# Synthesis of Functionalized Compounds Containing a Difluoromethylene Moiety

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By a two-step sequence, functionalized $CF_2$-containing compounds have been readily synthesized from $CF_2Br_2$. In the presence of $CrCl_3/Fe$, $CF_2Br_2$ added to both electron-deficient and electron-rich alkenes to give $CF_2Br$-containing compounds. Promoted by $Co^{III}/Zn$, these adducts reacted further with a further molecule of alkene to give various $CF_2$-containing compounds in good yields.

Since pharmaceuticals and agrochemicals containing a $CF_2$ group often show unique biological activities,[1] there is much interest in the introduction of this group into compounds. It has been reported that the $CF_2$ group has a steric profile similar to that of the $CH_2$ group but since it has both a very different polarity and reactivity,[1c] it could be regarded as an isopolar and isosteric replacement of oxygen.[2] Compounds containing a $CF_2$ group are usually synthesized through the general transformation $C{=}O \rightarrow CF_2$ brought about by (diethylamino)sulfur trifluoride (DAST)[3–4] and other reagents.[5–6] Such methods, however, although quite popular, necessitate use of both expensive reagents and special equipment. Although $CF_2Br_2$ and Zn powder could, in certain cases, bring about the conversion $C{=}O \rightarrow CF_2$, *via* a $:CF_2$ intermediate, product yields were low.[7] Lack of a general synthesis for such $CF_2$-bearing functionalized compounds has, therefore, hampered developments in this area. Whilst investigating the synthetic utility of $CF_2Br_2$, we found that the $CrCl_3/Fe$ redox system is an efficient catalyst for the addition of $CF_2Br_2$ to electron-deficient alkenes to give $CF_2Br$-containing products.[8] Since such products contain a terminal $CF_2Br$ group we surmised that the remaining bromine atom could, possibly, react with a further molecule of alkene. Experiments showed that such a bromine atom could be activated by cobaloxime/Zn, but not $CrCl_3/Fe$. Here, we describe a two-step strategy to synthesize $CF_2$-containing compounds.

## Results and Discussion

In the presence of $CrCl_3 \cdot 6H_2O$ as catalyst (30 mol%) and Fe powder (1.5 equiv.), $CF_2Br_2$ **1** readily reacted with electron-deficient alkenes **2** to give $CF_2Br$-containing products **3** in good to excellent yields. Under these conditions, no debromination or hydrodebromination products $:CF_2$ or $CF_2BrH$, respectively) were detected (Scheme 1). Ethanol and tetrahydrofuran proving to be the most suitable solvents although most additions were carried out in the former. Iron powder alone was insufficiently active to initiate such additions. Table 1 summarizes the reaction conditions and the yields.

Subsequently, it was found that the above described redox system also promoted the addition of $CF_2Br_2$ **1** to electron-rich alkenes (see Scheme 2). Such reactions were more rapid (*ca.* 10 h) than those with electron-deficient alkenes and gave a 1:1 adduct; this contrasts with the reactions of electron-deficient alkenes, where the bromine atom in the hydrocarbon part was reduced (Schemes 1 and 2).

Since the bromine atom remaining in compounds **3** and **5** allowed the possibility of further chemical transformation to give $CF_2$-containing compounds, addition with a further molecule of alkene was attempted. The bromine atom in the $CF_2Br$ group being relatively inert because of the presence of the neighbouring $\alpha$-$CH_2$ group. Initiators such as $CrCl_3/Fe$, $Cp_2TiCl_2/Fe$,[9] $Na_2S_2O_4/NaHCO_3$,[10] CuCl/ethanolamine[11] and palladium[12] *etc.*, failed to initiate further addition.

Nevertheless, since it was known that cobaloxime/Zn efficiently promoted the addition both of per(poly)fluoroalkyl iodides or bromides to electron-deficient alkenes[13] and of $CF_2BrP(O)(EtO)_2$ to various alkenes,[14] it was used to promote the addition of ethyl 4-bromo-4,4-difluorobutyrate **3a** and ethyl acrylate **2a** to give the 1:1 hydrodebromination adduct **6a** (see Scheme 3).

