Photoinduced Electron-transfer Reaction of Difluorodiiodomethane with Aza-aromatic Compounds and Enamines

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Irradiation of difluorodiiodomethane 1 with pyrroles, indole and imidazoles in dimethylformamide gives the corresponding trifluoromethylated products, whereas irradiation with enamines results in 2-trifluoromethyl ketones. A photoinduced electron-transfer mechanism is proposed.

Perhalogenomethanes CF_2XY (X, Y = Br, Cl) have been studied extensively as difluorocarbene precursors[1] and trifluoromethylating reagents.[2] They can also react with a variety of nucleophiles, such as carbanions,[3] phenolates,[4] thiophenolates,[5] mercaptides,[6] amines,[7] alkyl phosphites,[8] and benzeneselenol.[9] In contrast, we know very little about another simple perhalogenomethane, i.e. CF_2I_2 1, probably because this reagent is difficult to prepare. The only report on compound 1 was involved with its reaction with alkenes.[10] Previously, we have studied the reactions of perfluoroalkyl iodides, including 1,2-diiodotetrafluoroethane with aza-aromatic compounds[11] and various nucleophiles[12] and showed that these reactions were involved in an electron-transfer mechanism (ET). Recently, we found that compound 1 could be prepared conveniently by reaction of potassium or methyl bromodifluoroacetate and iodine in the presence of potassium iodide and copper(I) iodide,[13] and this made it possible to study this perhalogenomethane with a wider range of reactants. Herein we report its photoinduced reactions with aza-aromatic compounds and enamines.

Results and Discussion

When a mixture of CF_2I_2 1 and various kinds of aza-aromatic compounds in dimethylformide (DMF) was irradiated with UV light, trifluoromethylated but no difluoroiodomethylated or difluoromethylated derivatives were produced. Thus, photolysis of compound 1 and an excess of pyrrole 2 (1:2 = 1:3) in DMF afforded 2-(trifluoromethyl)pyrrole 3 and a small amount of 3-(trifluoromethyl)pyrrole 4 [equation (1)]. Evolved gases were shown by GC–MS spectroscopy to be CO, CHF_3, and $CF_2=CF_2$. The temperature rose to ~70 °C as the result of irradiation; however, the reaction did not take place at this temperature without irradiation, indicating that irradiation was essential.
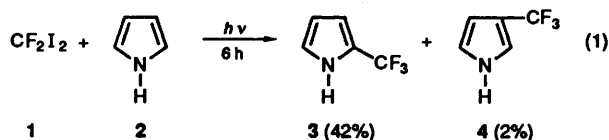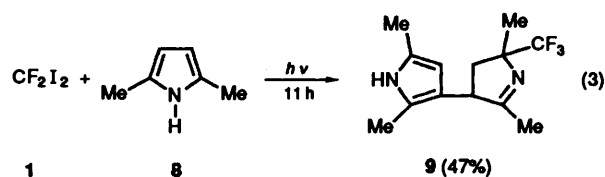
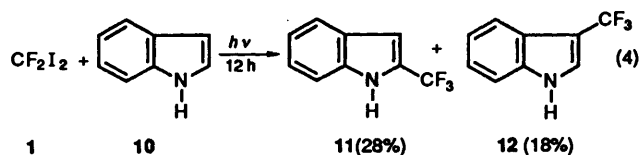Similarly, products 6 and 7 were obtained upon treatment of compound 1 with 1-methylpyrrole 5 [equation (2)].
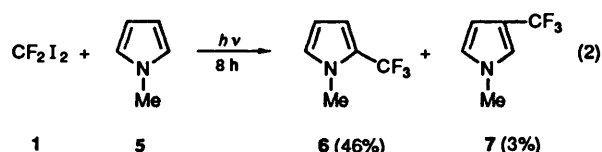
Unexpectedly, irradiation of a mixture of CF_2I_2 and 2,5-dimethylpyrrole 8 did not result in the formation of simple

substituted product but instead gave adduct 9 which was identified by MS, ^1H NMR, ^{13}C NMR, ^{19}F NMR spectroscopy and microanalysis [equation (3)].

