

Addition–cyclization of a diallylmalonic acid ester and related compounds with per(poly)fluoroalkyl iodides using a trichlorolanthanide [LnCl₃(cat.)]/Zn system

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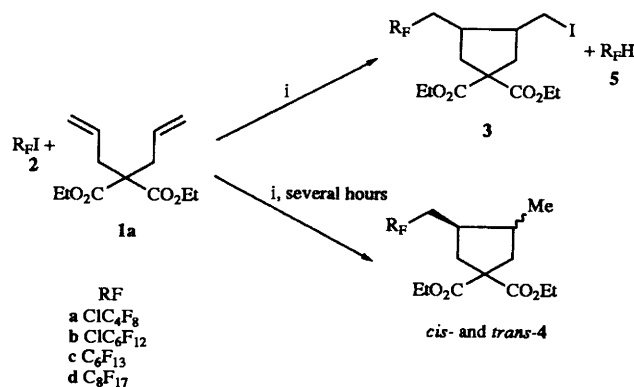
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A free-radical addition–cyclization of hepta-1,6-diene with per(poly)fluoroalkyl iodides initiated by LnCl₃(cat.)/Zn yields per(poly)fluoroalkyl-substituted cyclopentanes, *cis*-disubstituted compounds predominating.

Cyclization of hex-5-enyl radicals to cyclopentylmethyl radicals has been widely studied for mechanistic and synthetic reasons.¹ In related studies it has been reported that azoisobutyronitrile (AIBN) initiated the radical cyclization of hepta-1,6-diene with perfluoroalkyl iodides (R_FI) to give five-membered ring compounds, a preference for *trans*-disubstituted cyclopentanes derivatives being observed by Brace² in such reactions. Earlier, we reported that the addition of R_FI to alkenes promoted by LnCl₃(cat.)/Zn in tetrahydrofuran (THF) afforded hydroperfluoroalkylated products.³ We now report the stereoselective addition–cyclization of R_FI to diethyl diallylmalonates and related compounds initiated by the same system.

Results and discussion

Initially, we studied the reaction of diethyl diallylmalonate **1a** with ω-chlorooctafluorobutyl iodide (ClC₄F₈I, **2a**) in the presence of catalytic amount of YbCl₃ (10% mol) and zinc powder in THF (Scheme 1).



Scheme 1 Reagents and conditions: LnCl₃(cat.)/Zn, THF, 50–67 °C

Thus, typically, to a mixture of **1a** (10 mmol), LnCl₃ (1 mmol), THF (20 cm³) and zinc powder (0.65 g, 10 mmol) was added **2a** (15 mol) within 10 min. The mixture was stirred at 50–67 °C for several hours, and the reaction was monitored by GC and ¹⁹F NMR spectroscopy. The sole reaction product an isomeric mixture of compounds **4aa** was isolated as a colourless oil (67%). The ratio of isomers was determined from the integrated area of the newly formed CH₃ peaks in the ¹H NMR spectra. The structure of the major isomer was assigned through a series of selective decoupling experiments and two-dimensional ¹H NMR measurements. The 2D NOESY ¹H NMR spectrum clearly exhibits a cross-peak between H_c and H_d to confirm that the major isomer has a *cis* configuration (Fig. 1).

