# Reactions Involving Fluoride Ion. Part 35.[1] Fluorinated Derivatives of Benzyl Anions

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Hexafluoroisopropyl groups were introduced into fluorinated aromatic systems using 2H-pentafluoro-propene and caesium fluoride. Reaction with pentafluoronitrobenzene gave a fluorinated isoxazole and a mechanism is advanced for this reaction. Direct observation of fluorinated benzyl anion derivatives has been possible and effects on fluorine chemical shifts are discussed.

In earlier parts of this series we have described the generation and reactions of fluorinated-alkyl and -cycloalkyl anions and, in some cases,[1-3] we were successful in direct observation of carbanions by NMR spectroscopy. Benzyl anions and their derivatives are of particular interest in organic fluorine chemistry because of their relationship with σ-complexes formed in nucleophilic aromatic substitution processes,[4] *e.g.* **1a**, **1b**, and it seemed possible that direct observation of fluorinated analogues of **1b** might give insight into the effects of fluorine substitution on the process of nucleophilic aromatic substitution.
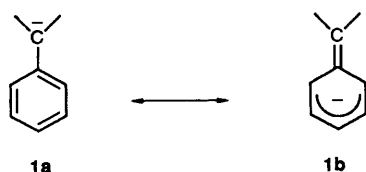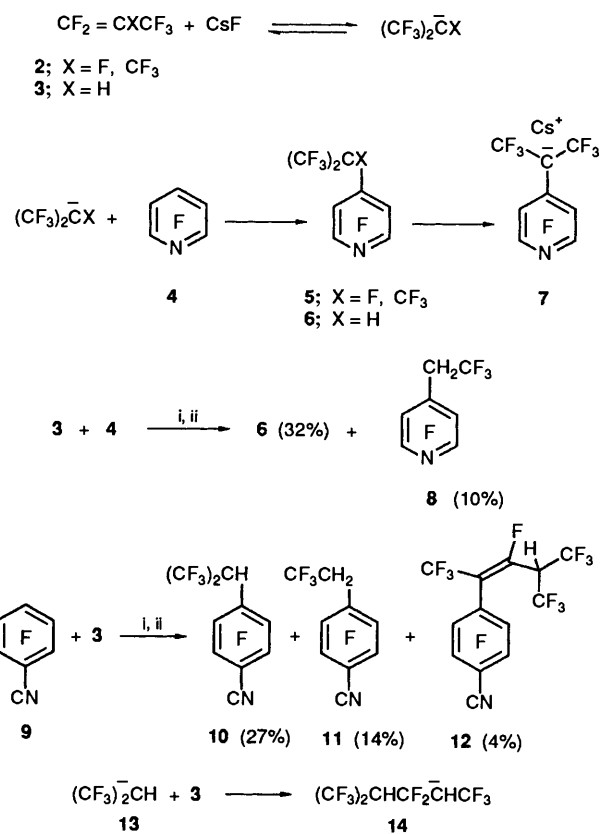

We have previously described negative Friedel Crafts processes to make various fluorinated alkylaromatic compounds [5,6] *e.g.* reactions of hexafluoropropene **2** and pentafluoro-pyridine **4**, giving **5** and we have applied this process to the formation of derivatives of benzyl anions through the use of 2H-pentafluoropropene **3** (Scheme 1). In this case, product **6** may react further with fluoride ion as base, giving the corresponding anion **7**; compound **6** had previously been made by an alternative route.[7] Reaction between **3** and **4** gave, after acid work-up, compound **6** plus a further compound **8** and the formation of **8** will be discussed later.
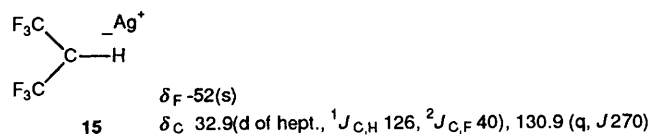
Pentafluorobenzonitrile **9** gave analogous products **10** and **11** but a compound **12** was also formed, which can be rationalized as arising from reaction between the intermediate anion **13** and the starting alkene **3**, to give the anion **14** which then reacts with **9**, prior to a fluoride ion induced elimination of hydrogen fluoride. It is well known that oligomers are formed from perfluoropropene with various fluoride ion sources; **3** did form higher molecular weight material on reaction with caesium fluoride but we were unable to separate the complex product mixture that was obtained. The products were apparently tars, which suggests that fluoride ion induced dehydrofluorination of the intermediate oligomers had taken place. We made several attempts to generate and observe the ion **13** but these were unsuccessful using caesium fluoride with 2H-pentafluoro-propene **3**. However, reaction of **3** with silver(I) fluoride gave a yellow–brown solution which, although light sensitive, gave NMR spectra consistent with the silver salt **15**.