Indole 10 also underwent a similar reaction, giving a mixture of compounds 11 and 12 [equation (4)]. No benzene-ring-

substituted products were found. Similar reaction of compound 1 with imidazole 13 and 2-methylimidazole 16 were as shown in equations (5) and (6). There were no N-trifluoromethylated products formed.
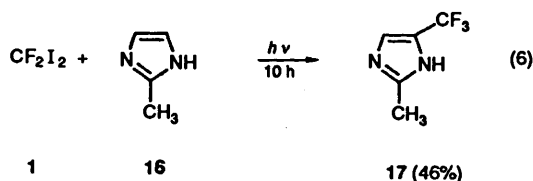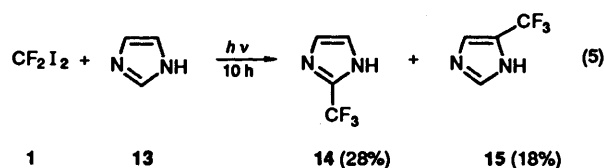
We are aware that charge-transfer complexes can be formed between amines and perfluoroalkyl iodides,[11,14] the existence of which results in an upfield shift in the chemical shift of CF_2I in the ^{19}F NMR spectrum. In the present case, it was found that on reaction of compound 1 with 2 or 5, the CF_2I_2 signal was shifted upfield (~3.5 ppm), indicating the formation of charge-transfer complexes. In order to elucidate the reaction mechanism, inhibition studies were carried out. Electron-transfer scavengers such as p-dinitrobenzene (DNB) and $Bu^t_2NO^·$ and the free radical inhibitor hydroquinone (HQ) suppressed the reaction significantly. For example, addition of 20 mol% of these reagents to the reaction mixture of substrates 1 and 5
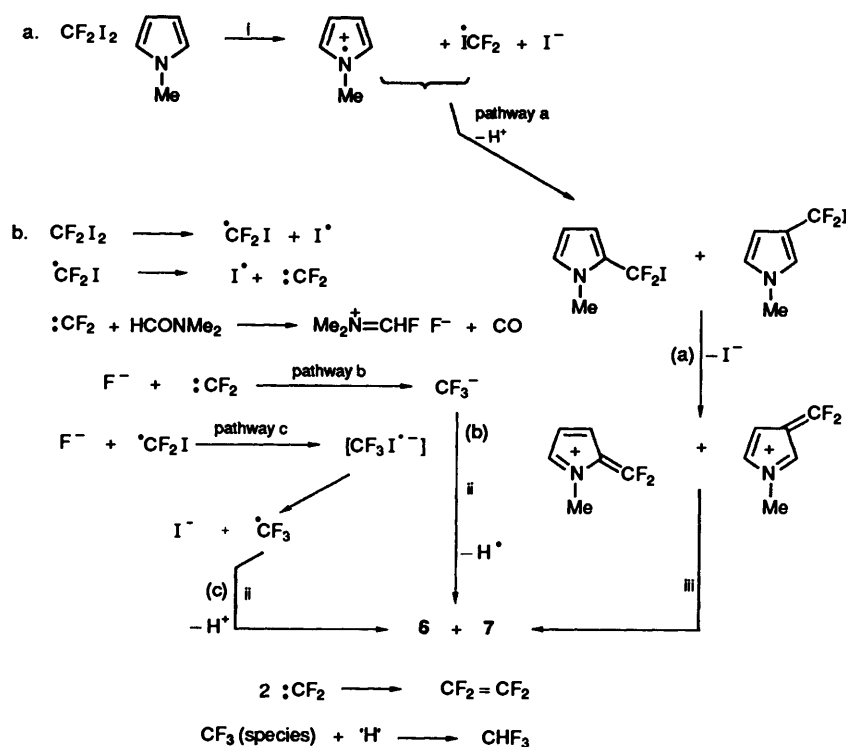
Scheme 1   Reagents and reaction conditions: i, PET; ii, 5'$^+$; iii, F$^-$

Table 1   Results of photoinduced reaction of difluorodiiodomethane 1 and enamines 18 at 70 °C

Entry	18^a	Time (t/h)	Products	Isolated yields
1	18a1	10	19a	40
2^b	18a1	8	19a	10
3^c	18a1	8	19a	40
4	18a2	7	19a	45
5^c	18a2	6	19a	65
6^d	18a2	6	19a	55
7^e	18a2	8	19a	20
8^f	18a2	8	19a	18
9^g	18a2	8	19a	10
11	18b1	6	19b	43
12^c	18b1	6	19b	68
13^d	18b1	6	19b	58
14	18b2	7	19b	34
15	18c1	9	19c	30
16	18c2	6	19c	36
17^c	18c2	6	19c	59
18	18d	12	19d	30
19^c	18d	12	19d	49

^{a} 1:18 = 1:2 in all the reactions. ^{b} The reaction proceeded without irradiation. ^{c} Me$_4$N$^+$F$^-$, in the same molar proportion as compound 1, was added. ^{d} KF, in the same molar proportion as compound 1, was added. ^{e} 20 mol% of p-DNB was added. ^{f} 20 mol% of Bu$^t{}_2$NO$^\cdot$ was added. ^{g} 20 mol% of HQ was added.

decreased the overall yields of products 6 and 7 greatly (30, 24 and 21%, respectively). All these results therefore point to the reaction being a photoinduced electron-transfer (PET) reaction (see Scheme 1).

