 61.35, H 5.15; found C 61.21, H 5.08%.

1,1-Difluoro-*cis*-2-methyl-*trans*-2-phenyl-*r*-3-([3-phenoxy]benzylthiomethyl)cyclopropane (7b) : 3-Phenoxy-α-toluenethiol [11, 12] (5.4 g, 25 mmol) was allowed to react with a vigorously stirred suspension of sodium hydride (0.72 g, 30 mmol) in tetrahydrofuran (25 mL). After 1 h, (2,2-difluoro-*cis*-3-methyl-*trans*-3-phenyl-*r*-1-cyclopropyl)methyl *p*-toluenesulfonate (**8b**, 8.8 g, 25 mmol) was added and the mixture was kept 1 h at 25 °C before being absorbed on silica gel. Column chromatography using fresh silica gel as the support and a 19 : 1 (v/v) mixture of pentane and diethyl ether as the eluent gave **7b** as a colorless oily liquid; 8.8 g (89%); mp -20 to -19 °C; n_D^{20} 1.5835. - ^{1}H-NMR ($CDCl_3$) : 7.2 (14 H, m), 3.76 (2 H, s), 2.75 (1 H, dd, *J* 13.8, 6.8), 2.59 (1 H, ddd, *J* 13.9, 8.9, 2.3), 1.89 (1 H, dddd, *J* ~ 15, 8.8, 6.8, 1.4), 1.37 (3 H, dd, *J* 2.8, 1.7). - ^{19}F-NMR ($CDCl_3$) : -81.6 (d, *J* 157), -65.7 (dd, *J* 157, 14). - MS : 396 (14%, M^+), 319 (22%), 213 (12%), 183 (100%). - Analysis : calc. for $C_{24}H_{22}F_2OS$ (396.50) C 72.70, H 5.59; found C 73.04, H 5.55%.

6. Carboxy Substituted *gem*-Difluorocyclopropanes and Esters Thereof

2,2-Difluoro-3,3-dimethyl-1-cyclopropanecarboxylic acid (4a) : 1,1-Difluoro-3-hydroxymethyl-2,2-dimethylcyclopropane (2,2-difluoro-3,3-dimethyl-1-cyclopropylmethanol, **3a**, 11.8 mL, 13.6 g, 100 mmol) were added dropwise and under stirring to a 10°C cold solution of potassium permanganate (32 g, 0.20 mol) and sodium hydroxide (20 g, 0.50 mol) in water (0.40 L). After 1 h at 25°C, a 20% aqueous solution (100 mL) of sodium hydrogen sulfite was added until the deep purple color had disappeared. Then the mixture was acidified with concentrated hydrochloric acid to pH 1. The aqueous phase was extracted with diethyl ether (5 x 100 mL). The combined organic layers were washed with brine (100 mL), dried and evaporated. The acid **4a** was obtained as white, shiny crystals; 12.8 g (85%); mp 62 - 64°C (crude); mp 66.5 - 67.5 °C (after recrystallization from hexane). - ^{1}H-NMR ($CDCl_3$) : 11.8 (1 H, s, very broad), 2.08 (1 H, dd, *J* 12.5, 1.5), 1.40 (3 H, dd, *J* 2.3, 1.2), 1.35 (3 H, s, fine structure). - ^{19}F-NMR ($CDCl_3$) : -81.2 (d, *J* 154), -68.4 (dd, *J* 154, 13.0). - MS : 150 (7%, M^+), 129 (58%), 105 (100%). - Analysis : calc. for $C_6H_8F_2O_2$ (150.13) C 48.00, H 5.37; found C 47.95, H 5.41%.

A sample of the acid **4a** (0.75 g, 5.0 mmol) was treated with a small excess of ethereal diazomethane. Distillation afforded an almost quantitative yield of **methyl 2,2-difluoro-3,3-dimethyl-1-cyclopropanecarboxylate**; bp 147 - 148°C; n_D^{20} 1.4004. - ^{1}H-NMR ($CDCl_3$) : 3.71 (3 H, s), 2.06 (1 H, dd, *J* 13.0, 1.5); 1.39 (3 H, dd, *J* 2.5, 1.4), 1.34 (3 H, s, fine structure). - ^{19}F-NMR ($CDCl_3$) : -82.1 (d, *J* 154), -69.5 (dd, *J* 154, 13). - MS : 164 (0.3%, M^+), 149 (53%), 105 (100%), 91 (62%), 77 (71%). - Analysis : calc. for $C_7H_{10}F_2O_2$ (164.15) C 51.22, H 6.14; found C 51.30, H 6.17%.