**Table 1** The addition of $CF_2Br_2$ **1** to electron-deficient alkenes **2** in ethanol with $CrCl_3/Fe$

| Entry | Alkene | Temp. (°C) | Time (h) | Product | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | **2a** | 60 | 20 | **3a** | 72 |
| 2 | **2a** | 60 | 20 | **3a** | 0[b] |
| 3 | **2b** | 60 | 20 | **3b** | 63 |
| 4 | **2c** | 60 | 24 | **3c** | 80 |
| 5 | **2d** | 60 | 28 | **3d** | 43 |
| 6 | **2e** | 65 | 20 | **3e** | 64[c] |
| 7 | **2f** | 70 | 20 | **3f** | 72 |
| 8 | **2g** | 60 | 20 | **3g** | 60 |
| 9 | **2h** | 60 | 18 | **3h** | 62 |
| 10 | **2i** | 75 | 20 | **3i** | 18 |

[a] Isolated yields. [b] Iron powder alone used. [c] Tetrahydrofuran was used as solvent.

$$\underset{\mathbf{1}}{CF_2Br_2} + \underset{\mathbf{2}}{RCH{=}CR'R''} \xrightarrow{CrCl_3/Fe} \underset{\mathbf{3}}{BrCF_2CHRCHR'R''}$$

| 2 | R | R′ | R″ | 3 |
|---|---|---|---|---|
| **a** | H | H | $CO_2Et$ | **a** |
| **b** | H | H | $CO_2Me$ | **b** |
| **c** | H | Me | $CO_2Et$ | **c** |
| **d** | Me | H | $CO_2Et$ | **d** |
| **e** | H | H | $CO_2H$ | **e** |
| **f** | H | H | $CONH_2$ | **f** |
| **g** | H | H | Ac | **g** |
| **h** | H | H | CN | **h** |
| **i** | –$(CH_2)_3CO$– | | H | **i** |

**Scheme 1**

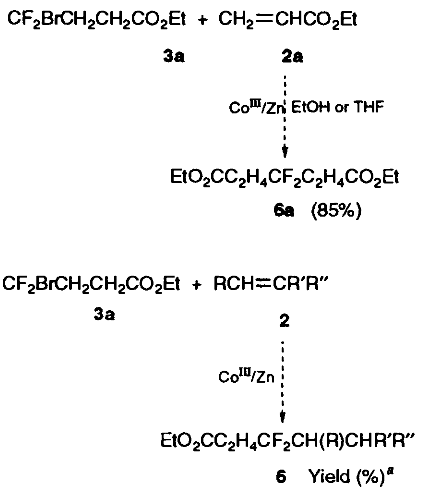
$$\underset{\mathbf{1}}{CF_2Br_2} + \underset{\mathbf{4}}{CH_2{=}CHC_4H_9} \xrightarrow[EtOH,\ 60\ ^\circ C]{CrCl_3/Fe} \underset{\mathbf{5}\ (96\%)}{BrCF_2CH_2CHBrC_4H_9}$$

**Scheme 2**

Neither the reduced product $HCF_2C_2H_4CO_2Et$ nor the zinc reagent $BrZnCF_2C_2H_4CO_2Et$ were detected as by-products. Although either ethanol or THF could be used as solvent, most of the additions were carried out in the former at room temperature.

Although ammonium chloride, bromide, acetate or formate accelerated the addition, 10–15% of $HCF_2CH_2CH_2CO_2Et$ as a by-product was detected ($^{19}F$ NMR).