No bis-adducts or telomers were obtained under these

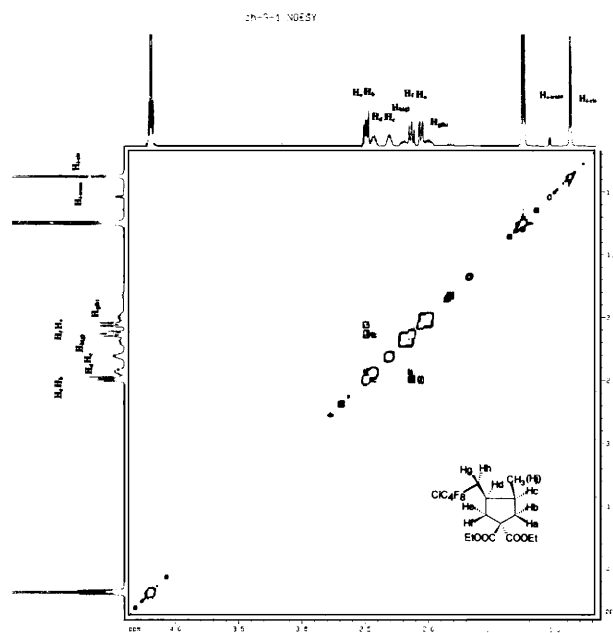


Fig. 1 600 MHz ¹H NMR 2D-¹H-¹H NOESY spectrum of **4aa**

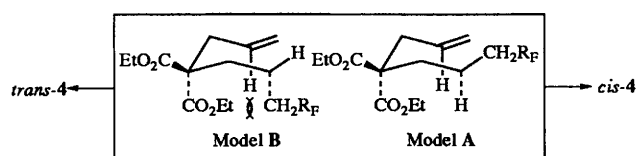
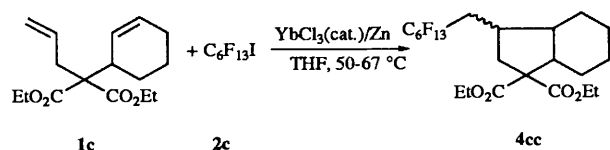
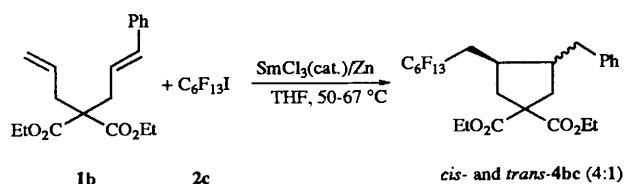
conditions. Formation of the by-product ClC₄F₈H **5a** was indicated by ¹⁹F NMR monitoring. GC analysis during the course of the reaction showed two product peaks, the amount of that with a shorter retention time increasing at the expense of the other as the reaction progressed. For the reaction of **2** with **1a**, by controlling the reaction time we could obtain, separately, the two products formed: by ¹H NMR and MS measurements, that with the short GC retention time was shown to be **4** and the other **3**. In order to obtain a good yield of compound **4**, it was necessary to heat the reaction mixture for 6–10 h. As summarized in Table 1 not only were the product yields little affected by the catalyst employed (*viz.* SmCl₃, YbCl₃, EuCl₃, YCl₃ and DyCl₃) but, similarly, the stereoselectivity of the cyclization products was almost unaffected by the alkyl group chain length. The high stereoselectivity observed in the reaction with **1a** may be explained in terms of Beckwith's chair-like transition state (Fig. 2) hypothesis:^{1b,4} thus, a stronger 1,3-diaxial interaction in molecular model **B** of the *trans* cyclization is absent in the *cis* cyclization model **A**.

The reaction of **1b** or **1c** with the iodide **2c** gave a mixture of *cis*- and *trans*-per(poly)fluoroalkylmethylcyclopentanes the *cis/trans* ratio of which decreased (4:1 for **1b**) as the steric effect of the substituent on the vinyl carbon increased (Scheme 2).

Table 1 $\text{LnCl}_3(\text{cat.})/\text{Zn}$ promoted addition–cyclization of per(poly)fluoroalkyl iodides **2** to hepta-1,6-diene **1**^a

Entry no.	Hepta-1,6-diene 1	R _F I 2	LnCl ₃	Time	Yield (%) ^b	4- <i>cis</i> : 4- <i>trans</i> ^c
1	1a	2a	YbCl ₃	20 min	3aa , 78 4aa , 11	10.6:1
2	1a	2b	YbCl ₃	25 min	3ab , 75 4aa , 10	10.0:1
3	1a	2c	SmCl ₃	30 min	3ac , 74 4ac , 10	11.0:1
4	1a	2d	EuCl ₃	30 min	3ad , 58 4ad , 12	11.4:1
5	1a	2a	YbCl ₃	6 h	4aa , 82	10.6:1
6	1a	2a	SmCl ₃	6 h	4aa , 80	10.5:1
7	1a	2a	EuCl ₃	6 h	4aa , 81	10.5:1
8	1a	2a	YCl ₃	6 h	4aa , 79	10.4:1
9	1a	2a	DyCl ₃	6 h	4aa , 76	10.3:1
10	1a	2b	YbCl ₃	6 h	4ab , 81	10.0:1
11	1a	2c	SmCl ₃	6 h	4ac , 79	11.0:1
12	1a	2d	EuCl ₃	6 h	4ad , 62	11.4:1
13	1b	2c	SmCl ₃	6 h	4bc , 60	4.0:1
14	1c	2c	YbCl ₃	6 h	4cc , 60	

^a Molar ratio **1**:**2**: LnCl_3 : Zn = 1.5:1:0.1:1. ^b Isolated yield based on **1**. ^c Ratio estimated by ¹H NMR.