The charge-transfer complex between compound 1 and aza-aromatics (using N-methylpyrrole 5 as an example) is photochemically stimulated to induce ET to generate the radical cation of compound 5 and difluoroiodomethyl radical. This is followed by three possible pathways. First, the difluoroiodomethyl radical directly attacks 5'$^+$ followed by deprotonation

to give 2- and 3-(difluoroiodomethyl)-N-methylpyrrole, which, similar to their bromine analogues, are unstable and easily eliminate iodide to form the corresponding cations. The cations then react with fluoride generated *in situ* to give the final products 6 and 7 (pathway a). The only route to the formation of F$^-$ is the known reaction of :CF$_2$ with DMF; the former is produced through α-elimination of $^\cdot$CF$_2$I.[16] The ensuing reactions might be divided into two sequences; one is the combination of F$^-$ and :CF$_2$ to form CF$_3{}^-$ (pathway b) and the other is to form $^\cdot$CF$_3$ *via* SET (pathway c). Both CF$_3{}^-$ and $^\cdot$CF$_3$ species react with 5'$^+$ to give the same products. The formation of gaseous by-products, CO, CF$_2$=CF$_2$, and CHF$_3$ can be easily explained by Scheme 1.

Enamines are also good substrates for this reaction because it was reported that α-CF$_2$X (X = Br, Cl) ketones can be easily synthesized from the reaction of enamines and CF$_2$X$_2$ (X = Br, Cl) even at room temperature without irradiation.[2a] We have also studied the reaction between compound 1 and enamines 18. Unlike species CF$_2$X$_2$ (X = Br, Cl),[2a] compound 1 did not react with enamines 18 in DMF even at 70 °C for several hours. Irradiation of a mixture of compound 1 and enamines 18 in DMF gave directly the trifluoromethylated products 19 and no stable difluoroiodomethylated compounds could be isolated (Scheme 2). The temperature rose to ~70 °C as a result of the irradiation. CF$_2$=CF$_2$, CHF$_3$ and CO were also detected in the reaction products. The addition of tetramethylammonium fluoride or potassium fluoride promoted the conversion. The results of the reaction are listed in Table 1.

The reaction could be partly suppressed by p-DNB, Bu$^t{}_2$NO$^\cdot$ and HQ (see entries 7–9 in Table 1); therefore we infer that the reaction might involve a PET mechanism similar to that of the reaction of compound 1 with aza-aromatic compounds (Scheme 1). The reactivity difference between species CF$_2$X$_2$ (X = Cl, Br) and CF$_2$I$_2$ may result mainly from the weaker electronic negativity of iodine and, therefore, the reaction of CF$_2$I$_2$ has to be initiated by irradiation.

Finally, the formation of the unexpected product 9 from reaction of compound 1 and 2,5-dimethylpyrrole 8 is not very
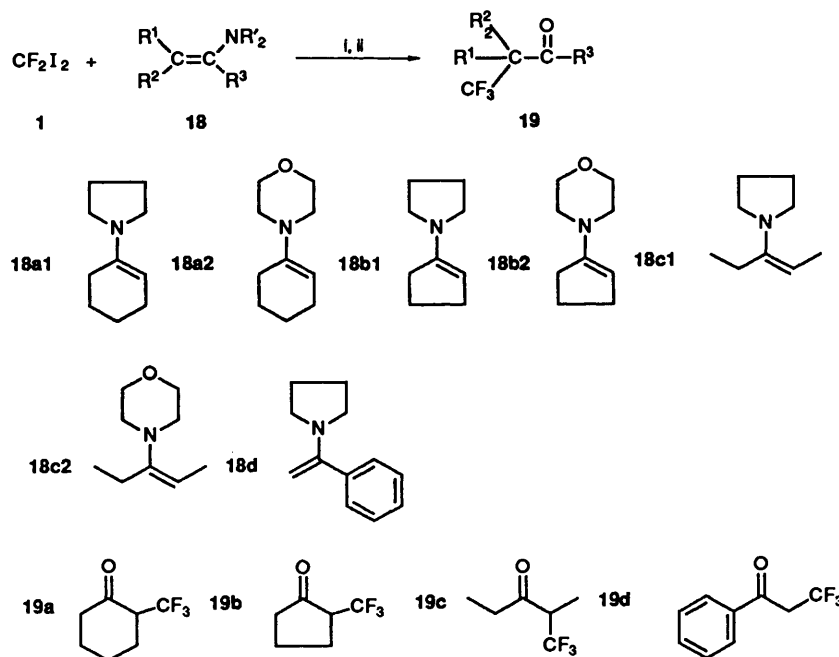
Scheme 2 *Reagents and conditions:* i, *hv*; ii, water

