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Mixed Organofluorine-Organosilicon Chemistry. 10. Allylation and Benzylation of Difluoroenoxysilanes. Application to the Synthesis of *gem*-Difluoroterpene Analogues

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Abstract: Acylsilane and trifluoromethyltrimethylsilane gave, under fluoride initiation, a difluoroenoxysilane which is used *in situ* in a Lewis acid catalyzed coupling with a prenyl ester or a benzylic bromide. The advantage of this one-pot procedure was illustrated by its use in the synthesis of *gem*-difluoro analogues of terpenes (dehydro-*ar*-curcumene and *ar*-turmerone). © 1999 Elsevier Science Ltd. All rights reserved.

Keywords : Fluorine and compounds ; Silicon and compounds ; Terpenes and terpenoids ; Allylation; benzylation

The growing interest in fluoro substituted compounds, especially for agrochemical and pharmaceutical use has been accompanied by the need of selective methods of introduction of fluorine and/or the development of versatile fluorinated building blocks. Among the various available methods for the synthesis of *gem*-difluoro compounds,[1] difluoroenoxysilanes **2** meet these requirements, as illustrated by several recently reported applications to the synthesis of α,α-difluoro keto derivatives. Originally described by the group of Ishihara,[2] who used chlorodifluoroketones as starting materials, difluoroenoxysilanes have also been prepared from different fluorinated raw materials such as trifluoroacetyltriphenylsilane,[3] trifluoromethyltrimethylsilane,[4] trifluoromethylketones.[5]

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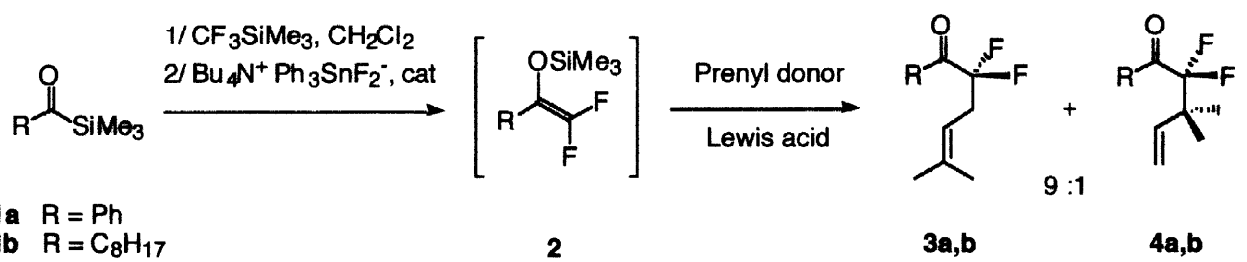
The strategy developped in our group, based on the reaction of acylsilanes with trifluoromethyltrimethylsilane (TFMTMS) in dichloromethane, allowed us to perform one-pot reactions under Lewis acid activation: aldol reactions,[4] glycosylations[6] and Michael reactions.[7] We report here new applications of this strategy, allylation and benzylation of difluoroenoxysilanes, whose usefulness is demonstrated by the synthesis of *gem*-difluoroanalogues of terpenes.

RESULTS AND DISCUSSION.

One-pot allylation and benzylation of difluoroenoxysilanes.

The overall process is depicted in Scheme 1. The prenylation conditions were studied using benzoyltrimethylsilane as starting compound. Reaction in dichloromethane with TFMTMS, initiated by tetrabutylammonium difluorotriphenylstannate[8] gave the corresponding difluoroenoxysilane. The prenyl donor and a Lewis acid were added to the reaction mixture. The results are reported in Table 1. Prenyl esters and zinc iodide proved to be suitable conditions (entry 1), however, an excess of the Lewis acid was necessary for preparative yields. We were able to perform this reaction with a catalytic amount of Lewis acid by using the $BiCl_3/ZnI_2$ system[9] (entry 2) or trimethylsilyltriflate (entries 3-6). Similar yields were obtained starting from an aromatic or an aliphatic acylsilane (entry 4). The reaction invariably led to the expected product contaminated with the S_N' type isomer (10 % determined by ^{19}F NMR). The ratio between the two isomers remained constant as seen from 3,3-dimethylallylbenzoate (entry 5) or 1,1-dimethylallylbenzoate (entries 6) which indicates a pure S_N1 mechanism.



