Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Metal-free, hydroacylation of C=C and N=N bonds *via* aerobic C-H activation of aldehydes, and reaction of the products thereof

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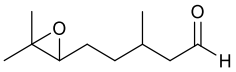
General Experimental

All reagents were purchased from Aldrich or AlfaAesar and were used as received without further purification. All hydroacylation reactions were carried out in carousel tubes (15 cm × 2 cm) equipped with an octagon-shaped magnetic stirrer bar (12.7 mm × 3 mm). Where described below petrol refers to petroleum ether (b.p. 40-60 °C). All reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel plates (254 μm). Flash column chromatography was carried out with Kiesegel 60M 0.04/0.063 mm (200-400 mesh) silica gel. ^{1}H NMR spectra were recorded at 300 MHz, 400 MHz, 500 MHz and 600 MHz and ^{13}C NMR at 75 MHz, 100 MHz, 125 MHz and 150 MHz on a Bruker AMX300, AMX400, AMX500 and AMX600 at 21 °C unless otherwise stated. The chemical shifts (δ) for ^{1}H and ^{13}C are quoted relative to residual signals of the solvent on the ppm scale. Coupling constants (*J* values) are reported in Hertz (Hz). Due to the broadness of the ^{13}C NMR signals in the pentafluorophenyl moiety these peaks have not been assigned. Mass spectra were obtained on a VG70-SE mass spectrometer. Infrared spectra were obtained on a Perkin Elmer Spectrum 100 FTIR Spectrometer operating in ATR mode. Optical rotations were measured using a Perkin Elmer 343 polarimeter. Chiral High Performance Liquid Chromatography (HPLC) was performed on a Varian HPLC instrument equipped with a manual injector, binary pump, and a UV detector (214 nm) using CHIRALCEL® OD column (4.6 mm x 250 mm, 10 μm) from Chiral Technologies (West Chester, PA) eluting with hexane:*i*-PrOH (99:1) with a flow rate of 0.6 mL/min.

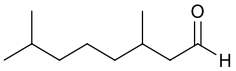
5-(3,3-dimethyloxiran-2-yl)-3-methylpentanal 5o[1]



To a stirring solution of (±)-citronellal (771 mg, 902 μL, 5.00 mmol) in CH_2Cl_2 (20 mL) was added dropwise a solution of *m*-CPBA (1.04 g, 6.00 mmol) in CH_2Cl_2 (10 mL) at 0 °C under argon. The reaction mixture was allowed to warm to 21 °C and stirred for a further 90 min. The reaction mixture was filtered and the filtrate washed with sat. K_2CO_3 (3 × 30 mL), dried ($MgSO_4$) and the solvent removed *in vacuo* to afford 5-(3,3-dimethyloxiran-2-yl)-3-methylpentanal **5o** as a 1:1 mixture of diastereoisomers (A and B) as a colourless oil (809 mg, 4.75 mmol, 95%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.76 (t, *J* = 2.0 Hz, 1H), 2.70-2.68 (m, 1H), 2.42 (ddd, *J* = 2.0, 3.5, 11.0 Hz, 1H), 2.30-2.25 (m, 1H), 2.14-2.09 (m, 1H), 1.60-1.42 (m, 4H), 1.30 (s, 3H), 1.26 (s, 3H

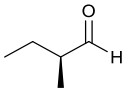
of diastereoisomer A, 1.5H), 1.26 (s, 3H of diastereoisomer B, 1.5H), 0.98 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.7 (CH), 202.6 (CH), 64.3 (CH_2), 64.2 (CH_2), 58.4 (C), 58.3 (C), 51.0 (CH_2), 50.9 (CH_2), 33.5 (CH_2), 27.9 (CH), 26.4 (CH_2), 26.4 (CH_2), 25.0 (CH_3), 19.9 (CH_3), 19.8 (CH_3), 18.7 (CH_3), 18.7 (CH_3); IR (thin film) 2960, 2927, 1722 cm^{-1}; LRMS (FAB) 193 (60, $[M+Na]^+$), 169 (100); HRMS (FAB) calcd for $C_{10}H_{18}O_2Na$ $[M+Na]^+$ 193.1205, observed 193.1208.

3,7-Dimethyloctanal 5r[2]



A stirring solution of (±)-citronellal (771 mg, 902 µL, 5.00 mmol) and Pd on activated C (1%, 250 mg) in MeOH (15 mL) was successively degassed and purged with H_2 three times and the solution left to stir under a H_2 atmosphere for 20 h. To work-up, the reaction mixture was filtered through a 50:50 mixture of silica and Celite, and the filtrate solvent removed *in vacuo* to afford 3,7-dimethyloctanal **5r** as a colourless oil (546 mg, 3.50 mmol, 70%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.76 (t, *J* = 2.5 Hz, 1H), 2.38 (ddd, *J* = 16.0, 5.5, 2.5 Hz, 1H), 2.22 (ddd, *J* = 16.0, 8.0, 2.5 Hz, 1H), 2.08-2.02 (m, 1H), 1.52 (nonet, *J* = 6.5 Hz, 1H), 1.36-1.12 (m, 6H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 203.4 (CH), 51.2 (CH_2), 39.1 (CH_2), 37.2 (CH_2), 28.3 (CH), 28.0 (CH), 24.8 (CH_2), 22.8 (CH_3), 22.7 (CH_3), 20.1 (CH_3); IR (thin film) 2955, 2927, 2870, 1726 cm^{-1}.

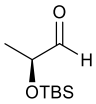
(*S*)-2-Methylbutanal 5x[3]



A two-necked flask was fitted with a pressure-equalising dropping funnel and a thermometer. The flask was charged with (*S*)-2-methylbutanol 151 (13.5 mL, 11.0 g, 0.13 mol), 2,2,6,6-tetramethylpiperidin-1-oxyl (0.20 g, 1.30 mmol), CH_2Cl_2 (40 mL), and a solution of KBr (1.48 g, 0.013 mol) in H_2O (6 mL). The reaction mixture was vigorously stirred and cooled to -10 °C, then aqueous NaOCl (2.4 M, 115 mL, 0.14 mol, pH 9.5) was added over 20 min, keeping the temperature of the reaction mixture between 10 and 15 °C. The mixture was stirred for a further 15 min, the orange organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (15 mL). The combined organic extracts were washed with 10% aqueous HCl (50 mL) containing KI (0.40 g, 0.03 mol), 10% aqueous $Na_2S_2O_3$ (50 mL) and H_2O (30 mL). The organic phase was dried over $MgSO_4$ and then distilled at atmospheric pressure through a 20 cm Vigreux distillation column to give (*S*)-2-methylbutanal **5x** as a colourless oil (8.8 g, 0.10 mol, 82%): b.p. 90-92 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.59 (d, *J* = 2.0 Hz, 1H), 2.24 (sextet of doublets, *J* = 7.0 and 2.0 Hz, 1H), 1.75-1.67 (m, 1H), 1.45-1.36 (m, 1H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.4 (C), 47.8 (CH), 23.5 (CH_2), 12.9 (CH_3), 11.3 (CH_3); IR (thin film) 2970, 2938, 2878, 1705 cm^{-1}; LRMS (CI) 87 (30, $[M+H]^+$), 74 (100); HRMS (CI)

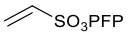
calcd for $C_5H_{11}O$ $[M+H]^+$ 87.0804, observed 87.0809; $[\alpha]_D$ = +35.0 (c 2.04, Acetone, 22.0 ºC), Lit. $[\alpha]_D$ = +35.5 (c 2.50, Acetone, 20.0 °C).[4]

(*S*)-2-[(*tert*-Butyldimethylsilyl)oxy]propanal 5y[5]



2-*tert*-Butylchlorodimethylsilane (7.95 g, 53.0 mmol) was added to a stirring solution of (*S*)-ethyl lactate (5.00 mL, 44.2 mmol) and imidazole (4.51 g, 67.1 mmol) in DMF (44 mL) and the reaction mixture left to stir at 21 °C for 30 min. The reaction mixture was diluted with H_2O (100 mL), extracted with Et_2O (3 × 100 mL), the combined organics washed with sat. NaCl (100 mL), dried ($MgSO_4$) and the solvent removed *in vacuo* to give crude ethyl (*S*)-2-[(tertbutyldimethylsilyl)oxy]propanoate (12.0 g). Diisobutylaluminium hydride (1.5 M in PhMe, 19.0 mL, 28.9 mmol) was added at 0.5 mL/min to a solution of (*S*)-2-[(tertbutyldimethylsilanyl)oxy]-propionic acid ethyl ester (4.42 g, 18.2 mmol) in Et_2O (150 mL) at -85 °C under an inert atmosphere. After addition was complete, the reaction was stirred for a further 10 min at -78 °C then quenched by the dropwise addition of MeOH (1.1 mL) and H_2O (3 mL). After warming to 21 °C and stirring for 90 min, finely ground Na_2SO_4 and $MgSO_4$ were added and the suspension stirred for 15 min, then filtered through a short plug of Celite and silica, eluting with Et_2O. The solvents were removed *in vacuo* and the crude residue purified by vacuum distillation to give (*S*)-2-[(tert-butyldimethylsilyl)oxy]propanal **5y** as a colourless oil (2.10 g, 11.1 mmol, 61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (d, *J* = 1.5 Hz, 1H), 4.10 (qd, *J* = 7.0 and 1.5 Hz, 1H), 1.28 (d, *J* = 7.0 Hz, 3H), 0.92 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.3 (CH), 73.8 (CH), 25.7 (CH_3), 18.5 (CH_3), 18.2 (CH_3), -4.8 (CH_3), -4.8 (CH_3); IR (thin film) 2952, 2931, 2859, 1742 cm^{-1}; $[\alpha]_D$ = -11.0 (c 2.51, $CHCl_3$, 22.0 ºC), Lit. $[\alpha]_D$ = -11.1 (*c* 1.50, $CHCl_3$, 20.0 °C).[5]

Ethenesulfonic acid pentafluorophenyl ester 14[6]



Pentafluorophenol (11.5 g, 62.5 mmol) and NEt_3 (19 mL, 137.5 mmol) in CH_2Cl_2 (20 mL) was added dropwise over 1 h to a solution at of 2-chloroethane sulfonyl chloride (10.13 g, 62.5 mmol) in CH_2Cl_2 (100 ml) at -78°C. The mixture was allowed to warm slowly to 21 °C and diluted with CH_2Cl_2 (100 mL) and washed with H_2O (100 mL), 2M HCl (2 × 100 mL) and sat. $NaHCO_3$ (2 × 100 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. Purification by column chromatography on silica gel (10% Et_2O/petrol) gave ethenesulfonic acid pentafluorophenyl ester **14** as a white solid (13.72 g, 50 mmol, 81%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.79 (dd, *J* = 9.8, 16.5 Hz, 1H), 6.53 (dd, *J* = 0.7, 16.5 Hz, 1H), 6.34 (dd, *J* = 0.7, 9.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.2 (C), 133.2 (CH), 131.7 (CH); IR (thin film) 2963, 1650, 1625 , 1520 cm^{-1}; LRMS (EI) 274 (46, $[M]^+$), 184 (47), 136 (17), 91 (100).

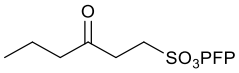
Typical procedure for the hydroacylation of PFPVS 14 in 1,4-dioxane - Method A

To a solution of ethenesulfonic acid pentafluorophenyl ester **14** (1 mmol) in 1,4-dioxane (1 mL) was added aldehyde (5 mmol) and the reaction mixture stirred at 300 rpm at 21 °C until reaction was complete by TLC. PhMe (2 mL) was added and the solvent removed *in vacuo* and the crude residue purified as described below to afford the desired ketone sulfonate ester.

Typical procedure for the hydroacylation of PFPVS 14 in H_2O - Method B

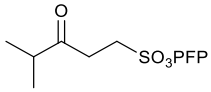
To a solution of ethenesulfonic acid pentafluorophenyl ester **14** (1 mmol) in H_2O (1 mL) was added aldehyde (2 mmol) and the reaction mixture stirred at 300 rpm at 21 °C until reaction was complete by TLC. The solvent removed *in vacuo* and the crude residue purified as described below to afford the desired ketone sulfonate ester.

3-Oxo-hexane-1-sulfonic acid pentafluorophenyl ester 15a[6]



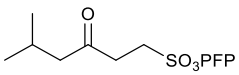
Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 3-oxo-hexane-1-sulfonic acid pentafluorophenyl ester **15a** as an off-white crystalline solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77-3.73 (m, 2H), 3.15-3.10 (m, 2H), 2.50 (t, *J* = 7.3, 2H), 1.71-1.59 (sextet, *J* = 7.3, 2H), 0.94 (t, *J* = 7.4, 3H): ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.9 (C), 47.0 (CH_2), 44.6 (CH_2), 35.9 (CH_2), 17.2 (CH_2), 13.6 (CH_3), IR (neat) 2964, 1716 cm^{-1}; LRMS (CI) 364 (100, $[M+NH_4]^+$); HRMS (ES) calcd for $C_{12}H_{15}F_5NO_4S$ $[M+NH_4]^+$ 364.0636; observed 364.0636.

4-Methyl-3-oxo-pentane-1-sulfonic acid pentafluorophenyl ester 15b[6]



Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 4-methyl-3-oxo-pentane-1-sulfonic acid pentafluorophenyl ester **15b** as a as a colourless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78-3.74 (m, 2H), 3.21-3.18 (m, 2H), 2.74-2.67 (septet, *J* = 6.9, 1H), 1.18 (d, *J* = 6.9, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.7 (C), 47.2 (CH_2), 41.0 (CH), 33.7 (CH_2), 18.1 (CH_3); IR (neat) 2976, 1716 cm^{-1}; LRMS (CI) 364 (100, $[M+NH_4]^+$); HRMS (ES) calcd for $C_{12}H_{15}F_5NO_4S$ $[M+NH_4]^+$. 364.0636; observed 364.0635.

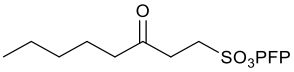
5-Methyl-3-oxo-hexane-1-sulfonic acid pentafluorophenyl ester 15c[6]



Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 5-methyl-3-oxo-hexane-1-sulfonic acid pentafluorophenyl ester **15c** as an off-white crystalline solid: m.p. 56-59 °C; ^{1}H NMR (300

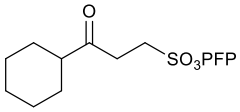
MHz, $CDCl_3$) δ 3.78-3.73 (m, 2H), 3.14-3.09 (m, 2H), 2.40 (d, *J* = 6.9, 2H), 2.18 (septet, *J* = 6.7, 1H), 0.95 (d, *J* = 6.6, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.7 (C), 51.6 (CH_2), 46.9 (CH_2), 36.4 (CH_2), 24.7 (CH), 22.5 (CH_3); IR (neat) 2964, 1720 cm^{-1}; LRMS (CI) 378 (100, $[M+NH_4]^+$); HRMS (ES) calcd for $C_{13}H_{13}F_5NO_4S$ $[M+NH_4]^+$. 378.0793; observed 378.0796.

3-Oxo-octane-1-sulfonic acid pentafluorophenyl ester 15d[7]



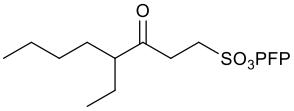
Using Methods A and B, reaction was complete after 3 h and 6 h, respectively. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 3-oxo-octane-1-sulfonic acid pentafluorophenyl ester **15d** as white crystals: m.p. 45-47 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 3.78-3.74 (m, 2H), 3.15-3.11 (m, 2H), 2.51 (t, *J* = 7.5 Hz, 2H), 2.16 (sextet, *J* = 7.5 Hz, 2H), 1.33-1.27 (m, 4H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.1 (C), 47.1 (CH_2), 42.8 (CH_2), 40.0 (CH_2), 31.3 (CH_2), 23.4 (CH_2), 22.4 (CH_2), 13.9 (CH_3); IR (solid) 2937, 2871, 1721 cm^{-1}; LRMS (CI) 375 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{14}H_{16}F_5O_4S$ $[M+H]^+$ 375.0690; observed 375.0685.

3-Cyclohexyl-3-oxo-propane-1-sulfonic acid pentafluorophenyl ester 15e[6]



Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 3-cyclohexyl-3-oxo-propane-1-sulfonic acid pentafluorophenyl ester **15e** as an off-white solid: m.p. 62-64 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.79-3.72 (m, 2H), 3.22-3.16 (m, 2H), 2.45 (tt, *J* = 3.5, 11.2, 1H), 1.97-1.64 (m, 5H), 1.48-1.15 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1 (C), 50.7 (CH), 47.1 (CH_2), 34.0 (CH_2), 28.4 (CH_2), 25.6 (CH_2), 25.5 (CH_2); IR (neat) 2934, 2855, 1706 cm^{-1}; LRMS (CI) 404 (100%, $[M+NH_4]^+$); HRMS (ES) calcd for $C_{15}H_{15}F_5NO_4S$ $[M+NH_4]^+$. 404.0949; observed 404.0949.

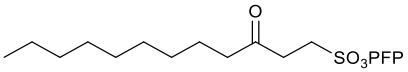
4-Ethyl-3-oxo-octane-1-sulfonic acid pentafluorophenyl ester 15f[6]



Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 4-ethyl-3-oxo-octane-1-sulfonic acid pentafluorophenyl ester **15f** as a as a colourless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 3.87-3.83 (m, 2H), 3.23-3.19 (m, 2H), 2.49 (tt, *J* = 5.7, 8.0, 1H), 1.68-1.64 (m, 2H), 1.54-1.47 (m, 2H), 1.34-1.27 (m, 2H), 1.27-1.20 (m, 2H), 0.90 (t, *J* = 7.2, 3H), 0.89 (t, *J* = 7.4, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9 (C), 54.0 (CH), 47.1 (CH_2), 35.6 (CH_2), 31.0 (CH_2), 29.8 (CH_2), 24.7 (CH_2), 22.8 (CH_2), 14.0 (CH_3), 11.8 (CH_3); IR (neat) 2934, 2962, 2875, 1714 cm^{-1}; LRMS (CI) 420 (14,

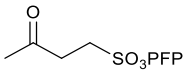
$[M+NH_4]^+$), 172 (100); HRMS (ES) calcd for $C_{16}H_{23}F_5NO_4S$ $[M+NH_4]^+$ 420.1262; observed 420.1265.

3-Oxo-dodecane-1-sulfonic acid pentafluorophenyl ester 15g[7]



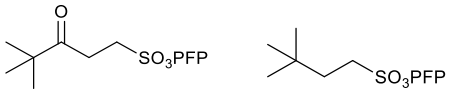
Using Methods A and B, reaction was complete after 3 h and 6 h, respectively. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 3-oxo-dodecane-1-sulfonic acid pentafluorophenyl ester **15g** as white crystals: m.p. 68-70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.75 (t, *J* = 7.5 Hz, 2H), 3.13 (t, *J* = 7.5 Hz, 2H), 2.51 (t, *J* = 7.5 Hz, 2H), 1.61 (t, *J* = 7.0 Hz, 2H), 1.29-1.21 (m, 12H), 0.87 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.1 (C), 47.0 (CH_2), 42.8 (CH_2), 35.9 (CH_2), 31.9 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 23.7 (CH_2), 22.7 (CH_2), 14.1 (CH_3); IR (solid) 2954, 2918, 2849, 1710 cm^{-1}; LRMS (CI) 431 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{18}H_{24}F_5O_4S$ $[M+H]^+$ 431.1310; observed 431.1307.

3-Oxo-butane-1-sulfonic acid pentafluorophenyl ester 15h[6]



Using Method A, reaction was complete after 1 h. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 3-oxo-butane-1-sulfonic acid pentafluorophenyl ester **15h** as a pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78-3.75 (m, 2H), 3.21-3.17 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4 (C), 46.9 (CH_2), 36.8 (CH_2), 29.8 (CH_3); IR (neat) 1724 cm^{-1}; LRMS (ES) 336 (100, $[M+NH_4]^+$); HRMS (ES) calcd for $C_{10}H_{11}F_5NO_4S$ $[M+NH_4]^+$ 336.0323; observed 336.0323.

4,4-Dimethyl-3-oxo-pentane-1-sulfonic acid pentafluorophenyl ester 15i and 3,3-dimethyl-butane-1-sulfonic acid pentafluorophenyl ester[6]

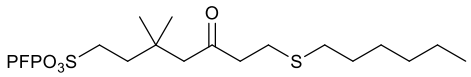


Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 4,4-dimethyl-3-oxo-pentane-1-sulfonic acid pentafluorophenyl ester and 3,3-dimethyl-butane-1-sulfonic acid pentafluorophenyl ester **15i** as an off-white solid.