Ethyl 4-bromo-4,4-difluorobutyrate **3a** was allowed to react with various electron-deficient and electron-rich alkenes (Scheme 3).




| Entry | Compd. 2 | R | R′ | R″ | 6 | Yield (%)[a] |
|---|---|---|---|---|---|---|
| 1 | **a** | H | H | $CO_2Et$ | **a** | 85 |
| 2 | **b** | H | H | $CO_2Me$ | **b** | 70[b] |
| 3 | **c** | H | Me | $CO_2Et$ | **c** | 72 |
| 4 | **d** | Me | H | $CO_2Et$ | **d** | 28 |
| 5 | **f** | H | H | $CONH_2$ | **f** | 52 |
| 6 | **h** | H | H | CN | **h** | 82 |
| 7 | **i** | $-(CH_2)_3CO-$ | | H | **i** | 48 |
| 8 | **j** | H | H | $CH_2Cl$ | **j**[c] | 77 |
| 9 | **k** | H | H | Bu | k | 80 |
| 10 | **l** | H | H | $C_2H_4COMe$ | l | 72 |
| 11 | **m** | H | H | OEt | m | 74 |

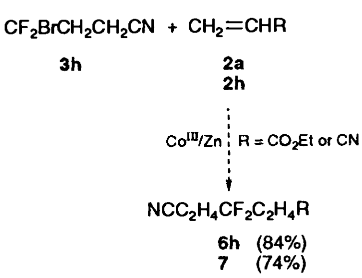
[a] Isolated yields. [b] THF was used as sovent. [c] The product was ethyl 4,4-difluorohept-6-enoate.

**Scheme 3**

Tetrahydrofuran was used as solvent with methyl acrylate **2b**, to avoid partial exchange of the methoxy group to a ethoxy group which was possible in ethanol.

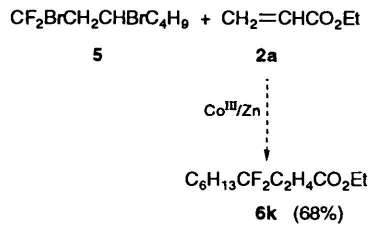
As a result mainly of steric hindrance, ethyl crotonate **2d** gave a lower yield (entries 3 and 4 in Scheme 3).

4-Bromo-4,4-difluorobutyronitrile **3h** was also similarly found to add to ethyl acrylate **2a** and acrylonitrile **2h** to give **6h** and **7** in 84 and 74% yields, respectively (Scheme 4)




**Scheme 4**

Finally, 1,3-dibromo-1,1-difluoroheptane **5** was allowed to react with **2a**. In this case, the terminal $CF_2$ added to ethyl




**Scheme 5**

acrylate, while the bromine atom in CHBr was reduced (Scheme 5).

In summary, various multi-functionalized $CF_2$-containing compounds have been readily synthesized from $CF_2Br_2$ in a two-step strategy.

## Experimental

All b.p.s are uncorrected. IR spectra were recorded on an IR-440 Shimadzu spectrometer using a thin film. $^{19}F$ NMR spectra were recorded on a Varian-360L (56.4 MHz) spectrometer in $CDCl_3$ or [$^2H_6$]acetone using $CF_3CO_2H$ as external standard. Chemical shifts in ppm were positive for upfield shifts. $^1H$ NMR spectra were recorded on an XL-200 (200 MHz) instrument or a Bruker machine (300 MHz) in $CDCl_3$ or [$^2H_6$]acetone. MS spectra were obtained on a Finnigan GC-MS-4021 or Finnigan-8430 spectrometer.

*Addition of* $CF_2Br_2$ *to Electron-deficient Alkenes initiated by* $CrCl_3$/Fe.—*Typical procedure.* A mixture of $CrCl_3{\cdot}6H_2O$ (0.53g, 2 mmol), iron powder (0.84 g, 15 mmol), $CF_2Br_2$ (2.1 g, 10 mmol) and ethyl acrylate **2a** (1.2 g, 12 mmol) in ethanol (15 $cm^3$) was stirred at the appropriate temperature for the stated time (see Table 1); the reaction was monitored by $^{19}F$ NMR spectrometry. At completion of the reaction, the mixture was poured into water (30 $cm^3$) and filtered. The filtrate was extracted with diethyl ether (3 × 20 $cm^3$) and the combined extracts were successively washed with saturated aqueous $NaHSO_3$, water and brine, dried ($Na_2SO_4$) and evaporated. The residue was either distilled *in vacuo* or column chromatographed with light petroleum (b.p. 60–90 °C)–ethyl acetate as eluent (95:5, v/v) to give the pure products.