(3-Phenoxy)benzyl 2,2-difluoro-3,3-dimethyl-1-cyclopropanecarboxylate (5a) : 3-Phenoxybenzyl alcohol (5.0 g, 25 mmol) was added to a vigorously stirred suspension of sodium hydride (0.12 g, 5.0 mmol) in tetrahydrofuran (10 mL). To the resulting mixture, a solution prepared from 2,2-difluoro-3,3-dimethyl-1-cyclopropanecarboxylic acid (**4a**, 3.8 g, 25 mmol) and *N,N'*-carbonyldiimidazole (4.5 g, 28 mmol) was added as soon as the gas evolution had ceased (approximately after 10 min). Some 20 min later the ester **5a** was isolated by column chromatography, using silica gel as the support and a 4 : 1 (v/v) mixture of pentane and diethyl ether as the eluant. A colorless liquid was collected; 7.6 g (94%), n_D^{20} 1.5343. - ^{1}H-NMR ($CDCl_3$) : 7.36 (3 H, symm. m), 7.1 (6 H, m), 5.14 (2 H, s), 2.13 (1 H, dd, *J* 12.5, 1.5), 1.39 (3 H, s, fine structure), 1.35 (3 H, s, fine structure). ^{1}H-NMR (C_6D_6) : 6.9 (9 H, m), 4.87 (1 H, d, *J* 12.5), 4.77 (1 H, d, *J* 12.5), 1.82 (1 H, dd, *J* 13.2, 1.5), 1.17 (3 H, dd, *J* 2.4, 1.5), 0.75 (3 H, s, fine structure). - ^{19}F-NMR ($CDCl_3$) : -81.4 (d, *J* 151), -69.0 (dd, *J* 151, 13). - MS : 332 (19%, M^+), 183 (100%), 114 (28%). - Analysis : calc. for $C_{19}H_{18}F_2O_3$ (332.35) C 68.67, H 5.46; found C 68.73, H 5.49%.

2,2-Difluoro-*cis*-3-methyl-*trans*-3-phenyl-*r*-1-cyclopropanecarboxylic acid (4b) : At -10 °C, 1,1-Difluoro-*r*-3-hydroxymethyl-*cis*-2-methyl-*trans*-2-phenylcyclopropane (4.0 g, 20 mmol) was slowly added to a vigorously stirred solution of potassium permanganate (6.3 g, 40 mmol) and sodium hydroxide (4.0 g, 100 mmol) in water (100 mL). After 1 h, the excess of permanganate was destroyed with a 20% aqueous solution of sodium hydrogen sulfite (20 mL). The mixture was acidified with concentrated hydrochloric acid to pH 1 and extracted with diethyl ether (4 × 25 mL). The combined organic layers were washed with brine (2 × 25 mL), dried and evaporated. The solid residue (3.9 g, 92%) was recrystallized from hexane; mp 105 - 107 °C. - ^{1}H-NMR ($CDCl_3$) : 11.8 (1 H, s, broad), 7.4 (5 H, m), 2.75 (1 H, dd, *J* 12.7, 1.2), 1.74 (3 H, s, fine structure). - ^{19}F-NMR ($CDCl_3$) : -80.0 (dd, *J* 150, 1), -62.1 (ddd, *J* 150, 13, 2). - MS : 212 (0.5%, M^+), 192 (35%), 147 (100%). - Analysis : calc. for $C_{11}H_{10}F_2O_2$ (212.20) C 62.26, H 4.75; found C 62.35, H 4.63%.

A sample of the acid **4b** (0.53 g, 2.5 mmol) was treated with a small excess of diazomethane. The **methyl 2,2-difluoro-*cis*-3-methyl-*trans*-3-phenyl-*r*-1-cyclopropanecarboxylate** (0.56 g, 99%) was isolated by distillation; bp 111 - 112 °C/10 mmHg; n_D^{20} 1.4868. - ^{1}H-NMR ($CDCl_3$) : 7.4 (5 H, m), 3.83 (3 H, s), 2.70 (1 H, dd, *J* 12.8, 1.8), 1.69 (3 H, dd, *J* 2.5, 1.7). - ^{19}F-NMR ($CDCl_3$) : -80.8 (dpent, *J* 151, 2), -63.0 (ddq, *J* 151, 13, 2). - MS : 226 (0.2%, M^+), 206 (28%), 178 (20%), 167 (26%), 147 (100%). - Analysis : calc. for $C_{12}H_{12}F_2O_2$ (226.22) C 63.71, H 5.35; found C 63.64, H 5.03%.

(3-Phenoxy)benzyl 2,2-difluoro-*cis*-3-methyl-*trans*-3-phenyl-*r*-1-cyclopropanecarboxylate (5b) : 3-Phenoxybenzyl alcohol (0.40 g, 2.0 mmol) was added to a vigorously stirred suspension of sodium hydride (5 mg, 0.2 mmol) in tetrahydrofuran (5 mL). 2,2-Difluoro-*cis*-3-methyl-*trans*-3-phenyl-*r*-1-cyclopropanecarboxylic acid (**5b**, 0.42 g, 2.0 mmol) and *N,N'*-carbonyldiimidazole (0.36 g, 2.2 mmol) were dissolved in tetrahydrofuran (5 mL). After 15 min, when the gas evolution had ceased, this solution was added to the reaction mixture containing the 3-phenoxybenzyl alcohol. Again 15 min later, silica gel (5 g) was added, the solvent evaporated and the dry powder poured on top of a column filled with a slurry of fresh silica gel (15 g) in hexane. Elution with a 4 : 1 (v/v) mixture of hexane and diethyl ether afforded **5b**; 0.76 g (96%); mp -15 to -12 °C. - ^{1}H-NMR ($CDCl_3$) : 7.3 (14 H, m), 5.24 (2 H, s), 2.74 (1 H, dd, *J* 13.5, 1.5), 1.66 (3 H, dd, *J* 2.5, 1.6). - ^{19}F-NMR ($CDCl_3$) : -80.6 (dpent, *J* 151, 2), -62.9 (ddq, *J* 151, 13, 2). - MS : 394 (11%, M^+), 183 (100%), 167 (10%). - Analysis : calc. for $C_{24}H_{20}F_2O_3$ (394.42) C 73.09, H 5.11; found C 73.24, H 5.21%.

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