clear and probably results from the addition of CF_3 onto the α-position of the pyrrole ring thus generating an allylic radical which attacks another molecule of the starting material, followed by some hydrogen shifts. A further study of this problem is being carried out.

Experimental

All b.p.s and m.p.s were uncorrected. ^1H NMR spectra were recorded on an XL-200Q instrument with $SiMe_4$ as external standard. *J* Values are given in Hz. The ^{13}C NMR spectrum was recorded on an AMX-600 instrument with $SiMe_4$ as internal standard. ^{19}F NMR spectra were obtained on a Varian EM-360L spectrometer, and chemical shifts in ppm were positive for upfield with CF_3CO_2H as internal standard. IR spectra were recorded for solid samples in KBr pellets for liquid samples on film, on a Shimadzu-440 spectrophotometer. Mass spectra were obtained on a Finnigan MS-4021 spectrometer. GC–MS spectra were recorded on a Finnigan GC-MS-4021 instrument. DMF was treated with CaH_2 before use. Light petroleum refers to the fraction boiling in the range 60–90 °C.

The Reaction of Compound 1 *with* 1-*Methylpyrrole* 5.—Under N_2, compound 1 (1.52 g, 5 mmol), 1-methylpyrrole 5 (1.22 g, 15 mmol) and DMF (5 cm³) were added to a Pyrex flask, which was connected to a gas collector, and then the mixture was irradiated with a 450 W medium-pressure mercury lamp at a distance of 10 cm for 8 h. The gases evolved were identified by GC–MS spectroscopy to be a mixture of carbon monoxide, fluoroform and tetrafluoroethylene. The solution was poured to water (20 cm³) and extracted with diethyl ether (10 cm³ × 3). The extract was washed successively with water (8 cm³ × 3) and saturated aq. NaCl (5 cm³) and then dried over $MgSO_4$. The ether was removed, the residue was distilled, and 1-methyl-2-(trifluoromethyl)pyrrole 6 (0.34 g, 46%) was obtained. ^{19}F NMR spectroscopy showed the presence of ~3% of 1-methyl-3-(trifluoromethyl)pyrrole 7 (δ_F 56.6 ppm), which was identified by its GC–MS spectrum, in the major compound 6. For compound 6: b.p. 82–84 °C (lit.,[18] 80–82 °C); v_{max}/cm^{-1} 3110, 1515, 1290 and 725; $\delta_H(CDCl_3)$ 3.75 (3 H, s), 6.00 (1 H, m), 6.48 (1 H, m) and 6.64 (1 H, m); $\delta_F(CDCl_3)$ 58.3; *m/z* 149

(M^+, 27.5%), 130 ($M^+ - F$, 13.7), 82 (100) and 69 (CF_3^+, 2.6).

2-(Trifluoromethyl)pyrrole 3 and 3-(trifluoromethyl)pyrrole 4 were obtained in a similar way. Compound 3: b.p. 102–104 °C (lit.,[18] 100–102 °C); v_{max}/cm^{-1} 3300, 1580, 1260 and 740; $\delta_H(CDCl_3)$ 6.05 (1 H, dd, *J* 3.5 and 2.5), 6.41 (1 H, dd, *J* 3.5 and 2.4), 6.63 (1 H, dd, *J* 2.5 and 2.4) and 6.99 (1 H, s); $\delta_F(CDCl_3)$ 59.0; 2% of isomer 4 was detected in compound 3 by ^{19}F NMR spectroscopy (δ_F 61.2 ppm).