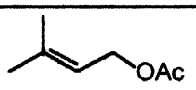
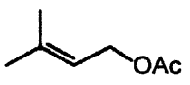
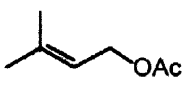
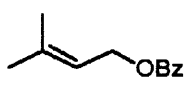
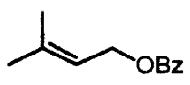
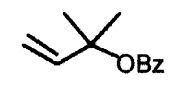
1a R = Ph
1b R = C_8H_{17} **2** **3a,b** **4a,b**

Scheme 1

We have already reported in our preliminary account[4] an example of benzylation with α-methylbenzylbromide, catalyzed by zinc iodide. The reaction did not work with benzylbromide, showing that only good S_N1 precursors are able to react. With such benzylic halides, zinc salts gave the best results. Some experimental aspects deserve to be emphasized. The first step of this process, the reaction of the acylsilane with TFMTMS under fluoride initiation, is an exothermic reaction. Owing to the low boiling point of TFMTMS (56 °C), the yields were optimized by mixing the reagents at low temperature (- 10 °C) and using a small excess of TFMTMS. We would like to emphasize that the use of a classical fluoride source such as tetrabutylammonium

fluoride is not suitable for our reaction since a further self condensation of the difluoroenoxysilane took place with such an initiator.[4]

Table 1. Prenylation reactions of difluoroenoxysilane.

Entry	Acylsilane	Prenyl donor		Lewis acid	yield (%)[a,b]
1	**1a**		5 eq.	ZnI_2 (5 eq.)	**3a+4a** 55%
2	**1a**		4 eq	$BiCl_3$ (0.1 eq.) + ZnI_2 (0.15 eq.)	**3a+4a** 47%
3	**1a**		2 eq.	TMSOTf (0.2 eq.)	**3a+4a** 65%
4	**1b**		3 eq.	TMSOTf (0.2 eq.)	**3b+4b** 51%
5	**1a**		3 eq.	TMSOTf (0.2 eq.)	**3a+4a** 61%
6	**1a**		3 eq.	TMSOTf (0.2 eq.)	**3a+4a** 54%

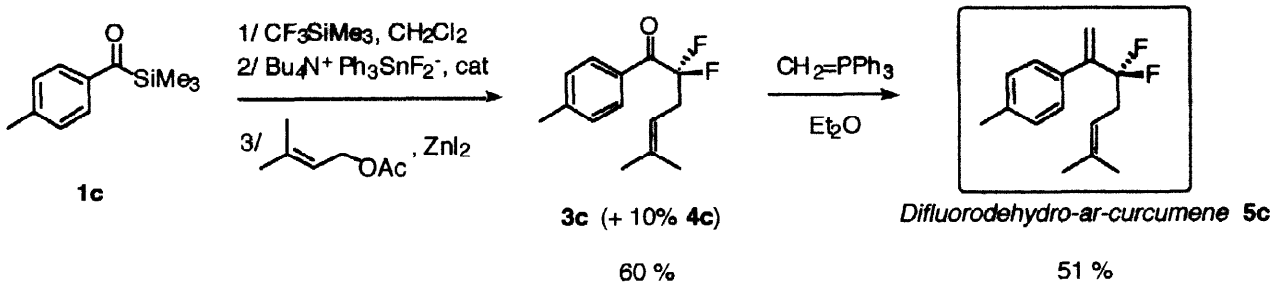
[a] Isolated mixture of **3** and **4** in a 9/1 ratio (^{19}F NMR). [b]Overall yield based on acylsilane.

Taking into account that the yields reported in the table are the overall yields from the starting acylsilane, this three component one-pot process can be considered as a useful method to synthesize *gem*-difluoro compounds.

Application to the synthesis of gem-difluoroterpene analogues.

