

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

Olivier Lefebvre, Thierry Brigaud and Charles Portella*

Laboratoire "Réactions Sélectives et Applications". Associé au CNRS (UMR 6519)
Université de Reims. Faculté des Sciences. BP 1039. 51687 Reims Cedex 2. France.

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Abstract: Acylsilane and trifluoromethyltrimethylsilane gave, under fluoride initiation, a difluoroenoxyasilane 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- α -curcumene and α -turmerone). © 1999 Elsevier Science Ltd. All rights reserved.

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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 difluoroenoxyasilanes **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, difluoroenoxyasilanes have also been prepared from different fluorinated raw materials such as trifluoroacetyltriphenylsilane,³ trifluoromethyltrimethylsilane,⁴ trifluoromethylketones.⁵

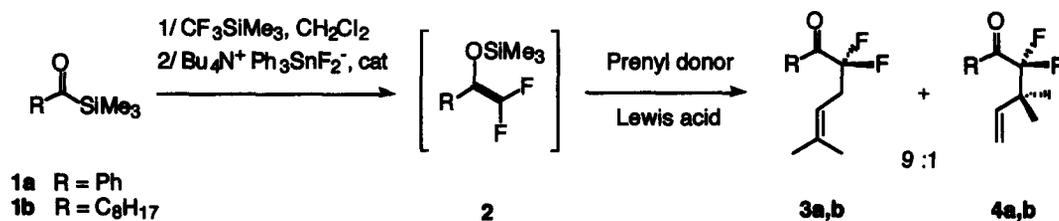
e-mail : charles.portella@univ-reims.fr ; fax : 33 (0)3 26 05 31 66

The strategy developed 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 glycosylations⁶ and Michael reactions.⁷ We report here new applications of this strategy, allylation and benzylation of difluoroenoxy silanes, whose usefulness is demonstrated by the synthesis of *gem*-difluoroanalogues of terpenes.

RESULTS AND DISCUSSION.

One-pot allylation and benzylation of difluoroenoxy silanes.

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 difluorotriphenylstannate⁸ gave the corresponding difluoroenoxy silane. 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 BiCl₃/ZnI₂ system⁹ (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 ¹⁹F 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.

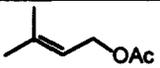
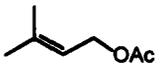
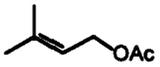
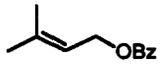
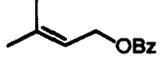
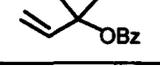


Scheme 1

We have already reported in our preliminary account⁴ 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 difluoroenoxy silane took place with such an initiator.⁴

Table 1. Prenylation reactions of difluoroenoxy silane.

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%

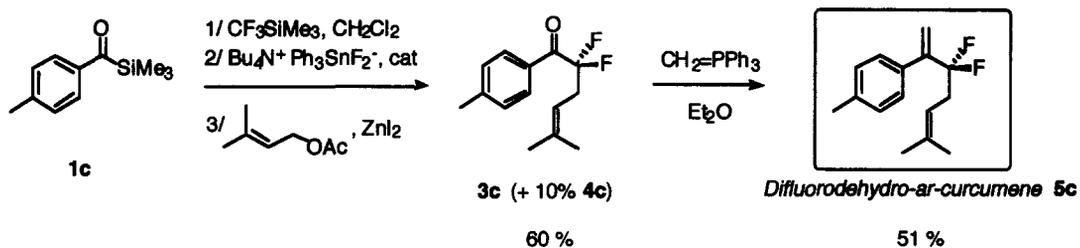
^a Isolated mixture of 3 and 4 in a 9/1 ratio (¹⁹F NMR). ^b Overall yield based on acylsilane.

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.