The Reaction of Compound 1 *with* 2,5-*Dimethylpyrrole* 8.—A mixture of compound 1 (3.04 g, 10 mmol) and 2,5-dimethylpyrrole 8 (2.85 g, 30 mmol) in DMF (10 cm³) was irradiated as above for 11 h. After work-up, the residue was purified by column chromatography on silica gel with diethyl ether–light petroleum (1 : 1) as eluent, to give *compound* 9 (1.22 g, 47%). M.p. 140–142 °C (Found: C, 60.4; H, 6.6; N, 10.6; F, 21.9. $C_{13}H_{17}N_2F_3$ requires C, 60.44; H, 6.65; N, 10.84; F, 22.07%); v_{max}/cm^{-1} 3250, 3200, 2920, 2850, 1455, 1195 and 940; $\delta_H(CDCl_3)$ 1.13 (3 H, s), 2.12 (3 H, s), 2.18 (3 H, s), 2.19 (3 H, s), 2.78 (1 H, dd, *J* 3.0 and 8.0), 3.06 (1 H, dd, *J* 4.5 and 8.0), 3.64 (1 H, dd, *J* 3.0 and 4.5), 5.57 (1 H, s) and 7.52 (1 H, w); $\delta_C[(CD_3)_2SO]$ 14.42 (s), 16.77 (s), 21.30 (s), 23.48 (s), 41.97 (s), 50.59 (s), 82.96 (q, J_{C-F} 24.1), 108.75 (s), 119.23 (s), 126.48 (s), 131.81 (q, J_{C-F} 28.18) and 181.90 (s); $\delta_F(CDCl_3)$ 78.5; *m/z* 258 (M^+, 56%), 243 ($M^+ - CH_3$, 16), 138 (27), 122 (100) and 69 (CF_3^+).

2-(*Trifluoromethyl*)*indole* 11 *and* 3-(*Trifluoromethyl*)*indole* 12.—Under N_2, compound 1 (1.52 g, 5 mmol) and indole 10 (1.75 g, 15 mmol) was added to DMF (10 cm³) and the mixture was irradiated as above for 30 h. After usual work-up, the solid residue was purified by column chromatography on silica gel with ethyl acetate–cyclohexane (1 : 2) as eluent. Compound 10 (0.52 g, 28%) and compound 11 (0.34 g, 18%) were obtained. For compound 10: m.p. 106–108 °C (lit.,[19] 107–108 °C); v_{max}/cm^{-1} 3400, 1160 and 1100; $\delta_H(CDCl_3)$ 6.91 (1 H, s), 7.59 (4 H, m) and 8.2 (1 H, s); $\delta_F(CDCl_3)$ 60.7; *m/z* 185 (M^+, 100%). For compound 11: m.p. 107–109 °C (lit.,[19] 107–108 °C); v_{max}/cm^{-1} 3400, 1350, 1185, 1130 and 1090; $\delta_H(CDCl_3)$ 6.62 (1 H, s), 7.61 (4 H, m) and 8.38 (1 H, s); $\delta_F(CDCl_3)$ 67.8; *m/z* 185 (M^+, 100%).

2-(*Trifluoromethyl*)*imidazole* **14** *and* 5-(*Trifluoromethyl*)-*imidazole* **15**.—Irradiation of CF_2I_2 (1.52 g, 5 mmol) and imidazole (2.04 g, 30 mmol) in DMF (6 cm^3) for 10 h afforded compound **12** (0.12 g, 18%) and compound **13** (0.18 g, 26%) which were purified, after usual work-up, by column chromatography on silica gel with diethyl ether–hexane (1:3) as eluent. Compound **14**: m.p. 145–147 °C (lit.,[20] 146–147 °C); δ_H-[(CD$_3$)$_2$SO] 6.80 (1 H, s) and 7.26 (2 H, s); δ_F[(CD$_3$)$_2$SO] 61.0; *m/z* 136 (M$^+$, 29.8%), 41 (C$_2$H$_3$N$^+$, 100) and 69 (CF$_3$$^+$, 5.6). Compound **15**: m.p. 150–152 °C (lit.,[13] 150–151 °C); ν_{max}/cm^{-1} 3300, 1540 and 1205; δ_H[(CD$_3$)$_2$SO] 6.50 (1 H, s), 7.62 (1 H, d, *J* 1.5) and 7.81 (1 H, d, *J* 1.5); δ_F[(CD$_3$)$_2$SO] 62.1; *m/z* 136 (M$^+$, 16.0%), 69 (CF$_3$$^+$, 6.8) and 41 (C$_2H_3N^+$, 100).