*Ethyl* 4-*bromo*-4,4-*difluorobutyrate* **3a**.[8] Colourless oil; b.p. 91–92 °C/40 mmHg; $\delta_F$ −32 (s, $CF_2Br$) ppm; $\delta_H$ 4.15 (q, $^3J_{HH}$ 7, 2 H, $OCH_2$), 3.2–2.2 (m, 4 H, $CH_2CH_2$) and 1.25 (t, $^3J_{HH}$ 7, 3 H, OEt).

*Methyl* 4-*bromo*-4,4-*difluorobutyrate* **3b**. Colourless oil; b.p. 65–67 °C/20 mmHg, $\delta_F$ −32 (s, $CF_2Br$); $\delta_H$ 3.8 (s, 3 H, $OCH_3$), 3.2–2.2 (m, 4 H, $CH_2CH_2$), $\nu_{max}/cm^{-1}$ 1740s (C=O), 1220, 1180s (C–F), 1060s; *m/z* (%) 217 ($M^+$, 3.18), 138 ($M^+$ − Br, 9.81), 137 ($M^+$ − HBr, 100), 89 ($M^+$ − $CF_2Br$, 45.9) (Found: C, 27.5; H, 3.3. Calc. for $C_5H_7BrF_2O_2$: C, 27.65; H, 3.22%).

*Ethyl* 4-*bromo*-4,4-*difluoro*-2-*methylbutyrate* **3c**. Colourless oil; b.p. 72–74 °C/15 mmHg; $\delta_F$ −34 (s, $CF_2Br$); $\delta_H$ 4.4 (q, 2 H, $^3J_{HH}$ 7, OEt), 3.6–2.2 (m, 3 H, $CH_2CH$) and 1.00 (t, $^3J_{HH}$ 7, 6 H, OEt + $CH_3$); $\nu_{max}/cm^{-1}$ 1740s (C=O), 1220, 1180s (C–F) and 1020s; *m/z* (%) 245 ($M^+$, 2.56, $^{79}Br$), 246 ($M^+$, 195, $^{81}Br$), 200 (49.3), 137 (100) (Found: C, 34.2; H, 4.6; Br, 32.9; F, 15.6. Calc. for $C_7H_{11}BrF_2O_2$: C, 34.29; H, 4.49; Br, 32.65; F, 15.51%).

*Ethyl* 4-*bromo*-4,4-*difluoro*-3-*methylbutyrate* **3d**. Colourless oil; b.p. 71–73 °C/15 mmHg; $\delta_F$ −33 (m, $CF_2Br$); $\delta_H$ 4.3 (q, 2 H, $^3J_{HH}$ 7, OEt), 2.8–1.5 (m, 6 H, $CH_2CH$ + $CH_3$) and 1.38 (t, $^3J_{HH}$ 7, 3 H, OEt); $\nu_{max}/cm^{-1}$ 1735s (C=O), 1200; 1160s (C–F), 1020s; *m/z* (%) 245 ($M^+$ + 1, 5.68, $^{79}Br$), 247 ($M^+$ + 1, 4.72, $^{81}Br$) and 137 (100) (Found: C, 34.2; H, 4.6; Br, 32.9; F, 15.3. Calc. for $C_7H_{11}BrF_2O_2$: C, 34.3; H, 4.5; Br, 32.65; F, 15.5%).