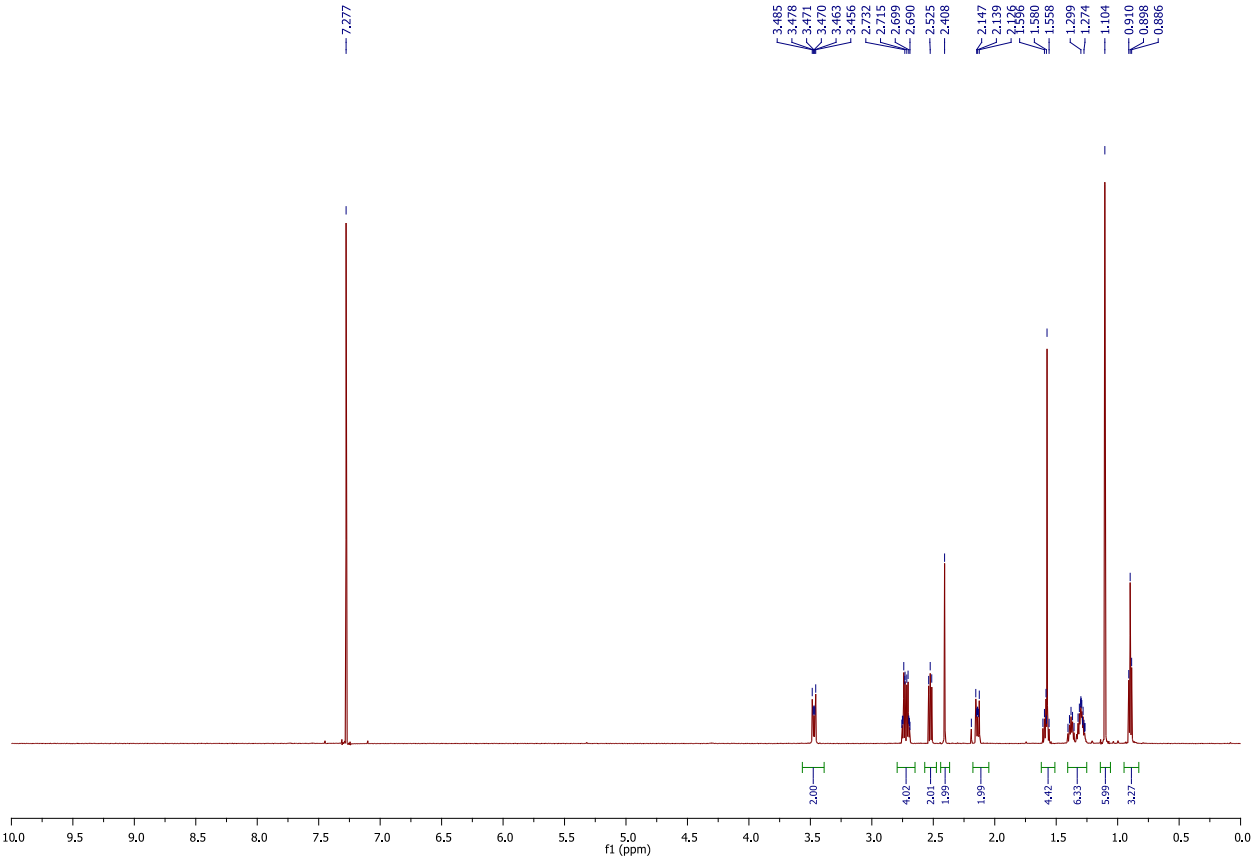
Data for 4,4-dimethyl-3-oxo-pentane-1-sulfonic acid pentafluorophenyl ester **15i**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.76-3.72 (m, 2H), 3.26-3.20 (m, 2H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.4 (C), 47.5 (CH_2), 44.3 (C), 30.8 (CH_2), 26.3 (CH_3); IR (neat) 2971, 1710 cm^{-1}; LRMS (CI) 378 (65%, $[M+NH_4]^+$); HRMS (ES) calcd for $C_{13}H_{13}F_5O_4S$ $[M+NH_4]^+$. 378.0793; observed 378.0797.

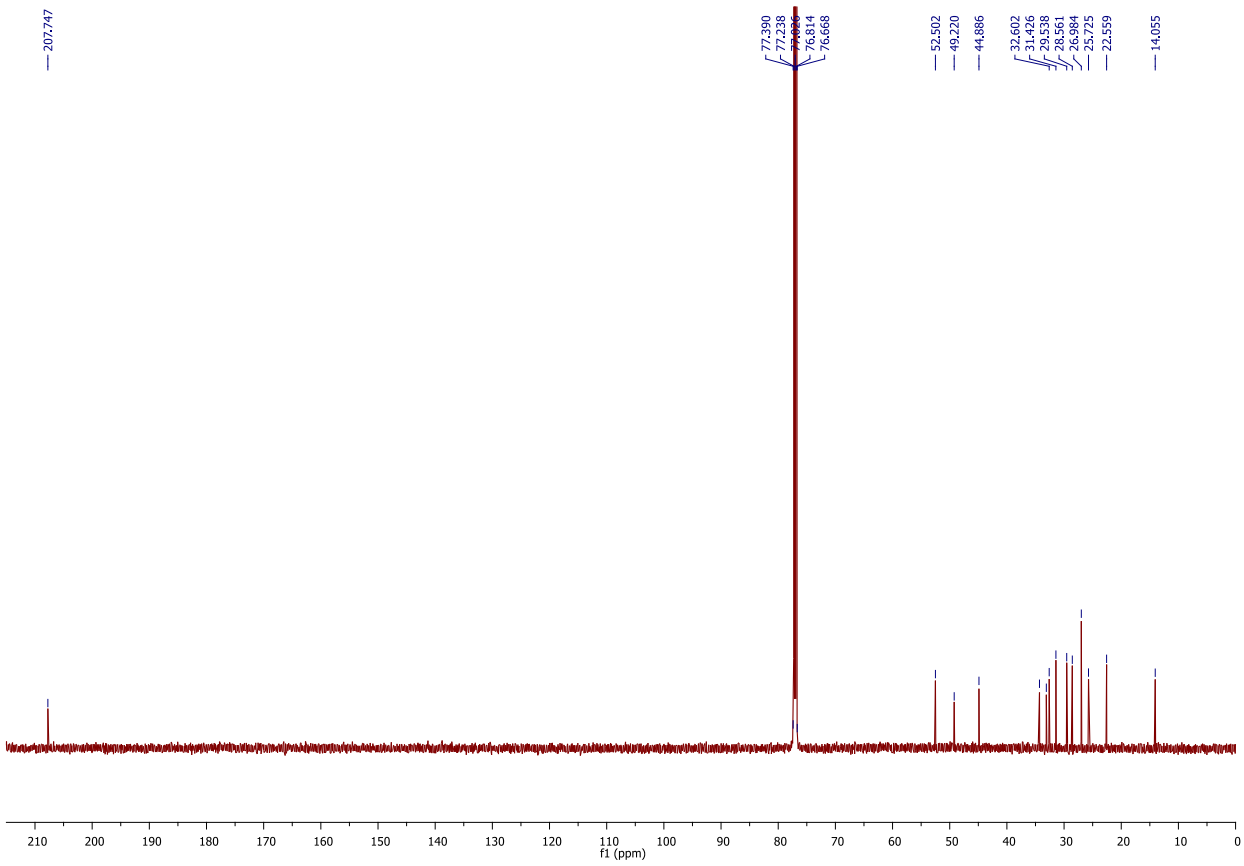
Data for 3,3-dimethyl-butane-1-sulfonic acid pentafluorophenyl ester: m.p. 40-43 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.51-3.33 (m, 2H), 2.02-1.85 (m, 2H), 1.00 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.7 (CH_2), 36.5 (CH_2), 31.0 (C), 28.8 (CH_3); IR (neat) 2958, 1519 cm^{-1}; LRMS (CI) 361 (50, $[M+H]^+$), 177 (38), 113 (100); HRMS (ES) calcd for $C_{13}H_{14}F_5O_4S$ $[M+H]^+$ 361.0533; observed 361.0541.

Pentafluorophenyl 6-(hexylthio)-3,3-dimethyl-4-oxohexane-1-sulfonate 19



Using Method A, reaction was complete after 1 h. The crude reaction mixture was dissolved in CH_2Cl_2 (3 mL), and n-hexanethiol (154 mg, 1.30 mmol) and DBU (304 mg, 2.00 mmol) were added. The reaction mixture was left to stir for 1 h. The solvent was removed *in vacuo* and the crude residue purified by flash column chromatography (30-60% CH_2Cl_2/Petrol) gave pentafluorophenyl 6-(hexylthio)-3,3-dimethyl-4-oxohexane-1-sulfonate **19** as a pale yellow oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.49-3.46 (m, 2H), 2.76-2.69 (m, 4H), 2.53 (t, J = 7.5 Hz, 2H), 2.41 (s, 2H), 2.15-2.13 (m, 2H), 1.60-1.56 (m, 2H), 1.40-1.27 (m, 6H), 1.10 (s, 6H), 0.90 (t, J = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.7 (C), 52.5 (CH_2), 49.2 (CH_2), 44.5 (CH_2), 34.3 (CH_2), 33.1 (C), 32.6 (CH_2), 31.4 (CH_2), 29.5 (CH_2), 28.6 (CH_2), 27.0 (CH_3), 25.7 (CH_2), 22.6 (CH_2), 14.1 (CH_3); IR (thin film) 2959, 2854, 1715, 1520, 1182 cm^{-1}; LRMS (CI) 505 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{21}H_{30}F_5O_4S_2$ $[M+H]^+$ 505.1506, observed 505.1487.

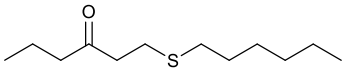




Typical procedure for the synthesis of γ-keto-sulfides 22 - Method C

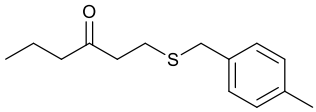
To a solution of pentafluorophenyl 3-oxohexane-1-sulfonate **15a** (1 mmol) in CH_2Cl_2 (3 mL) was added thiol (1.3 mmol) and DBU (2 mmol), and the reaction mixture stirred at 300 rpm at 21 °C for 1 h. The solvent was removed *in vacuo* and the crude residue purified as described below to afford the desired γ-keto-sulfide.

1-Hexylsulfanyl-hexan-3-one 22a[7]



Using Method C. Purification by flash column chromatography (60% CH_2Cl_2/petrol to neat CH_2Cl_2) afforded 1-hexylsulfanyl-hexan-3-one **22a** as a colourless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.72-2.70 (m, 2H), 2.69-2.65 (m, 2H), 2.49 (t, *J* = 7.5, 2H), 2.39 (t, *J* = 7.5 Hz, 2H), 1.62-1.55 (m, 4H), 1.38-1.23 (m, 6H), 0.90 (t, *J* = 7.5 Hz, 3H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.8 (C), 45.1 (CH), 42.9 (CH_2), 32.6 (CH_2), 31.5 (CH_2), 29.6 (CH_2), 28.6 (CH_2), 25.9 (CH_2), 22.6 (CH_2), 17.3 (CH_2), 14.1 (CH_3), 13.8 (CH_3); IR (thin film) 2959, 2927, 1714 cm^{-1}; LRMS (CI) 217 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{12}H_{25}OS$ $[M+H]^+$ 217.1626; observed 217.1621.

1-(4-Methyl-benzylsulfanyl)-hexan-3-one 22b[7]

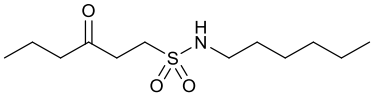


Using Method C. Purification by flash column chromatography (60% CH_2Cl_2/petrol to neat CH_2Cl_2) afforded 1-(4-methyl-benzylsulfanyl)-hexan-3-one **22b** as a colourless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 3.68 (s, 2H), 2.66-2.58 (m, 4H), 2.34 (t, *J* = 7.5 Hz, 2H), 2.32 (s, 3H), 1.59 (septet, *J* = 7.5 Hz, 2H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.6 (C), 136.8 (C), 135.2 (C), 129.3 (CH), 128.8 (CH), 45.0 (CH_2), 42.5 (CH_2), 36.5 (CH_2), 25.3 (CH_2), 21.1 (CH), 17.3 (CH_2), 13.8 (CH_3); IR (thin film) 2962, 2928, 2871, 1712, 1535, 1516 cm^{-1}; LRMS (CI) 237 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{14}H_{21}OS$ $[M+H]^+$ 237.1313; observed 237.1318.

Typical procedure for the synthesis of sulfonamides 23-25a - Method D

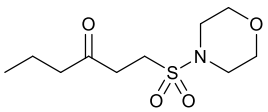
To a solution of pentafluorophenyl 3-oxohexane-1-sulfonate **15a** (79 mg, 0.29 mmol) in NMP (2.5 mL) was added dropwise a solution of amine (0.58 mmol) in NMP (1 mL) at 0 °C. After addition was complete, the reaction mixture was warmed to 21 °C and stirred for 4 h. To work-up, the reaction mixture was diluted with Et_2O (20 mL), washed with sat. LiCl (3 × 20 mL), sat. $NaHCO_3$ (3 × 20 mL), 2M HCl (3 × 20 mL), dried ($MgSO_4$) and the solvent removed *in vacuo* to afford the desired sulfonamide.

***N*-Hexyl-3-oxohexane-1-sulfonamide 23a**[7]



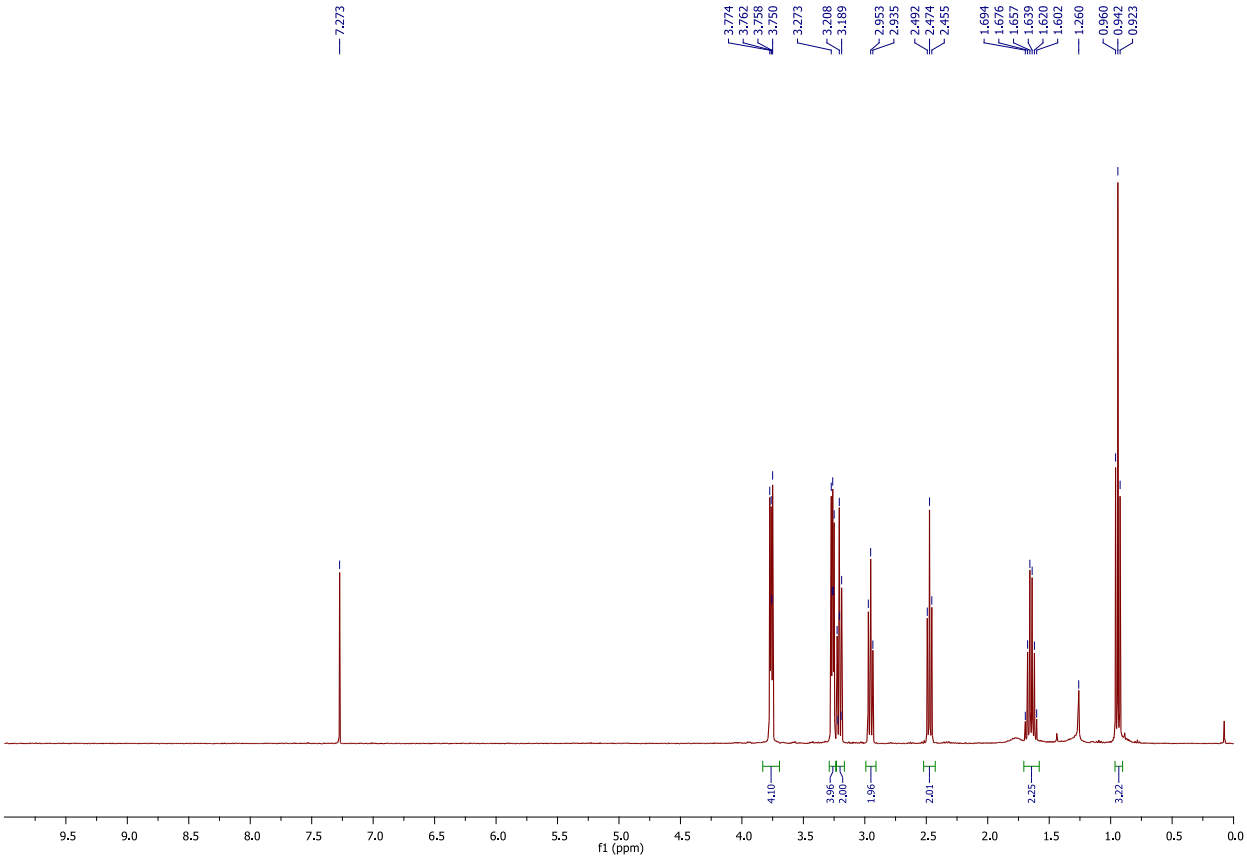
Using Method D, *N*-hexyl-3-oxohexane-1-sulfonamide **23a** was isolated as a white solid (64 mg, 0.25 mmol, 82%): m.p. 67-69 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.12 (br t, *J* = 6.0 Hz, 1H, NH), 3.34-3.31 (m, 2H), 3.12 (q, *J* = 7.0 Hz, 2H), 2.97-2.94 (m, 2H), 2.47 (t, *J* = 7.5 Hz, 2H), 1.63 (sextet, *J* = 7.5 Hz, 2H), 1.57 (quintet, *J* = 7.5 Hz, 2H), 1.38-1.24 (m, 6H), 0.94 (t, *J* = 7.5 Hz, 3H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.1 (C), 46.6 (CH_2), 44.8 (CH_2), 43.4 (CH_2), 36.5 (CH_2), 33.3 (CH_2), 30.2 (CH_2), 26.3 (CH_2), 22.5 (CH_2), 17.2 (CH_2), 14.0 (CH_3), 13.7 (CH_3); IR (solid) 3288, 2957, 2930, 2859, 1703, 1312, 1136 cm^{-1}; LRMS (CI) 264 (45, $[M+H]^+$), 102 (100); HRMS (CI) calcd for $C_{12}H_{26}NO_3S$ $[M+H]^+$ 264.1633, observed 264.1624.

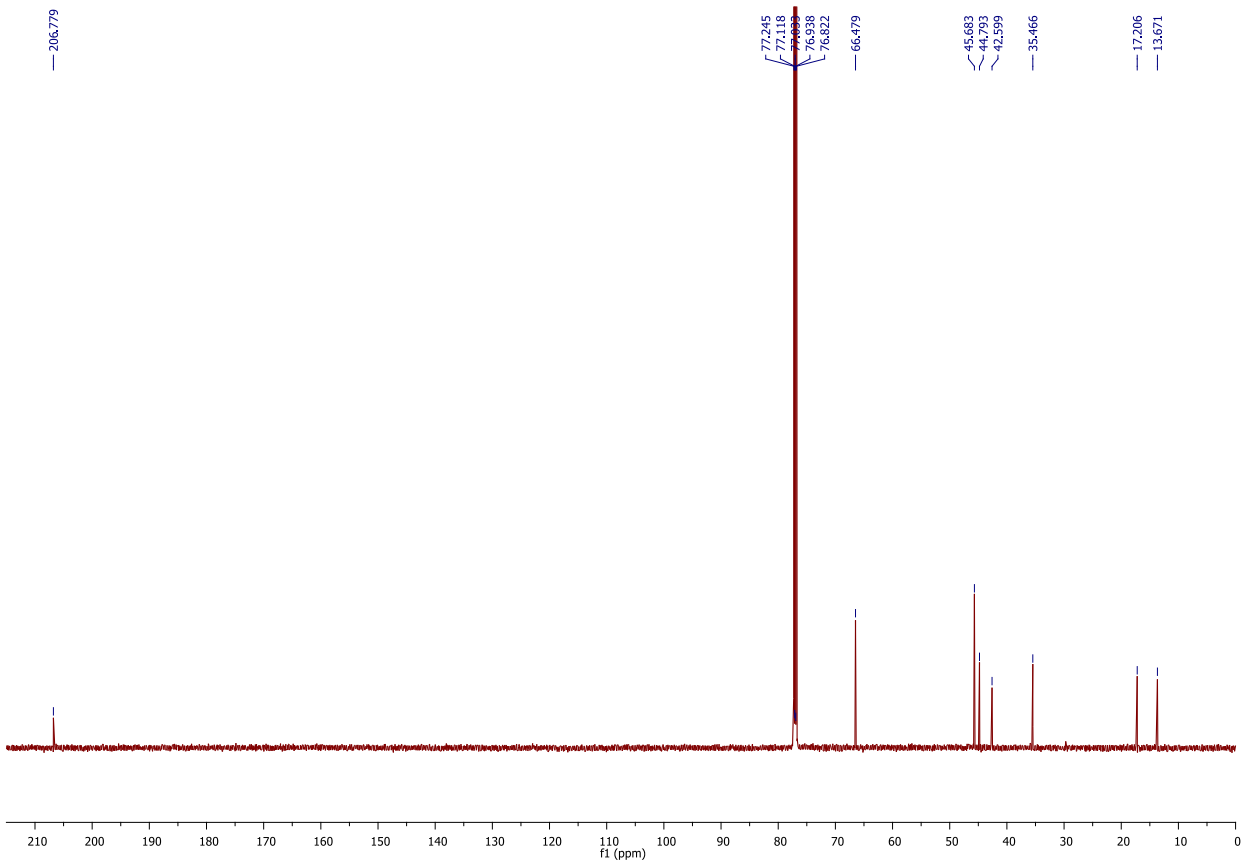
1-(Morpholin-4-ylsulfonyl)hexan-3-one 24a



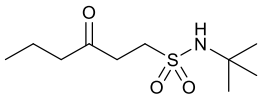
Using Method D, 1-(morpholin-4-ylsulfonyl)hexan-3-one **24a** was isolated as a yellow solid (23 mg, 0.09 mmol, 32%): m.p. 45-48 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78-3.75 (m, 4H), 3.27-3.25 (m, 4H), 3.23-3.20 (m, 2H), 2.98-2.95 (m, 2H), 2.48 (t, *J* = 7.0 Hz, 2H), 1.67 (sextet, *J* = 7.0

Hz, 2H), 0.93 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8 (C), 66.5 (CH_2), 45.7 (CH_2), 44.8 (CH_2), 42.6 (CH_2), 35.5 (CH_2), 17.2 (CH_2), 13.7 (CH_3); IR (solid) 2964, 2926, 2860, 1716, 1344, 1157 cm^{-1}; LRMS (CI) 250 (20, $[M+H]^+$), 163 (35), 99 (100); HRMS (CI) calcd for $C_{10}H_{20}NO_4S$ $[M+H]^+$ 250.1113, observed 250.1107.

