Difluorocyclopropenes

Ringing the Changes: A Remarkable Carbene-Free Synthesis of Difluorocyclopropenes**

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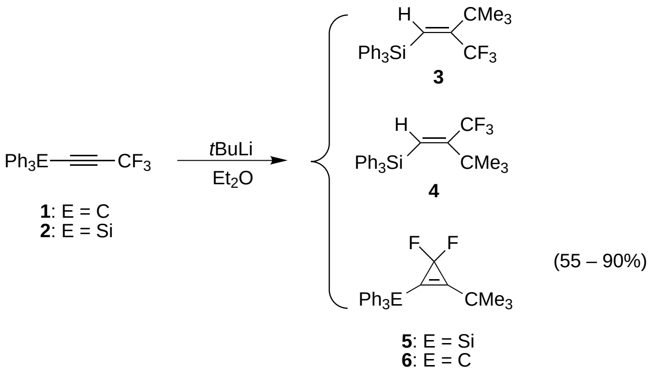
In recent years there has been resurgent interest in the chemistry of fluorinated compounds because of their potential pharmaceutical, agrochemical, and materials applications.[1] We have been investigating new methods for the selective introduction of small fluorocarbon fragments and have recently reported a new and facile route to trifluoropropynyl derivatives.[2] In seeking to extend to these systems our recent work on the reactivity of organometallic fluorovinyl compounds,[3] we have discovered a remarkable transformation, which results in the facile formation of *gem*-difluorocyclopropenyls in good yields.

The trifluoropropynyls $Ph_3EC\equiv CCF_3$ (**1**: E = C, **2**: E = Si) are readily prepared by the reaction of Ph_3EX (X = Cl, Br) with trifluoropropynyllithium ($LiC\equiv CCF_3$), derived from hydrofluorocarbon HFC-245fa ($CF_3CH_2CF_2H$) as we have previously described,[2] and isolated as air- and moisture-stable solids. These materials are characterized by singlet resonances at around $\delta_F = -50$ ppm in the ^{19}F NMR spectra, and three quartet signals in the ^{13}C NMR spectra, ($\delta_C = 90$–120 ppm), with infrared absorptions ($C\equiv C$ stretch) at approximately 2200 cm^{-1}.

Given the versatility of silanes as organotransfer reagents[4] and in fluoro/hydro-desilylation chemistry,[5] compound **2** constitutes a potentially useful substrate for derivatization. The reaction of **2** with organolithium reagents was thus explored as a route to some novel β-CF_3-substituted vinylic systems. However, when an ethereal solution of **2** was treated with 1 equivalent of *t*BuLi at −78 °C and then allowed to warm to ambient temperature over 5 h, workup afforded an unexpected product mixture (Scheme 1). Multinuclear (^1H, ^{19}F) NMR studies revealed a significant proportion of (*Z*)-$Ph_3SiCH{=}C(tBu)CF_3$ (**3**), which was assigned on the basis of H-F coupling constants and a discernible NOE interaction between the alkenic and *tert*-butyl proton resonances, and trace levels of the *E* isomer **4** (*Z*/*E* 14:1). The major product (55 % by integration) was characterized by a low-frequency singlet ^{19}F NMR resonance ($\delta_F = -103.1$ ppm) and additional *tert*-butyl resonances in the ^1H and ^{13}C NMR spectra; no further alkenic protons were observed. Efforts to separate these materials chromatographically proved unsuccessful, owing to their limited stability on the column, as did recrystallization. However, the slow evaporation of a dichloromethane/hexane solution, did afford isomerically enriched single crystals.



Scheme 1. Products from the *t*BuLi reaction with group 14 trifluoropropynyl derivatives.

Surprisingly, X-ray analysis revealed the presence of both **4** (12 %) and the *gem*-difluorocyclopropenyl **5** (88 %, Figure 1), within the same crystal.[6] The presence of **5** is consistent with the observed NMR data, the low-frequency ^{19}F resonance being characteristic of other *gem*-difluorocyclopropenes.[7] Moreover, we observed three cyclopropenic