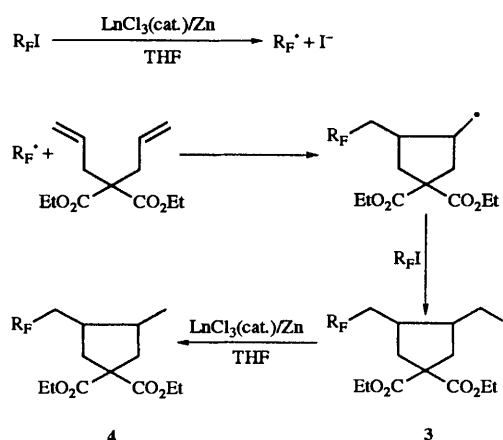
**Fig. 2****Scheme 2**

The suggested pathway of the present reaction is outlined in Scheme 3.

In conclusion, these results demonstrate that the free-radical reaction of per(poly)fluoroalkyl iodides with hepta-1,6-diene promoted by $\text{LnCl}_3(\text{cat.})/\text{Zn}$ provides a new method for the synthesis of per(poly)fluoroalkylmethylcyclopentanes in good yield.

Experimental

All bps are uncorrected. IR spectra were measured with a Shimadzu IR-440 spectrometer using liquid films. ¹H NMR spectra were recorded on AM-300 and AMX-600 spectrometers at 300 or 600 MHz with TMS as internal standard. ¹⁹F NMR spectra were recorded on EM-3601 spectrometer at 56.4 MHz using TFA as external standard. *J* Values are recorded in Hz. Mass spectra were taken on a Finnigan GC-MS-4021 spectrometer. Elemental analyses were obtained by the Elemental Analysis Group of SIOC. GC analyses were carried out on a Shimadzu GC-9A using a 3 m column coated with OV-101 or QF-1.

**Scheme 3**

General procedure for the addition–cyclization of R_FI with a 1,6-diene using $\text{LnCl}_3(\text{cat.})/\text{Zn}$

Preparation of diethyl 3-methyl-4-(perfluoroalkyl)methylcyclopentane-1,1-dicarboxylates **4.** To a stirred solution of hepta-1,6-diene **1** (10 mmol), zinc powder (0.65 g, 10 mmol) and anhydrous LnCl_3 (0.1 mmol) in THF (20 cm³) was added the per(poly)fluoroalkyl iodide **2** (15 mmol) and the mixture stirred at 50–67 °C for 6–10 h. After the completion of the reaction as monitored by GC and ¹⁹F NMR spectroscopy, the mixture was poured into aq. HCl (6 mol dm⁻³; 10 cm³) and extracted with ether (3 × 30 cm³). The organic layer was successively washed with saturated aq. NaHCO₃ and brine, dried (Na₂SO₄) and evaporated. Distillation of the residual liquid under reduced pressure gave pure compound **4**.

Preparation of diethyl 3-iodomethyl-4-(perfluoroalkyl)methylcyclopentane-1,1-dicarboxylates **3.** To a stirred solution of hepta-1,6-diene **1** (10 mmol), zinc powder (0.65 g, 10 mmol) and anhydrous LnCl_3 (0.1 mmol) in THF (20 cm³) was added per(poly)fluoroalkyl iodide **2** (15 mmol) and the mixture stirred at 50–67 °C for 20–30 min. After this the reaction was quenched with aq. HCl (6 mol dm⁻³; 10 cm³) and the mixture worked up as above. Fractionation of the residue yielded the major product **3** and the minor product **4**.