4-*Bromo*-4,4-*difluorobutyric acid* **3e**. Colourless oil; b.p. 90–92 °C/2 mmHg; $\delta_F$ −31.6 (s, $CF_2Br$); $\delta_H$ 10.8 (s br, 1 H, $CO_2H$) and 3.2–2.8 (m, 4 H, $CH_2CH_2$); $\nu_{max}/cm^{-1}$ 3400vs (OH), 1740s (C=O), 1180, 1110s (C–F); *m/z* (%) 2303 ($M^+$, 0.19, $^{79}Br$), 185 ($M^+ - H_2O$, 4.5), 123 ($M^+$ − Br, 5.6), 103 (100) and 77 (46) (Found: C, 24.2; H, 2.7; Br, 39.2; F, 19.0. Calc. for $C_4H_5BrF_2O_2$: C, 23.65; H, 2.46; Br, 39.41; F, 18.92%).

4-*Bromo*-4,4-*difluorobutyramide* **3f**. $\delta_F$ −33 (s, $CF_2Br$); $\delta_H$ 10 (br, 2 H, $NH_2$) and 2.5 (m, 4 H, $CH_2CH_2$); $\nu_{max}/cm^{-1}$ 3450, 3300vs (NH), 1780s (C=O), 1220, 1180s (C–F); *m/z* (%) 201 ($M^+$, 1.75, $^{79}Br$), 203 ($M^+$, 1.74, $^{81}Br$), 122 ($M^+$ − Br, 100) and 77 (46) (Found: C, 23.9; H, 2.7; Br, 40.7; F, 19.3; N, 6.8. Calc. for $C_4H_6BrF_2NO$: C, 23.76; H, 2.97; Br, 39.60; F, 18.81; N, 6.93%).

1-*Bromo*-1,1-*difluoropentan*-4-*one* **3g**. Colourless oil (slowly turned from colourless to deep brown at room temperature); b.p. 75–77 °C/40 mmHg; $\delta_F$ −34 (s, $CF_2Br$); $\delta_H$ 2.5 (m, 4 H, $CH_2CH_2$) and 2.1 (s, 3 H, $CH_3$); $\nu_{max}/cm^{-1}$ 1720s (C=O) and 1220s (C–F); *m/z* (%) 201 ($M^+$ + 1, 2.13, $^{79}Br$), 203 ($M^+$ + 1, 2.08, $^{81}Br$), 121 ($M^+$ − Br, 29) and 44 (100) (Found: C, 29.4; H, 3.3; Br, 39.55; F, 18.1. Calc. for $C_5H_7BrF_2O$: C, 29.85; H, 3.48; Br, 39.80; F, 18.91%).

4-*Bromo*-4,4-*difluorobutyronitrile* **3h**. Colourless oil; b.p. 85–87 °C/40 mmHg; $\delta_F$ −31.5 (s, $CF_2Br$); $\delta_H$ 3.6–2.8 (m, $C_2H_4$); $\nu_{max}/cm^{-1}$ 2200w (CN), 1220, 1180s (C–F); *m/z* (%) 183 ($M^+$, 4.65, $^{79}Br$), 185 ($M^+$, 4.87, $^{81}Br$), 104 ($M^+$ − Br, 100) and 54 ($M^+ - CF_2Br$, 67) (Found: C, 26.4; H, 2.3; Br, 43.8; F, 21.0; N, 7.6. Calc. for $C_4H_4BrF_2N$: C, 26.09; H, 2.17; Br, 43.48; F, 20.65; N, 7.61%).

3-*Bromodifluoromethylcyclohexanone* **3i**. Light yellow oil; b.p. 67–68 °C/2 mmHg; $\delta_F$ −28 (s, $CF_2Br$); $\delta_H$ 3.8–1.5 (m, cyc-H); $\nu_{max}/cm^{-1}$ 1730s (C=O), 1200s (C–F); *m/z* (%) 227 ($M^+$ + 1, 27.81, $^{79}Br$), 229 ($M^+$ + 1, 25.01, $^{81}Br$), 147 ($M^+$ − Br, 100) and 97 ($M^+ - CF_2Br$ − 33); [Found: (HRMS): *m/z* 225.9812 ($^{79}Br$). Calc. for $C_7H_9BrF_2O$: 225.9802 ($^{79}Br$)].