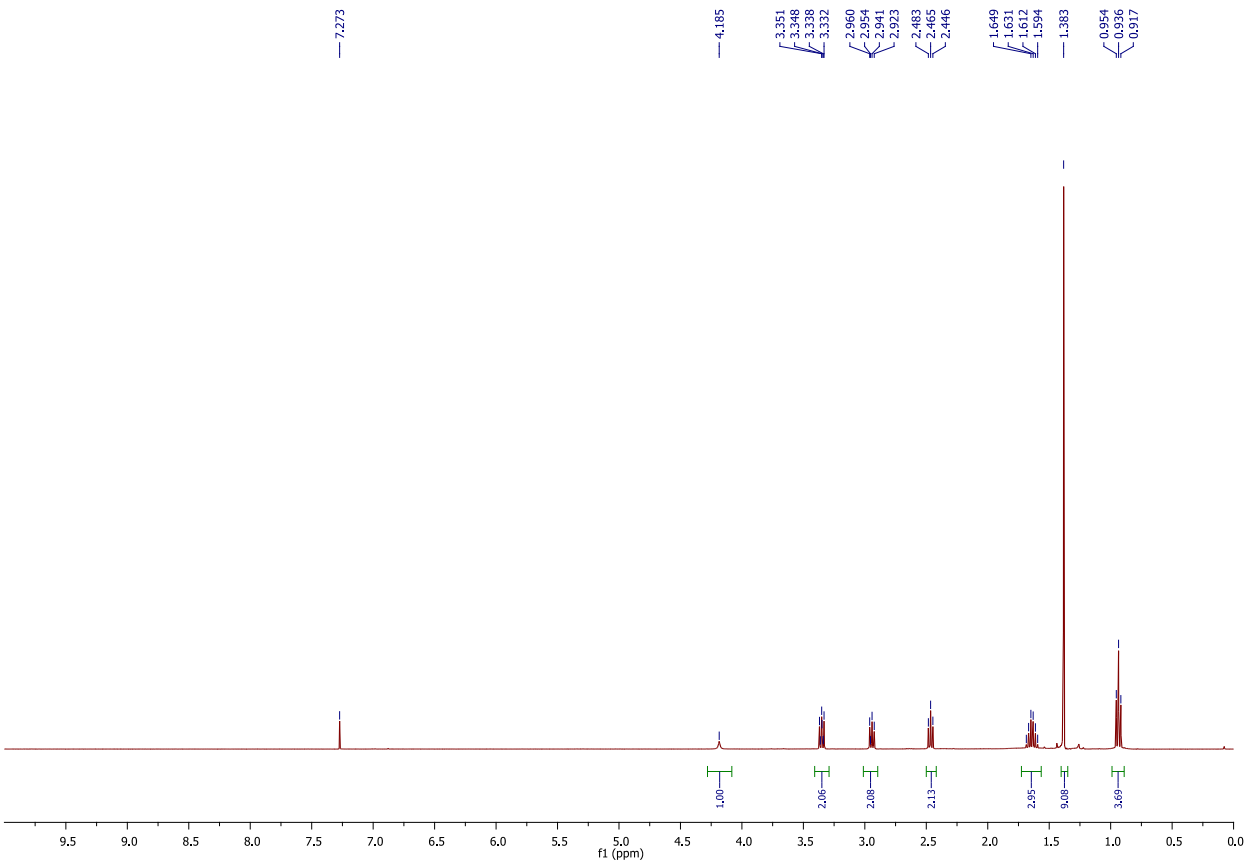


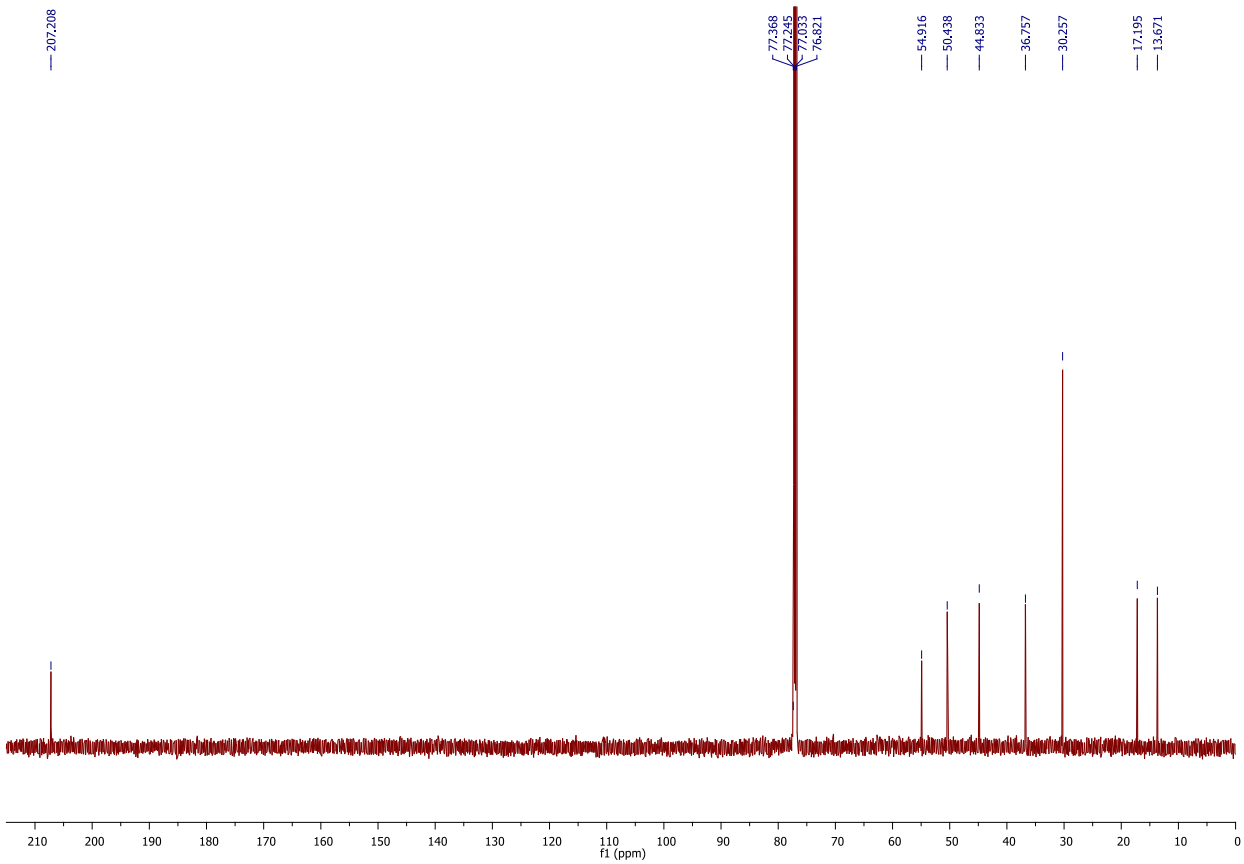


***N*-*tert*-Butyl-3-oxohexane-1-sulfonamide 25a**

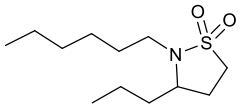


Using Method D, *N*-tert-butyl-3-oxohexane-1-sulfonamide **25a** was isolated as a colourless oil (27 mg, 0.11 mmol, 40%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.18 (br s, NH, 1H), 3.37-3.33 (m, 2H), 2.96-2.92 (m, 2H), 2.46 (t, *J* = 7.0 Hz, 2H), 1.64 (sextet, *J* = 7.0 Hz, 2H), 1.41 (s, 9H), 0.93 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.2 (C), 54.9 (C), 50.4 (CH_2), 44.8 (CH_2), 36.8 (CH_2), 30.3 (CH_3), 17.2 (CH_2), 13.7 (CH_3); IR (thin film) 3288, 2966, 2940, 2875, 1716, 1316, 1135 cm^{-1}; LRMS (CI) 236 (15, $[M+H]^+$), 220 (25), 163 (100); HRMS (CI) calcd for $C_{10}H_{22}NO_3S$ $[M+H]^+$ 236.1320, observed 236.1325.



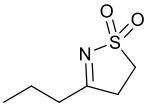


2-Hexyl-3-propyl-1,2-thiazolidine 1,1-dioxide 26[7]

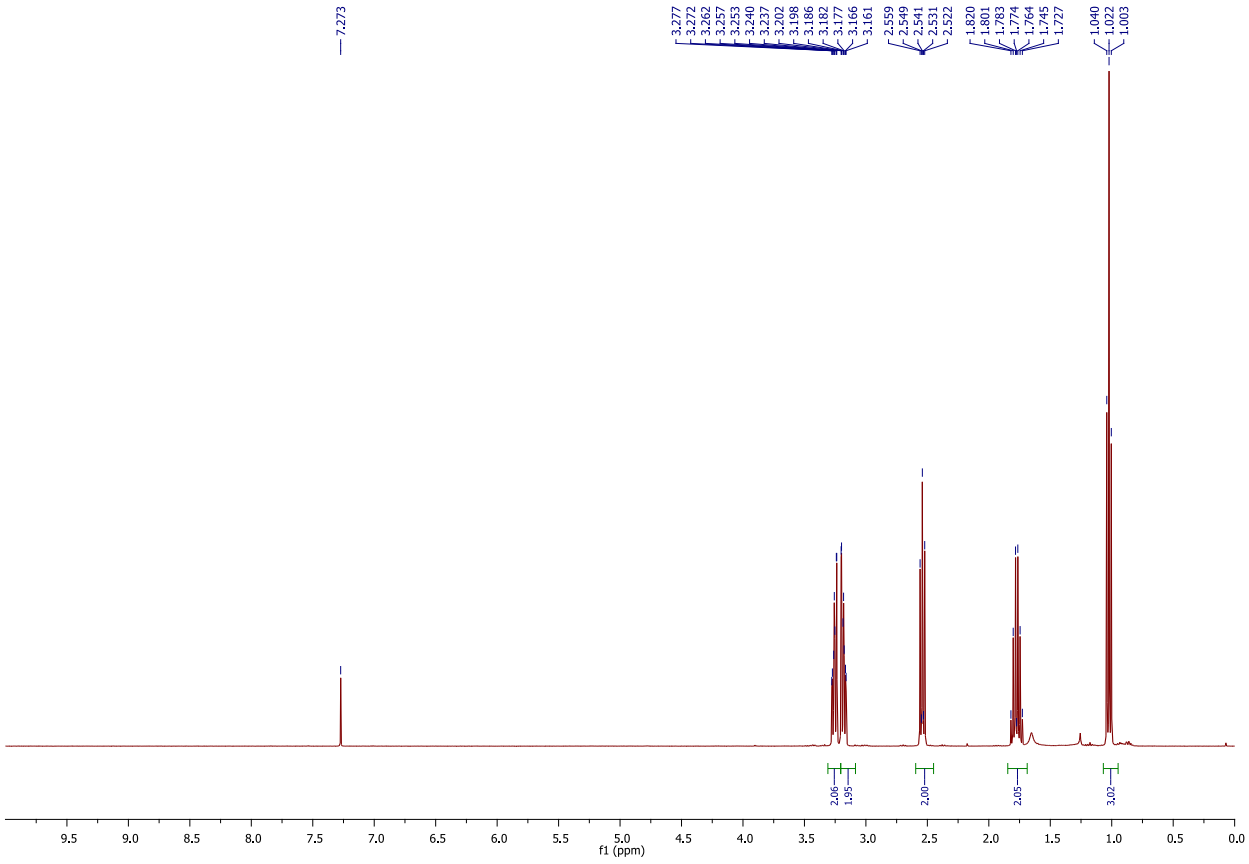


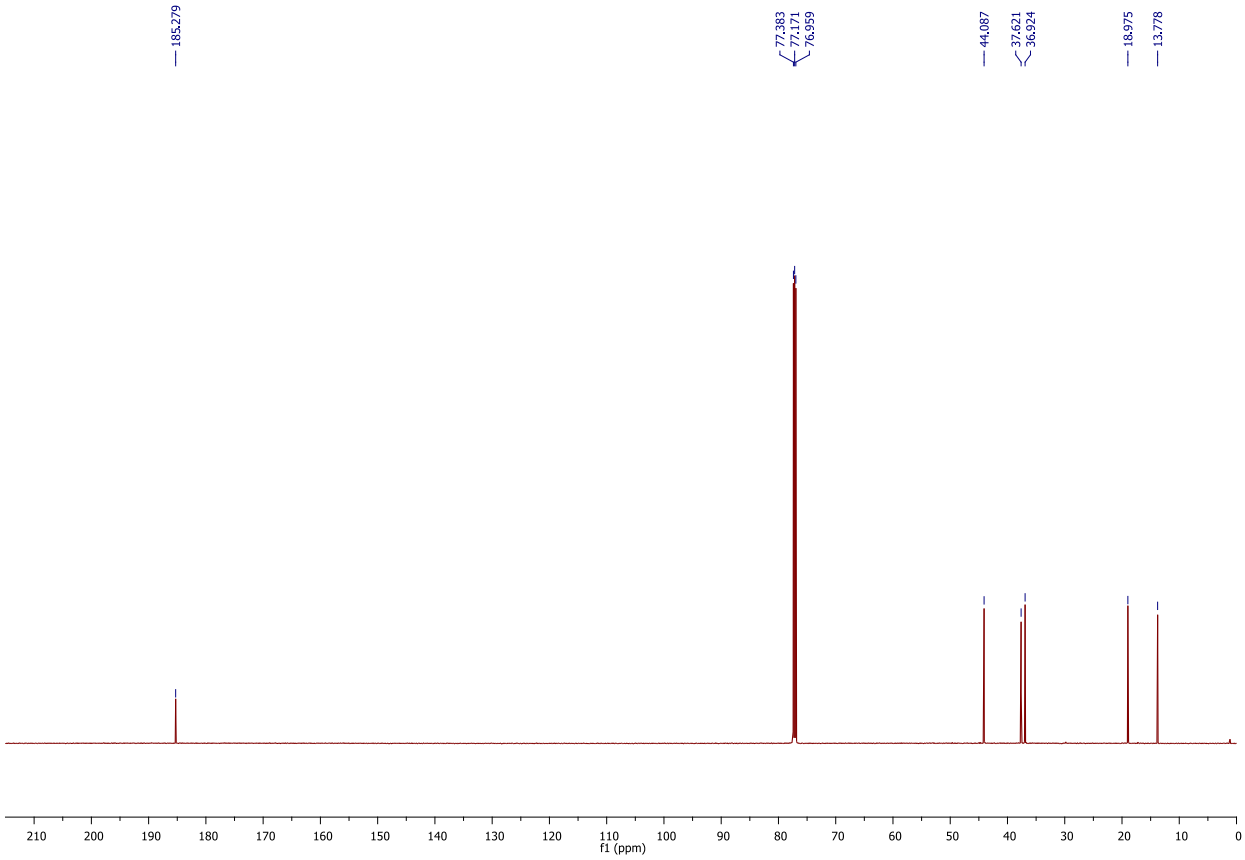
A solution of *N*-hexyl-3-oxohexane-1-sulfonamide **23a** (50 mg, 0.19 mmol) in TFA (4 mL) was left to stir at 21 °C for 15 min. Then was added sodium cyanoborohydride (12 mg, 0.19 mmol) and the reaction mixture left to stir for 30 min. Then was added further sodium cyanoborohydride (24 mg, 0.38 mmol) and the reaction mixture left to stir for a further 20 min. The solvent was removed *in vacuo*, the crude residue diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (3 × 100 mL) and 2M HCl (3 × 100 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude residue was purified by column chromatography (50% Et_2O/petrol) to afford 2-hexyl-3-propyl-isothiazolidine 1,1-dioxide **26** as a colourless oil (41 mg, 0.17 mmol, 87%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.34-3.30 (m, 1H), 3.22 (ddd, *J* = 12.5, 8.0, 4.5 Hz, 1H), 3.16 (ddd, *J* = 12.5, 8.0, 7.0 Hz, 1H), 3.03-2.97 (m, 2H), 2.44-2.37 (m, 1H), 2.06-2.00 (m, 1H), 1.75-1.70 (m, 1H), 1.65-1.24 (m, 11H), 0.98 (t, *J* = 7.5 Hz, 3H). 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 58.1 (CH), 46.5 (CH_2), 43.8 (CH_2), 36.0 (CH_2), 31.5 (CH_2), 28.6 (CH_2), 26.7 (CH_2), 25.0 (CH_2), 22.6 (CH_2), 17.8 (CH_2), 14.1 (CH_3), 14.1 (CH_3); IR (thin film) 2957, 2930, 2872, 1305, 1134 cm^{-1}; LRMS (CI) 248 (60, $[M+H]^+$), 204 (100); HRMS (CI) calcd for $C_{12}H_{26}NO_2S$ $[M+H]^+$ 248.1684, observed 248.1686.

3-Propyl-4,5-dihydro-1,2-thiazole 1,1-dioxide 27

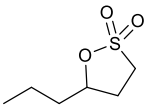


To a solution of pentafluorophenyl 3-oxohexane-1-sulfonate **15a** (0.29 mmol) in CH_2Cl_2 (2 mL) was bubbled through NH_3 (g) for 45 min at 0 °C. Then the reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with 2M HCl (3 × 20 mL) and sat. K_2CO_3 (3 × 20 mL), dried ($MgSO_4$) and the solvent removed *in vacuo* to afford 3-propyl-4,5-dihydro-isothiazole 1,1-dioxide **27** as a white solid (31 mg, 0.19 mmol, 67%): m.p. 68-70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.28-2.24 (m, 2H), 3.20-3.16 (m, 2H), 2.54 (t, *J* = 7.5 Hz, 2H), 1.77 (sextet, *J* = 7.5 Hz, 2H), 1.02 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.9 (C), 44.0 (CH_2), 37.5 (CH_2), 36.8 (CH_2), 18.9 (CH_2), 13.7 (CH_3); IR (solid) 2966, 2929, 2872, 1617, 1326, 1144 cm^{-1}; LRMS (CI) 162 (100, $[M+H]^+$); HRMS (CI) calcd for $C_6H_{12}NO_2S$ $[M+H]^+$ 162.0589, observed 162.0591.

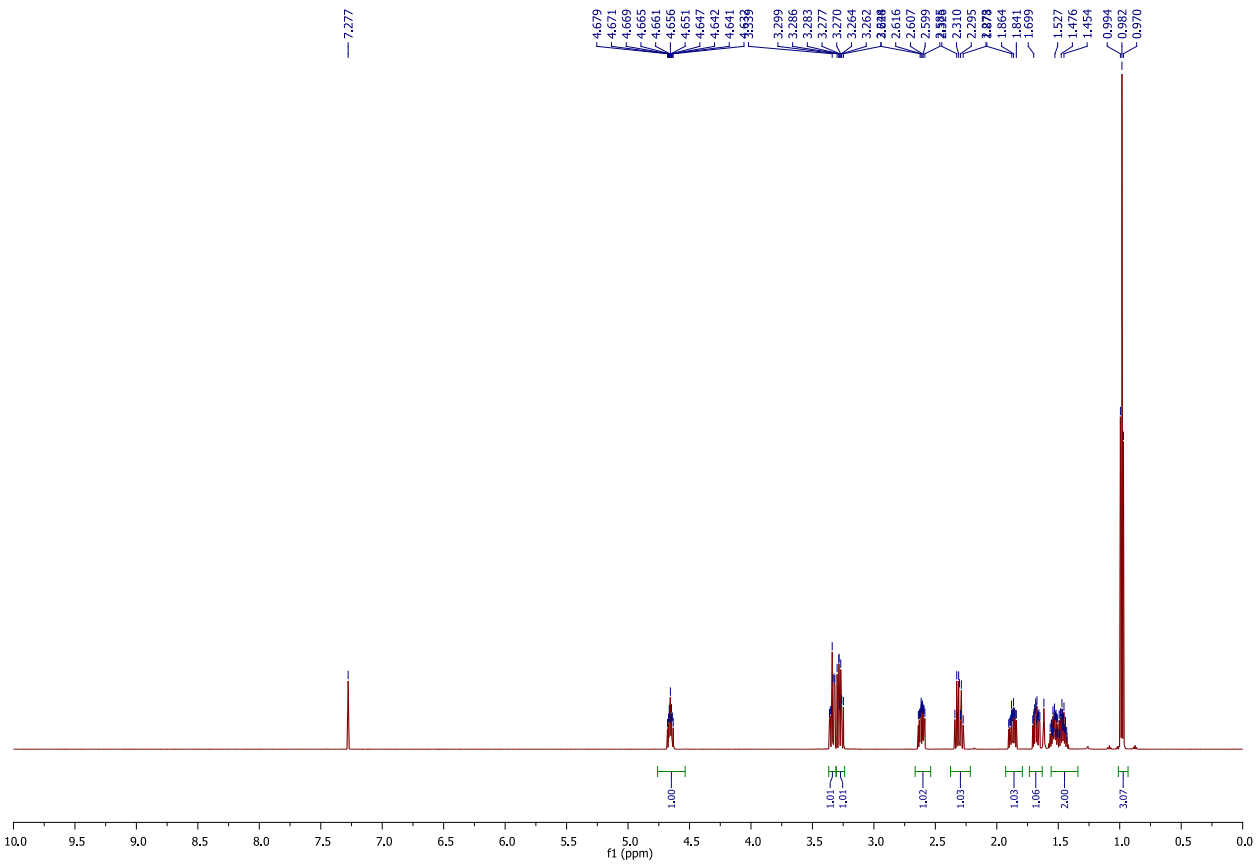


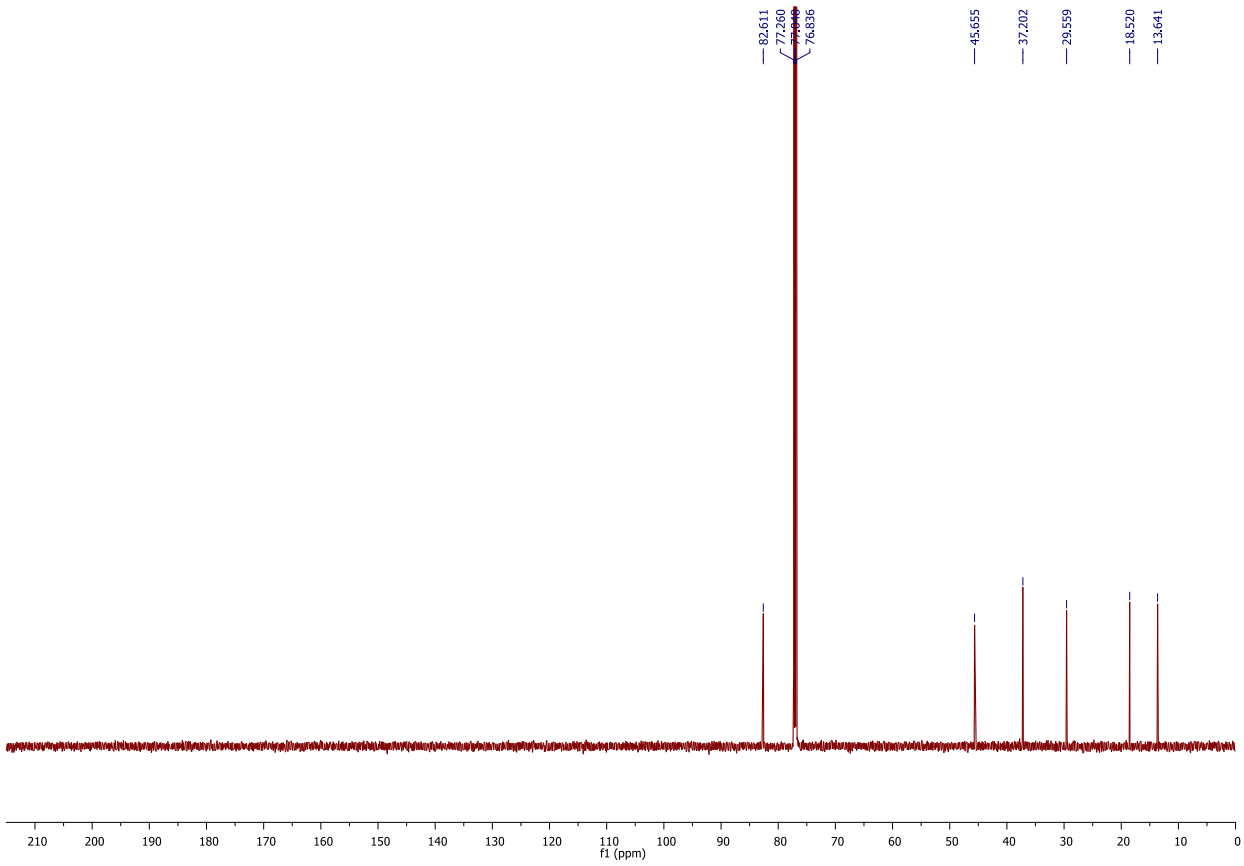


5-Propyl-1,2-oxathiolane 2,2-dioxide 29

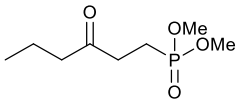


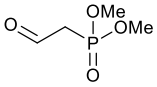
To a mixture of pentafluorophenyl 3-oxohexane-1-sulfonate **15a** (100 mg, 0.29 mmol) and sodium borohydride (22 mg, 0.58 mmol) was added CH_2Cl_2 (4 mL) and MeOH (12 mL) and the reaction mixture left to stir for 30 min. Then was added further sodium borohydride (22 mg, 0.58 mmol) and the reaction mixture left to stir for a further 10 min. The solvents were removed *in vacuo*, the crude residue diluted with Et_2O (50 mL), washed with sat. $NaHCO_3$ (3 × 100 mL), dried ($MgSO_4$) and the solvent removed *in vacuo* to afford 5-propyl-1,2-oxathiolane 2,2-dioxide **29** as a colourless oil (33 mg, 0.20 mmol, 71%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.66 (ddt, *J* = 12.0, 8.5, 5.0 Hz, 1H), 3.34 (ddd, *J* = 12.0, 9.0, 4.0 Hz, 1H), 3.27 (ddd, *J* = 12.0, 9.5, 8.0 Hz, 1H), 2.64-2.57 (m, 1H), 2.34-2.37 (m, 1H), 1.89-1.84 (m, 1H), 1.71-1.65 (m, 1H), 1.57-1.42 (m, 2H), 0.98 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 82.6 (CH), 45.7 (CH_2), 37.2 (CH_2), 29.6 (CH_2), 18.5 (CH_2), 13.6 (CH_3); IR (thin film) 2963, 2877, 1340, 1157 cm^{-1}; LRMS (CI) 165 (100, $[M+H]^+$); HRMS (CI) calcd for $C_6H_{13}O_3S$ $[M+H]^+$ 165.0585, observed 165.0587.