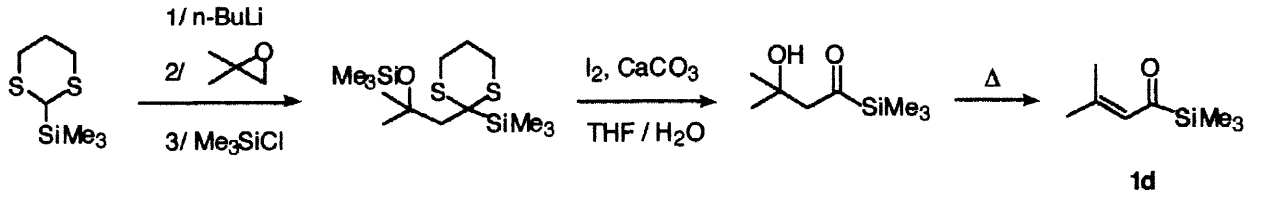
The following applications in the terpene series illustrate the usefulness of this methodology. The specific properties induced by fluorine have prompted organic chemists and biochemists to investigate this field and several reports deal with fluorosubstituted terpenes and pheromones.[10] Most of the reported syntheses were based on the building block approach. The interest of our methodology is based on its highly convergent character. Starting from readily prepared acylsilanes, the one-pot procedure described above and, if necessary, a simple transformation of the product leads to *gem*-difluoroterpenes in a few steps.

The one-pot prenylation of *p*-methylbenzoyl(trimethyl)silane **1c** yielded the difluoroketone (with 10% of the isomer **4c**) in 60 % overall yield. The mixture was submitted to a Wittig olefination to give the difluoro compounds **5c** and **6c** (9/1 ratio). The difluoro analogue of dehydro-*ar*-curcumene **5c** was obtained as a unique product after purification by silicagel chromatography in 51 % yield (Scheme 2).

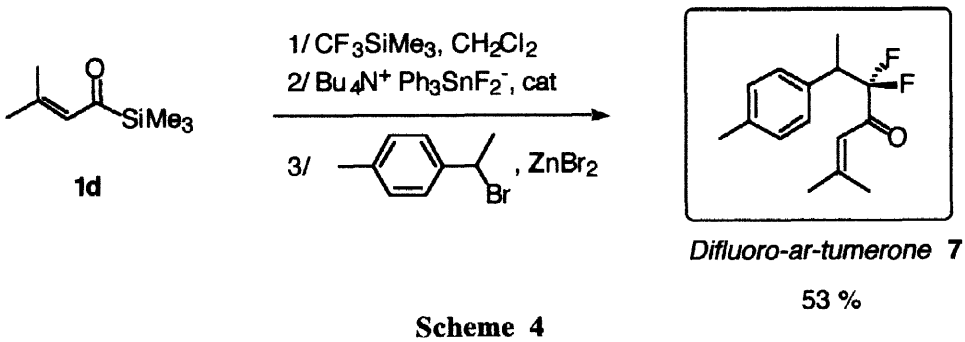


Scheme 2

In this example, the tolyl part of the terpene derivative came from the starting acylsilane. The versatility of the methodology is illustrated by the synthesis of the difluoroanalogue **7** of *ar*-turmerone, where the tolyl moiety is a part of the benzyl donor. *Ar*-turmerone is a sesquiterpene displaying an antitumor activity.[11] This synthesis needed the acylsilane **1d** which was prepared from isobutene oxide by a procedure similar to the one we have recently reported (Scheme 3).[12] The corresponding difluoroenoxysilane was generated *in situ* in the conditions described above, then 1-bromo-1-tolylethane and zinc bromide was added to the reaction mixture to give the difluoro-*ar*-turmerone **7** in 53 % overall yield (Scheme 4).



Scheme 3



Scheme 4

Summary

These results extend the chemical scope of the combined acylsilane-trifluoromethyltrimethylsilane as a synthetic equivalent of difluoroenoxysilane. The latter was prenylated or benzylated *in situ* to yield the corresponding α,α-difluoro ketone. The straightforward synthesis of difluoroterpenes analogues demonstrates the usefulness of the methodology. Current investigation in this field will be reported in a forthcoming paper.

EXPERIMENTAL

General methods.