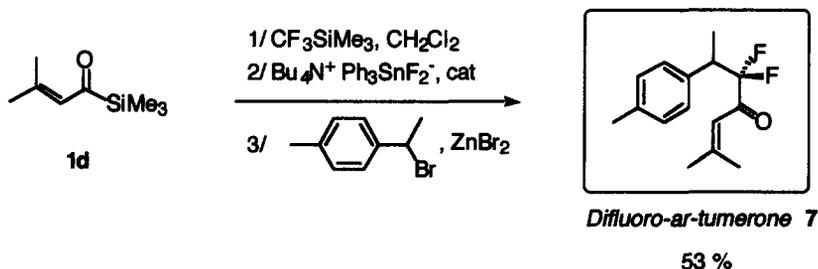
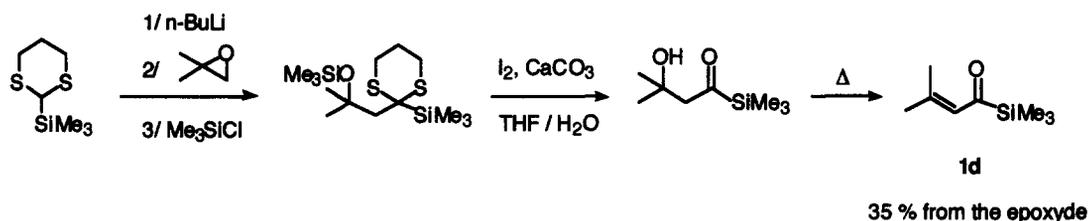
Application to the synthesis of *gem*-difluoro terpene analogues.

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*-difluoro terpenes 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- α -curcumene 5c was obtained as a unique product after purification by silicagel chromatography in 51% yield (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 difluoroenoxy silane was generated *in situ* in the conditions described above, then 1-bromo-1-tolyloethane and zinc bromide was added to the reaction mixture to give the difluoro-*ar*-turmerone **7** in 53% overall yield (Scheme 4).



Summary

These results extend the chemical scope of the combined acylsilane-trifluoromethyltrimethylsilane as a synthetic equivalent of difluoroenoxy silane. 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. ^1H , ^{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 ^1H 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). ^1H NMR 0.18 (s, 9H, 3 CH_3), 0.86 (t, $^3J_{\text{HH}} = 6.0$, 3H, CH_3), 1.24 (s, 10H, 5 CH_2), 1.49 (quint, $^3J_{\text{HH}} = 7.0$, 2H, CH_2), 2.55 (t, $^3J_{\text{HH}} = 7.0$, 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 (CO), 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 $\text{C}_{12}\text{H}_{26}\text{OSi}$: 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). ^1H NMR 0.37 (s, 9H, 3 CH_3), 2.40 (s, 3H, CH_3), 7.27 (dm, $^3J_{\text{HH}} = 8.2$, 2H), 7.75 (dt, $^3J_{\text{HH}} = 8.2$, $^4J_{\text{HH}} = 1.8$, 2H), ^{13}C NMR -1.4 (3 CH_3), 21.6 (CH_3), 127.6 (C_{aro}), 129.2 (C_{aro}), 139.1 (C_{aro}), 143.4 (C_{aro}), 234.7 (CO), 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 $\text{C}_{11}\text{H}_{16}\text{OSi}$: 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, ClSiMe₃ (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 Et₂O (3 X 50 mL), the organic layer was washed with brine, dried over MgSO₄ and the solvent was evaporated under reduced pressure. The silyl dithiane derivative was purified by silicagel column chromatography (CH₂Cl₂/EP 10/90 ;45% yield). Pale yellow liquid. ¹H NMR 0.12 (s, 9H, 3 CH₃), 0.26 (s, 9H, 3 CH₃), 1.43 (s, 6H, 2 CH₃), 2.16 (s, CH₂), 2.42-2.53 (m, 4H, 2 CH₂), 2.97-3.03 (m, 2H, CH₂), ¹³C NMR -1.3 (3 CH₃), 3.0 (3 CH₃), 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 NaHCO₃ (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 Na₂S₂O₃ was added and the crude mixture was extracted with Et₂O. The organic layer was washed with brine, dried over MgSO₄ 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 CH₃), 1.20 (s, 6H, 2 CH₃), 2.78 (s, 2H, CH₂), ¹³C NMR -3.6 (3 CH₃), 29.4 (2CH₃), 57.5 (CH₂), 70.3, 253.2 (CO), I.R. (film) 3480 (S), 2972 (S), 1631 (S), 1375 (m), 1251 (S), 848 (S).