Compound **3aa**: colourless oil, bp 98–100 °C/0.01 mmHg (Found: C, 33.7; H, 3.4; Cl, 5.8; F, 25.1; I, 22.8. C₁₇H₂₀ClF₈IO₄ requires C, 33.88; H, 3.34; F, 25.22; Cl, 5.88; I, 21.06%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1730, 1720 (s, C=O), 1250 and 1100 (CF); δ_{H} 1.25

(t, $^3J_{\text{HH}}$ 7.0, 6 H), 2.0–2.8 (m, 8 H), 3.1 (dt, $^3J_{\text{HH}}$ 8, $^2J_{\text{HH}}$ 16.0, 1 H), 3.3 (dd, $^3J_{\text{HH}}$ 4, $^2J_{\text{HH}}$ 16.0, 1 H) and 4.2 (q, $^3J_{\text{HH}}$ 7.0); δ_{F} -9.0 (s, 2 F), 36.5 (m, 2 F), 38.5 (s, 2 F) and 44 (s, 2 F); m/z 603 (M, 100%) and 474 (M - C₂H₅, 70).

Compound **3ab**: colourless oil, bp 120–124 °C/0.01 mmHg (Found: C, 33.7; H, 3.1; Cl, 5.1; F, 32.1; I, 17.9. C₁₉H₂₀ClF₁₂IO₄ requires C, 32.48; H, 2.87; F, 32.44; Cl, 5.05; I, 18.05%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1730, 1720 (s, C=O), 1250 and 1200 (CF); δ_{H} 1.25 (t, $^3J_{\text{HH}}$ 7.0, 6 H), 2.0–2.8 (m, 8 H), 3.1 (dt, $^3J_{\text{HH}}$ 8, $^2J_{\text{HH}}$ 16.0, 1 H), 3.3 (dd, $^3J_{\text{HH}}$ 4, $^2J_{\text{HH}}$ 16.0, 1 H), 4.2 (q, $^3J_{\text{HH}}$ 7.0); δ_{F} -8.5 (s, 2 F), 37.0 (m, 2 F) and 43.5–47.5 (m, 8 F); m/z 703 (M, 100%) and 573 (M - C₂H₅ - 1, 65).

Compound **3ac**: colourless oil, bp 114–116 °C/0.02 mmHg (Found: C, 33.5; H, 3.1; F, 34.2; I, 18.9. C₁₉H₂₀F₁₃IO₄ requires C, 33.25; H, 2.94; F, 35.99; I, 18.49%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1730, 1720 (s, C=O), 1250 and 1150 (CF); δ_{H} 1.25 (t, $^3J_{\text{HH}}$ 7.0, 6 H), 2.0–2.8 (m, 8 H), 3.1 (dt, $^3J_{\text{HH}}$ 8, $^2J_{\text{HH}}$ 16.0, 1 H), 3.3 (dd, $^3J_{\text{HH}}$ 4, $^2J_{\text{HH}}$ 16.0, 1 H), 4.2 (q, $^3J_{\text{HH}}$ 7.0); δ_{F} 4.5 (s, 2 F), 38.0 (m, 2 F), 44.0–48.0 (m, 6 F) and 50 (s, 2 F); m/z 578 (M, 100%) and 505 (M - CO₂Et, 74).

Compound **3ad**: colourless oil, bp 125–126 °C/0.02 mmHg (Found: C, 32.2; H, 2.45; F, 42.3; I, 16.1. C₂₁H₂₀F₁₇IO₄ requires C, 32.08; H, 2.56; F, 41.08; I, 16.14%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1730, 1720 (s, C=O), 1250 and 1200 (CF); δ_{H} 1.25 (t, $^3J_{\text{HH}}$ 7.0, 6 H), 2.0–2.8 (m, 8 H), 3.1 (dt, $^3J_{\text{HH}}$ 8, $^2J_{\text{HH}}$ 16.0, 1 H), 3.3 (dd, $^3J_{\text{HH}}$ 4, $^2J_{\text{HH}}$ 16.0, 1 H) and 4.2 (q, $^3J_{\text{HH}}$ 7.0); δ_{F} 4.5 (s, 2 F), 38.0 (m, 2 F), 44.0–48.0 (m, 6 F) and 50 (s, 2 F); m/z 784 (M, 100%) and 638 (M - 2 × CO₂Et, 63).