Melting points are uncorrected. FT-IR spectra were run on a MIDAS corporation apparatus. ^{1}H,^{19}F, and ^{13}C NMR spectra were recorded on a BRUKER AC-250 spectrometer in $CDCl_3$ as the solvent. All chemical shifts are reported in parts per million against internal tetramethylsilane for ^{1}H and ^{13}C NMR spectra and $CFCl_3$ for ^{19}F NMR spectra. MS data were obtained on a Fison VG autospec apparatus at 70 eV in the electron impact mode. Elemental analyses were performed with a Perkin Elmer CHN 2400 apparatus. All reactions were monitored by TLC (Merck F 254) or GC. GC analyses were performed on a HP 5890 chromatograph equipped with a polydimethylsiloxane HP ultra I column and a flame ionization detector. Silicagel Merck 9385 (40-63 mm) was used for flash chromatography. Tetrabutylammonium difluorotriphenylstannate was prepared following the literature procedure.[8] The puriss. quality of dichloromethane from Fluka was used for the prenylation and benzylation reactions.

Acylsilanes preparations.

The acylsilanes **1a**,**1b** and **1c** were synthesized by the Brook and Corey method.[13]

Trimethylnonanoylsilane (1b). Pale yellow liquid (CH_2Cl_2/petroleum ether : 20/80). ^{1}H NMR 0.18 (s, 9H, 3 CH_3), 0.86 (t, $^{3}J_{HH}$= 6.0, 3H, CH_3), 1.24 (s, 10H, 5 CH_2), 1.49 (quint, $^{3}J_{HH}$= 7.0, 2H, CH_2), 2.55 (t, $^{3}J_{HH}$= 7.0, 2H, CH_2), ^{13}C NMR -3.2 (3 CH_3), 14.0 (CH_3), 22.1 (CH_2), 22.6 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 31.8 (CH_2), 48.5 (CH_2), 248.5 (*C*O), I.R. (film) 2910 (S), 2840 (S), 1620 (S), 1240 (m), 840 (S), MS m/e (%) 214 (M^+, 2), 199 (2), 129 (14), 101 (7), 75 (15), 73 (10), Anal. Calcd for $C_{12}H_{26}OSi$:C, 67.22; H, 12.22. Found : C, 67.35; H, 12.65.

***p*-Methylbenzoyltrimethylsilane (1c).** Yellow liquid (CH_2Cl_2/petroleum ether : 20/80). ^{1}H NMR 0.37 (s, 9H, 3 CH_3), 2.40 (s, 3H, CH_3), 7.27 (dm, $^{3}J_{HH}$= 8.2, 2H), 7.75 (dt, $^{3}J_{HH}$= 8.2, $^{4}J_{HH}$= 1.8, 2H), ^{13}C NMR -1.4 (3 *C*H_3), 21.6 (*C*H_3), 127.6 (C_{aro}), 129.2(C_{aro}), 139.1 (C_{aro}), 143.4 (C_{aro}), 234.7 (*C*O), I.R. (film) 2959 (m), 1724 (m), 1595 (S), 1250 (m), 1219 (S), 1172 (S), 841 (S), MS m/z (%) 192 (M^+, 8), 177 (82), 149 (51), 119 (100), Anal. Calcd for $C_{11}H_{16}OSi$:C, 68.70; H, 8.38. Found : C, 68.93; H, 8.54.

Synthesis of 3-methyl-1-oxo-but-2-enyltrimethylsilane (1d).

2-(2-Methyl-2-trimethylsilyloxypropyl)-2-trimethylsilyl-1,3-dithiane. To a solution of 2-trimethylsilyl-1,3-dithiane (15.31 g; 0.08 mol) in THF (200 mL), was added *n*-BuLi (33.1 mL 2.5 M in hexane; 0.082 mol) at 0°C. After 1h stirring at this temperature, isobutene oxide (5g; 0,069 mol) was added and after 2h, $ClSiMe_3$ (13,1 mL; 1,5 eq.) was added. The reaction was allowed to stir overnight at room temperature. After hydrolysis with brine the crude mixture was extracted with Et_2O (3 X 50 mL), the organic layer was washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The silyl dithiane derivative was purified by silicagel column chromatography (CH_2Cl_2/EP 10/90 ;45% yield). Pale yellow liquid. ^1H NMR 0.12 (s, 9H, 3 CH_3), 0.26 (s, 9H, 3 CH_3), 1.43 (s, 6H, 2 CH_3), 2.16 (s, CH_2), 2.42-2.53 (m, 4H, 2 CH_2), 2.97-3.03 (m, 2H, CH_2), ^{13}C NMR -1.3 (3 CH_3), 3.0 (3 CH_3), 23.7, 24.9, 26.2, 31.3, 38.0, 50.6, 76.1, I.R. (film) 1253 (S), 2910 (S) , 2961 (S), MS m/z (%) 336 (M^+, 25), 264 (27), 205 (40), 191 (45), 159 (42), 131 (100)