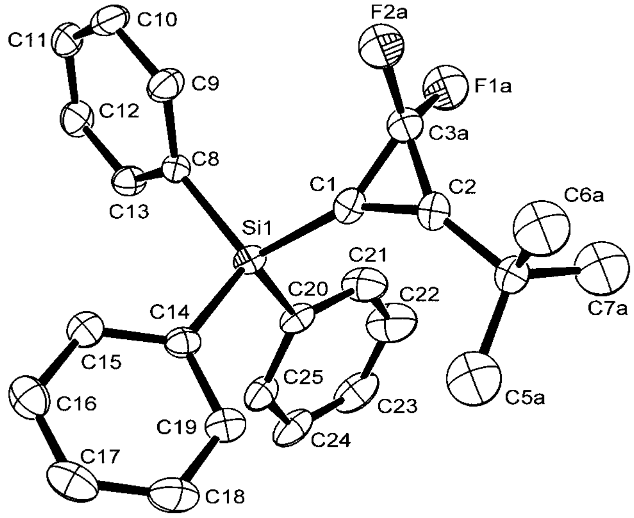


Figure 1. ORTEP representation of **5** with thermal ellipsoids set at the 30 % probability level and hydrogen atoms omitted for clarity. The numbering scheme is directly transposable to compound **6**, with C1′ replacing Si1. Selected data (Å, °) for **5**. C1-C2 1.329(4), C2-C3 1.371(4), C1-C3 1.402(4), C3-F1a 1.384(4), C3-F2a 1.369(4); C2-C1-C3 60.2(2), C1-C2-C3 62.6(2), C2-C3-C1 57.27(19), Si1-C1-C2 151.2(2), C1-C2-C4 147.2(3). Selected data for **6**. C1-C2 1.324(3), C2-C3 1.427(3), C1-C3 1.429(3), C3-F1a 1.379(3), C3-F2a 1.375(3); C2-C1-C3 62.2(16), C1-C2-C3 62.47(15), C2-C3-C1 55.23(14), C1′-C1-C2 148.2(2), C1-C2-C4 152.0(3).

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[**] This work was supported by the Engineering and Physical Sciences Research Council (EPSRC) and UMIST. We gratefully acknowledge Honeywell Specialty Chemicals for a donation of HFC-245fa and the EPSRC for support of the UMIST NMR (GR/L52246), FT-IR/Raman (GR/M30135), and X-ray (Research Initiative Grant) facilities.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

DOI: 10.1002/ange.200250756

^{13}C NMR resonances in the region $\delta_C = 160–100$ ppm; each one a well-defined triplet.

The formation of **5** is optimized when **2** is treated with *t*BuLi at ambient temperature over 20 h, whereupon **5** accounts for 80 % of the product mixture. Significantly, comparable conditions also result in cyclization of the trityl alkyne **1**, thus precluding the possibility that cyclization involves the participation of silicon d orbitals. Indeed, **1** has proven to be the most viable substrate, since difluorocyclopropene **6**[8] accounts for 90 % of the reaction products.

This remarkably facile cyclization presumably occurs by elimination of LiF from the lithiated intermediate (*E*)-$Ph_3EC(Li){=}C(tBu)CF_3$, driven by the steric strain associated with the introduction of a *t*Bu group *cis* to the Ph_3E fragment. This is supported by ab initio calculations of the related alkene (*E*)-$Me_3SiCH{=}C(tBu)CF_3$ at the B3LYP/6-311 + G* level,[9] which reveal an energy minimum with a significantly distorted geometry (Si-C=C = 140.1°, C=C-*t*Bu = 127.8°). Consequently, the eclipsing fluorine atom approaches the alkenic hydrogen center at 2.119 Å (C–F···H = 59.2°), significantly closer than the sum of the contact radii (2.67 Å).[10] This would be enhanced in the lithiated intermediate, thus predisposing it to elimination of LiF. Significantly, these distortions are also evident in the single-crystal structure of **4** (Figure 2),[11] obtained in a subsequent experiment. Once again, an extremely short H···F interaction (2.13(2) Å) is apparent, clearly enforced by an opening of the alkene geometry (Si-C=C = 139.37(18)°, C=C-*t*Bu = 127.4(2)°). The steric argument is supported by ongoing investigations of the interaction of **2** with other, smaller organolithium reagents, RLi (R = Ph, *n*Bu, Me) and $LiAlH_4$, whereupon cyclization occurs only at trace levels. Indeed, for the limiting case, (*E*)-$R_3SiCH{=}CHCF_3$ (**7**: R = Me), ab initio calculations reveal a more typical geometry (Si-C=C = 125.3°, C=C-H = 122.9°) with a significantly reduced H···F interaction (2.407 Å).[12] We note that similar Li···F interactions are also believed to play an important role in the mechanism of *ortho* metallation of fluoroaromatic compounds.[13]