Reaction of **3** with pentafluoronitrobenzene **16** gave **17**, **18** and, remarkably, the isoxazole **19** (Scheme 2) and this observation prompted various mechanistic probes to be applied.

We can summarise the results of these probes as follows: (a)

2; X = F, CF$_3$
3; X = H

4   **5;** X = F, CF$_3$ **7**
                6; X = H

$$3 + 4 \xrightarrow{\text{i, ii}} 6 \ (32\%) + $$

8 (10%)

9   **10** (27%)   **11** (14%)   **12** (4%)

$$(CF_3)_2\bar{C}H + 3 \longrightarrow (CF_3)_2CHCF_2\bar{C}HCF_3$$
13   **14**

Scheme 1 *Reagents:* i, CsF, tetraglyme, room temp.; ii, dil. HCl

δ_F -52(s)
15 δ_C 32.9(d of hept., $^1J_{C,H}$ 126, $^2J_{C,F}$ 40), 130.9 (q, J270)

reaction of a sample of the pure compound **17** with caesium fluoride, rapidly formed the anion **20**. (b) The anion **20** gradually decomposed to form **18**. (c) Compound **18** did not form any isoxazole **19** under the same conditions and therefore cannot be on the reaction path to **19**. (d) A pure sample of **17** with added **16** gave a product containing **19**; **16**; **17** and **18**. (e) Isoxazole **19** formation increased with increased concentration of reagents. Therefore, we conclude that the formation of **19** is bimolecular.