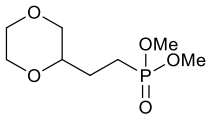




Hydroacylation of dimethyl vinyl phosphonate with n-butanal in 1,4-dioxane at 20 °C[8,9]







To a stirring solution of dimethyl vinyl phosphonate (136 mg, 1 mmol) in 1,4-dioxane (1 mL) was added n-butanal (361 mg, 5 mmol) and the reaction mixture stirred at 20 °C for 144 h. The reaction mixture was concentrated *in vacuo* and purified by column chromatography (neat CH_2Cl_2 to 5% CH_3OH/CH_2Cl_2) to give dimethyl (3-oxohexyl)phosphonate **31a**, dimethyl (2-oxoethyl)phosphonate[1] **32** and dimethyl [2-(1,4-dioxan-2-yl)ethyl]phosphonate **33.**

Data for dimethyl (3-oxohexyl)phosphonate **31a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.67 (dt, $J_{H\text{-}P}$ = 15.5 and J = 7.5 Hz, 2H), 2.38 (t, J = 7.5 Hz, 2H), 2.00 (dt, $J_{H\text{-}P}$ = 18.0 and J = 7.5 Hz, 2H), 1.59 (sextet, J = 7.5 Hz, 2H), 0.89 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.1 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 52.5 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 44.6 (CH_2), 35.3 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 18.3 (d, $J_{C\text{-}P}$ = 143.0 Hz, CH_2), 17.3 (CH_2), 13.7 (CH_3); IR (thin film) 2960, 1715, 1245 cm^{-1}; LRMS (CI) 209 (100, $[M+H]^+$); HRMS (CI) calcd for $C_8H_{18}O_4P$ $[M+H]^+$ 209.0943, observed 209.0947.

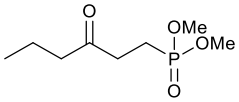
Data for dimethyl (2-oxoethyl)phosphonate[1] **32**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.68 (td, J = 3.0 Hz, $J_{H\text{-}P}$ = 1.5 Hz, 1H), 3.81 (d, $J_{H\text{-}P}$ = 11.5 Hz, 6H), 3.10 (dd, $J_{H\text{-}P}$ = 22.0 and J = 3.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.6 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH), 53.1 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 42.1 (d, $J_{C\text{-}P}$ = 128.0 Hz, CH_2); IR (thin film) 2954, 2859, 1720, 1240 cm^{-1}; LRMS (CI) 153 (100, $[M+H]^+$); HRMS (CI) calcd for $C_4H_{10}O_4P$ $[M+H]^+$ 153.0317, observed 153.0318.

Data for dimethyl [2-(1,4-dioxan-2-yl)ethyl]phosphonate **33**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.80-3.69 (m, 10H), 3.62-3.53 (m, 2H), 3.27 (dd, J = 11.5, 10.0 Hz, 1H), 2.04-1.95 (m, 1H), 1.82-1.62 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 74.7 (d, $J_{C\text{-}P}$ = 16.0 Hz, CH), 70.9 (CH_2), 66.7 (CH_2), 66.5 (CH_2), 52.3 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 52.3 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 24.4 (d, $J_{C\text{-}P}$ = 4.5 Hz, CH_2), 20.2 (d, $J_{C\text{-}P}$ = 142.0 Hz, CH_2); IR (thin film) 2957, 2853, 1244 cm^{-1}; LRMS (FAB) 247 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_8H_{17}NaO_5P$ $[M+Na]^+$ 247.0711, observed 247.0714.

Typical procedure for hydroacylation of vinyl phosphonate 30 - Method E

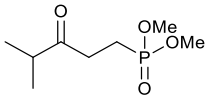
To a solution of vinyl phosphonate **30** (1 mmol) in 1,4-dioxane (1 mL) was added aldehyde (5 mmol) and the reaction mixture stirred at 300 rpm at 60 °C for 24 h unless otherwise stated below. The reaction mixture was concentrated *in vacuo* and the crude residue purified as described below.

Dimethyl (3-oxohexyl)phosphonate 31a[9]

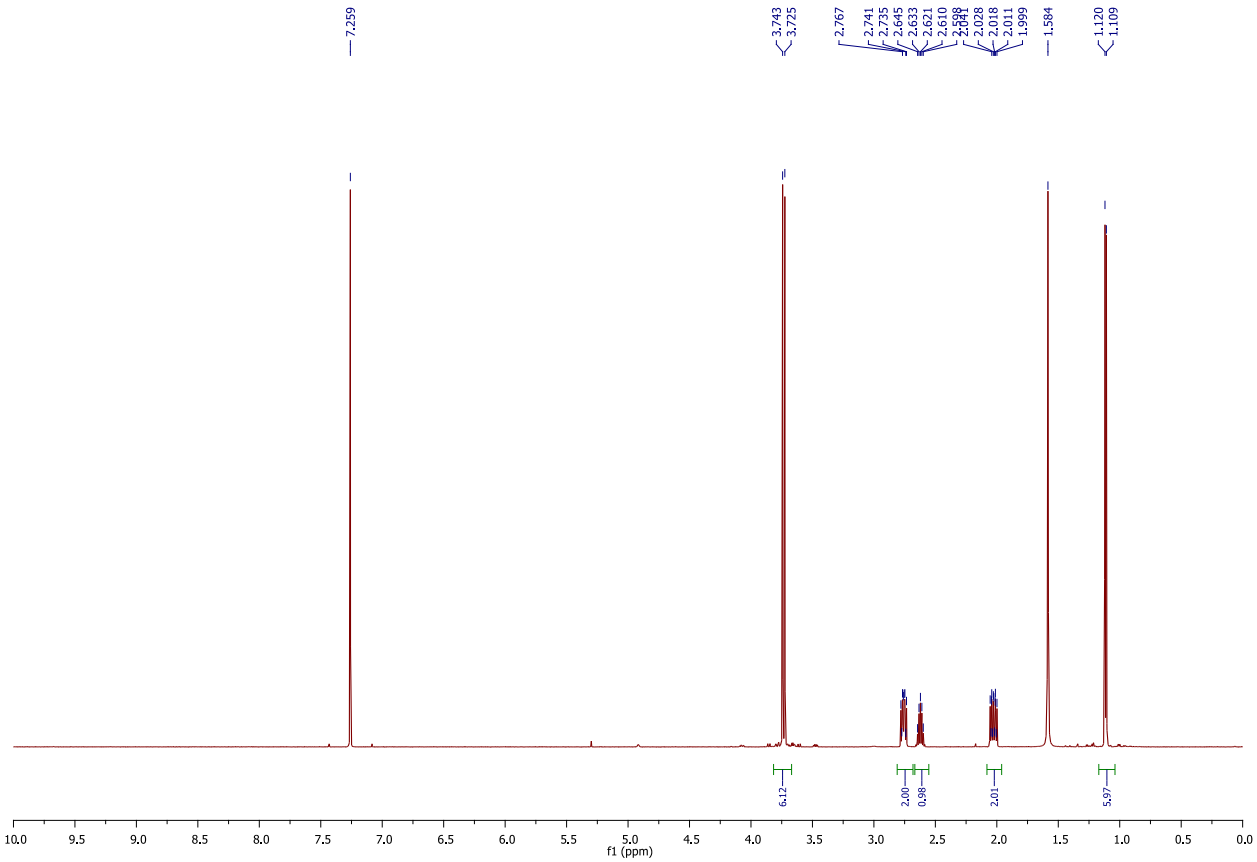


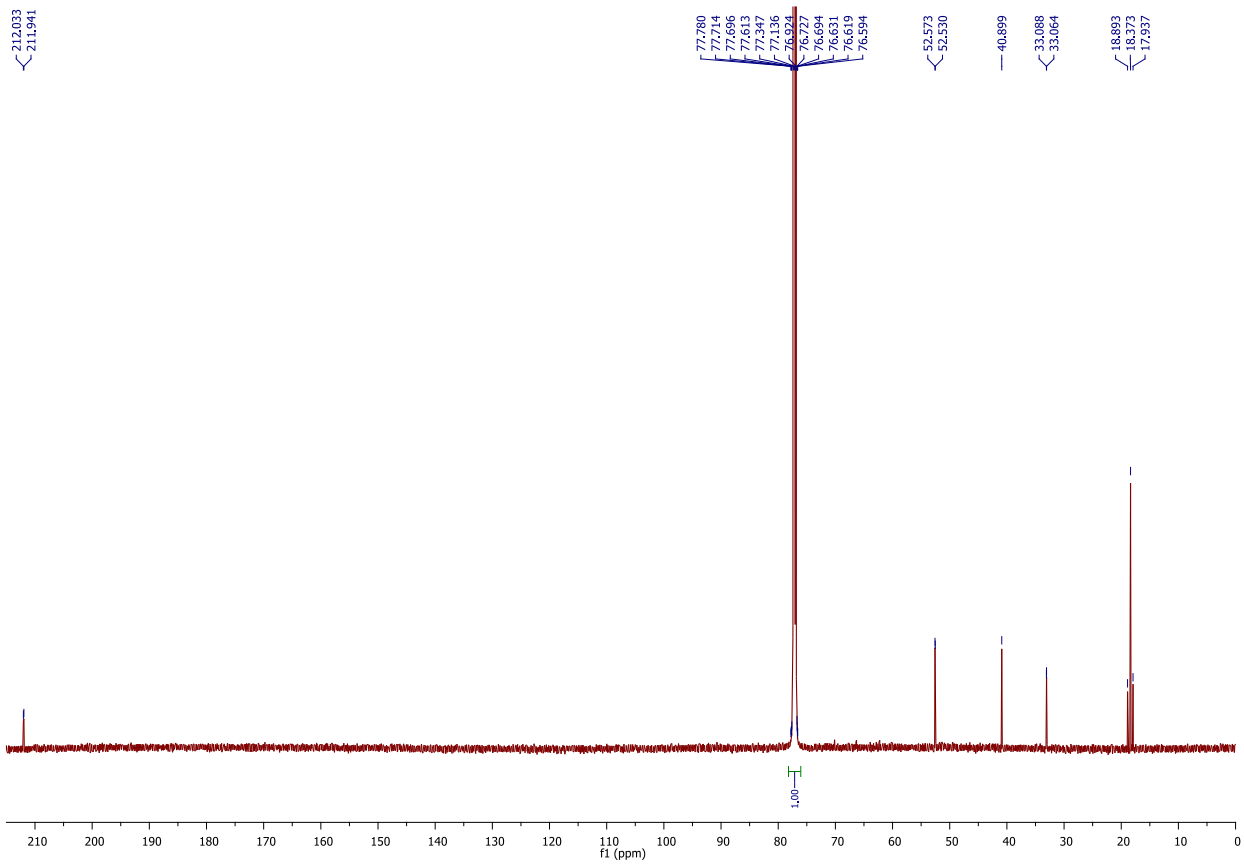
Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% MeOH/CH_2Cl_2) gave dimethyl (3-oxohexyl)phosphonate **31a** as a colourless oil (146 mg, 0.70 mmol, 70%). Data matched that as described above.

Dimethyl (4-methyl-3-oxopentyl)phosphonate 31b

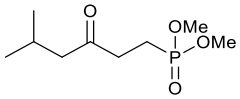


Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% MeOH/CH_2Cl_2) gave dimethyl (4-methyl-3-oxopentyl)phosphonate **31b** as a colourless oil (83 mg, 0.40 mmol, 40%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.73 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.75 (dt, $J_{H\text{-}P}$ = 15.5 and J = 7.0 Hz, 2H), 2.31 (septet, J = 7.0 Hz, 1H), 2.03 (dt, $J_{H\text{-}P}$ = 18.0 and J = 7.0 Hz, 2H), 1.11 (d, J = 7.0 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.0 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 52.5 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 40.9 (CH), 33.0 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 18.4 (CH_3), 18.3 (d, $J_{C\text{-}P}$ = 144.0 Hz, CH_2); IR (thin film) 2965, 2853, 1713, 1242 cm^{-1}; LRMS (EI) 208 (20, $[M]^+$), 165 (100); HRMS (EI) calcd for $C_8H_{17}O_4P$ $[M]^+$ 208.0859, observed 208.0863.



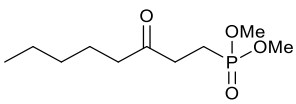


Dimethyl (5-methyl-3-oxohexyl)phosphonate 31c[9]



Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% MeOH/CH_2Cl_2) gave (dimethyl (5-methyl-3-oxohexyl)phosphonate **31c** as a colourless oil (144 mg, 0.65 mmol, 65%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.74 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.69 (dt, $J_{H\text{-}P}$ = 15.5 and J = 7.5 Hz, 2H), 2.31 (d, J = 7.0 Hz, 2H), 2.15 (nonet, J = 7.0 Hz, 1H), 2.03 (dt, $J_{H\text{-}P}$ = 18.0 and J = 7.5 Hz, 2H), 0.89 (d, J = 7.0 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.3 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 52.4 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 51.6 (CH_2), 35.7 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 24.7 (CH), 22.5 (CH_3), 18.2 (d, $J_{C\text{-}P}$ = 144.0 Hz, CH_2); IR (thin film) 2957, 2873, 1714, 1245 cm^{-1}; LRMS (ES) 245 (100, $[M+Na]^+$); HRMS (ES) calcd for $C_9H_{19}O_4PNa$ $[M+Na]^+$ 245.0919, observed 245.0915.

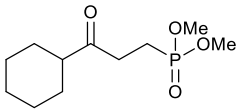
Dimethyl (3-oxooctyl)phosphonate 31d[9]



Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% MeOH/CH_2Cl_2) gave dimethyl (3-oxooctyl)phosphonate **31d** as a colourless oil (170 mg, 0.72 mmol, 72%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.74 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.72 (dt, $J_{H\text{-}P}$ = 15.5 and J = 7.5 Hz, 2H),

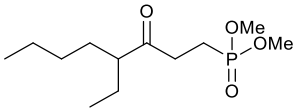
2.43 (t, J = 7.5 Hz, 2H), 2.00 (dt, $J_{H\text{-}P}$ = 18.0 and J = 7.5 Hz, 2H), 1.59 (quintet, J = 7.5 Hz, 2H), 1.35-1.24 (m, 4H), 0.89 (t, J = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.3 (d, $J_{C\text{-}P}$ = 14.0 Hz C), 52.4 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 42.6 (CH_2), 35.2 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 31.4 (CH_2), 23.5 (CH_2), 22.4 (CH_2), 18.2 (d, $J_{C\text{-}P}$ = 143.0 Hz, CH_2), 13.9 (CH_3); IR (thin film) 2956, 2934, 2856, 1717, 1243 cm^{-1}; LRMS (FAB) 259 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_{10}H_{21}O_4PNa$ $[M+Na]^+$ 259.1076, observed 259.1070.

Dimethyl (3-cyclohexyl-3-oxopropyl)phosphonate 31e[9]

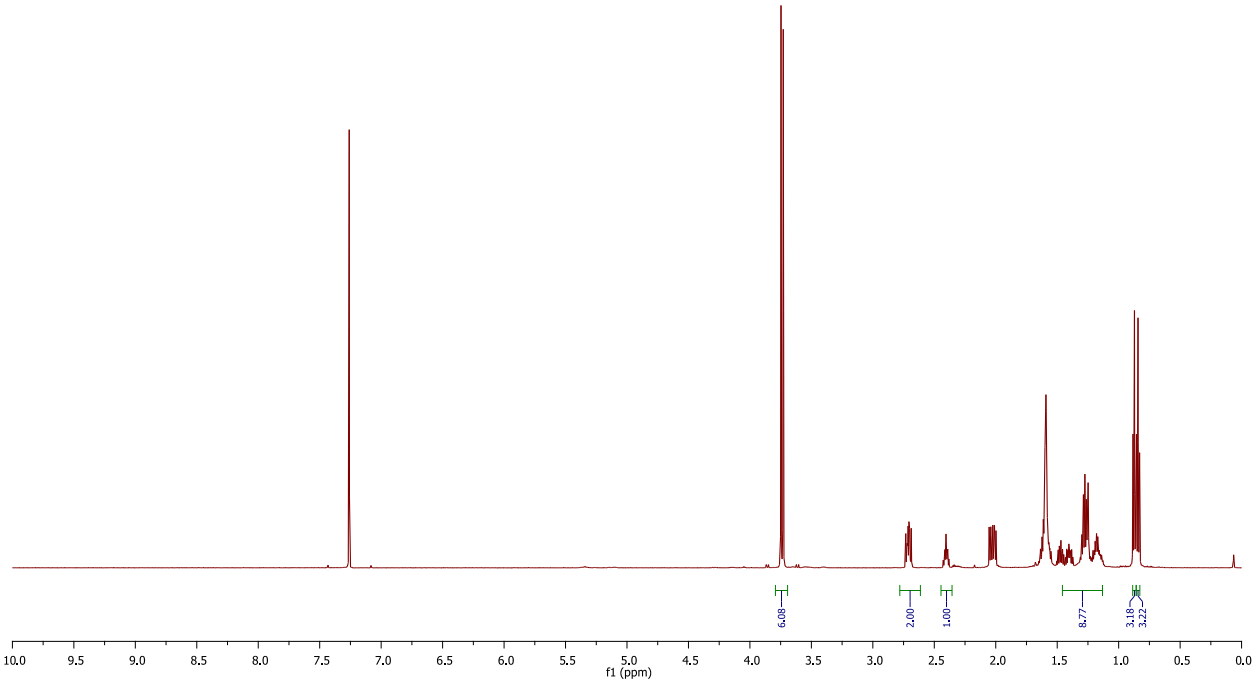


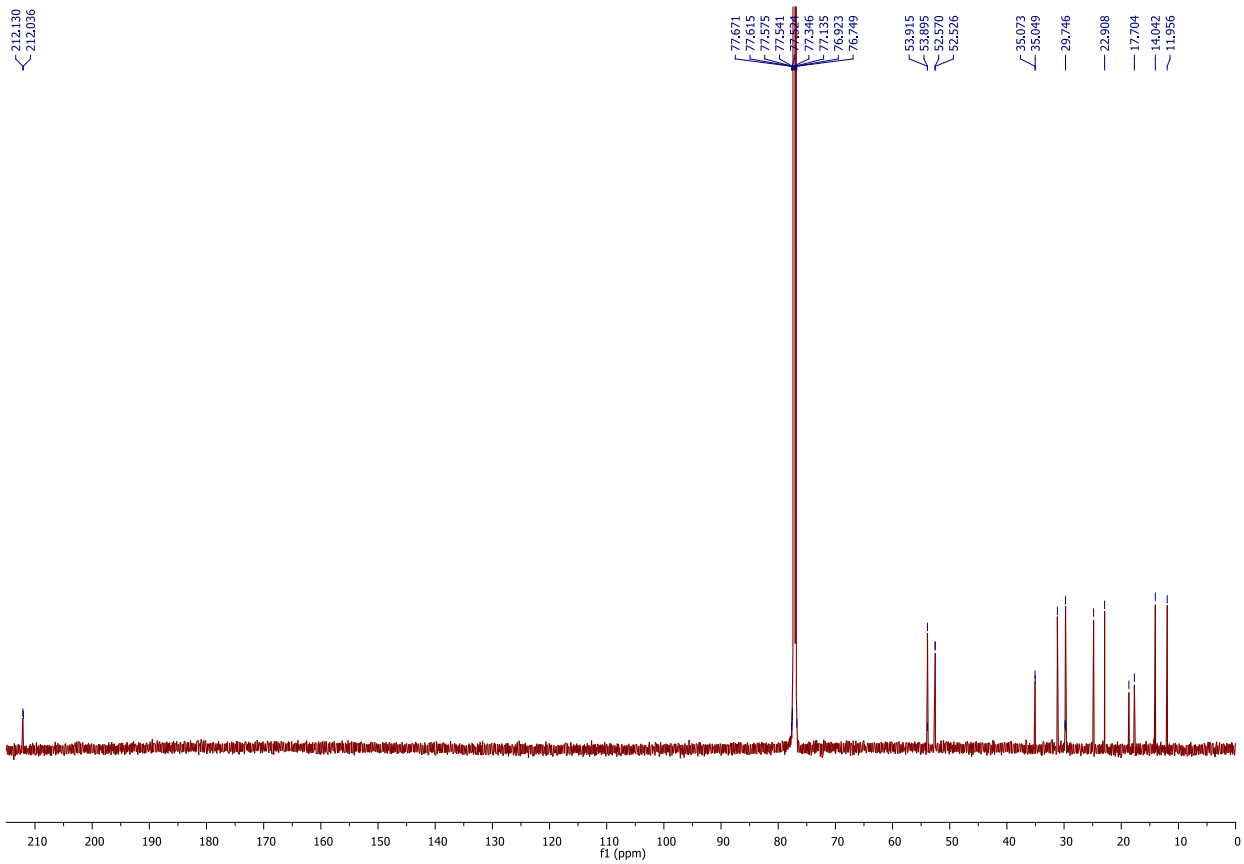
Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% MeOH/CH_2Cl_2) gave dimethyl (3-cyclohexyl-3-oxopropyl)phosphonate **31e** as a colourless oil (149 mg, 0.60 mmol, 60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.74 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.75 (dt, $J_{H\text{-}P}$ = 15.5 and J = 7.5 Hz, 2H), 2.36 (tt, J = 11.0, 3.0 Hz, 1H), 2.00 (dt, $J_{H\text{-}P}$ = 18.0 and J = 7.5 Hz, 2H), 1.87-1.18 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.1 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 52.4 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 50.7 (CH), 33.2 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 28.5 (CH_2), 25.8 (CH_2), 25.6 (CH_2), 18.2 (d, $J_{C\text{-}P}$ = 143.0 Hz, CH_2); IR (thin film) 2930, 2854, 1709, 1243 cm^{-1}; LRMS (EI) 248 (100, $[M]^{+\cdot}$); HRMS (EI) calcd for $C_{11}H_{21}O_4P$ $[M]^{+\cdot}$ 248.1172, observed 248.1176.