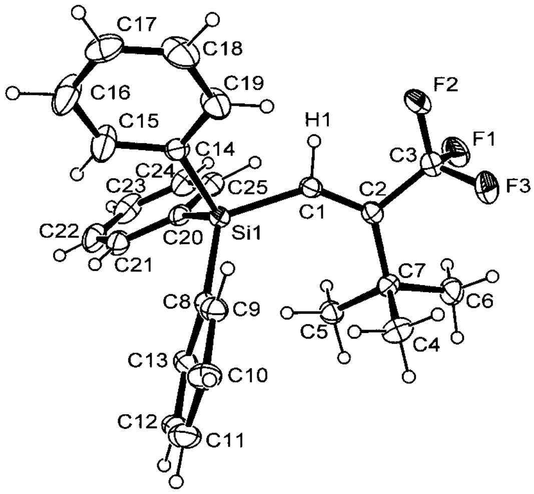

Figure 2. ORTEP representation of **4** with thermal ellipsoids set at the 30% probability level. Selected data (Å, °): C1-C2 1.341(3), C2-C3 1.510(3), C3-C1 1.345(3), C3-F2 1.344(3), C3-F3 1.345(3); C1-C2-C7 127.4(2), C1-C2-C3 115.9(2), Si1-C1-C2 139.37(18), C2-C1-C7 116.68(16), Si1-C1-H1 110.1(13).

The cyclization pathway is also inhibited when operating at reduced temperature. Thus, when **2** and *t*BuLi interact at −60 °C, **5** is obtained, along with **4**, only as a trace contaminant (2.5 %) in admixture with **3** (95 %). This preference for *syn* addition would suggest the intermediacy of a lithium π complex, favored by the decreased nucleophilicity of *t*BuLi under these conditions. Support for this has been obtained through the use of tmeda to enhance solvation, and thus nucleophilicity, of the *t*BuLi, which results in a lower specificity of addition. In these experiments, **3** was generated with varying amounts of the *E* isomer, consistent with inhibition of the π complex and also of LiF elimination to afford **5**.

In conclusion, the reaction of the group 14 trifluoropropynyl compounds $Ph_3EC{\equiv}CCF_3$ (E = C, Si) with sterically demanding organolithium reagents results in a facile and efficient cyclization to afford the respective triphenyl-2-*tert*-butyl-3,3-difluorocyclopropenyl compounds. This circumvents the use of difluorocarbene sources, as in more classical synthetic protocols, and is readily controlled under mild conditions. The potential for Si–C cleavage and selective transfer of organic components from organosilanes renders this discovery a significant advance in small-ring chemistry, which we continue to explore.

Experimental Section

Reagents were obtained from commercial vendors and used as supplied. NMR spectra were recorded as $CDCl_3$ solutions at 298 K, on Bruker DPX 200 (^{19}F NMR spectra at 188.310 MHz) or DPX 400 (^{13}C NMR and Dept-135 spectra at 100.155 MHz, ^1H NMR spectra at 400.4 MHz) spectrometers and referenced to external $CFCl_3$ and TMS, respectively.

2: A stirred solution of HFC-245fa (2.16 cm³, 21.28 mmol) in diethyl ether (300 cm³) was treated with *n*BuLi (2.5 M, 25.5 cm³, 63.75 mmol) at −10 °C under N_2. After 15 min, Ph_3SiCl (4.15 g, 14.07 mmol) in diethyl ether (40 cm³) was added, whilst maintaining the temperature at −10 °C. The mixture was then allowed to stir and attain ambient temperature overnight. Hexane (160 cm³) was added to precipitate the inorganic salts, the settled mixture was then filtered through celite, and the filtrate was concentrated in vacuo. Purification on a silica column, eluting with 50:50 toluene/hexane, afforded **2** as a pale yellow solid (4.229 g, 85 %). M.p. 110 °C; elemental analysis: calcd for $C_{21}H_{15}F_3Si$: C 71.6, H 4.3, F 16.2; found: C 71.9, H 4.5, F 16.0; $\delta_F = -50.4$ ppm; $\delta_C = 135.4$ (s; CH), 131.6 (s; C), 131.1 (s; CH), 128.8 (s; CH), 113.3 (q, $J_{CF} = 258.7$ Hz; CF_3), 93.8 (q, $J_{CF} = 51.6$ Hz; C_β), 90.3 ppm (q, $J_{CF} = 5.8$ Hz; C_α); $\delta_H = 7.7–7.4$ ppm (m; Ph); $\tilde{\nu}_{max}$ 2204 (C≡C str), 1245, 1151, 1114 cm^{-1} (C–F str).