(3-Methylbut-2-enoyl)trimethylsilane (1d). The dehydration 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 CH₃), 1.86 (s, 3H, CH₃), 2.07 (s, 3H, CH₃), 6.53 (t, ⁴J_{HH}= 1.2, CH), ¹³C NMR -3.3 (3 CH₃), 21.0 (CH₃), 27.4 (CH₃), 126.9 (CH), 150.1, 237.7 (CO), 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 difluoroenoxyasilane. To a solution of acylsilane (1.5 mmol) and trifluoromethyltrimethylsilane (0.3 mL, 1.89 mmol) in CH₂Cl₂ (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 difluoroenoxyasilane was monitored by GC and it was used in the next step in a one-pot procedure.

ZnI₂ catalysis. To a solution of difluoroenoxyasilane (1.5 mmol) in CH₂Cl₂ (15 mL) was added the prenylester (2.25 mmol) and ZnI₂ (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 NaHCO₃ solution the crude mixture was extracted with CH₂Cl₂ (4 x 20mL), the organic layer was washed with brine, dried over MgSO₄ and the solvent was evaporated under reduced pressure. The crude product was purified by silicagel column chromatography.

BiCl₃ / ZnI₂ catalysis. The prenyl acetate (3 mmol), BiCl₃ (0.15 mmol) and freshly sublimated ZnI₂ (0.225 mmol) were added to the solution of difluoroenoxyasilane at room temperature and the reaction mixture was stirred at room temperature until consumption of the difluoroenoxyasilane. The work up procedure was the same as above.

TMSOTf catalysis. TMSOTf (0.3 mmol) was added to the solution of difluoroenoxyasilane 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 (CH₂Cl₂/EP 10/90). ¹H NMR 1.63 (s, 3H, CH₃), 1.74 (s, 3H, CH₃), 2.94 (td, ³J_{HH}= 17.4, ³J_{HF}= 7.3, 2H, CH₂), 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). ¹³C NMR 17.9 (CH₃), 26.1 (CH₃), 33.4 (t, ²J_{CF}= 23.6, CH₂), 113.0 (CH), 119.2 (t, J_{CF}= 254.0, CF₂), 128.6, 130.0, 134.1, 137.2, 138.2, 189.6 (t, ²J_{CF}= 31.5, CO). ¹⁹F NMR -99.9 (t, ³J_{HF}= 17.4, 2F, CF₂). 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 C₁₃H₁₄O₂F₂: 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 CH₃), 5.12-5.19 (m, 2H), 6.03 (dd, ³J_{HH}= 17.5, ³J_{HF}= 10.8, 1H), 7.35-7.63 (m, 3H), 8.04 (d, ³J_{HH}= 9.5, 2H). ¹⁹F NMR -107.9 (s).