Dealing first with the formation of **18**, it seems likely that this involves an SET process from the anion **20**, to any available acceptor in the system *e.g.* **16** or the carbon acid **17** itself (see Scheme 3).
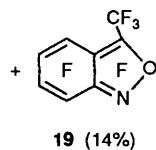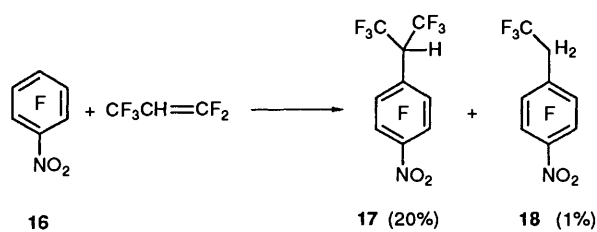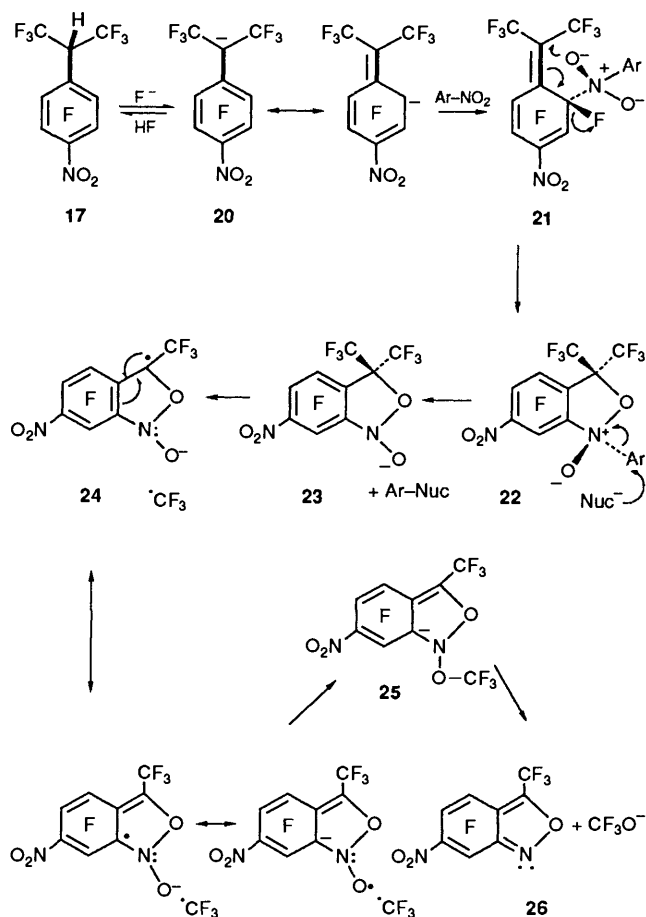
Scheme 2
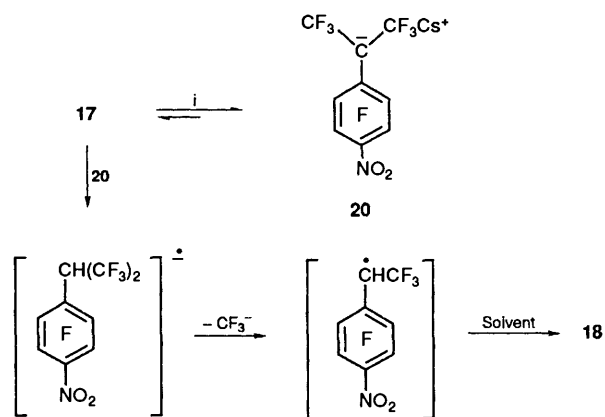
Scheme 3 *Reagents and conditions:* i, CsF, tetraglyme, room temp.

Taking all of the observations together, our proposals for the process for formation of the isoxazole **19**, are contained in Scheme 4. First, it is highly unlikely that the nitro group migrates because it was observed that the anion **20** is formed first and it would be difficult to envisage a nitro group migrating from or within **20**; therefore, the scheme incorporates a nitro group from another molecule, to form the isoxazole system, while eventually losing the original group by nucleophilic displacement by fluoride ion.

It seems reasonable that **20** reacts with pentafluoronitro-benzene **16** or with **17** giving **21**, which can obviously cyclise to **22**. Loss of the polyfluoroaryl group could then occur through nucleophilic displacement, by various nucleophiles in the system, giving **23**. At this point, we need to propose a mechanism for elimination of both trifluoromethyl and oxygen, and this seems highly unlikely unless trifluoromethyl first migrates to oxygen. This step should not be controversial because it is yielding a highly stabilised radical **24**, before collapsing to give **25**. The process **23–25** is highly reminiscent of a Stevens-type process.[8] The loss of trifluoromethoxide from **25** would follow.