1: M.p. 150 °C; elemental analysis: calcd for $C_{22}H_{15}F_3$: C 78.6, H 4.5, F 16.9; found: C 78.8, H 4.3, F 16.6; $\delta_F = -50.0$ ppm; $\delta_C = 143.2$ (s; C), 129.4 (s; CH), 128.8 (s; CH), 127.9 (s; CH), 114.8 (q, $J_{CF} = 256.9$ Hz; CF_3), 93.9 (q, $J_{CF} = 6.7$ Hz; C_α), 72.6 (q, $J_{CF} = 52.2$ Hz; C_β), 55.8 ppm (br s, Ph_3C); $\delta_H = 7.7–7.4$ (m; Ph); $\tilde{\nu}_{max}$ 2256 (C≡C str), 1276, 1145, 1091 cm^{-1} (C–F str).

Reaction with nucleophiles: Typically, a solution of **1** (0.500 g, 1.49 mmol) in diethyl ether (15 cm³) was treated with *t*BuLi (1.5 M, 1.0 cm³, 1.50 mmol) at ambient temperature under N_2 and stirred for 20 h. The reaction was quenched with methanol (3 cm³) and hexane was added to precipitate the inorganic components, then filtered through celite, and the filtrate was concentrated in vacuo. Purification on silica, eluting with 50:50 CH_2Cl_2/hexane afforded the pure product **6** in 60 % yield. M.p. 143 °C; elemental analysis: calcd for $C_{26}H_{24}F_2$: C 83.4, H 6.5, F 10.2; found: C 83.2, H 6.8, F 10.5; $\delta_F = -105.9$ ppm; $\delta_C =$ 143.0 (s; C), 128.5 (s; CH), 127.2 (s; CH), 126.1 (s; CH), 136.1 (t, $J_{CF} =$ 10 Hz; C_β), 131.2 (t, $J_{CF} = 10.6$ Hz; C_α), 103.8 (t, $J_{CF} = 272$ Hz; CF_2), 58.1 (brs; Ph_3C), 30.3 (s; CMe_3), 27.1 ppm (s; $C(CH_3)_3$); $\delta_H = 7.7–7.4$ (m; Ph), 1.02 ppm (s; $(CH_3)_3$); $\tilde{\nu}_{max} = 1781$ (C=C str), 1292, 1147 cm^{-1} (C−F str).

5: $\delta_F = -103.1$ ppm; $\delta_C = 134.6$ (s; CH), 130.9 (s; C), 129.3 (s; CH), 127.1 (s; CH), 157.9 (t, $J_{CF} = 8.3$ Hz; C_β), 124.6 (t, $J_{CF} = 13.1$ Hz; C_α), 108.2 (t, $J_{CF} = 271$ Hz; CF_2), 29.7 (s; CMe_3), 27.4 ppm (s; $C(CH_3)_3$); $\delta_H = 7.7–7.4$ (m; Ph), 1.1 ppm (s; $(CH_3)_3$); $\tilde{\nu}_{max} = 1729$ (C=C str), 1261, 1149 cm^{-1} (C−F str).

3: M.p. 89 °C; elemental analysis: calcd for $C_{25}H_{25}F_3Si$: C 73.2, H 6.1, F 13.9; found: C 73.4, H 6.1, F 13.5; $\delta_F = -60.7$ ppm (d, $J_{HF} =$ 1.5 Hz); $\delta_C = 134.7$ (s; CH), 134.1 (s; C); 128.6 (s; CH), 127.0 ($J_{SiC} =$ 29 Hz; CH), 155.7 (q, $J_{CF} = 23.7$ Hz; C_β), 126.2 (q, $J_{CF} = 4.8$ Hz; C_α), 123.2 (q, $J_{CF} = 279$ Hz; CF_3), 35.3 (s; CMe_3), 29.7 ppm (s; $C(CH_3)_3$); $\delta_H = 7.7–7.4$ (m; Ph), 6.9 (q, $J_{HF} = 1.5$ Hz; =CH), 1.06 ppm (s; $(CH_3)_3$); $\tilde{\nu}_{max} = 1429$ (C=C str), 1257, 1157, 1120 cm^{-1} (C−F str).