Dimethyl (4-ethyl-3-oxooctyl)phosphonate 31f

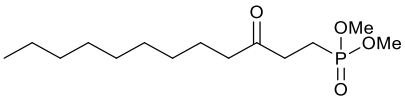


Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% MeOH/CH_2Cl_2) gave dimethyl (4-ethyl-3-oxooctyl)phosphonate **31f** as a colourless oil (137 mg, 0.52 mmol, 52%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.73 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.71 (dt, $J_{H\text{-}P}$ = 11.5 and J = 7.5 Hz, 2H), 2.43-2.38 (m, 1H), 2.02 (dt, $J_{H\text{-}P}$ = 18.0 and J = 7.0 Hz, 2H), 1.60-1.15 (m, 8H), 0.87 (t, J = 7.5 Hz, 3H), 0.84 (t, J = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.0 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 53.9 (CH), 52.5 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 35.0 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 31.2 (CH_2), 29.7 (CH_2), 24.8 (CH_2), 22.9 (CH_2), 18.6 (d, $J_{C\text{-}P}$ = 144.0 Hz, CH_2), 14.0 (CH_3), 12.0 (CH_3); IR (thin film) 2958, 2929, 2857, 1713, 1247 cm^{-1}; LRMS (EI) 264 (25, $[M]^+$), 165 (100); HRMS (EI) calcd for $C_{12}H_{25}O_4P$ $[M]^+$ 264.1485, observed 264.1489.

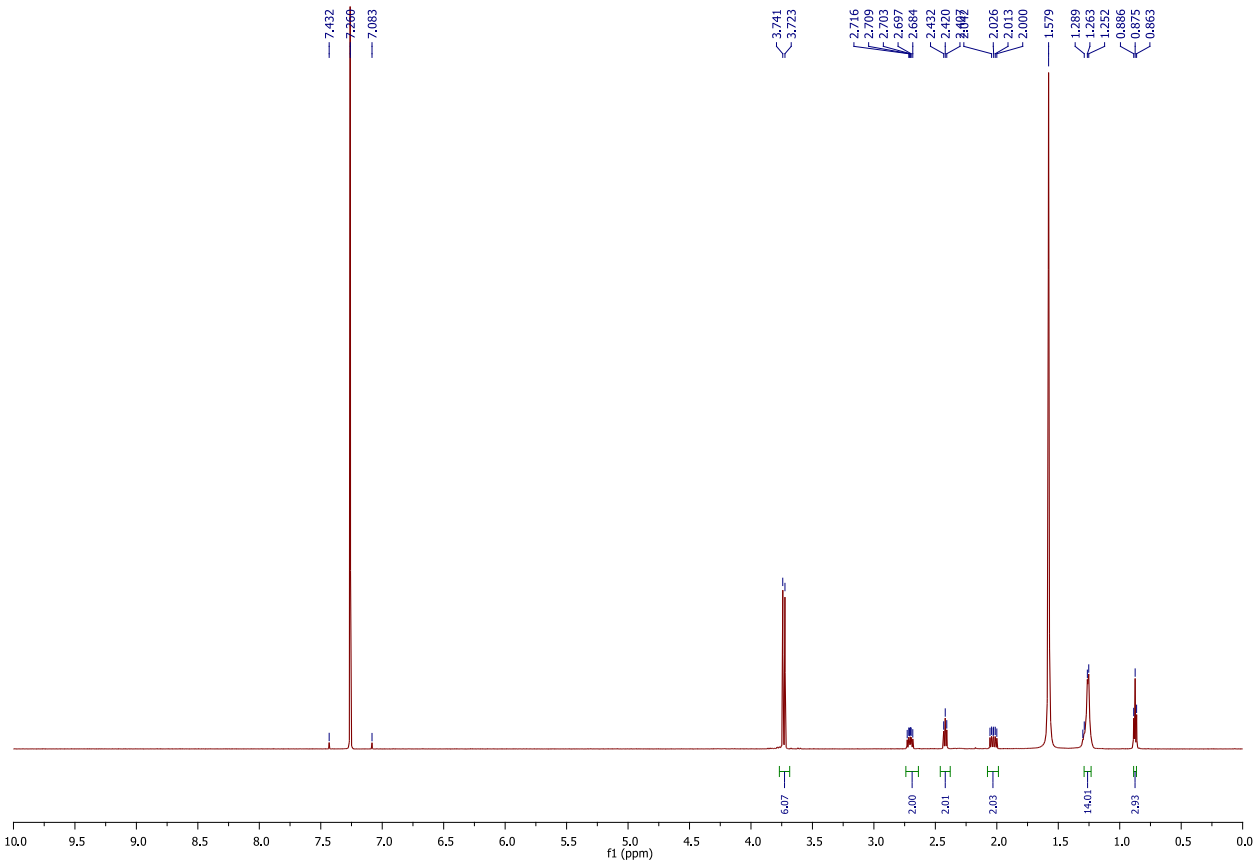


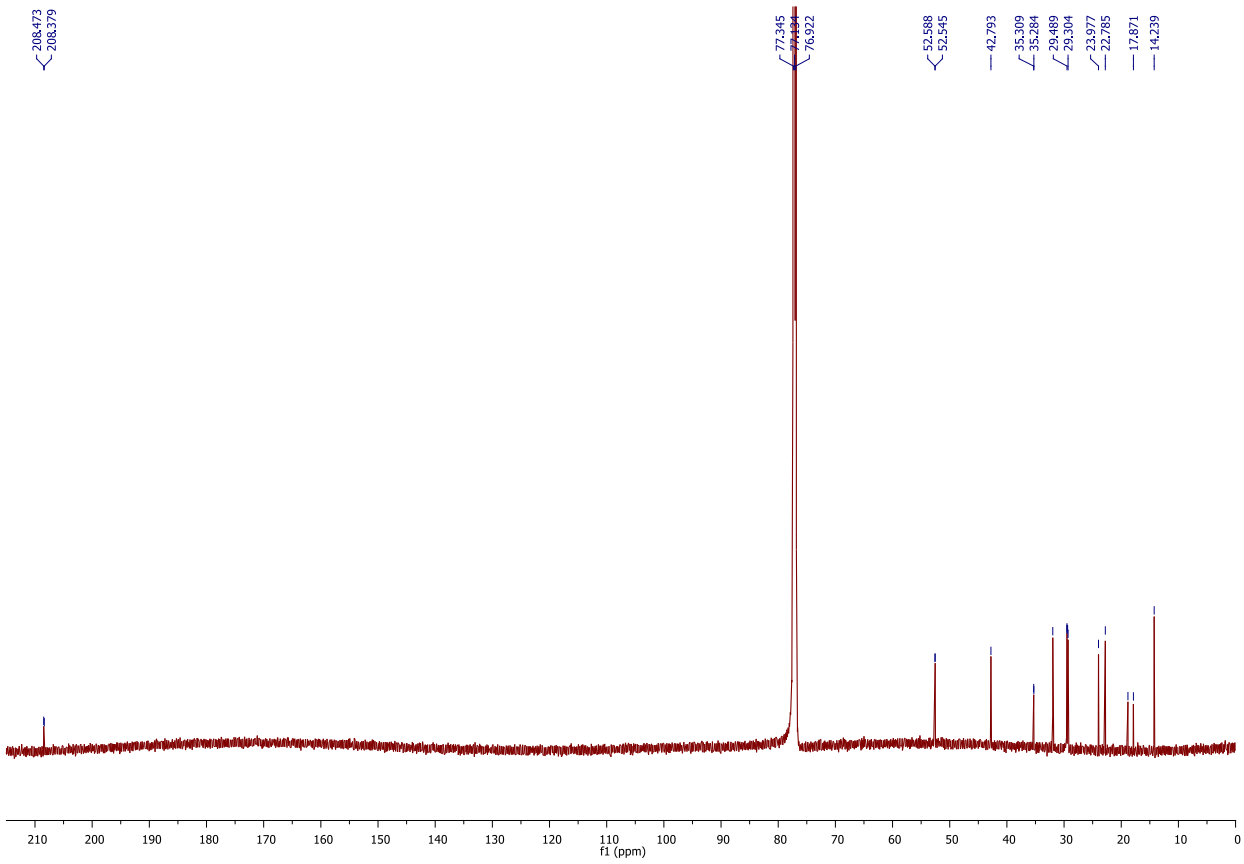


Dimethyl (3-oxododecyl)phosphonate 31g

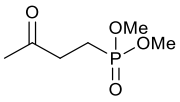


Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% MeOH/CH_2Cl_2) gave dimethyl (3-oxododecyl)phosphonate **31g** as a colourless oil (161 mg, 0.55 mmol, 55%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.73 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.71 (dt, $J_{H\text{-}P}$ = 11.5 and J = 7.5 Hz, 2H), 2.42 (t, J = 7.5 Hz, 6H), 2.02 (dt, $J_{H\text{-}P}$ = 18.0 and J = 7.0 Hz, 2H), 1.28-1.24 (m, 14H), 0.87 (t, J = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.4 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 52.5 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 42.8 (CH_2), 35.3 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 32.0 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 24.0 (CH_2), 22.8 (CH_2), 18.6 (d, $J_{C\text{-}P}$ = 144.0 Hz, CH_2), 14.2 (CH_3); IR (thin film) 2925, 2854, 1720, 1213 cm^{-1}; LRMS (CI) 293 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{14}H_{30}O_4P$ $[M+H]^+$ 293.1882, observed 293.1890.



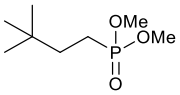


Dimethyl (3-oxobutyl)phosphonate 31h[9]



Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% MeOH/CH_2Cl_2) gave dimethyl (3-oxobutyl)phosphonate **31h** as a colourless oil (122 mg, 0.68 mmol, 68%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.74 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.76 (dt, $J_{H\text{-}P}$ = 15.5 and J = 7.5 Hz, 2H), 2.18 (s, 3H), 2.02 (dt, $J_{H\text{-}P}$ = 18.0 and J = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 205.7 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 52.5 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 36.2 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 29.7 (CH_3), 18.2 (d, $J_{C\text{-}P}$ = 143.0 Hz, CH_2); IR (thin film) 2958, 1717, 1239 cm^{-1}; LRMS (EI) 180 (5, $[M]^{+\cdot}$), 110 (100); HRMS (EI) calcd for $C_6H_{13}O_4P$ $[M]^{+\cdot}$ 180.0546, observed 180.0548.

Dimethyl (3,3-dimethylbutyl)phosphonate[9]



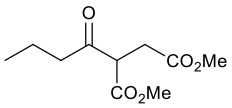
Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% CH_3OH/CH_2Cl_2) to give dimethyl (3,3-dimethylbutyl)phosphonate as a colourless oil (89 mg, 0.46 mmol, 46%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.75 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 1.74-1.67 (m, 2H), 1.50-1.46 (m, 2H), 0.89 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 52.4 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 35.7 (d, $J_{C\text{-}P}$ = 4.0

Hz, CH_2), 30.4 (d, J_{C-P} = 18.0 Hz, C), 28.7 (CH_3), 20.1 (d, J_{C-P} = 140.0 Hz, CH_2); IR (thin film) 2955, 2868, 1245 cm^{-1}; LRMS (CI) 195 (100, $[M+H]^+$); HRMS (CI) calcd for $C_8H_{20}O_3P$ $[M+H]^+$ 195.1150, observed 195.1153.

Typical procedure for the hydroacylation of alkenes 35, 40, 41, 43 and 45 - Method F

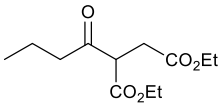
To a solution of alkene (1 mmol) in 1,4-dioxane (3 mL) was added aldehyde (5 mmol) and the reaction mixture stirred at 300 rpm at 60 °C for the time specified below. The solvent removed *in vacuo* and the crude residue purified as described below to afford the desired hydroacylation product.

2-Butyryl-succinic acid dimethyl ester 36a[10]



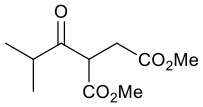
Using Method F, reaction was complete after 3 days. Purification by column chromatography (10-30% Et_2O/petrol) gave 2-butyryl-succinic acid dimethyl ester **36a** and its enol tautomer in a >95:<5 ratio as a colourless oil (151 mg, 0.70 mmol, 70%). Only the ^1H NMR peaks for 2-butyryl-succinic acid dimethyl ester have been assigned as it predominates: ^1H NMR (500 MHz, $CDCl_3$) δ 3.95 (dd, *J* = 8.0, 6.5 Hz, 1H), 3.71 (s, 3H), 3.64 (s, 3H), 2.94 (dd, *J* = 17.5, 8.0 Hz, 1H), 2.80 (dd, *J* = 17.5, 6.5 Hz, 1H), 2.65 (dt, *J* = 17.5, 7.5 Hz, 1H), 2.61 (dt, *J* = 17.5, 7.5 Hz, 1H), 1.59 (sextet, *J* = 7.5 Hz, 2H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.8 (C), 171.8 (C), 168.9 (C), 53.8 (CH), 52.7 (CH_3), 52.0 (CH_3), 44.6 (CH_2), 32.1 (CH_2), 16.8 (CH_2), 13.4 (CH_3); IR (thin film) 2959, 2880, 1734, 1717 cm^{-1}; LRMS (CI) 217 (100, $[M+H]^+$), 185 (27); HRMS (CI) calcd for $C_{10}H_{17}O_5$ $[M+H]^+$ 217.1076, observed 217.1072.

2-Butyryl-succinic acid diethyl ester 42[10]



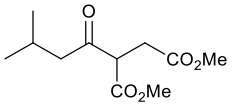
Using Method F, reaction was complete after 4 days. Purification by column chromatography (10-20% Et_2O/petrol) gave 2-butyryl-succinic acid diethyl ester **42** and its enol tautomer in a >95:<5 ratio as a colourless oil (146 mg, 0.60 mmol, 60%). Only the ^1H NMR peaks for 2-butyryl-succinic acid diethyl ester have been assigned as it predominates: ^1H NMR (400 MHz, $CDCl_3$) δ 4.21 (q, *J* = 7.0, 2H), 4.12 (q, *J* = 7.0 Hz, 2H), 3.97 (dd, *J* = 8.5, 6.0 Hz, 1H), 2.98 (dd, *J* = 17.5, 8.5 Hz, 1H), 2.83 (dd, *J* = 17.5, 6.0 Hz, 1H), 2.70 (dt, *J* = 17.5, 7.0 Hz, 1H), 2.61 (dt, *J* = 17.5, 7.0 Hz, 1H), 1.65 (sextet, *J* = 7.0 Hz, 2H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.24 (t, *J* = 7.0 Hz, 3H), 0.93 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.0 (C), 171.4 (C), 168.5 (C), 61.8 (CH_2), 61.0 (CH_2), 54.0 (CH), 44.6 (CH_2), 32.4 (CH_2), 16.8 (CH_2), 14.1 (CH_3), 14.0 (CH_3), 13.5 (CH_3); IR (thin film) 2967, 2881, 1736, 1719 cm^{-1}; LRMS (CI) 245 (60, $[M+H]^+$), 199 (100); HRMS (CI) calcd for $C_{12}H_{21}O_5$ $[M+H]^+$ 245.1389, observed 245.1382.

2-Isobutyryl-succinic acid dimethyl ester 36b[10]



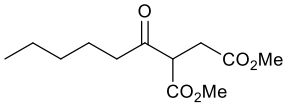
Using Method F, reaction was complete after 5 days. Purification by column chromatography (5-30% Et_2O/petrol) gave 2-isobutyryl-succinic acid dimethyl ester **36b** as a colourless oil (45 mg, 0.21 mmol, 21%). Only the ^1H NMR peaks for 2-isobutyryl-succinic acid dimethyl ester **36b** have been assigned as it predominates: ^1H NMR (600 MHz, $CDCl_3$) δ 4.20 (dd, *J* = 8.0 and 6.5 Hz, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 2.99-2.94 (m, 2H), 2.65 (dd, *J* = 17.5 and 6.5 Hz, 1H), 1.18 (d, *J* = 7.0 Hz, 3H), 1.14 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.8 (C), 171.8 (C), 169.1 (C), 52.8 (CH), 52.1 (CH_3), 52.0 (CH_3), 40.7 (CH_2), 32.3 (CH), 18.6 (CH_3), 17.8 (CH_3); IR (thin film) 2949, 2886, 1736, 1714 cm^{-1}; LRMS (CI) 217 (15, $[M+H]^+$), 86 (100); HRMS (CI) calcd for C10H17O5 $[M+H]^+$ 217.1076, observed 217.1066.

2-(3-Methyl-butyryl)-succinic acid dimethyl ester 36c[10]



Using Method F, reaction was complete after 3 days. Purification by column chromatography (10-30% Et_2O/petrol) gave 2-(3-methyl-butyryl)-succinic acid dimethyl ester **36c** and its enol tautomer in a >95:<5 ratio as a colourless oil (131 mg, 0.57 mmol, 57%). Only the ^1H NMR peaks for 2-(3-methyl-butyryl)-succinic acid dimethyl ester have been assigned as it predominates: ^1H NMR (600 MHz, $CDCl_3$) δ 3.98 (dd, *J* = 8.0, 6.5 Hz, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 3.01 (dd, *J* = 17.0, 8.0 Hz, 1H), 2.85 (dd, *J* = 17.0, 6.5 Hz, 1H), 2.58 (dd, *J* = 17.0, 7.5 Hz, 1H), 2.53 (dd, *J* = 17.0, 6.5 Hz, 1H), 2.24-2.17 (m, 1H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 203.4 (C), 171.8 (C), 168.9 (C), 54.2 (CH), 52.7 (CH_3), 52.1 (CH_3), 51.5 (CH_2), 32.1 (CH_2), 24.1 (CH), 22.5 (CH_3), 22.2 (CH_3); IR (thin film) 2957, 1738, 1719 cm^{-1}; LRMS (EI) 230 (15, $[M]^{+\cdot}$), 199 (100); HRMS (EI) calcd for $C_{11}H_{18}O_5$ $[M]^{+\cdot}$ 230.1149, observed 230.1143.

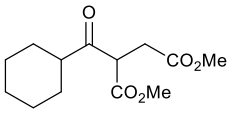
2-Hexanoyl-succinic acid dimethyl ester 36d[10]



Using Method F, reaction was complete after 3 days. Purification by column chromatography (10-30% Et_2O/petrol) gave 2-hexanoyl-succinic acid dimethyl ester **36d** and its enol tautomer in a >95:<5 ratio as a colourless oil (185 mg, 0.76 mmol, 76%). Only the ^1H NMR peaks for 2-hexanoyl-succinic acid dimethyl ester have been assigned as it predominates: ^1H NMR (400 MHz, $CDCl_3$) δ 4.00 (dd, *J* = 8.0, 6.5 Hz, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 3.00 (dd, *J* = 17.5, 8.0 Hz, 1H), 2.84 (dd, *J* = 17.5, 6.5 Hz, 1H), 2.71 (dt, *J* = 17.5, 7.5 Hz, 1H), 2.61 (dt, *J* = 17.5, 7.5 Hz, 1H), 1.59 (sextet, *J* = 7.5 Hz, 2H), 1.36-1.22 (m, 4H) 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150

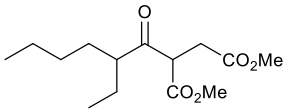
MHz, $CDCl_3$) δ 204.0 (C), 171.9 (C), 169.0 (C), 53.8 (CH_3), 52.8 (CH_3), 52.1 (CH), 42.8 (CH_2), 32.2 (CH_2), 31.1 (CH_2), 23.1 (CH_2), 22.4 (CH_2), 13.9 (CH_3); IR (thin film) 2959, 2934, 1738, 1720 cm^{-1}; LRMS (CI) 245 (15, $[M+H]^+$), 213 (85), 99 (100); HRMS (CI) calcd for $C_{12}H_{21}O_5$ $[M+H]^+$ 245.1389, observed 245.1382.

2-Cyclohexanecarbonyl-succinic acid dimethyl ester 36e[10]



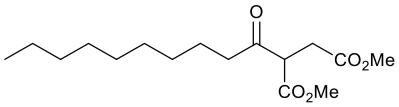
Using Method F, reaction was complete after 10 days. Purification by column chromatography (10-30% Et_2O/petrol) gave 2-cyclohexanecarbonyl-succinic acid dimethyl ester **36e** and its enol tautomer in a >95:<5 ratio as a colourless oil. Only the ^1H NMR peaks for 2-cyclohexanecarbonyl-succinic acid dimethyl ester have been assigned as it predominates: ^1H NMR (600 MHz, $CDCl_3$) δ 3.95 (dd, *J* = 8.0, 6.5 Hz, 1H), 3.75 (s, 3H), 3.65 (s, 3H), 2.96 (dd, *J* = 17.5, 8.0 Hz, 1H), 2.84 (dd, *J* = 17.5, 6.5 Hz, 1H), 2.68 (tt, *J* = 11.0, 3.5 Hz, 1H), 2.03-1.97 (m, 1H), 1.84-1.77 (m, 3H), 1.72-1.67 (m, 1H), 1.47-1.40 (m, 1H), 1.35-1.19 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.0 (C), 171.8 (C), 169.1 (C), 52.8 (CH), 52.1 (CH_3), 52.1 (CH_3), 50.6 (CH), 32.3 (CH_2), 28.9 (CH_2), 27.9 (CH_2), 25.8 (CH_2), 25.7 (CH_2), 25.3 (CH_2); IR (thin film) 2934, 2855, 1740, 1711 cm^{-1}; LRMS (ES^-) 255 (70, $[M-H]^-$), 208 (100); HRMS (ES^-) calcd for $C_{13}H_{19}O_5$ $[M-H]^-$ 255.1232, observed 255.1234.

