Hydrofluorocarbon 245fa: a versatile new synthon in alkyne chemistry

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The CFC replacement 1,1,1,3,3-pentafluoropropane (HFC 245fa) has been established as a convenient source of trifluoropropynyllithium under mild conditions; a range of novel and known trifluoropropynyl-containing systems has been prepared in a one-pot procedure.

Over recent years there has been a surge of interest in the chemistry of fluorinated compounds, with particular focus on the development of systems with pharmaceutical, agrochemical and materials applications.[1,2] We have been actively involved in the investigation of systems bearing the trifluorovinyl (CF=CF$_2$) group,[3] which is readily introduced by means of trifluorovinyllithium, obtained *via* the low-temperature reaction of hydrofluorocarbon 134a (1,1,1,2-tetrafluoroethane, CF$_3$CH$_2$F) with two equivalents of *n*-butyllithium.[4] This has led us to screen a range of commercially available HFCs for similar reactivity and potential as synthetic precursors. Here we report that HFC-245fa (1,1,1,3,3-pentafluoropropane, CF$_3$CH$_2$CF$_2$H) is a convenient source of the trifluoropropynyl anion, through its reaction with 3 equivalents of *n*-butyllithium.

Introduction of the trifluoropropynyl group to organic and organometallic systems has classically been achieved through the use of the respective organolithium,[5] Grignard[6] or organozinc[7] reagents. In each case, reliance upon trifluoropropyne as a precursor incurs experimental difficulties, associated with the handling of a gaseous reagent (b.p. −48 °C), and has significant cost implications. Recently, two independent reports have suggested that 3,3,3-trifluoro-2-bromopropene serves as an experimentally and economically more viable precursor for trifluoropropynyl lithium,[8] which is generated by reaction of the propene with two equivalents of LDA at −78 °C, in THF. However, availability of the fluorocarbon and the necessity for low reaction temperatures remain prohibitive factors, particularly for large-scale applications.

In contrast, we have found that HFC-245fa (**1**, b.p. 15 °C), which has recently gone into mass production, affords good yields of trifluoropropynyllithium under comparatively mild conditions. Thus, the treatment of a diethyl ether solution of **1** with three equivalents of *n*-BuLi at −10 °C leads to good yields of trifluoropropynyllithium **4**, presumably by means of the process illustrated in Scheme 1. Efforts to isolate intermediates **2** and **3** have been unsuccessful, as have attempts to trap the anions from deprotonation of **1** or **2**, though preliminary deuterolysis experiments indicate a predominance of **4**, suggesting a largely concerted mechanism
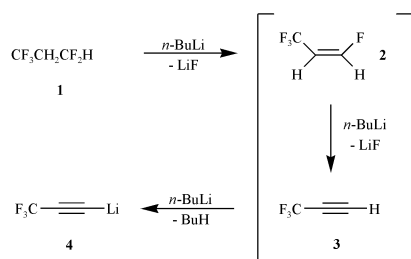
Reagent **4**, generated in this fashion, is stable for several hours when held below 0 °C, but decomposes rapidly above this temperature to afford an intractable material. Stability is significantly reduced when THF is used in place of ether, **4** having a lifetime of a few minutes at −78 °C. Treatment of **4**, generated as described, with ethereal solutions of a range of electrophiles, allows for preparation of the respective trifluoropropynyl compounds, typically in good to excellent yields. In this way a range of organic and organometallic derivatives has been prepared (Fig. 1). In a typical reaction,[9] an ethereal solution of triphenyltin chloride was added to a stirred solution of **4**, at −10 °C, then the mixture allowed to warm slowly to ambient temperature overnight. The reaction is conveniently monitored by ^{19}F-NMR spectroscopy; extracts withdrawn from the mixture revealing gradual loss of the complex multiplet resonances associated with HFC-245fa at −64.3 and −116.8 ppm, and concomitant development of a singlet at −50.8 ppm, with attendant tin satellites (J_{SnF} 12 Hz). The product was isolated as a pale yellow solid by addition of an excess of hexane, to precipitate the inorganic salts, and subsequent concentration of the filtered solution *in vacuo*. The presence of an acetylenic unit was confirmed by the infrared spectrum, which exhibits a strong absorption at 2183 cm^{-1} (C≡C str.) and by multinuclear NMR studies. The CF$_3$ unit inferred by the ^{19}F-NMR spectrum, is also apparent in the ^{13}C-NMR spectrum as a quartet resonance ($^1J_{CF}$ 260 Hz) at 111.5 ppm. Additionally, two further quaternary resonances are observed at δ_C 94.5 and 91.8, which also exhibit quartet multiplicities. Coupling constants of 50 and 6 Hz allow for assignment of the resonances to the β and α acetylenic carbon atoms respectively.

Verification of the trifluoropropynyl group was obtained by an analogous reaction with 0.5 equivalents of HgCl$_2$, affording a moderate yield of Hg(CCCF$_3$)$_2$. The ^{13}C-NMR spectrum again consists of three characteristic quartet resonances in the region 120–90 ppm, each exhibiting satellite coupling to mercury, the magnitude of which diminishes with increasing
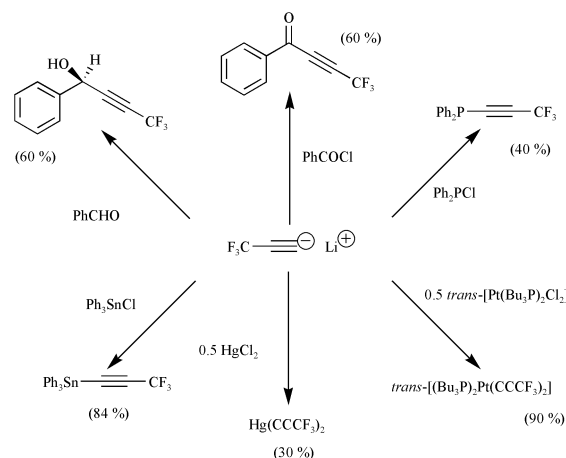

Scheme 1 *Conditions.* Diethyl ether, −10 °C.