The NMR spectra of compounds **6**, **10** and **17** are particularly interesting regarding rotational isomerism arising from restricted rotation of the hexafluoroisopropyl groups. We have previously reported on the NMR spectra of various per-fluoroisopropyl systems[9] and, recently, an analysis of perfluoro-4-*sec*-butylpyridine **27** has been carried out.[10] The resonances arising from 3- and 5-fluorine atoms in **6**, **10** and **17** are non-equivalent at room temperature and coalescence temperatures were determined for each of these systems. It is interesting that the values are higher than that recorded for **27**, which is surprising because we would not have expected the barrier to rotation to be less for the bulkier group. We attribute the effect to some hydrogen-bonding between the hydrogen of the hexa-fluoroisopropyl group and the ring fluorine in **6**, **10** and **17** (see
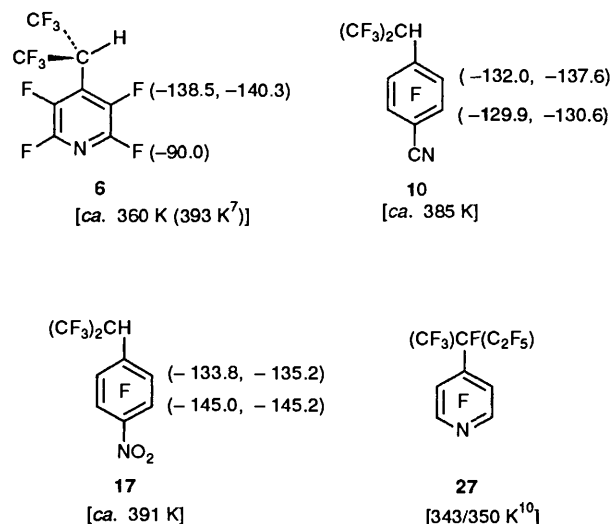

Scheme 4

Fig. 1 ^{19}F Chemical shifts (298 K); [observed coelescence *T*].

Fig. 1). Note also that the barrier is significantly higher for **17** than for **6** and this suggests buttressing arising from the larger steric requirement of the nitro group than ring nitrogen.
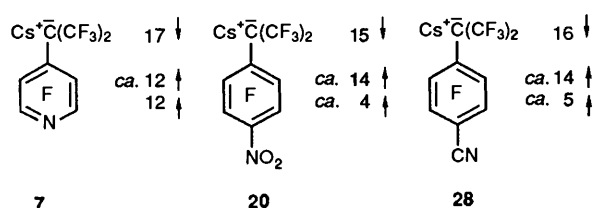
Fig. 2 Changes in δ_F on ionization, with reference to the corresponding carbon acids

Formation of anions from **6**, **10** and **17** occurred readily on stirring with caesium fluoride in a solvent. The equilibrium was essentially entirely towards the anion, because, in one case **7**, the anion was generated from the corresponding alkene,[11] by adding caesium fluoride, and the resultant chemical shifts of the anion were essentially the same as those observed by generation from **17**. It is clear then, that we have been able to observe fluorinated derivatives of benzyl anions directly. More difficult, is the interpretation of chemical shifts (Fig. 2); in comparison with the corresponding carbon acids, the anions each showed substantial downfield shifts for trifluoromethyl groups, which is consistent with known effects of charge on fluorine at adjacent sites,[1] but the resonances corresponding to ring fluorines each showed upfield shifts. It is known that fluorine resonances attached to charged sites should be moved upfield and the magnitude of this effect in **20** and **28** is also consistent with the anticipated differing charge densities in the ring, but the essentially equivalent effect shown by **7** is difficult to understand. Nevertheless, the fact that fluorine atoms *ortho-* and *meta-* to the reaction site show an effect in the same direction, at least parallels what has been observed in nucleophilic aromatic substitution in highly fluorinated systems.[4]

Experimental

^{19}F NMR spectra were measured using a Brüker AC250, with trichlorofluoromethane as internal reference; upfield shifts are quoted as negative, J values are given in Hz. Gas chromatography was carried out using columns packed with 20% diisodecyl phthalate on Chromosorb P (Column A), 10% silicone rubber SE-30 on Chemosorb P (Column O), and 20% Krytox fluid on Chromosorb W (Column K). Mass spectra were recorded on V.G. 7070E instrument.