Compound **4aa**: colourless oil, bp 96 °C/0.1 mmHg (Found: C, 43.1; H, 4.4; F, 31.9; Cl, 7.7. C₁₇H₂₁ClF₈O₄ requires C, 42.83; H, 4.44; Cl, 7.44; F, 31.88%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1720, 1730 (s, C=O), 1250 and 1120 (CF); δ_{H} 0.95 (d, $^3J_{\text{HH}}$ 7.1), 1.02 (d, $^3J_{\text{HH}}$ 6.3) (3 H), 1.25 (t, $^3J_{\text{HH}}$ 7.0, 6 H), 1.99 (td, $^3J_{\text{HH}}$ 22.9, $^2J_{\text{HH}}$ 15.0, $^3J_{\text{HH}}$ 5.7, 1 H), 2.06 (ABX, $^3J_{\text{HH}}$ 3.8, $^3J_{\text{HH}}$ 10.4, $^2J_{\text{HH}}$ 14.0, 1 H), 2.13 (ABX, $^2J_{\text{HH}}$ 13.3, $^3J_{\text{HH}}$ 10.4, $^3J_{\text{HH}}$ 2.94), 2.20 (m, $^3J_{\text{HF}}$ 21.8, $^2J_{\text{HH}}$ 15.0, $^3J_{\text{HH}}$ 6.4, 1 H), 2.50 (ABX, $^2J_{\text{HH}}$ 14.0, $^3J_{\text{HH}}$ 7.3, $^3J_{\text{HH}}$ 6.7, 2 H) and 4.20 (t, $^3J_{\text{HH}}$ 7.0, 4 H); δ_{F} -9.5 (s, 2 F), 38.0 (m, 2 F), 44.0 (s, 2 F) and 46 (s, 2 F); m/z 475 (M - 1, 60%) and 241 (M - ClC₄F₈, 100).

Compound **4ab**: colourless oil, bp 128 °C/0.15 mmHg (Found: C, 39.7; H, 3.8; Cl, 6.4; F, 40.1. C₁₉H₂₁ClF₁₂O₄ requires C, 39.56; H, 3.67; Cl, 6.15; F, 39.52%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1720, 1735s (C=O), 1250 and 1200 (CF); δ_{H} 0.95 (d, $^3J_{\text{HH}}$ 7.1), 1.02 (d, $^3J_{\text{HH}}$ 6.3) (3 H), 1.25 (t, $^3J_{\text{HH}}$ 7.0, 6 H), 1.99 (td, $^3J_{\text{HF}}$ 22.9, $^2J_{\text{HH}}$ 15.0, $^3J_{\text{HH}}$ 5.7, 1 H), 2.06 (ABX, $^3J_{\text{HH}}$ 3.8, $^3J_{\text{HH}}$ 10.4, $^2J_{\text{HH}}$ 14.0, 1 H), 2.13 (ABX, $^2J_{\text{HH}}$ 13.3, $^3J_{\text{HH}}$ 10.4, $^3J_{\text{HH}}$ 2.94), 2.20 (m, $^3J_{\text{HF}}$ 21.8, $^2J_{\text{HH}}$ 15.0, $^3J_{\text{HH}}$ 6.4, 1 H), 2.50 (ABX, $^2J_{\text{HH}}$ 14.0, $^3J_{\text{HH}}$ 7.3, $^3J_{\text{HH}}$ 6.7, 2 H) and 4.20 (t, $^3J_{\text{HH}}$ 7.0, 4 H); δ_{F} -8.20 (s, 2 F), 38.2 (m, 2 F), 44.0–46.0 (m, 6 F) and 48 (s, 2 F); m/z 576 (M, 56%) and 242 (M - ClC₆F₁₂ + 1, 100).

Compound **4ac**: colourless oil, bp 118 °C/0.2 mmHg (Found: C, 40.7; H, 3.7; F, 44.1. C₁₉H₂₁F₁₃O₄ requires C, 40.73; H, 3.78; F, 44.08%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1730, 1740s (C=O), 1250 and 1200 (CF);

δ_{H} 0.95 (d, $^3J_{\text{HH}}$ 7.1), 1.02 (d, $^3J_{\text{HH}}$ 6.3) (3 H), 1.25 (t, $^3J_{\text{HH}}$ 7.0, 6 H), 1.99 (td, $^3J_{\text{HF}}$ 22.9, $^2J_{\text{HH}}$ 15.0, $^3J_{\text{HH}}$ 5.7, 1 H), 2.06 (ABX, $^3J_{\text{HH}}$ 3.8, $^3J_{\text{HH}}$ 10.4, $^2J_{\text{HH}}$ 14.0, 1 H), 2.13 (ABX, $^2J_{\text{HH}}$ 13.3, $^3J_{\text{HH}}$ 10.4, $^3J_{\text{HH}}$ 2.94), 2.20 (m, $^3J_{\text{HF}}$ 21.8, $^2J_{\text{HH}}$ 15.0, $^3J_{\text{HH}}$ 6.4, 1 H), 2.50 (ABX, $^2J_{\text{HH}}$ 14.0, $^3J_{\text{HH}}$ 7.3, $^3J_{\text{HH}}$ 6.7, 2 H) and 4.20 (t, $^3J_{\text{HH}}$ 7.0, 4 H); δ_{F} 4.2 (s, 2 F), 36.0 (m, 2 F), 44.0–46.0 (m, 6 F) and 48 (s, 2 F); m/z 560 (M, 20%) and 412 (M - 2 × CO₂Et - 2, 100).