4: $\delta_F = -56.7$ ppm (d, $J_{HF} = 1.5$ Hz), $\delta_H = 7.7–7.4$ (m; Ph), 6.7 ppm (q, $J_{HF} = 1.5$ Hz; =CH), 1.1 (s; $(CH_3)_3$).

Crystallography: Single crystals were obtained by the slow evaporation of CH_2Cl_2/hexane solutions. Diffraction data were recorded on a Nonius κ-CCD 4-circle diffractometer using graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å) at 150(2) K. Structure data were solved by direct methods, with full-matrix least-squares refinement on F^2 using the SHELX-97[14] program; absorption corrections by the multiscan method were applied with the SORTAV program. Non-hydrogen atoms were refined with anisotropic thermal parameters: all hydrogen atoms were located in the data. Figures were generated using ORTEP-3 for Windows.[15] CCDC-199460 (**4**), -199461 (**5**), and -199462 (**6**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

Ab initio calculations**:** Calculations were performed with the Gaussian 98 package, Revision A.7,[16] running on a Sun Enterprise HPC 4500 workstation. Geometries were optimized at the B3LYP/6-311+G* level and characterized as minima by frequency calculations.

Received: December 12, 2002 [Z50756]

Keywords: alkynes · cyclization · fluorine · small-ring systems · structure elucidation · synthetic methods

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[6] Crystal data for $C_{25}H_{24}F_2Si$ (**5**): 0.25 × 0.15 × 0.05 mm^3, monoclinic, $P121/n1$, $a = 15.7382(4)$ Å, $b = 8.8148(2)$ Å, $c =$ 16.2312(5) Å, $\alpha = 90.0000(10)$, $\beta = 103.0830(10)$, $\gamma =$ 90.0000(10)°, $V = 2193.29(10)$ Å^3, $\rho_{calcd} = 1.183$ Mg m^{-3}, $\theta_{max} =$ 27.45°, reflections/unique/parameters. 36277/4973/300, $F(000)$ 824, $\mu = 0.130$ mm^{-1}, $T_{max} = 1.039$, $T_{min} = 0.968$, $R = 0.0699$, $wR2 = 0.1515$, Largest diff. peak + hole 0.244, −0.218 e Å^{-3}.

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[9] Selected geometric data (Å, °) for (*E*)-$Me_3SiCH{=}C(tBu)CF_3$: C1-C2 1.344, C2-C3 1.526, C3-F2 1.351, C3-F1 1.359, C3-F3 1.361; Si1-C1-C2 140.1, C1-C2-C7 127.8, C1-C2-C3 115.9, C3-C2-C7 116.2, Si1-C1-H1 106.8.

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[11] Crystal data for $C_{25}H_{25}F_3Si$ (**4**): 0.20 × 0.25 × 0.03 mm^3, monoclinic, $P21/c$, $a = 14.5669(5)$ Å, $b = 9.8256(3)$ Å, $c =$ 15.4721(6) Å, $\alpha = 90$, $\beta = 90.4580(10)$, $\gamma = 90$°, $V =$ 2214.43(13) Å^3, $\rho_{calcd} = 1.231$ Mg m^{-3}, θ_{max} 24.98°, reflections/unique/parameters 13196/3837/362, $F(000)$ 864, $\mu =$ 0.139 mm^{-1}, $T_{max} = 0.9959$, $T_{min} = 0.9728$, $R = 0.0463$, $wR2 =$ 0.1128, Largest diff. peak + hole 0.215, −0.232 e Å^{-3}.

[12] Selected geometric data (Å, °) for **7**: C1-C2 1.333, C2-C3 1.498, C3-F2 1.349, C3-F1 1.358, C3-F3 1.358; Si1-C1-C2 125.3, C1-C2-H2 122.9, C1-C2-C3 124.3, C3-C2-H2 112.7, Si1-C1-H1 117.9.

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