Reactions of 2H-*Pentafluoropropene* **3**.—(*a*) *With penta-fluoropyridine* **4**. A mixture containing pentafluoropyridine **4** (24.5 g, 145.2 mmol), dry caesium fluoride (36.3 g, 238.8 mmol), tetraglyme (55 cm³) and 2H-pentafluoropropene **3** (18.1 g, 137.4 mmol) contained in a flexible gas reservoir was stirred at room temperature for 6.5 h. Recovered volatiles (1.7 g) were shown by IR spectroscopic analysis to consist mainly of 2H-pentafluoro-propene **3**. The crude residue was then added to hydrochloric acid (400 cm³; 10%) and, after ether extraction (3 × 80 cm³), the extracts were combined and dried (MgSO₄). Careful removal of the ether (Vigreux column) followed by vacuum transfer of the residue into a cold trap gave a colourless oil, distillation of which gave pentafluoropyridine **4** (b.p. 83–85 °C) (4.6 g, 30.7 mmol, 21% recovery) and a two component mixture [ratio *ca.* 4:1 (by GC)] (13.6 g) (b.p. 120–140 °C) and a residue (*ca.* 13 g). A portion of the volatile mixture was separated by preparative scale gas chromatography (130 °C, column O) yielding perfluoro-4-(2H-hexafluoroisopropyl)pyridine **6**[7] [total yield *ca.* 10.9 g, 36 mmol, 32% based on **4** (calculated by analytical-scale glc)] (Found: C, 32.2; H, 0.5; N, 4.7%; M⁺, 301. Calc. for C₈HF₁₀N: C, 31.9; H, 0.3; N, 4.65%; *M*, 301); δ_F −64.5 (6 F, s, 2 × CF₃), −90.0 (2 F, s, F-2, -6), −138.5 (1 F,

s, F-3 or -5) and −140.3 (1 F, s, F-5 or -3); and *tetrafluoro-4-(2,2,2-trifluoroethyl)pyridine* **8** [total yield *ca.* 2.7 g, 12 mmol, 10% based on **4** (calculated by analytical scale glc): (Found: C, 35.9; H, 0.9; N, 5.6%; M⁺, 233. C₇H₂F₇N requires C, 36.1; H, 0.9; N, 6.0%; *M*, 233); δ_F, −65.4 (3 F, t, *J* 10, CH₂CF₃), −89.9 (2 F, s, F-2, -6) and −143.3 (2 F, s, F-3, -5); δ_H 3.7 (q, *J*, 10).