(3-Hydroxy-3-methylbutanoyl)trimethylsilane. To a solution of silyl dithiane (7.68g) and $NaHCO_3$ (4 eq.) in THF (100 mL) was added iodine (3 eq.) by small portion at 0°C. After 4h at room temperature, a saturated solution of $Na_2S_2O_3$ was added and the crude mixture was extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure.The crude product was used in the next step without purification. Yellow liquid. ^1H NMR 0.17 (s, 9H, 3 CH_3), 1.20 (s, 6H, 2 CH_3), 2.78 (s, 2H, CH_2), ^{13}C NMR -3.6 (3 CH_3), 29.4 (2CH_3), 57.5 (CH_2), 70.3, 253.2 (*C*O), I.R. (film) 3480 (S), 2972 (S), 1631 (S), 1375 (m), 1251 (S), 848 (S).

(3-Methylbut-2-enoyl)trimethylsilane (1d). The dehydratation of the previous β-hydroxyacylsilane was carried out by distillation under reduce pressure (20 mm Hg) giving 3.7g of **1d** (35 % overall yield from the epoxide). Yellow liquid. ^1H NMR 0.17 (s, 9H, 3 CH_3), 1.86 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 6.53 (t, $^4J_{HH}$= 1.2, CH), ^{13}C NMR -3.3 (3 CH_3), 21.0 (CH_3), 27.4 (CH_3), 126.9 (CH), 150.1, 237.7 (*C*O), I.R. (film) 2970 (S), 1639 (S), 1572 (m), 1250 (S), 844 (S), MS m/z (%) 202 (M^+, 100).

Prenylation, general procedure.

In situ preparation of the difluoroenoxysilane. To a solution of acylsilane (1.5 mmol) and trifluoromethyltrimethylsilane (0.3 mL, 1.89 mmol) in CH_2Cl_2 (5 mL) under Argon was added a catalytic amount of tetrabutylammonium difluorotriphenylstannate (54 mg, 0.075 mmol). The reaction mixture was stirred 5 min at 0°C, then 25 min at room temperature. When the reaction was carried out at -20 °C, 1.05 eq. of trifluoromethyltrimethylsilane were enough to achieve a complete transformation of the acylsilane. The

formation of the difluoroenoxysilane was monitored by GC and it was used in the next step in a one-pot procedure.

ZnI_2 catalysis. To a solution of difluoroenoxysilane (1.5 mmol) in CH_2Cl_2 (15 mL) was added the prenylester (2.25 mmol) and ZnI_2 (7.5 mmol) at room temperature. The reaction was monitored by GC and an additional amount of prenylester (2 x 2.25 mmol) was added to complete the reaction. After hydrolysis with a saturated $NaHCO_3$ solution the crude mixture was extracted with CH_2Cl_2 (4 x 20mL), the organic layer was washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude product was purified by silicagel column chromatography.

$BiCl_3$ / ZnI_2 catalysis. The prenyl acetate (3 mmol), $BiCl_3$ (0.15 mmol) and freshly sublimated ZnI_2 (0.225 mmol) were added to the solution of difluoroenoxysilane at room temperature and the reaction mixture was stirred at room temperature until consumption of the difluoroenoxysilane. The work up procedure was the same as above.

TMSOTf catalysis. TMSOTf (0.3 mmol) was added to the solution of difluoroenoxysilane cooled down to -20°C. The prenyl ester (4.5 mmol) was then slowly added at this temperature for 4-6h with a syringe. The work up procedure was the same as above.

As prenylation products could not be separated from the other isomer (9/1 ratio), the analyses were performed on the mixture.