2-*Methyl*-5-(*trifluoromethyl*)*imidazole* **17**.—M.p. 176–178 °C (lit.,[20] 179–180 °C); ν_{max}/cm^{-1} 3320, 2960, 1450 and 770; δ_H[(CD$_3$)$_2$SO] 2.33 (3 H, s), 6.50 (1 H, s) and 7.44 (1 H, s); δ_F[(CD$_3$)$_2$SO] 62.6; *m/z* 150 (M$^+$, 32%), 69 (CF$_3$$^+$, 6.0) and 55 (C$_3H_5N^+$, 100).

Photoinduced Reaction of CF_2I_2 *with Enamines* **18**.—*Typical procedure.* Under nitrogen, compound **18a1** (1.51 g, 10 mmol) was added to a solution of compound **1** (1.52 g, 5 mmol) in DMF (5 cm^3) in a Pyrex flask. The system was connected to a gas collector and was then exposed, while being stirred, to a medium-pressure mercury lamp (450 W) at a distance of 10 cm. The system's temperature rose to ~70 °C within 20 min and carbon monoxide, fluoroform, and tetrafluoroethylene, which were identified by GC–MS, were evolved slowly. After *ca.* 10 h, ^{19}F NMR spectroscopy indicated that 88% of **1** had been consumed. Aq. hydrochloric acid (5%) was then added dropwise until the solution was acid (pH 5). The solution was stirred at room temperature for another 3 h, then was poured into water (20 cm^3) and extracted with dichloromethane (10 cm^3 × 3). After the organic phase had been washed successively with water (10 cm^3 × 3) and saturated aq. sodium chloride (8 cm^3) and dried over MgSO$_4$, the solvent was evaporated off under reduced pressure. The oily residue was distilled under reduced pressure, to give 2-(trifluoromethyl)cyclohexanone **19a** (0.33 g, 40%). In the presence of tetramethylammonium fluoride (0.47 g, 5 mmol), compound **19a** (0.58 g, 70%) was obtained similarly. B.p. 84–86 °C at 22 mmHg (lit.,[17] 90–92 °C at 30 mmHg); ν_{max}/cm^{-1} 1725 (C=O) and 1185 (CF$_3$); δ_H(CDCl$_3$) 1.42–1.71 (6 H, m), 2.40 (2 H, t) and 4.95 (1 H, t); δ_F(CDCl$_3$) 65.8; *m/z* 166 (M$^+$, 7.2%), 124 (M$^+$ – CH$_2$CO, 24.0), 55 (C$_3$H$_3$O$^+$, 100) and 42 (CH$_2$CO$^+$, 62.9).

2-(*Trifluoromethyl*)*cyclopentanone* **19b**. B.p. 80–82 °C at 30 mmHg; ν_{max}/cm^{-1} 1730 (C=O) and 1190 (CF$_3$); δ_H(CDCl$_3$) 1.29–1.68 (4 H, m), 2.51 (2 H, t) and 4.10 (1 H, t); δ_F(CDCl$_3$) 65.0; *m/z* 153 (M$^+$ + 1, 15.1%), 77 (22.8), 69 (CF$_3$$^+$, 10.6) and 55 (100).

2-(*Trifluoromethyl*)*pentan-3-one* **19c**. B.p. 85–87 °C at 200 mmHg (lit.,[17] 68–70 °C at 134 mmHg); ν_{max}/cm^{-1} 1705 (C=O), 1540, 1205 (CF$_3$) and 780; δ_H(CDCl$_3$) 4.22 (2 H, s) and 7.70 (5 H, m); δ_F(CDCl$_3$) 74.7; *m/z* 188 (M$^+$, 20.2%) and 105 (M$^+$ – C$_2$H$_2$F$_3$$^+$, 100).

Phenyl 2,2,2-*trifluoroethyl ketone* **19d**. B.p. 78–80 °C/180

mmHg; ν_{max}/cm^{-1} 2950, 1730 (C=O) and 1190 (CF$_3$); δ_H(CDCl$_3$) 1.05 (3 H, t), 1.32 (3 H, d), 2.62 (2 H, q) and 3.85 (1 H, m); δ_F(CDCl$_3$) 72.0; *m/z* 155 (M$^+$ + 1, 15.4%) and 57 (C$_3$H$_5$O$^+$, 100).

Acknowledgements

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