(*b*) *With pentafluorobenzonitrile* **9**. A mixture containing pentafluorobenzonitrile **9** (37.2 g, 193 mmol), caesium fluoride (39.2 g, 258 mmol), tetraglyme (50 cm³) and 2H-pentafluoro-propene **3** (23.2 g, 176 mmol) contained in a flexible gas reservoir was rapidly stirred at room temperature for a period of 6 h, during which time the reservoir collapsed. Volatile material was (3.4 g) isolated by vacuum transfer, sealed in an NMR tube, and shown by fluorine NMR spectroscopy to consist mainly of 2H-pentafluoropropene **3**. The residual product was filtered and washed with dry acetone. Water (50 cm³) mixed with concentrated hydrochloric acid (15 cm³) was then added. Ether extraction (3 × 70 cm³), drying (MgSO₄) and the removal of the ether by rotary evaporation yielded a brown oil (*ca.* 35 g). Distillation (37 mmHg) yielded: fraction (a) (82–85 °C) (15.0 g); fraction (b) (107–113 °C) (8.7 g); fraction (c) (115–125 °C) (7.3 g); fraction (d) (<150 °C, 0.1 mmHg) (1.5 g). Fraction (a) was shown (by GC) to be pentafluorobenzonitrile (44% recovery). By GC–MS the remaining fractions were shown to be three component mixtures in the combined ratio *ca.* 3:1:1. The major two components were separated by preparative scale gas chromatography (carbowax column, 115 °C) and identified as *perfluoro-4-(2H-hexafluoroisopropyl)benzonitrile* **10** (GC yield *ca.* 10.2 g, 31 mmol, 27% yield based on **9**) (Found: C, 37.0; H, 0.3; N, 4.5%; M⁺, 325. C₁₀HF₁₀N requires: C, 36.9; H, 0.3; N, 4.3%; *M*, 325); δ_F −64.3 (6 F, m, 2 × CF₃), −129.9 (1 F, s, F-2 or -6), −130.6 (1 F, s, F-6 or -2), −132.0 (1 F, m, F-3 or 5) and 137.6 (1 F, s, F-5 or -3); δ_H 4.8 (hept., *J* 7.7); δ_C 97.3 (m, C-1), 106.3 (s, CN), 145.6 (d, *J* 261.0, C-2), 147.2 (d of m, *J*, 264.0, C-3 or -5), 147.6 (d of m, *J* 260.1, C-5 or -3), 112.3 (t, *J* 14, C-4), 46.2 [hept., *J* 33.1, C(CF₃)₂] and 121.5 (q, *J* 283.5, CF₃); (broad band decoupled spectrum); *tetrafluoro-4-(2,2,2-trifluoro-ethyl)benzonitrile* **11** (yield *ca.* 4.2 g, 16 mmol, 14% based on **3**) (Found: M⁺, 257. C₉H₂F₇N requires *M*, 257); δ_F −65.8 (3 F, s, CF₃), −132.2 (2 F, m) and −138.2 (2 F, m); δ_F 3.7 (q, *J* 9.1). The minor isomer crystallised from fraction (d) and was identified as *perfluoro-4-[4H-decafluoro(4-methylpent-2-en-2-yl)]benzoni-trile* **12** (1.5 g isolated, *ca.* 4% total yield calc. by GC on **3**) (Found: C, 36.1; H, 0.5; N, 2.9%; M⁺, 437. C₁₃HF₁₄N requires: C, 35.7; H, 0.2; N, 3.2%; *M*, 437); m.p. 141 °C; δ_F −60.0 (3 F, d, *J* 20.2, CF₃C=), −91.6 (1 F, s, CF₃C=F), −63.9 [6 F, s, C(CF₃)₂], −131.6 (2 F, m, F-2, -6) and −135.7 (2 F, s, F-3, 5); δ_H 5.1 (d of hept., *J* 28.4, 7.3); δ_C 121.3 (q, *J* 275.3, CF₃C=), 110.5 (d or m, *J* *ca.* 38, CF₃C=), 156.8 (d, *J* 288.0, C=CF), 50.0 [d of m, *J* 138.5, C(CF₃)₂], 122.0 [q, *J* 285.2, C(CF₃)₂], 98.5 (t, *J* 19, C-1), 107.7 (t, *J* *ca.* 3.5, CN), 146.1 (ddt, *J* 253.5, 14.7, 3.2, aromatic CF), 150.0 (ddt, *J* 260.6, 16.4, 4.7, aromatic CF) and 112.7 (t, *J* *ca.* 38, C-4).

(*c*) *With pentafluoronitrobenzene* **16**.—A mixture containing pentafluoronitrobenzene **16** (13.0 g, 61.0 mmol), dry caesium fluoride (14.1 g, 93.3 mmol), dry tetraglyme (20 cm³) and 2H-pentafluoropropene **3** (7.1 g, 53.4 mmol) was rapidly stirred at room temperature for 14 h, during which time the gas reservoir collapsed. A volatile product (1.9 g), isolated by vacuum transfer, was sealed in an NMR tube and shown to consist mainly of 2H-pentafluoropropene **3**, together with some 1,1,1,3,3,3-hexafluoropropane. The remaining product (9.9 g; total recovery 58%), a yellow liquid, was analysed by GC (column 'O', 170 and 240 °C) and shown to contain a complex mixture of components. This mixture was separated into four main fractions, according to retention time, by preparative