1,1-*Dibromo*-1,1-*difluoroheptane* **5**. Colourless oil; b.p. 95–98 °C/45 mmHg (lit.,[15] b.p. 78–80 °C/25 mmHg); $\delta_F$ −34.5 (s, $CF_2Br$); $\delta_H$ 4.3 (m, 1 H, CHBr), 3.05 (m, 2 H, $CH_2CF_2$) and 2.2–1.0 (m, 9 H, $C_4H_9$).

*Addition of* $BrCF_2C_2H_4R$ *to Alkenes initiated by* $Co^{III}$/Zn.—*General procedure*. A mixture of bromo(pyridine) cobaloxime(III) (0.1 mmol),[13] zinc powder (0.65 g, 10 mmol) and ethanol (20 cm$^3$) was vigorously stirred at room temperature under $N_2$ for *ca.* 30 min during which time, the colour of the suspension changed from brown to light green; further starting material (10 mmol) and the alkene **2** (12 mmol) were then added to it. After the mixture had been stirred at room temperature for *ca.* 1 day, the reaction being monitored by $^{19}F$ NMR spectroscopy, work-up as above gave the corresponding products.

*Diethyl* 4,4-*difluoropimelate* **6a**. Colourless oil; b.p. 110–112 °C/3 mmHg; $\delta_F$ 24 (s, $CF_2$); $\delta_H$ 4.16 (q, $^3J_{HH}$ 7, 4 H, 2 × OEt), 2.5–2.0 (m, 8 H, 2 × $C_2H_4$) and 1.36 (t, $^3J_{HH}$ 7, 6 H, 2 × Me); $\nu_{max}/cm^{-1}$ 1740s (C=O), 1260, 1200s (C–F); *m/z* (%) 253 ($M^+$ + 1, 49.85), 207 ($M^+$ − OEt, 63.5), 233 (82.79) and 159 (100) (Found: C, 52.4; H, 7.3; F, 15.2. Calc. for $C_{11}H_{18}F_2O_4$: C, 52.38; H, 7.14; F, 15.08%).

*Ethyl methyl* 4,4-*difluoropimelate* **6b**. Colourless oil; b.p. 120 °C/4 mmHg; $\delta_F$ 24 (s, $CF_2$); $\delta_H$ 4.16 (q, $^3J_{HH}$ 7, 2 H, OEt), 3.4 (s, 3 H, $CH_3$), 2.5–2.0 (m, 8 H, 2 × $C_2H_4$) and 1.36 (t, $^3J_{HH}$ 7, 3 H, $CH_3$); $\nu_{max}/cm^{-1}$ 1760, 1740 (s, C=O), 1260, 1200 (s, C–F); *m/z* (%) 239 ($M^+$ + 1, 100) (Found: C, 50.4; H, 6.7; F, 15.4. Calc. for $C_{10}H_{16}F_2O_4$: C, 50.42; H, 6.72; F, 15.79%).

*Diethyl* 4,4-*difluoro*-2-*methylpimelate* **6c**. Colourless oil; b.p. 107–108 °C/1 mmHg; $\delta_F$ 24 (s, $CF_2$); $\delta_H$ 4.16 (q, $^3J_{HH}$ 7, 4 H, 2 × OEt), 2.8–1.6 (m, 7 H, $C_2H_4$ + $CH_2CH$), 1.36 (t, $^3J_{HH}$ 7, 6 H, 2 × $CH_3$) and 1.11 (d, $^3J_{HH}$ = 2, 3 H, $CH_3$); $\nu_{max}/cm^{-1}$ 1740s (C=O) and 1200s (C–F); *m/z* (%) 267 ($M^+$ + 1, 31.69), 247 (100), 221 (80.52), 201 (17.08) and 85 (89) [Found (HRMS): 266.1330. Calc. for $C_{12}H_{20}F_2O_4$: 266.1324].