5,5-Difluoro-2-methyl-tetradec-2-en-6-one (3b). Colorless liquid (CH₂Cl₂/EP 10/90). ¹H NMR 0.87 (t, ³J_{HH}= 6.1, 3H, CH₃), 1.13-1.39 (m, 10H, 5 CH₂), 1.52-1.68 (m, 2H, CH₂), 1.62 (s, 3H, CH₃), 1.72 (s, 3H, CH₃), 2.62 (t, ³J_{HH}= 7.3, 2H, CH₂), 2.70 (td, ³J_{HF}= 16.8, ³J_{HH}= 7.6, 2H, CH₂), 5.08 (tm, ³J_{HH}= 7.3). ¹³C NMR 14.1 (CH₃), 17.9 (CH₃), 22.5, 22.6, 25.8 (CH₃), 28.9, 29.1, 29.2, 31.8, 32.1 (t, ²J_{CF}= 20.4, CH₂CF₂), 36.8, 112.7 (t, ³J_{CF}= 3.9, CH), 117.8 (t, J_{CF}= 253.9, CF₂), 138.4 (s, CH=C), 200.7 (t, ²J_{CF}= 30.5, CO). ¹⁹F NMR -106.8 (t, ³J_{HF}= 16.8, 2F, CF₂). 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). 1H 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). 1H 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, $^2J_{CF}=30.5$, CO). ^{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 (6 mL) 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 20 mL). 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. 1H 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). 1H 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, $^3J_{\text{HH}}=17.5$, $^3J_{\text{HH}}=11.1$, 1H, CH), 7.09 (d, $^3J_{\text{HH}}=8$, 2H_{aro}), 7.25 (d, $^3J_{\text{HH}}=8$, 2H_{aro}). ^{19}F NMR -95.5 (t, $^3J_{\text{HF}}=15.9$, 2F, CF₂).

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. H₂SO₄ on NaBr) during 30 min. The reaction mixture was washed with a saturated NaHCO₃ solution. The organic layer was dried over Na₂SO₄ 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, $^3J_{\text{HH}}=6.9$, 3H, CH₃), 2.36 (s, 3H, CH₃), 5.23 (q, $^3J_{\text{HH}}=6.9$, 1H, CH), 7.17 (d, $^3J_{\text{HH}}=7.1$, 2H), 7.35 (dd, $^3J_{\text{HH}}=7.1$, $^4J_{\text{HH}}=1.8$, 2H). ^{13}C NMR 21.1 (CH₃), 26.7 (CH₃), 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 difluoroenoxyasilane prepared from **1d** (1.5 mmol) in CH₂Cl₂ (5 mL) was added the 1-bromo-1-*p*-tolylethane (0.4 mL) and ZnBr₂ (405 mg, 1.8 mmol, 1.2 eq.). The reaction mixture was stirred 5h at room temperature. After hydrolysis with a saturated NaHCO₃ solution the crude mixture was extracted with CH₂Cl₂ (3 x 20mL), the organic layer was washed with brine, dried over MgSO₄ and the solvent was evaporated under reduced pressure. The crude product was purified by silicagel column chromatography (CH₂Cl₂/EP 10/90) to give pure **7** in 53 % yield. Colorless liquid. ^1H NMR 1.41 (d, $^3J_{\text{HH}}=7.3$, 3H, CH₃), 1.91 (d, $^4J_{\text{HH}}=1.2$, 3H, CH₃), 2.14 (d, $^4J_{\text{HH}}=1.2$, 3H, CH₃), 2.33 (s, 3H, CH₃), 3.48 (ddq, $^3J_{\text{HF}}=17.2$, $^3J_{\text{HF}}=15.3$, $^3J_{\text{HH}}=6.8$, 1H, CH), 6.24 (m, 1H, CH), 7.11 (d, $^3J_{\text{HH}}=8.4$, 2H), 7.18 (d, $^3J_{\text{HH}}=8.4$, 2H). ^{13}C NMR 14.0 (d, $^3J_{\text{C-F}}=3.9$, CH₃), 21.0 (CH₃), 21.5 (CH₃), 28.2 (CH₃), 42.7 (t, $^2J_{\text{C-F}}=22.6$, CH), 117.8 (s, C=CH), 118.5 (t, $J_{\text{CF}}=257.9$, CF₂), 127.1, 128.9, 129.0, 134.5 (d, $^3J_{\text{CF}}=3.9$), 137.2 (d, $^3J_{\text{CF}}=3.9$), 190.1 (t, $^2J_{\text{CF}}=28.5$, CO). ^{19}F NMR -112.3 (dd, $J_{\text{AB}}=255.5$, $^3J_{\text{HF}}=15.3$, 1F), -114.7 (dd, $J_{\text{AB}}=255.5$, $^3J_{\text{HF}}=15.3$, 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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