2,2-Difluoro-5-methyl-1-phenylhex-4-en-1-one (3a). Colorless liquid (CH_2Cl_2/EP 10/90). ^1H NMR 1.63 (s, 3H, CH_3), 1.74 (s, 3H, CH_3), 2.94 (td, $^3J_{HH}$= 17.4, $^3J_{HH}$= 7.3, 2H, CH_2), 5.20 (ttm, $^3J_{HH}$= 7.3, $^4J_{HH}$= 1.4, 1H), 7.49 (t, $^2J_{HH}$= 6.9, 2H), 7.63 (t, $^3J_{HH}$= 6.7, 1H), 8.11 (d, $^3J_{HH}$= 7.3, 2H). ^{13}C NMR 17.9 (CH_3), 26.1 (CH_3), 33.4 (t, $^2J_{CF}$= 23.6, CH_2), 113.0 (*C*H), 119.2 (t, J_{CF}= 254.0, CF_2), 128.6 , 130.0 , 134.1 , 137.2, 138.2, 189.6 (t, $^2J_{CF}$= 31.5, *C*O). ^{19}F NMR -99.9 (t, $^3J_{HF}$= 17.4, 2F, CF_2). I.R. (film) 2948 (m), 2862 (m), 1703 (S), 1599 (m), 1174 (S), 1057 (S) cm^{-1}. MS m/z (%) 224 (M^+, 18), 204 (60), 189 (65), 156 (12), 105 (100). Anal. Calcd for $C_{13}H_{14}O_2F_2$:C, 69.63; H, 6.29; Found : C, 69.52; H, 6.46.

2,2-Difluoro-3,3-dimethyl-1-phenylpent-4-en-1-one (4a). ^1H NMR 1.28 (s, 6H, 2 CH_3), 5.12-5.19 (m, 2H), 6.03 (dd, $^3J_{HH}$= 17.5, $^3J_{HH}$= 10.8, 1H), 7.35-7.63 (m, 3H), 8.04 (d, $^3J_{HH}$= 9.5, 2H). ^{19}F NMR -107.9 (s).

5,5-Difluoro-2-methyl-tetradec-2-en-6-one (3b). Colorless liquid (CH_2Cl_2/EP 10/90). ^1H NMR 0.87 (t, $^3J_{HH}$= 6.1, 3H, CH_3), 1.13-1.39 (m, 10H, 5 CH_2), 1.52-1.68 (m, 2H, CH_2), 1.62 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 2.62 (t, $^3J_{HH}$= 7.3, 2H, CH_2), 2.70 (td, $^3J_{HF}$= 16.8, $^3J_{HH}$= 7.6, 2H, CH_2), 5.08 (tm, $^3J_{HH}$= 7.3). ^{13}C NMR 14.1 (CH_3), 17.9 (CH_3), 22.5, 22.6, 25.8 (CH_3), 28.9, 29.1, 29.2, 31.8, 32.1 (t, $^2J_{CF}$= 20.4, CH_2CF_2), 36.8, 112.7 (t, $^3J_{CF}$= 3.9, *C*H), 117.8 (t, J_{CF}= 253.9, CF_2), 138.4 (s, CH=*C*), 200.7 (t, $^2J_{CF}$= 30.5, *C*O). ^{19}F NMR -106.8 (t, $^3J_{HF}$= 16.8, 2F, CF_2). I.R. (film) 2926 (S), 2856 (m), 1744 (m), 1462 (S), 1104 (S), 1059 (S) cm^{-1}.

MS m/z (%) 261 (M+1, 32), 167 (68), 141 (100). Anal. Calcd for $C_{15}H_{26}O_2F_2$: C, 69.20; H, 10.06; Found : C, 69.29; H, 10.23.

4,4-Difluoro-3,3-dimethyltridec-1-en-5-one (4b). ^{1}H NMR 0.87 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.22-1.39 (m, 10H, 5 CH_2), 1.52-1.68 (m, 2H, CH_2), 2.62 (t, $^3J_{HH}$= 7.3, 2H, CH_2), 5.04 (d, $^3J_{HH}$= 17.2, 1H), 5.17 (d, $^3J_{HH}$= 10.7, 1H), 5.93 (dd, $^3J_{HH}$= 17.2, $^3J_{HH}$= 10.7, 1H). ^{19}F NMR -115.4 (s, 2F, CF_2).