*Diethyl* 4,4-*difluoro*-3-*methylpimelate* **6d**. Colourless oil; b.p. 103–105 °C/1 mmHg; $\delta_F$ 29 (AB, $^3J_{AB}$ 240, $CF_2$); $\delta_H$ 4.26 (q, $^3J_{HH}$ 7, 4 H, 2 × OEt), 2.9–1.8 (m, 7 H, $C_2H_4$ + $CH_2CH$) and 1.36 (t, $^3J_{HH}$ 7, 9 H, 3 × $CH_3$); $\nu_{max}/cm^{-1}$ 1740, 1735s (C=O), 1260, 1200s (C–F); *m/z* (%) 267 ($M^+$ + 1, 68.56), 247 (100), 221 (32.22) and 201 (17.5) [Found (HRMS): 266.1322. Calc. for $C_{12}H_{20}F_2O_4$: 266.1324].

6-*Ethoxycarbonyl*-4,4-*difluorohexanoamide* **6f**. $\delta_F$ 24 (s, $CF_2$); $\delta_H$ 4.2 (q, $^3J_{HH}$ 7, 2 H, OEt), 2.9 (s, 2 H, $NH_2$), 2.8–1.8 (m, 8 H, 2 × $C_2H_4$) and 1.36 (t, $^3J_{HH}$ 7, 3 H, $CH_3$); $\nu_{max}/cm^{-1}$ 3400, 3200s ($NH_2$), 1740, 1640s (C=O), 1190s (C–F); *m/z* (%) 224 ($M^+$ + 1, 100), 204 ($M^+$ − HF, 58.47), 178 (83.05) and 160 (22.46) (Found: C, 48.15; H, 7.1; N, 2.9. Calc. for $C_9H_{15}F_2NO_3$: C, 48.43; H, 6.73; N, 6.28%); [Found (HRMS): 223.1042. Calc. for $C_9H_{15}F_2NO_3$: 223.1015].

*Ethyl* 6-*cyano*-4,4-*difluorohexanoate* **6h**. Colourless oil; b.p. 133–135 °C/1 mmHg; $\delta_F$ 25.5 (s, $CF_2$); $\delta_H$ 4.12 (q, $^3J_{HH}$ 7, 2 H, OEt), 2.8–1.9 (m, 8 H, 2 × $C_2H_4$) and 1.36 (t, $^3J_{HH}$ 7, 3 H, $CH_3$); $\nu_{max}/cm^{-1}$ 2200w (CN), 1740s (C=O), 1200s (C–F); *m/z* (%) 206 ($M^+$ + 1, 100), 160 ($M^+$ − OEt, 58), 140 (18.50) and 112 (24) (Found: C, 52.0; H, 6.65; N, 6.8. Calc. for $C_9H_{13}F_2NO_2$: C, 52.68; H, 6.34; N, 6.83%); [Found (HRMS): 205.0899. Calc. for $C_9H_{13}F_2NO_2$: 205.0910].

*Ethyl* 4,4-*difluoro*-4-(3′-*oxocyclohexyl*)*butyrate* **6i**. Colourless oil; b.p. 128–130 °C/1 mmHg; $\delta_F$ 30 (s, $CF_2$); $\delta_H$ 4.16 (q, $^3J_{HH}$ 7, 2 H, OEt), 2.8–1.6 (m, 13 H) and 1.36 (t, $^3J_{HH}$ 7, 3 H, $CH_3$); $\nu_{max}/cm^{-1}$ 1740, 1720s (C=O), 1200s (C–F); *m/z* (%) 249 ($M^+$ + 1, 100), 229 ($M^+$ − F, 67.20), 228 ($M^+$ − HF, 64.02), 209 (35.84) and 180 (41.23) (Found: C, 58.25; H, 7.2; F, 15.8. Calc. for $C_{12}H_{18}F_2O_3$: C, 58.06; H, 7.26; F, 15.32%); [Found (HRMS): 228.1130 ($M^+$ − HF). Calc. for ($M^+$ − HF): 228.1157].