scale GC (column 'O', 180 °C) and the major fractions were investigated; the second fraction contained two main components and separation by preparative scale GC (column 'K', 80 °C) gave pentafluoronitrobenzene **16** (2.2 g) and *perfluoro-(3-methyl-2,1-benzisoxazole)* **19** (1.4 g, 14.1%), a colourless liquid, b.p. 162–164 °C (Found: C, 36.9; F, 51.6%; N, 5.6%; M^+, 259.928; C_8F_7NO requires C, 37.1; F, 51.35; N, 5.4%; M, 258.986); λ_{max}/nm 216 (ε 5900), 243 (ε 4800) and 286 (ε 1900); δ_F −63.3 (3 F, d, J 9.2, CF_3), −138.7 (1 F, m, F-4), −157.0 (2 F, m, overlapping F-5, -6) and −146.8 (1 F, m, F-7); δ_C 148.7 (q, J 41.4, C-3), 118.8 (q, J 272.4, CF_3), 138.3 (ddd, J 271.3, 13.4, 3.7, C-4), 104.8 (d, J 19.3, C-4a), 143.6 (dt, J 261.9, 14.3, C-5), 138.7, (d of t, J 253.8, 14.6, C-6), 132.6 (ddd, J 258.8, 14.0, 4.9, C-7) and 148.9 (m, C-7a). The third fraction contained one major component, purified by preparative GC (column 'O', 180 °C). This was identified as *perfluoro-4-(2H-hexafluoroisopropyl)-1-nitrobenzene* **17**, a pale yellow liquid, (2.7 g, 20.2%), b.p. 193–194 °C (Found: C, 31.4; F, 55.4; N, 3.8. $C_9F_{10}HNO$ requires C, 31.3; F, 55.1; N, 4.1%] δ_F −64.0 (6 F, s, 2 × CF_3), −145.0 (1 F, s, F-2 or -6), −145.2 (1 F, s, F-6 or -2), −133.8 (1 F, s, F-3 or -5) and −135.2 (1 F, s, F-5 or -3); δ_H 4.8 (hept., J 8). The fourth (longest retention time) fraction contained four components and one of these was separated (column 'O', 190 °C) and identified as *tetrafluoro-1-nitro-2-(2,2,2-trifluoroethyl)benzene* **18**, a yellow liquid, (0.09 g); (M^+, 277. $C_8H_2F_7NO_2$ requires M, 277); δ_F −65.0 (3 F, s, F-4b), −147.2 (2 F, s, F-2, -6), −138.4 (2 F, s, F-3, - 5); δ_H 3.6 (q, J 10).

Formation of Observable Anions.—(*a*) *Using silver fluoride (in the dark).* 2*H*-Pentafluoropropene **3** (2.2 g, 17.0 mmol) was transferred *in vacuo* into a dry Rotoflo tube containing acetonitrile (10 cm³) and silver fluoride (2.3 g, 18 mmol). The tube was agitated for 2 h and after this time, no sample of **3** could be recovered. Rapid filtering through Celite and a sinter under dry nitrogen gave a yellow–brown solution (which deposited a silver mirror if exposed to light). From its NMR spectra (see Discussion section) it was deduced that the solution contained 2*H*-hexafluoroisopropylsilver **15**.

(*b*) *Ion* **20**, *generated from* **17**. Caesium fluoride was added to a very pure sample of compound **17** (*ca.* 40 mg) in tetraglyme (0.5 cm³), contained in a dry NMR tube. After 30 min all of the

resonances attributed to compound **17** had been replaced by resonances attributed to the caesium salt **20**: δ_F −49.1 (6 F, s, 2 × CF_3), −147.1 (2 F, s, aromatic CF) and −150.2 (2 F, s, aromatic CF).

(*c*) *Anion* **7**, *generated from* **6**. In an analogous experiment to that described in (*b*), ion **7** was generated on a similar time scale giving: δ_F −47.8 (6 F, s, 2 × CF_3), −102.3 (2 F, s, F-2, -6) and −151.1 (2 F, s, F-3, -5).

(*d*) *Anion* **28**, *generated from* **10**. Ion **28** was similarly generated, showing: δ_F −48.1 (6 F, s, 2 × CF_3), −142.1 (2 F, s, aromatic CF) and −145.3 (2 F, s, aromatic CF).

Acknowledgements

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