2-(2-Ethyl-hexanoyl)-succinic acid dimethyl ester 36f[10]



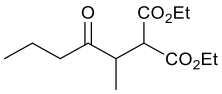
Using Method F, reaction was complete after 9 days. Purification by column chromatography (10-30% Et_2O/petrol) gave 2-(2-ethyl-hexanoyl)-succinic acid dimethyl ester **36f** as a 50:50 mixture of diastereoisomers and their enol tautomers in a >95:<5 ratio as a colourless oil. Only the ^1H NMR peaks for 2-(2-ethyl-hexanoyl)-succinic acid dimethyl ester have been assigned as it predominates: ^1H NMR (400 MHz, $CDCl_3$) δ 4.14 (m, 1H), 3.78-3.68 (m, 6H), 2.95-2.73 (m, 3H), 1.74-1.61 (m, 2H), 1.55-1.20 (m, 6H), 0.96-0.80 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.7 (C), 206.6 (C), 171.8 (C), 171.8 (C), 168.9 (C), 168.8 (C), 54.4 (CH), 54.3 (CH), 52.7 (CH), 52.6 (CH_3), 52.5 (CH), 52.1 (CH_3), 31.9 (CH_2), 31.9 (CH_2), 31.0 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 24.6 (CH_2), 23.5 (CH_2), 22.8 (CH_2), 13.9 (CH_3), 11.7 (CH_3), 11.4 (CH_3); IR (thin film) 2957, 2932, 1740, 1717 cm^{-1}; LRMS (ES^-) 271 (100, $[M-H]^-$); HRMS (ES^-) calcd for $C_{14}H_{23}O_5$ $[M-H]^-$ 271.1545, observed 271.1558.

2-Decanoyl-succinic acid dimethyl ester 36g[10]



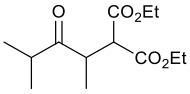
Using Method F, reaction was complete after 9 days. Purification by column chromatography (10-30% Et_2O/petrol) gave 2-decanoyl-succinic acid dimethyl ester **36g** and its enol tautomer in a >95:<5 ratio as a colourless oil (180 mg, 0.60 mmol, 60%). Only the ^1H NMR peaks for 2-decanoyl-succinic acid dimethyl ester have been assigned as it predominates: ^1H NMR (500 MHz, $CDCl_3$) δ 4.00 (dd, *J* = 8.5, 6.5 Hz, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 2.99 (dd, *J* = 17.5, 8.0 Hz, 1H), 2.85 (dd, *J* = 17.5, 6.5 Hz, 1H), 2.65 (dt, *J* = 17.5, 7.5 Hz, 1H), 2.61 (dt, *J* = 17.5, 7.5 Hz, 1H), 1.59 (sextet, *J* = 7.5 Hz, 2H), 1.33-1.23 (m, 12H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0 (C), 171.9 (C), 167.0 (C), 53.8 (CH), 52.7 (CH_3), 52.0 (CH_3), 42.8 (CH_2), 32.2 (CH_2), 31.9 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 23.4 (CH_2), 22.7 (CH_2), 14.1 (CH_3); IR (thin film) 2959, 2926, 2856, 1742, 1720 cm^{-1}; LRMS (ES^-) 299 (100, $[M-H]^-$); HRMS (ES^-) calcd for $C_{16}H_{27}O_5$ $[M-H]^-$ 299.1858, observed 299.1860.

2-(1-Methyl-2-oxo-pentyl)-malonic acid diethyl ester 44a[10]



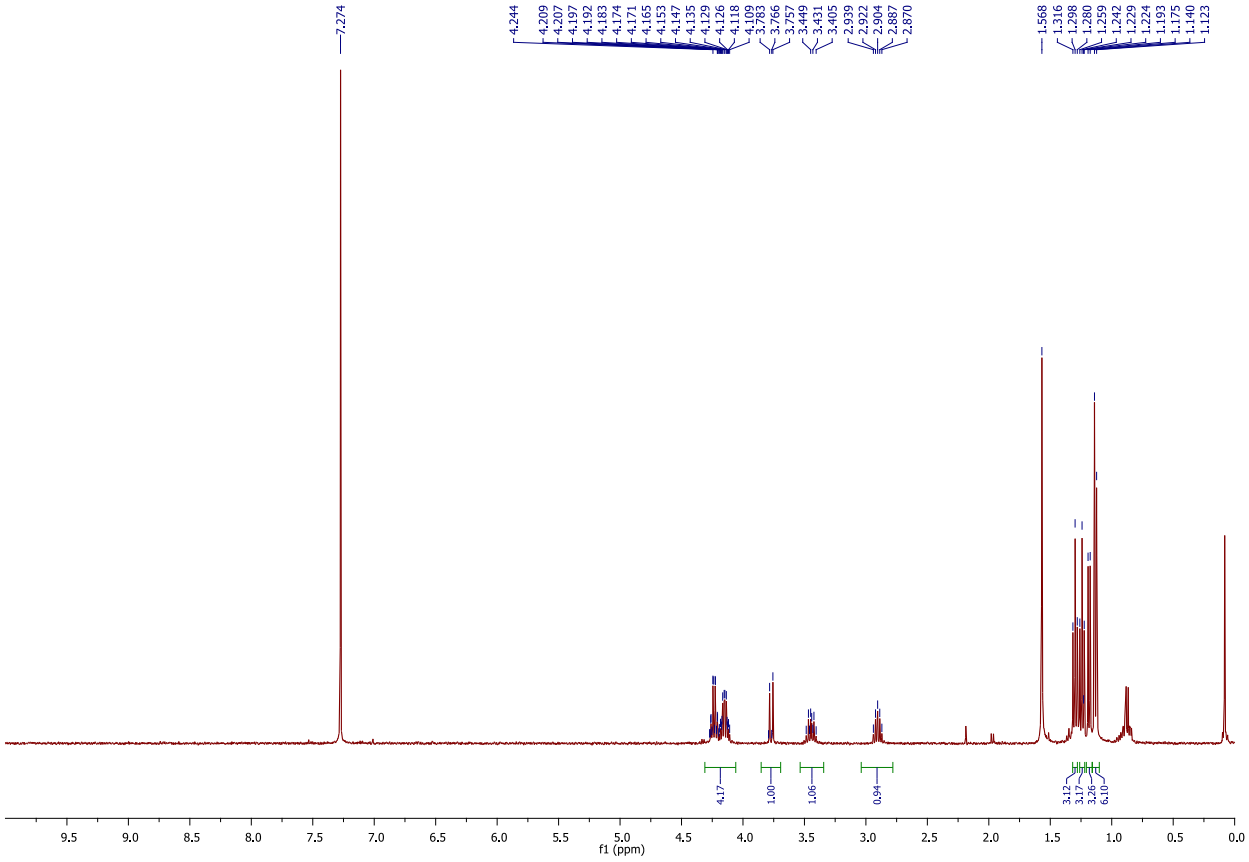
Using Method F, reaction was complete after 3 days. Purification by column chromatography (10-30% Et_2O/petrol) gave 2-(1-methyl-2-oxo-pentyl)-malonic acid diethyl ester **44a** as a colourless oil (181 mg, 0.70 mmol, 70%): ^1H NMR (400 MHz, $CDCl_3$) δ 4.26-4.11 (m, 4H), 3.77 (d, *J* = 10.5 Hz, 1H), 3.27 (dq, *J* = 10.5, 7.0 Hz, 1H), 2.58 (t, *J* = 7.0 Hz, 2H), 1.65 (sextet, *J* = 7.0 Hz, 2H), 1.29 (t, *J* = 7.0 Hz, 3H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.7 (C), 168.7 (C), 168.6 (C), 62.0 (CH_2), 61.6 (CH_2), 54.5 (CH), 45.0 (CH), 43.4 (CH_2), 16.9 (CH_2), 14.7 (CH_3), 14.2 (CH_3), 14.0 (CH_3), 13.8 (CH_3); IR (thin film) 2967, 2933, 1759, 1733, 1715 cm^{-1}; LRMS (CI) 259 (15, $[M+H]^+$), 213 (100); HRMS (CI) calcd for $C_{13}H_{23}O_5$ $[M+H]^+$ 259.1545, observed 259.1548.

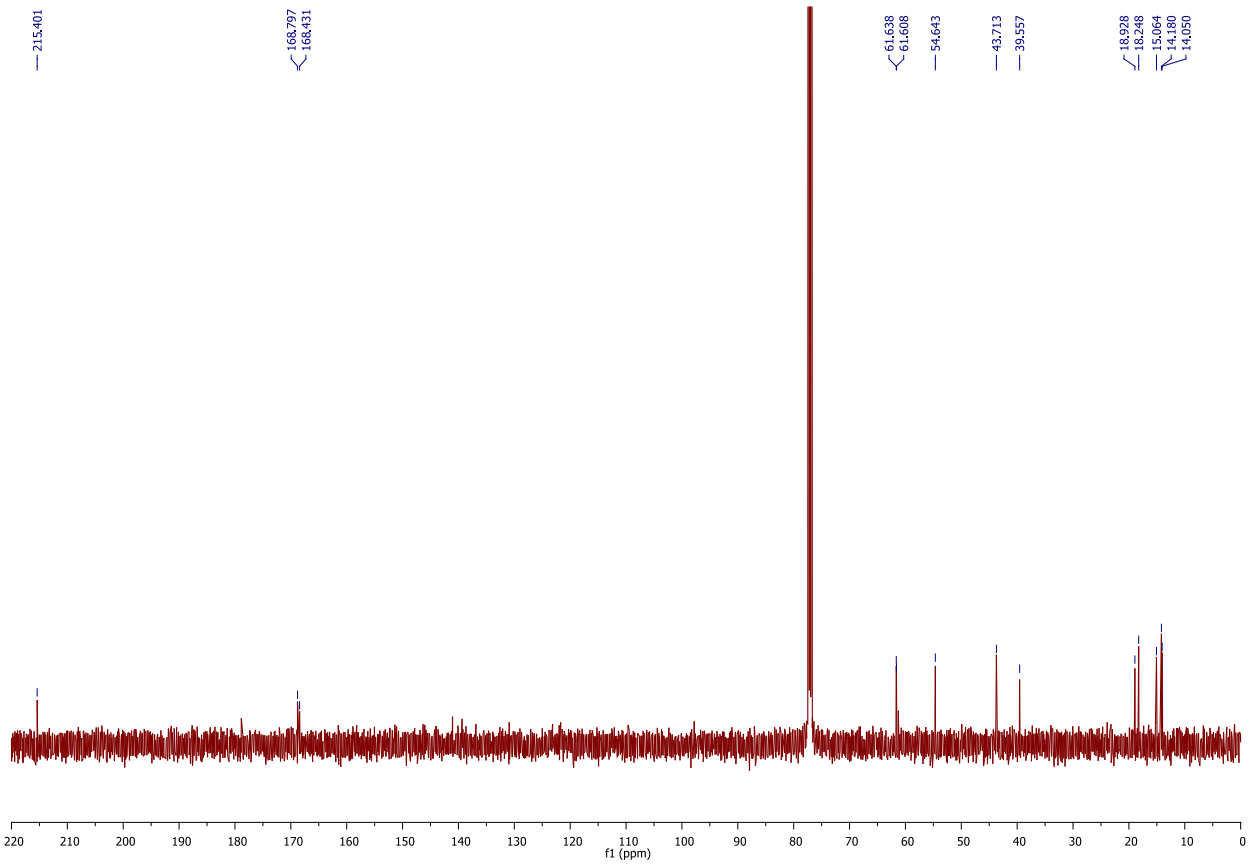
2-(4-Methyl-3-oxo-pentyl)-malonic acid diethyl ester 44b



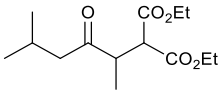
Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-30% Et_2O/petrol) gave 2-(4-methyl-3-oxo-pentyl)-malonic acid diethyl ester **44b** as a colourless oil (108 mg, 0.42 mmol, 42%): ^1H NMR (400 MHz, $CDCl_3$) δ 4.26-4.12 (m, 4H), 3.77 (d, *J* = 10.5 Hz, 1H), 3.44 (dq, *J* = 10.5, 7.0 Hz, 1H), 2.90 (septet, *J* = 7.0 Hz, 1H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.18 (d, *J* = 7.0 Hz, 3H), 1.13 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 215.4 (C), 168.8 (C), 168.4 (C), 61.6 (CH_2), 61.6 (CH_2), 54.7 (CH), 43.7 (CH), 39.5 (CH), 18.9 (CH_3), 18.2 (CH_3), 15.1 (CH_3), 14.2 (CH_3), 14.1 (CH_3); IR (thin film)

2977, 2939, 1751, 1734, 1714 cm^{-1}; LRMS (ES) 281 (100, $[M+Na]^+$); HRMS (ES) calcd for $C_{13}H_{22}O_5Na$ $[M+Na]^+$ 281.1365, observed 281.1360.



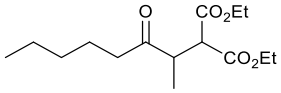


2-(1,4-Dimethyl-2-oxo-pentyl)-malonic acid diethyl ester 44c[10]



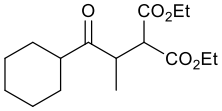
Using Method F, reaction was complete after 3 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(1,4-dimethyl-2-oxo-pentyl)-malonic acid diethyl ester **44c** as a colourless oil (163 mg, 0.60 mmol, 60%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.24-4.12 (m, 4H), 3.74 (d, *J* = 10.5 Hz, 1H), 3.22 (dq, *J* = 10.5, 7.5 Hz, 1H), 2.50 (dd, *J* = 17.0, 6.0 Hz, 1H), 2.44 (dd, *J* = 17.0, 7.5 Hz, 1H), 2.17 (nonet, *J* = 7.0 Hz, 1H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.10 (d, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.1 (C), 168.6 (C), 168.5 (C), 61.6 (CH_2), 61.5 (CH_2), 54.3 (CH), 50.3 (CH_2), 45.3 (CH), 23.8 (CH), 22.6 (CH_3), 22.4 (CH_3), 14.5 (CH_3), 14.1 (CH_3), 14.0 (CH_3); IR (thin film) 2960, 2870, 1746, 1733, 1713 cm^{-1}; LRMS (EI) 272 (10, $[M]^{+\cdot}$), 227 (85), 189 (100); HRMS (EI) calcd for $C_{14}H_{24}O_5$ $[M]^{+\cdot}$ 272.1618, observed 272.1621.

2-(1-Methyl-2-oxo-heptyl)-malonic acid diethyl ester 44d[10]



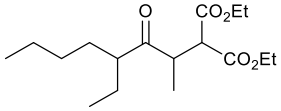
Using Method F, reaction was complete after 3 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(1-methyl-2-oxo-heptyl)-malonic acid diethyl ester **44d** as a colourless oil (206 mg, 0.72 mmol, 72%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.25-4.10 (m, 4H), 3.74 (d, *J* = 10.5 Hz, 1H), 3.27 (dq, *J* = 10.5, 7.5 Hz, 1H), 2.57 (t, *J* = 7.5 Hz, 2H), 1.65-1.56 (m, 2H), 1.35-1.22 (m, 10H), 1.11 (t, *J* = 7.5 Hz, 3H), 0.89 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.8 (C), 168.7 (C), 168.5 (C), 61.6 (CH_2), 61.5 (CH_2), 54.4 (CH), 44.9 (CH), 41.4 (CH_2), 31.3 (CH_2), 23.1 (CH_2), 22.5 (CH_2), 14.7 (CH_3), 14.1 (CH_3), 14.0 (CH_3), 14.0 (CH_3); IR (thin film) 2963, 2935, 1749, 1733, 1717 cm^{-1}; LRMS (CI) 287 (12, $[M+H]^+$), 241 (85), 230 (70), 187 (100); HRMS (CI) calcd for $C_{15}H_{27}O_5$ $[M+H]^+$ 287.1853, observed 287.1859.

2-(2-Cyclohexyl-1-methyl-2-oxo-ethyl)-malonic acid diethyl ester 44e[10]



Using Method F, reaction was complete after 3 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(2-cyclohexyl-1-methyl-2-oxo-ethyl)-malonic acid diethyl ester **44e** as a colourless oil (221 mg, 0.74 mmol, 74%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.22 (qd, *J* = 7.0, 2.0 Hz, 2H), 4.17-4.10 (m, 2H), 3.75 (d, *J* = 10.5 Hz, 1H), 3.41 (dq, *J* = 10.5, 7.5 Hz, 1H), 2.62 (tt, *J* = 11.5, 3.0 Hz, 1H), 2.04 (m, 1H), 1.83-1.78 (m, 3H), 1.69-1.64 (m, 1H), 1.46-1.38 (m, 1H), 1.34-1.17 (m, 10H), 0.92 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 214.6 (C), 168.8 (C), 168.4 (C), 61.6 (CH_2), 61.5 (CH_2), 54.5 (CH), 49.6 (CH), 43.7 (CH), 29.1 (CH_2), 28.3 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 25.6 (CH_2), 14.9 (CH_3), 14.1 (CH_3), 14.0 (CH_3); IR (thin film) 2981, 2932, 2856, 1749, 1732, 1709 cm^{-1}; LRMS (ES^+) 321 (100, $[M+Na]^+$); HRMS (ES^+) calcd for $C_{16}H_{26}O_5Na$ $[M+Na]^+$ 321.1666, observed 321.1678.

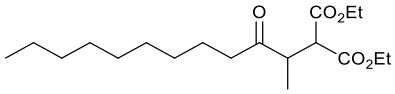
2-(3-Ethyl-1-methyl-2-oxo-heptyl)-malonic acid diethyl ester 44f[10]



Using Method F, reaction was complete after 6 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(3-ethyl-1-methyl-2-oxo-heptyl)-malonic acid diethyl ester **44f** as a 50:50 mixture of diastereoisomers as a colourless oil (163 mg, 0.52 mmol, 52%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.26-4.19 (m, 2H), 4.18-4.23 (m, 2H), 3.75-3.71 (m, 1H), 3.41-3.24 (m, 1H), 2.68-2.62 (m, 1H), 1.82-1.63 (m, 2H), 1.51-1.44 (m, 1H), 1.42-1.10 (m, 5H), 1.29 (t, *J* = 7.0 Hz, 3H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.16-1.13 (m, 3H), 0.95-0.82 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 214.1 (C), 168.8 (C), 168.4 (C), 168.3 (C), 61.6 (CH_2), 61.5 (CH_2), 61.5 (CH_2), 61.5 (CH_2), 54.1 (CH), 54.0 (CH), 51.5 (CH), 51.2 (CH), 45.0 (CH), 44.9 (CH), 31.0 (CH_2), 29.9 (CH_2), 29.2

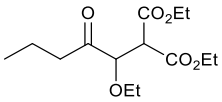
(CH_2), 22.8 (CH_2), 24.6 (CH_2), 23.0 (CH_2), 22.9 (CH_2), 22.8 (CH_2), 14.5 (CH_3), 14.4 (CH_3), 14.1 (CH_3), 14.0 (CH_3), 14.0 (CH_3), 12.1 (CH_3), 11.4 (CH_3); IR (thin film) 2962, 2934, 2875, 1753, 1734, 1710 cm^{-1}; LRMS (ES^+) 337 (100, $[M+Na]^+$), 269 (30); HRMS (ES^+) calcd for $C_{17}H_{30}O_5Na$ $[M+Na]^+$ 337.1991, observed 337.2011.

2-(1-Methyl-2-oxo-undecyl)-malonic acid diethyl ester 44g[10]



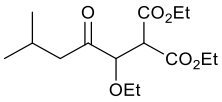
Using Method F, reaction was complete after 6 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(1-methyl-2-oxo-undecyl)-malonic acid diethyl ester **44g** as a colourless oil (246 mg, 0.72 mmol, 72%): ^1H NMR (500 MHz, $CDCl_3$) δ 4.21 (d, *J* = 7.0 Hz, 2H), 4.17-4.11 (m, 2H), 3.75 (d, *J* = 10.5 Hz, 1H), 3.22 (dq, *J* = 10.5, 7.5 Hz, 1H), 2.57 (t, *J* = 7.5 Hz, 2H), 1.61-1.54 (m, 2H), 1.32-1.21 (m, 18H), 1.10 (d, *J* = 7.5 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.8 (C), 168.7 (C), 168.6 (C), 61.7 (CH_2), 61.6 (CH_2), 54.5 (CH), 45.0 (CH), 41.5 (CH_2), 31.9 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 23.5 (CH_2), 22.7 (CH_2), 14.8 (CH_3), 14.1 (CH_3), 14.1 (CH_3), 14.0 (CH_3); IR (thin film) 2927, 2855, 1750, 1734, 1717 cm^{-1}; LRMS (ES^+) 365 (100, $[M+Na]^+$), 283 (30); HRMS (ES^+) calcd for $C_{19}H_{34}O_5Na$ $[M+Na]^+$ 365.2318, observed 365.2304.

2-(1-Ethoxy-2-oxo-pentyl)-malonic acid diethyl ester 46a[10]



Using Method F, reaction was complete after 7 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(1-ethoxy-2-oxo-pentyl)-malonic acid dimethyl **46a** as a colourless oil: ^1H NMR (500 MHz, $CDCl_3$) δ 4.29 (d, *J* = 7.5 Hz, 1H), 4.25-4.17 (m, 4H), 3.91 (d, *J* = 7.5 Hz, 1H), 3.69-3.60 (m, 2H), 2.68 (dt, *J* = 18.0, 7.0 Hz, 1H), 2.51 (dt, *J* = 18.0, 7.0 Hz, 1H), 1.65 (sextet, *J* = 7.0 Hz, 2H), 1.28-1.24 (m, 6H), 1.19 (t, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.5 (C), 167.0 (C), 167.0 (C), 82.4 (CH), 67.8 (CH_2), 61.8 (CH_2), 61.7 (CH_2), 54.5 (CH), 41.1 (CH_2), 16.5 (CH_2), 15.4 (CH_3), 14.1 (CH_3), 14.0 (CH_3), 13.8 (CH_3); IR (thin film) 2978, 2934, 2873, 1744, 1724 cm^{-1}; LRMS (CI) 289 (100, $[M+H]^+$), 243 (40), 217 (47); HRMS (CI) calcd for $C_{14}H_{25}O_6$ $[M+H]^+$ 289.1651, observed 289.1648.