2,2-Difluoro-5-methyl-1-*p*-tolylhex-4-en-1-one (3c). Colorless liquid (CH_2Cl_2/EP 10/90). ^{1}H NMR 1.64 (s, 3H, CH_3), 1.75 (d, $^4J_{HH}$= 1.2, 3H, CH_3), 2.44 (s, 3H, CH_3), 2.92 (td, $^3J_{HF}$= 17.4, $^3J_{HH}$= 7.3, 2H, CH_2), 5.21 (tm, $^3J_{HH}$= 7.3, 1H), 7.30 (d, $^3J_{HH}$= 8.6, 2H), 8.01 (d, $^3J_{HH}$= 8.6, 2H). ^{13}C NMR 14.0 (CH_3), 22.6 (CH_3), 32.9 (t, $^2J_{CF}$= 25.6, CH_2), 33.9, 118.6 (t, J_{CF}= 240.2, CF_2), 127.9, 128.7, 130.3, 132.5, 151.6 (t, $^2J_{CF}$= 25.6, C=CH), 196.1 (t, $^2J_{CF}$= 30.5, *C*O). ^{19}F NMR -99.9 (t, $^3J_{HF}$= 17.4, 2F, CF_2). I.R. (film) 2918 (m), 2862 (m), 1703 (S), 1599 (m), 1450 (m), 1174 (m), 1057 (m) cm^{-1}.

2,2-Difluoro-3,3-dimethyl-1-*p*-tolylpent-4-en-1-one (4c). ^{19}F NMR -107.8 (s).

Difluorodehydro-ar-curcumene preparation.

3,3-Difluoro-6-methyl-2-*p*-tolylhepta-1,5-diene (5c). To a solution of methyltriphenyl-phosphonium bromide (0.479 g, 1.34.mmol, 1.26 eq.) in ether (6mL) was added nBuLi (0.536 mL of a 2.5M solution in hexane; 1.34 mmol; 1.26 eq.) at room temperature After 0.5h stirring at RT, a 9/1 mixture of **3c** and **4c** (0.250 g; 1.06 mmol) solution in ether (5 mL) was added dropwise to the deep red solution. The reaction mixture was refluxed for 16h and was hydrolyzed with water (15 mL). The crude mixture was filtered and was extracted with ether (3 x 20mL). The organic layer was washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude product was purified by silicagel column chromatography (CH_2Cl_2/EP 2/98) giving pure **5c** in 51% yield. Colorless liquid. ^{1}H NMR 1.47 (s; 3H, CH_3), 1.71 (d, $^4J_{HF}$= 1.2, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.64 (td, $^3J_{HF}$= 15.9, $^3J_{HH}$= 7.3, 2H, CH_2), 5.09 (tm, $^3J_{HH}$= 7.3, 1H, CH), 5.45 (m, 1H), 5.68 (m, 1H), 7.18 (d, $^3J_{HH}$= 8.43, 2H), 7.33 (d, $^3J_{HH}$= 8.43, 2H). ^{13}C NMR 17.8 (CH_3), 21.2 (CH_3), 25.8 (CH_3), 35.6 (t, $^2J_{CF}$=26.6, CH_2), 114.8 (m, CH), 117.5 (t, $^3J_{CF}$= 8.7, CH_2), 122.2 (t, J_{CF}= 243.1, CF_2), 128.0 (CH), 129.0 (CH), 134.3 , 136.4, 137.9, 144.7 (t, $^2J_{CF}$= 23.2). ^{19}F NMR -95.5 (t, $^3J_{HF}$= 15.9, 2F, CF_2). I.R. (film) 2920 (S), 1514 (m), 1450 (m), 1051 (S) cm^{-1}. MS m/e (%) 236 (M+, 17), 193 (100). Anal. Calcd for $C_{15}H_{18}F_2$:C, 76.24; H, 7.68; Found : C, 76.61; H, 7.94.