Compound **4ad**: colourless oil, bp 104 °C/0.1 mmHg (Found: C, 37.9; H, 3.1; F, 47.9. C₂₁H₂₁F₁₇O₄ requires C, 38.20; H, 3.21; F, 48.91%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1730, 1740 (s, C=O), 1245 and 1100 (CF); δ_{H} 0.95 (d, $^3J_{\text{HH}}$ 7.1), 1.02 (d, $^3J_{\text{HH}}$ 6.3) (3 H), 1.25 (t, $^3J_{\text{HH}}$ 7.0, 6 H), 1.99 (td, $^3J_{\text{HF}}$ 22.9, $^2J_{\text{HH}}$ 15.0, $^3J_{\text{HH}}$ 5.7, 1 H), 2.06 (ABX, $^3J_{\text{HH}}$ 3.8, $^3J_{\text{HH}}$ 10.4, $^2J_{\text{HH}}$ 14.0, 1 H), 2.13 (ABX, $^2J_{\text{HH}}$ 13.3, $^3J_{\text{HH}}$ 10.4, $^3J_{\text{HH}}$ 2.94), 2.20 (m, $^3J_{\text{HF}}$ 21.8, $^2J_{\text{HH}}$ 15.0, $^3J_{\text{HH}}$ 6.4, 1 H), 2.50 (ABX, $^2J_{\text{HH}}$ 14.0, $^3J_{\text{HH}}$ 7.3, $^3J_{\text{HH}}$ 6.7, 2 H) and 4.20 (t, $^3J_{\text{HH}}$ 7.0, 4 H); δ_{F} 5.5 (s, 2 F), 38.0 (m, 2 F), 43.0–48.0 (m, 6 F) and 50 (s, 2 F); m/z 658 (M - 2, 100%), 242 (M - 2 × CO₂Et - 1, 90).

Compound **4bc**: colourless oil, bp 130–132 °C/0.2 mmHg (Found: C, 47.25; H, 4.0; F, 38.8. C₂₅H₂₅F₁₃O₄ requires C, 47.18; H, 3.96; F, 38.81%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1730, 1720 (s, C=O), 1240 and 1120 (CF); δ_{H} 0.85 (t, $^3J_{\text{HH}}$ 7.3), 1.25 (t, $^3J_{\text{HH}}$ 7.3) (6 H), 1.5–2.2 (m, 8 H), 2.6 (m, 2 H), 4.0–4.2 (q, $^3J_{\text{HH}}$ 7.3, 4 H) and 7.0–7.25 (m, 5 H); δ_{F} 4.2 (s, 2 F), 36.0 (m, 2 F), 44.0–46.0 (m, 6 F) and 48 (s, 2 F); m/z 635 (M - 1, 100%) and 563 (M - CO₂Et, 58).

Compound **4cc**: colourless oil, bp 100–102 °C/1 mmHg (Found: C, 44.0; H, 4.2; F, 41.1. C₂₂H₂₅F₁₃O₄ requires C, 44.01; H, 4.20; F, 41.13%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1740, 1720 (s, C=O), 1240 and 1200 (CF); δ_{H} 0.85–2.5 (m, 19 H), 2.7 (dd, $^3J_{\text{HH}}$ 1.7, 1 H), 3.0 (d, $^3J_{\text{HH}}$ 2.4, 1 H) and 4.2 (q, $^3J_{\text{HH}}$ 7.1, 4 H); δ_{F} 4.2 (s, 2 F), 36.0 (m, 2 F), 44.0–46.0 (m, 6 F) and 48 (s, 2 F); m/z 601 (M - 1, 10.0%), 526 (M - CO₂Et, 30) and 453 (m, 2 × CO₂Et, 100).

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