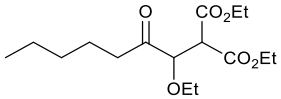
2-(1-Ethoxy-4-methyl-2-oxo-pentyl)-malonic acid diethyl ester 46c[10]



Using Method F, reaction was complete after 5 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(1-ethoxy-4-methyl-2-oxo-pentyl)-malonic acid diethyl ester **46c** as a colourless oil (257 mg, 0.85 mmol, 85%): ^1H NMR (600 MHz, $CDCl_3$) δ 4.31 (d, *J* = 7.5 Hz, 1H), 4.26-4.17 (m, 4H), 3.94 (d, *J* = 7.5 Hz, 1H), 3.72-3.62 (m, 2H), 2.68 (dd, *J* = 17.5, 7.0 Hz,

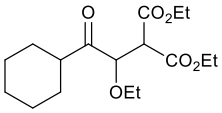
1H), 2.52 (dt, *J* = 17.5, 6.5 Hz, 1H), 2.19 (nonet, *J* = 6.5 Hz, 1H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.7 (C), 167.0 (C), 167.0 (C), 82.4 (CH), 67.8 (CH_2), 61.8 (CH_2), 61.7 (CH_2), 54.1 (CH), 47.9 (CH_2), 23.6 (CH), 22.7 (CH_3), 22.5 (CH_3), 15.4 (CH_3), 14.0 (CH_3), 13.9 (CH_3); IR (thin film) 2978, 2960, 2874, 1744, 1732 cm^{-1}; LRMS (CI) 303 (5, $[M+H]^+$), 285 (10), 211 (100); HRMS (CI) calcd for $C_{15}H_{27}O_6$ $[M+H]^+$ 303.1808, observed 303.1805.

2-(1-Ethoxy-2-oxo-heptyl)-malonic acid diethyl ester 46d[10]



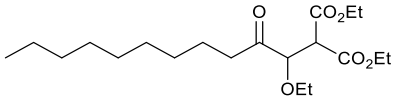
Using Method F, reaction was complete after 3 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(1-ethoxy-2-oxo-heptyl)-malonic acid diethyl ester **46d** as a colourless oil (275 mg, 0.87 mmol, 87%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.32 (d, *J* = 7.5 Hz, 1H), 4.25-4.17 (m, 4H), 3.93 (d, *J* = 7.5 Hz, 1H), 3.69-3.61 (m, 2H), 2.74 (dt, *J* = 18.0, 7.5 Hz, 1H), 2.60 (dt, *J* = 18.0, 7.5 Hz, 1H), 1.60 (quintet, *J* = 7.5 Hz, 2H), 1.34-1.24 (m, 10H), 1.21 (t, *J* = 7.0 Hz, 3H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.7 (C), 167.0 (C), 167.0 (C), 82.3 (CH), 67.7 (CH_2), 61.7 (CH_2), 61.7 (CH_2), 54.5 (CH), 39.1 (CH_2), 31.3 (CH_2), 22.7 (CH_2), 22.5 (CH_2), 15.4 (CH_3), 14.0 (CH_3), 14.0 (CH_3), 14.0 (CH_3); IR (thin film) 2978, 2959, 2932, 1750, 1736 cm^{-1}; LRMS (ES^+) 339 (100, $[M+Na]^+$); HRMS (ES^+) calcd for $C_{16}H_{28}O_6Na$ $[M+Na]^+$ 339.1784, observed 339.1769.

2-(2-Cyclohexyl-1-ethoxy-2-oxo-ethyl)-malonic acid diethyl ester 46e[10]



Using Method F, reaction was complete after 3 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(2-cyclohexyl-1-ethoxy-2-oxo-ethyl)-malonic acid diethyl ester **46e** as a colourless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.52 (d, *J* = 8.0 Hz, 1H), 4.27-4.15 (m, 4H), 3.98 (d, *J* = 8.0 Hz, 1H), 3.71-3.62 (m, 2H), 2.86 (tt, *J* = 11.5, 2.0 Hz, 1H), 1.94-1.89 (m, 1H), 1.85-1.79 (m, 3H), 1.72-1.67 (m, 1H), 1.44-1.19 (m, 14H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.4 (C), 167.2 (C), 167.1 (C), 81.0 (CH), 67.3 (CH_2), 61.7 (CH_2), 61.7 (CH_2), 53.7 (CH), 46.8 (CH), 29.0 (CH_2), 27.8 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 25.5 (CH_2), 15.5 (CH_3), 14.1 (CH_3), 14.0 (CH_3); IR (thin film) 2979, 2933, 2856, 1747, 1734, 1716 cm^{-1}; LRMS (ES^+) 351 (100, $[M+Na]^+$); HRMS (ES^+) calcd for $C_{17}H_{28}O_6Na$ $[M+Na]^+$ 351.1784, observed 351.1773.

2-(1-Ethoxy-2-oxo-undecyl)-malonic acid diethyl ester 46g[10]



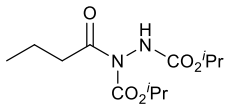
Using Method F, reaction was complete after 5 days. Purification by column chromatography (5-20% Et_2O/petrol) gave 2-(1-ethoxy-2-oxo-undecyl)-malonic acid diethyl ester **46g** as a colourless

oil (331 mg, 0.89 mmol, 89%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.35 (d, *J* = 7.0 Hz, 1H), 4.25-4.15 (m, 4H), 3.91 (d, *J* = 7.0 Hz, 1H), 3.69-3.60 (m, 2H), 2.68 (dt, *J* = 18.0, 7.0 Hz, 1H), 2.51 (dt, *J* = 18.0, 7.0 Hz, 1H), 1.60-1.55 (m, 2H), 1.28-1.18 (m, 21H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.7 (C), 167.0 (C), 167.0 (C), 82.4 (CH), 67.8 (CH_2), 61.8 (CH_2), 61.8 (CH_2), 54.5 (CH), 39.3 (CH_2), 31.9 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 23.1 (CH_2), 22.7 (CH_2), 15.4 (CH_3), 14.2 (CH_3), 14.1 (CH_3), 14.0 (CH_3); IR (thin film) 2926, 2856, 1749, 1733 cm^{-1}; LRMS (ES$^+$) 395 (100, $[M+Na]^+$); HRMS (ES$^+$) calcd for $C_{20}H_{36}O_6Na$ $[M+Na]^+$ 395.2410, observed 395.2423.

Typical procedure for the hydroacylation of DIAD 47 – Method G

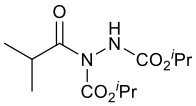
To a mixture of azodicarboxylate (1.2 mmol) and H_2O (500 μL) was added aldehyde (1.0 mmol) and the reaction mixture stirred at 300 rpm at 21 °C for the time specified below. The solvent was removed *in vacuo* and the crude residue purified as described below.

Dipropan-2-yl 1-butanoylhydrazine-1,2-dicarboxylate 48a[11]



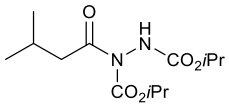
Using Method G, reaction was complete after 24 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-butanoylhydrazine-1,2-dicarboxylate **48a** as a colourless oil (249 mg, 0.91 mmol, 91%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.58 (br s, NH, 1H), 5.03 (septet, *J* = 6.5 Hz, 1H), 4.97 (septet, *J* = 6.5 Hz, 1H), 2.94-2.74 (m, 2H), 1.69 (sextet, *J* = 7.5 Hz, 2H), 1.34-1.17 (m, 12H), 0.96 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9 (C), 155.2 (C), 152.8 (C), 72.2 (CH), 70.5 (CH), 39.1 (CH_2), 22.0 (CH_3), 21.8 (CH_3), 18.2 (CH_2), 13.8 (CH_3); IR (thin film) 3317, 2982, 2938, 1736, 1717 cm^{-1}; LRMS (CI) 275 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{12}H_{23}N_2O_5$ $[M+H]^+$ 275.1607, observed 275.1609.

Dipropan-2-yl 1-(2-methylpropanoyl)hydrazine-1,2-dicarboxylate 48b[11]

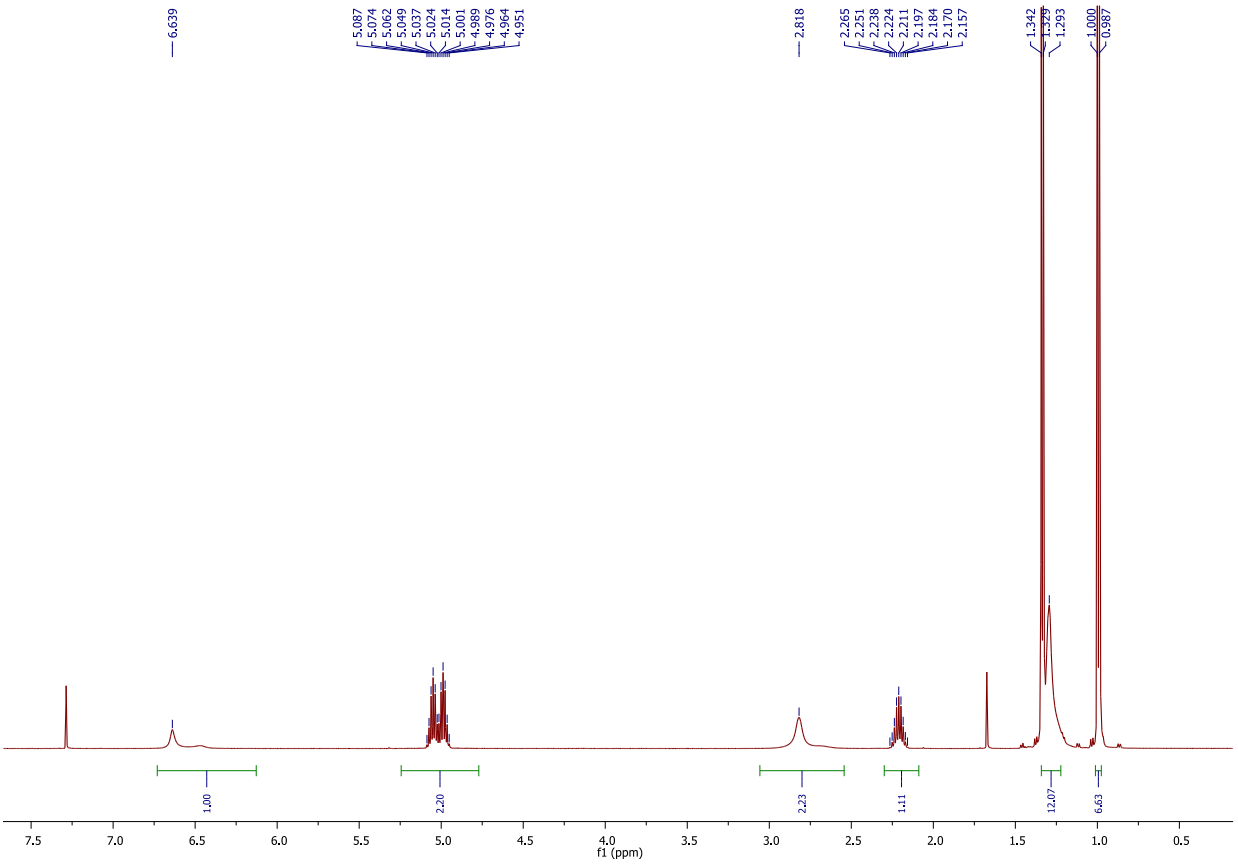


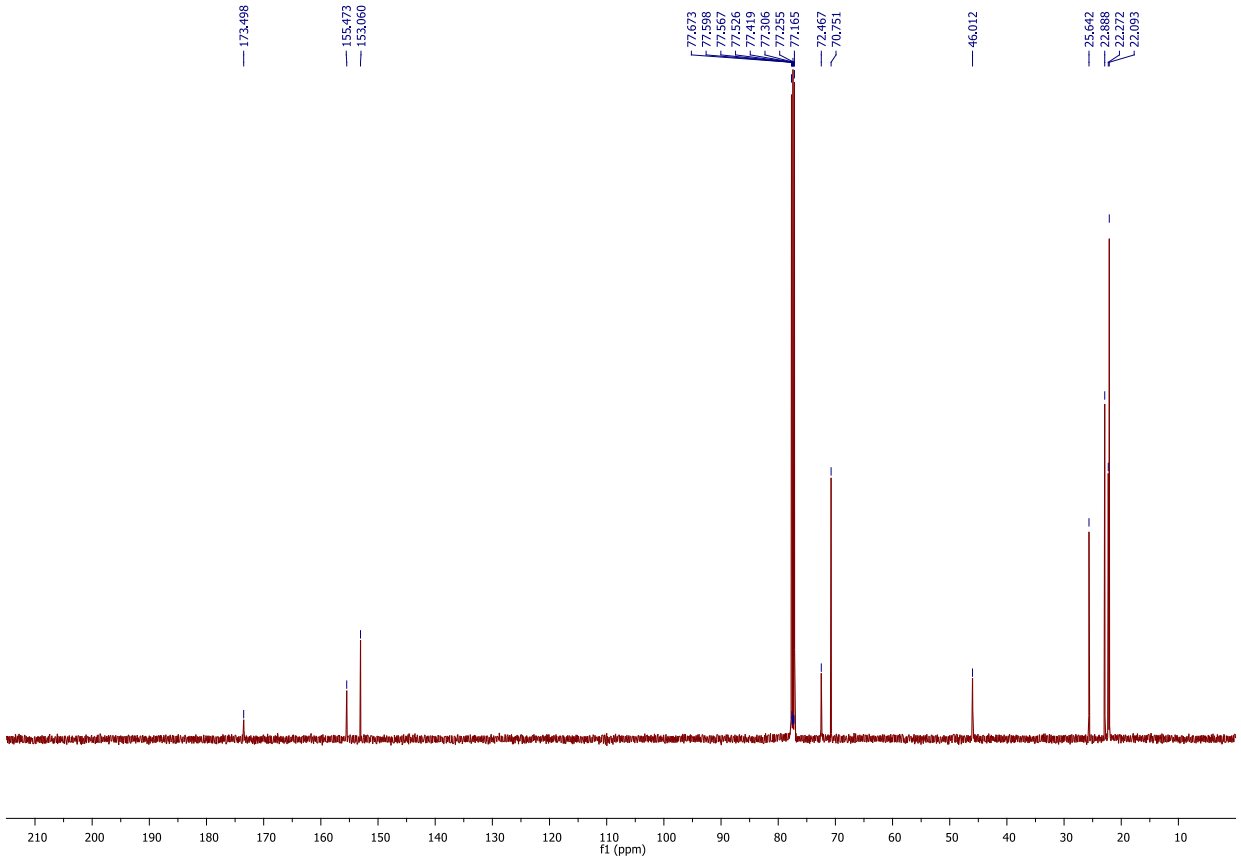
Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-(2-methylpropanoyl)hydrazine-1,2-dicarboxylate **48b** as a colourless oil (217 mg, 0.79 mmol, 79%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.76 (br s, NH, 1H), 5.00 (septet, *J* = 6.5 Hz, 1H), 4.93 (septet, *J* = 6.5 Hz, 1H), 3.60 (septet, *J* = 7.0 Hz, 1H), 1.33-1.12 (m, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.4 (C), 155.3 (C), 152.7 (C), 72.2 (CH), 70.4 (CH), 34.4 (CH), 22.0 (CH_3), 21.8 (CH_3), 19.4 (CH_3); IR (thin film) 3322, 2982, 2938, 1736, 1718 cm^{-1}; LRMS (CI) 275 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{12}H_{23}N_2O_5$ $[M+H]^+$ 275.1607, observed 275.1598.

Dipropan-2-yl 2-(3-methylbutanoyl)hydrazine-1,2-dicarboxylate 48c

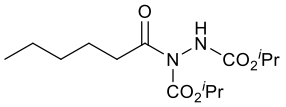


Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave diisopropyl 2-(3-methylbutanoyl)hydrazine-1,2-dicarboxylate **48c** as a colourless oil (228 mg, 0.79 mmol, 79%).^{1}H NMR (500 MHz, $CDCl_3$) δ 6.55 (br s, NH, 1H), 5.02 (septet, *J* = 6.5 Hz, 1H), 4.96 (septet, *J* = 6.5 Hz, 1H), 2.92-2.57 (m, 2H), 2.18 (nonet, *J* = 6.5 Hz, 1H), 1.33-1.17 (m, 12H), 0.97 (d, *J* = 6.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2 (C), 155.2 (C), 152.7 (C), 72.1 (CH), 70.4 (CH), 45.7 (CH_2), 25.3 (CH), 22.6 (CH_3), 21.9 (CH_3), 21.8 (CH_3); IR (thin film) 3317, 2982, 2874, 1736, 1718 cm^{-1}; LRMS (CI) 289 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{13}H_{25}N_2O_5$ $[M+H]^+$ 289.1764, observed 289.1760.

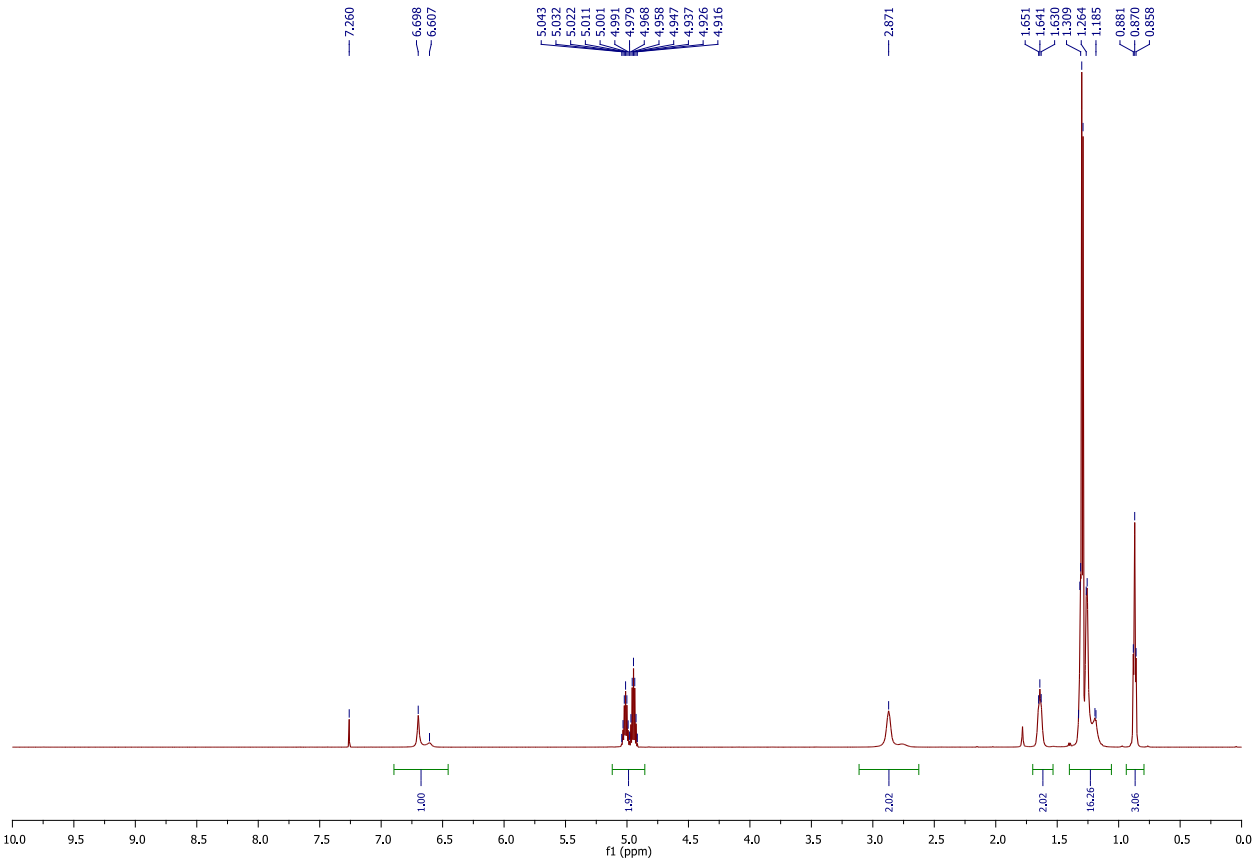


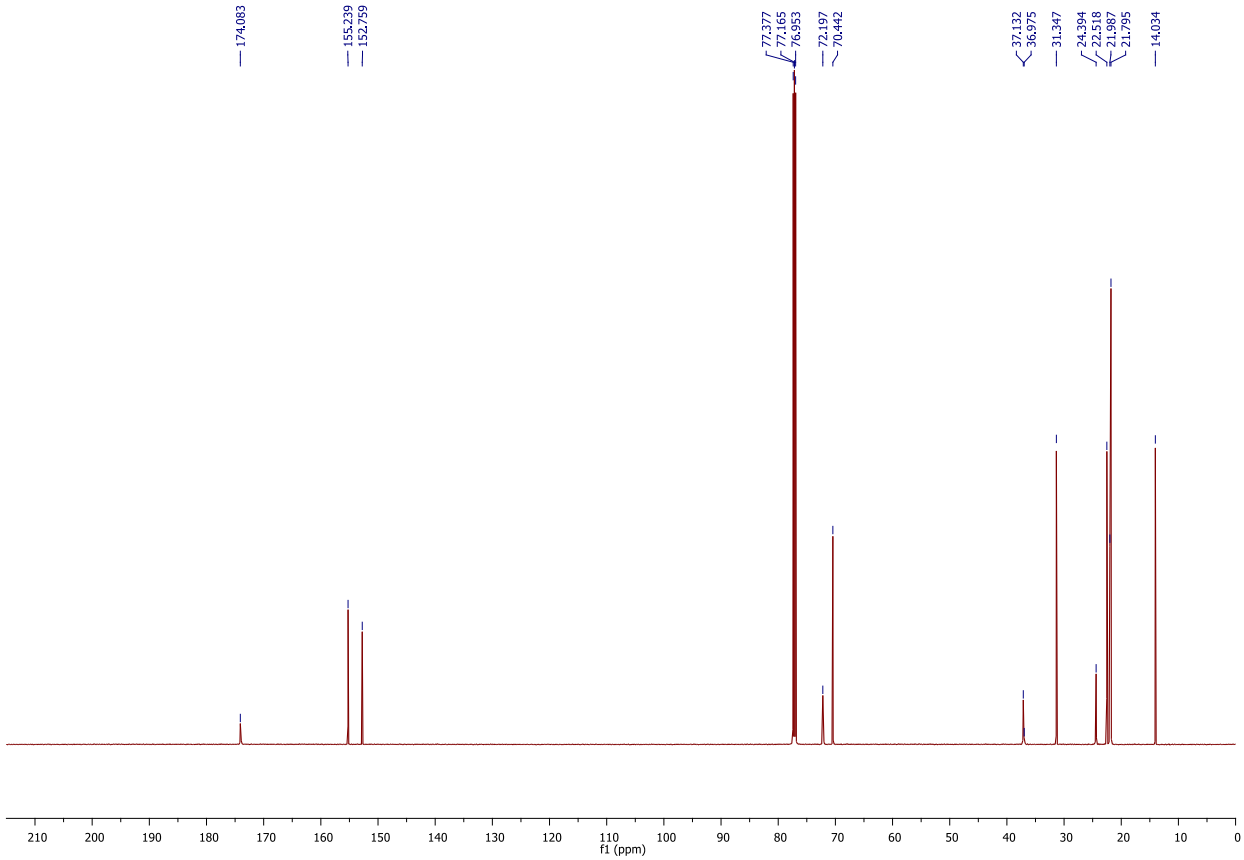


Dipropan-2-yl 1-hexanoylhydrazine-1,2-dicarboxylate 48d

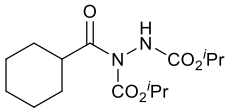


Using Method G, reaction was complete after 72 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-hexanoylhydrazine-1,2-dicarboxylate **48d** as a colourless oil (266 mg, 0.88 mmol, 88%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.70 (br s, NH, 1H), 5.01 (septet, *J* = 6.5 Hz, 1H), 4.94 (septet, *J* = 6.5 Hz, 1H), 2.87-2.75 (m, 2H), 1.64 (t, *J* = 7.0 Hz, 2H), 1.32-1.17 (m, 16H), 0.86 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0 (C), 155.2 (C), 152.8 (C), 72.2 (CH), 70.4 (CH), 37.1 (CH_2), 31.3 (CH_2), 24.4 (CH_2), 22.5 (CH_2), 22.0 (CH_3), 21.8 (CH_3), 14.0 (CH_3); IR (thin film) 3316, 2982, 2938, 2874, 1734, 1720 cm^{-1}; LRMS (ES) 301 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{14}H_{25}N_2O_5$ $[M-H]^-$ 301.1764, observed 301.1763.