*Ethyl* 4,4-*difluorohept*-6-*enoate* **6j**. Colourless oil; b.p. 85–87 °C/40 mmHg; $\delta_F$ 24 (s, $CF_2$); $\delta_H$ 5.4 (m, 1 H, $CH{=}CH_2$), 4.8 (m, 2 H, $CH{=}CH_2$), 4.0; $\nu_{max}/cm^{-1}$ 1740s (C=O), 1640m (C=C) and 1200s (C–F); *m/z* (%) 193 ($M^+$ + 1, 26.43), 173 ($M^+$ − F, 100), 147 (100), 127 (11.83), 85 (29.9) and 131 (38.48) [Found (HRMS): 192.1002. Calc. for $C_9H_{14}F_2O_2$: 192.0956].

*Ethyl* 4,4-*difluorodecanoate* **6k**. Colourless oil; b.p. 103–105 °C/3 mmHg; $\delta_F$ 24 (s, $CF_2$); $\delta_H$ 4.16 (q, $^3J_{HH}$ 7, 2 H, OEt), 2.8–1.6 (m, 13 H) and 1.36 (t, $^3J_{HH}$ 7, 3 H, $CH_3$); $\nu_{max}/cm^{-1}$ 1740, 1720s (C=O), 1200s (C–F); *m/z* (%) 273 ($M^+$ + 1, 1.08), 217 ($M^+$ − HF, 39.37), 189 ($M^+$ − OEt, 23) and 43 (100) (Found: C, 61.1; H, 9.0: F, 15.42. Calc. for $C_{12}H_{22}F_2O_2$: C, 61.1; H, 9.37; F, 16.10%).

*Ethyl* 4,4-*difluoro*-9-*oxodecanoate* **6l**. Colourless oil; b.p. 125–127 °C/1 mmHg; $\delta_F$ 24 (s, $CF_2$); $\delta_H$ 4.16 (q, $^3J_{HH}$ 7, 2 H, OEt), 2.6–1.3 (m, 12 H), 2.0 (s, 3 H, Ac) and 1.36 (t, $^3J_{HH}$ 7, 3 H, $CH_3$); $\nu_{max}/cm^{-1}$ 1740, 1720s (C=O), 1180, 1160s (C–F); *m/z* (%) 251 ($M^+$ + 1, 5.62), 231 (31.11), 207 ($M^+$ − Ac, 1.49), 187 (14.97), 173 (23.77) and 43 (100) (Found: F, 15.2. Calc. for $C_{12}H_{20}F_2O_3$: F, 15.20%).

*Ethyl* 4,4-*difluoro*-7-*oxanonanoate* **6m**. Colourless oil; b.p. 108–110 °C/1 mmHg; $\delta_F$ 24 (s, $CF_2$); $\delta_H$ 4.16 (q, $^3J_{HH}$ 7, 2 H, OEt), 3.8 (m, 4 H, 2 × $OCH_2$), 2.8–1.7 (m, 6 H) and 1.36 (t, $^3J_{HH}$ 7, 6 H, 2 × $CH_3$); $\nu_{max}/cm^{-1}$ 1740s (C=O), 1260, 1200s (C–F); *m/z* (%) 225 ($M^+$ + 1, 35.86), 205 ($M^+$ − HF, 100), 179 ($M^+$ − OEt, 38.95) and 159 (32.470), 59 (75) [Found: 14.25. (HRMS): 224.1219. Found: 224.1149. Calc. for $C_{10}H_{18}F_2O_3$: F, 14.9%].

1,5-*Dicyano*-3,3-*difluoropentane* **7**. $\delta_F$ 21 (s, $CF_2$); $\delta_H$ 2.6–1.6 (m, 2 × $C_2H_4$); $\nu_{max}/cm^{-1}$ 2230w (CN) 1200s (C–F); *m/z* (%) 159 ($M^+$ + 1, 56.26), 139 (5.13), 55 (100) and 54 (89) [Found (HRMS): 159.0751 ($M^+$ + 1). Calc. for $C_7H_8F_2N_2$: 159.0746 ($M^+$ + 1)].

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