3,3-Difluoro-4,4-dimethyl-2-*p*-tolylhexa-1,5-diene (6c). ^{1}H NMR 1.01 (d, $^4J_{HH}$= 1.1, 6H, 2 CH_3), 2.33 (s, CH_3), 4.91 (d, $^3J_{HH}$= 11.1, 1H, CH), 4.95 (d, $^3J_{HH}$= 17.5, 1H, CH), 5.40 (m, 1H, CH), 5.59 (m, 1H, CH), 5.80

(dd, $^3J_{HH}$= 17.5, $^3J_{HH}$= 11.1, 1H, CH), 7.09 (d, $^3J_{HH}$= 8, $2H_{aro}$), 7.25 (d, $^3J_{HH}$= 8, $2H_{aro}$). ^{19}F NMR -95.5 (t, $^3J_{HF}$= 15.9, 2F, CF_2).

Difluoro-ar-turmerone synthesis.

1-Bromo-1-*p*-tolylethane. A solution of 1-*p*-tolylethanol (8g, 0.058 mol) in toluene (60 mL) was submitted to a HBr bubbling (generated from a dropwise addition of conc. H_2SO_4 on NaBr) during 30 min. The reaction mixture was washed with a saturated $NaHCO_3$solution. The organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give pure 1-bromo-1-*p*-tolylethane in 85% yield. Colorless liquid. ^1H NMR 2.06 (d, $^3J_{HH}$= 6.9, 3H, CH_3), 2.36 (s, 3H, CH_3), 5.23 (q, $^3J_{HH}$= 6.9, 1H, CH), 7.17 (d, $^3J_{HH}$= 7.1, 2H), 7.35 (dd, $^3J_{HH}$= 7.1, $^4J_{HH}$= 1.8, 2H). ^{13}C NMR 21.1 (CH_3), 26.7 (CH_3), 49.7, 126.6, 129.2, 138.1, 140.3. I.R. (film) 2974 (m), 2920 (m), 1514 (m), 1441 (m), 1178 (S), 817 (S) cm^{-1}. MS m/z (%) 119 (M^+- Br, 100).

3,3-Difluoro-6-methyl-2-*p*-tolylhept-5-en-4-one (7). To a solution of difluoroenoxysilane prepared from **1d** (1.5 mmol) in CH_2Cl_2 (5 mL) was added the 1-bromo-1-*p*-tolylethane (0.4 mL) and $ZnBr_2$ (405 mg, 1.8 mmol, 1.2 eq.). The reaction mixtures was stirred 5h at room température. After hydrolysis with a saturated $NaHCO_3$ solution the crude mixture was extracted with CH_2Cl_2 (3 x 20mL), the organic layer was washed with brine, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude product was purified by silicagel column chromatography (CH_2Cl_2/EP 10/90) to give pure **7** in 53 % yield. Colorless liquid. ^1H NMR 1.41 (d, $^3J_{HH}$= 7.3, 3H, CH_3), 1.91 (d, $^4J_{HH}$= 1.2, 3H, CH_3), 2.14 (d, $^4J_{HH}$= 1.2, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.48 (ddq, $^3J_{HF}$= 17.2, $^3J_{HF}$= 15.3, $^3J_{HH}$= 6.8, 1H, CH), 6.24 (m, 1H, CH), 7.11 (d, $^3J_{HH}$= 8.4, 2H), 7.18 (d, $^3J_{HH}$= 8.4, 2H). ^{13}C NMR 14.0 (d, $^3J_{C\text{-}F}$= 3.9, *C*H_3), 21.0 (*C*H_3), 21.5 (*C*H_3), 28.2 (*C*H_3), 42.7 (t, $^2J_{C\text{-}F}$= 22.6, *C*H), 117.8 (s, C=*C*H), 118.5 (t, J_{CF}= 257.9, *C*F_2), 127.1, 128.9, 129.0, 134.5 (d, $^3J_{CF}$= 3.9), 137.2 (d, $^3J_{CF}$= 3.9), 190.1 (t, $^2J_{CF}$= 28.5, *C*O). ^{19}F NMR -112.3 (dd, J_{AB}=255.5, $^3J_{HF}$= 15.3, 1F), -114.7 (dd, J_{AB}=255.5, $^3J_{HF}$= 15.3, 1F). I.R. (film) 2982 (m), 2943 (m), 2924 (m), 1703 (S), 1614 (S), 1446 (m), 1099 (m), 1055 (m), 851 (m) cm^{-1}. MS m/z (%)252 (M+, 24), 232 (36), 119 (100).

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