Fig. 1 Reactions of trifluoropropynyllithium, derived from HFC-245fa, with a range of electrophiles (yields in parentheses, based on substrate).

J_{CF}.[10] Analogous data has been obtained for a range of novel and known organometallic and phosphorus based systems, which have been prepared in good yield.

HFC-245fa is an equally versatile synthon for organic chemistry; reagent **4** readily reacting with a range of organic substrates to afford the anticipated products in good yield. Thus, when ethereal PhCHO and **4** are allowed to react for 4 h, quenching with methanol, followed by an aqueous work-up allows for isolation of 4,4,4-trifluoro-1-phenyl-2-butyn-1-ol in 60% yield. Similarly, the reaction of **4** with benzoyl chloride afforded the anticipated (1-phenyl)trifluoropropyn-1-one upon aqueous work-up. Both materials were purified by distillation and characterised as previously described, spectroscopic data being consistent with literature reports.[8,11] All materials afforded satisfactory microanalysis.

In conclusion, the potentially useful trifluoropropynyl group can be introduced to a wide range of systems *via* a convenient, one-pot reaction, employing readily available starting materials. The commercial availability of HFC-245fa and the relatively mild conditions employed render trifluoropropynyllithium more widely available than ever before, its availability being comparable to that of any other organolithium. Significantly, for the first time, trifluoropropynyllithium is now an economically viable proposition for industrial-scale applications.

Notes and references

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9 *Typical reaction.* HFC-245fa (0.25 cm³, 2.46 mmol) as solution in ether (80 cm³) is held at −10 °C, while *n*-BuLi (2.5 M in hexane, 2.7 cm³, 6.75 mmol) is added, maintaining the temperature. After 10 min. Ph₃SnCl (0.867 g, 2.25 mmol) as solution in ether is added, maintaining −10 °C, then the mixture allowed to warm slowly to r.t. and stir overnight. An excess of hexane (150 cm³) is added then the settled mixture filtered through Celite®. Concentration of the resulting solution *in vacuo* affords a pale yellow solid, which is purified by column chromatography on silica gel, eluting with 1:1 toluene/hexane.

10 *Selected characterising data (CDCl₃). Ph₃SnCCCF₃*: δ_F –50.8 (s), δ_C 111.5 (C, q J_{CF} 260 Hz), 94.5 (C, q J_{CF} 50 Hz), 91.8 (C, q, J_{CF} 6 Hz). Anal. (Calcd.) C 57.1 (57.0), H 3.6 (3.4), F 12.6 (12.8). ν(C≡C) 2183 cm⁻¹. *Hg(CCCF₃)₂*: δ_F −51.6 (s, J_{HgF} 39 Hz). δ_C 116 (C, q J_{CF} 7, J_{HgC} 2726 Hz), 111.2 (C, q J_{CF} 258, J_{HgC} 69 Hz), 89.9 (C, q J_{CF} 51, J_{HgC} 675 Hz). Anal. (Calcd.) C 18.2 (18.6), F 30.5 (29.5). ν(C≡C) 2202 cm⁻¹. *Ph₂PCCCF₃*: δ_F −50.9 (d, J_{PF} 6 Hz). δ_P −34.5 (q, J_{PF} 6 Hz). δ_C 111.6 (C, qd J_{CF} 259, J_{CP} 1.4 Hz), 90.3 (qd. J_{CF} 52, J_{CP} 1.2 Hz), 85.7 (C, dq. J_{CF} 7, J_{CP} 31 Hz). Anal. (Calcd.) C 64.9 (64.7), H 3.7 (3.6), F 20.2 (20.4). ν(C≡C) 2198 cm⁻¹. *[(Bu₃P)₂Pt(CCCF₃)₂]*: δ_F −46.7 (t, J_{PF} 3, J_{PtF} 13 Hz). δ_P 4.35 (septet.J_{PF} 3, J_{PtP} 2245 Hz). δ_C 113 (C, qt. J_{CF} 254, J_{CP} 1.5 Hz), 107.9 (C, m), 93.8 (C, qt. J_{CF} 47, J_{CP} 2 Hz). Anal. (Calcd.) C 47 (46), H 7.1 (7.0), P 6.6 (7.5). ν(C≡C) 2130 cm⁻¹. *PhCH(OH)CCCF₃*: δ_F −50.9 (d, J_{HF} 2.6 Hz). δ_C 114 (C, q J_{CF} 258 Hz), 86.9 (C, q J_{CF} 6.5 Hz), 73.8 (C, q J_{CF} 53 Hz), 64.4 (CH, s). Anal. (Calcd.) C 60.15 (60.0), H 3.5 (3.5), F 28.8 (28.5). ν(C≡C) 2278 cm⁻¹. *PhCOCCCF₃*: δ_F −51.6 (s). δ_C 163.7 (C, s), 114.1 (C, q, J_{CF} 259 Hz), 81.3 (C, q, J_{CF} 6 Hz), 75.4 (C, q, J_{CF} 54 Hz). Anal. (Calcd.) C 60.9 (60.6), H 2.6 (2.5), F 28.5 (28.6). ν(C≡C) 2272 cm⁻¹.

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