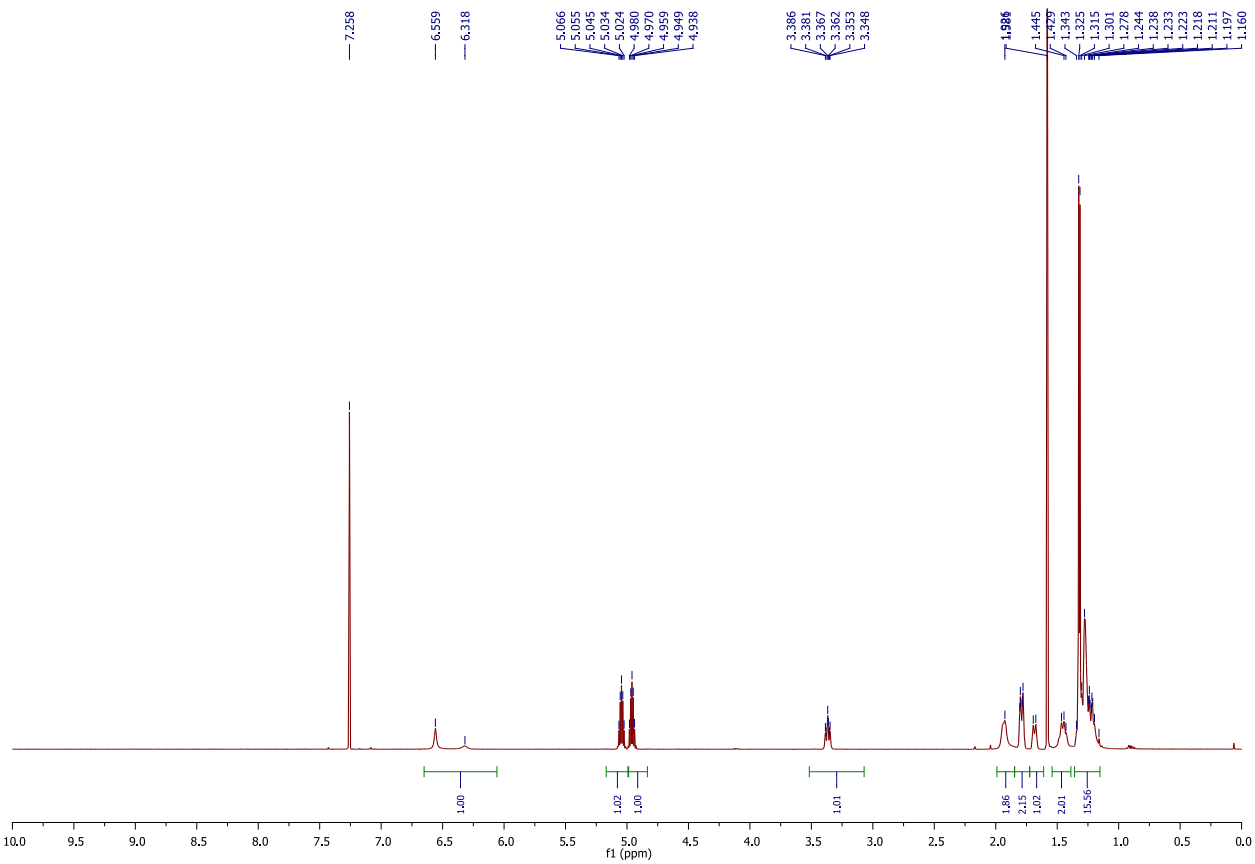


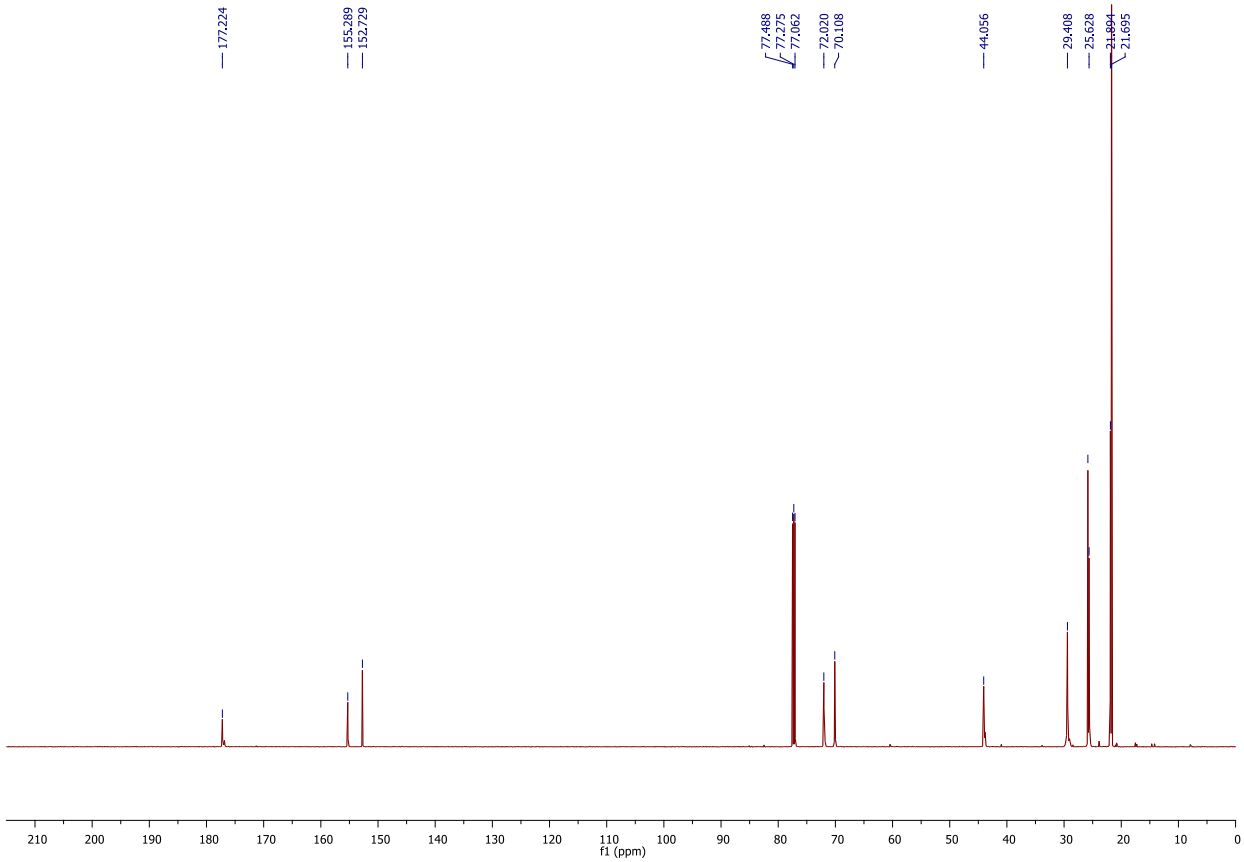


Dipropan-2-yl 1-(cyclohexanecarbonyl)hydrazine-1,2-dicarboxylate 48e

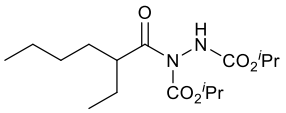


Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-(cyclohexanecarbonyl)hydrazine-1,2-dicarboxylate **48e** as a colourless oil (264 mg, 0.84 mmol, 84%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.55 (br s, NH, 1H), 5.04 (septet, *J* = 6.5 Hz, 1H), 4.97 (septet, *J* = 6.5 Hz, 1H), 3.37 (tt, *J* = 11.5 and 3.0 Hz, 1H), 1.96-1.91 (m, 2H), 1.81-1.76 (m, 2H), 1.71-1.65 (m, 1H), 1.48-1.41 (m, 2H), 1.34-1.18 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2 (C), 155.3 (C), 152.8 (C), 72.0 (CH), 70.1 (CH), 44.1 (CH), 29.4 (CH_2), 25.8 (CH_2), 25.6 (CH_2), 21.9 (CH_3), 21.7 (CH_3); IR (thin film) 3318, 2983, 2933, 2856, 1726, 1719 cm^{-1}; LRMS (ES) 313 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{15}H_{25}N_2O_5$ $[M-H]^-$ 313.1763, observed 313.1765.

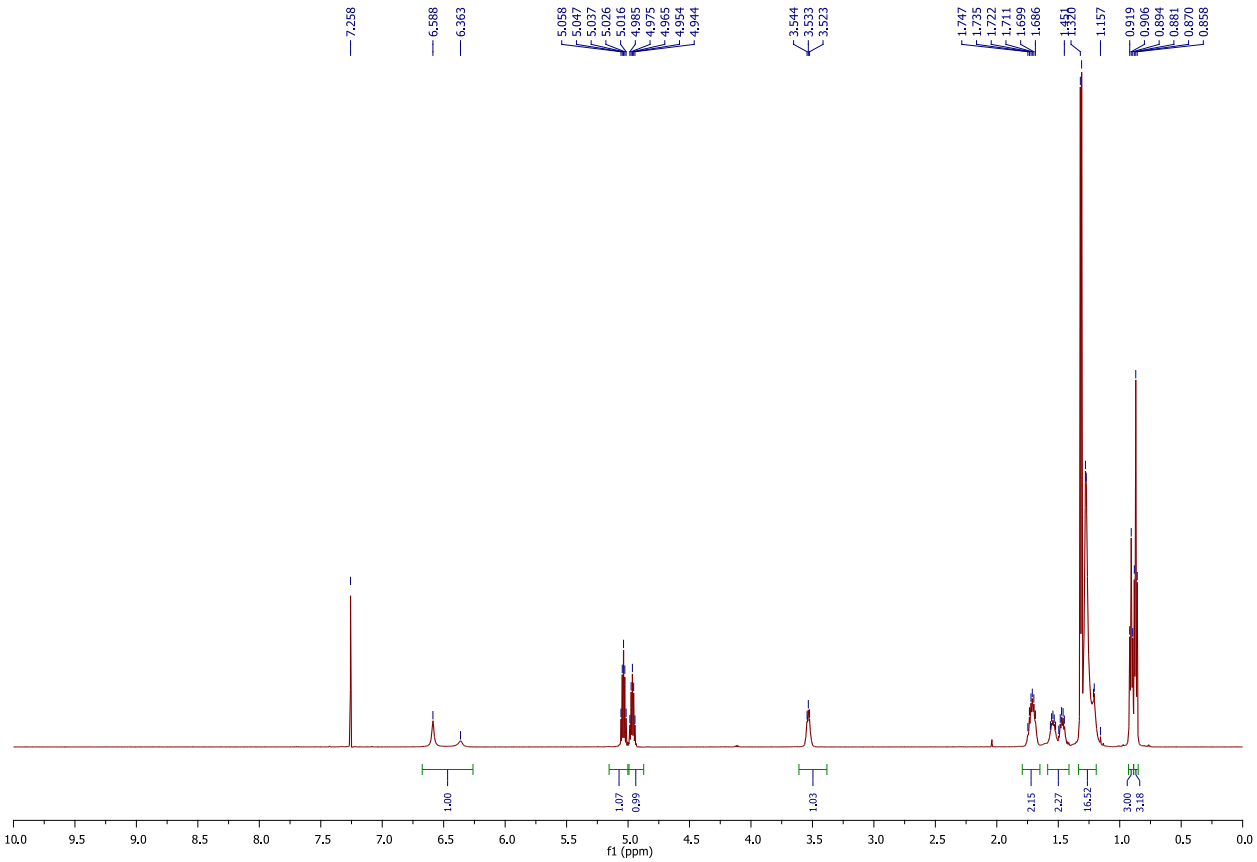


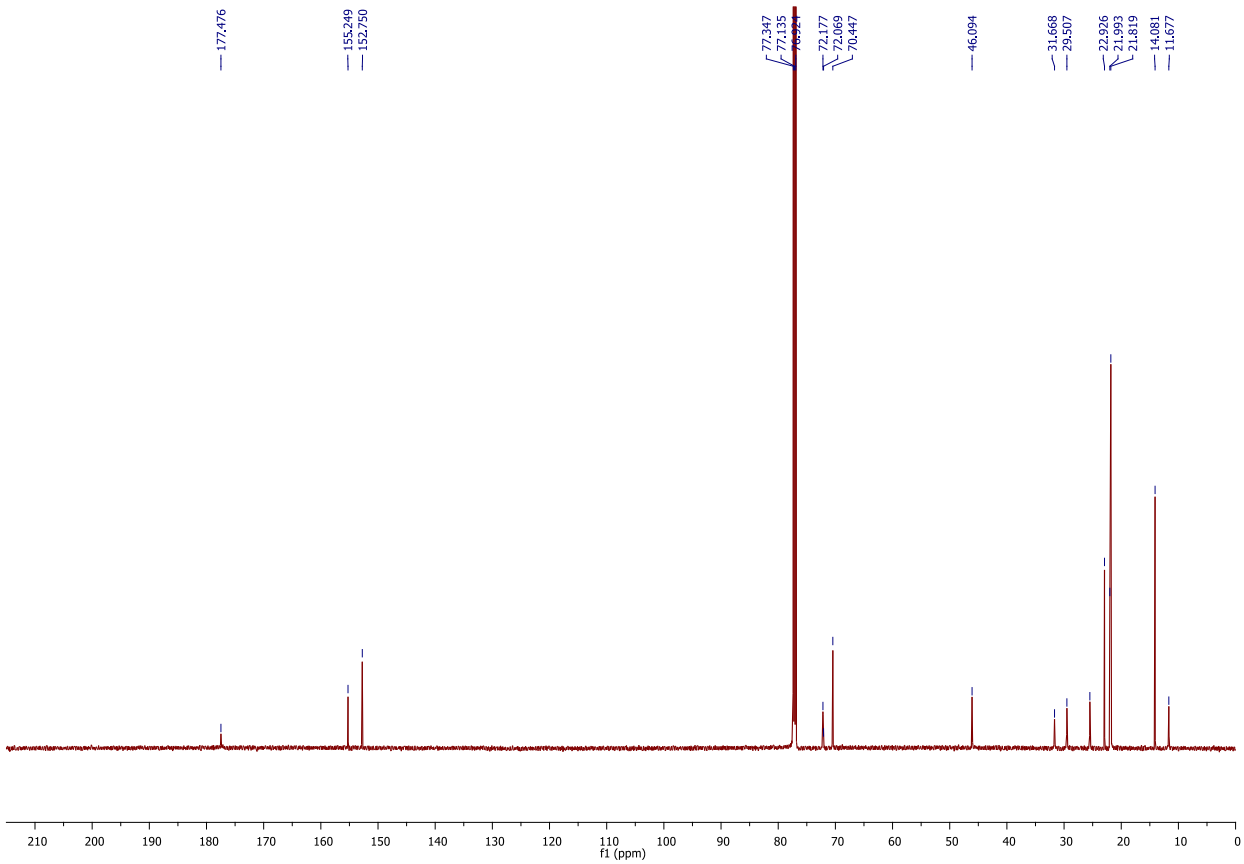


Dipropan-2-yl 1-(2-ethylhexanoyl)hydrazine-1,2-dicarboxylate 48f

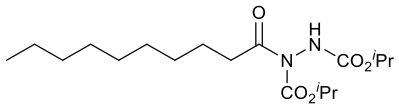


Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-(2-ethylhexanoyl)hydrazine-1,2-dicarboxylate **48f** as a colourless oil (284 mg, 0.86 mmol, 86%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.58 (br s, NH, 1H), 5.04 (septet, *J* = 6.5 Hz, 1H), 4.96 (septet, *J* = 6.5 Hz, 1H), 3.53 (app. quintet, *J* = 6.0 Hz, 1H), 1.75-1.66 (m, 2H), 1.57-1.42 (m, 2H), 1.33-1.17 (m, 16H), 0.90 (t, *J* = 7.5 Hz, 3H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.5 (C), 155.3 (C), 152.8 (C), 72.2 (CH), 70.5 (CH), 46.1 (CH), 31.7 (CH_2), 29.5 (CH_2), 25.5 (CH_2), 22.9 (CH_2), 22.0 (CH_3), 21.8 (CH_3), 14.1 (CH_3), 11.7 (CH_3); IR (thin film) 3317, 2963, 2935, 2875, 1736, 1721 cm^{-1}; LRMS (FAB) 353 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_{16}H_{30}N_2NaO_5$ $[M+Na]^+$ 353.2052, observed 353.2053.

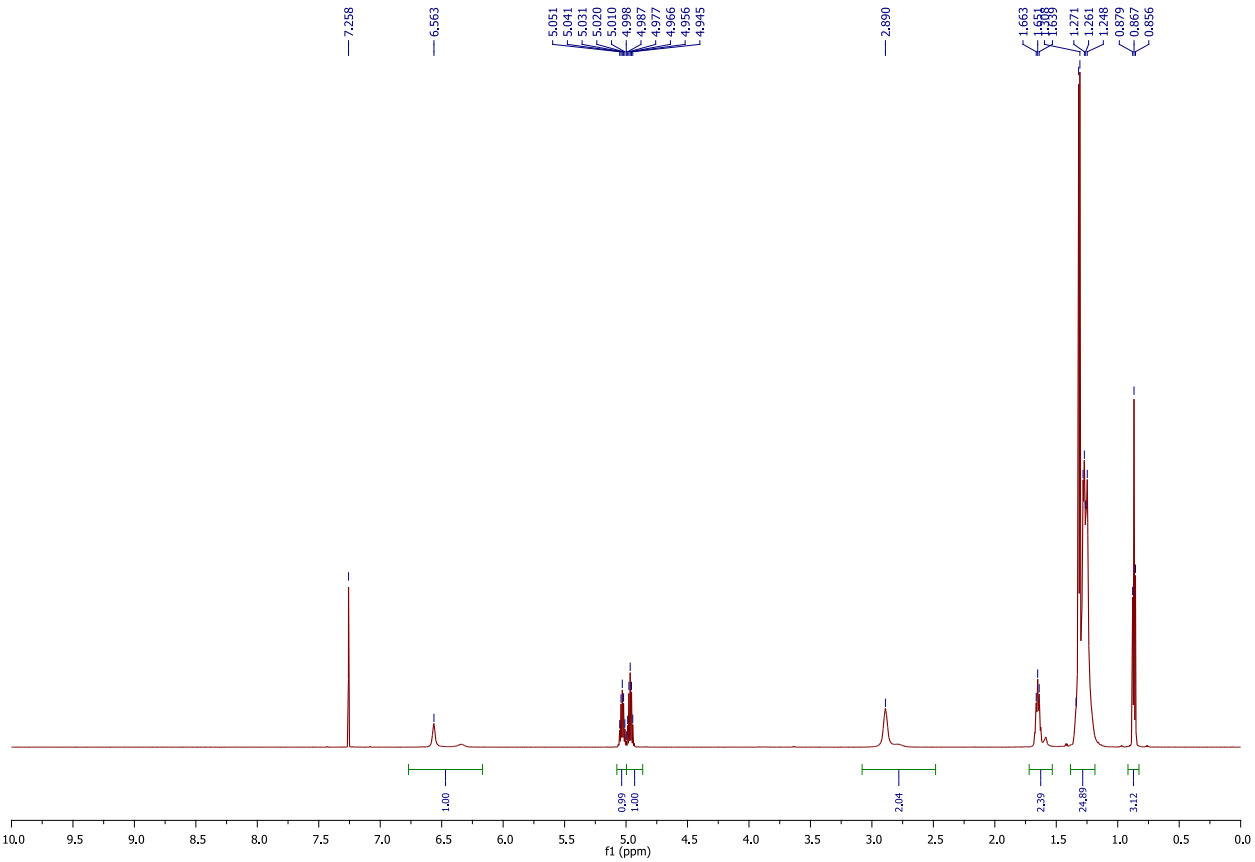


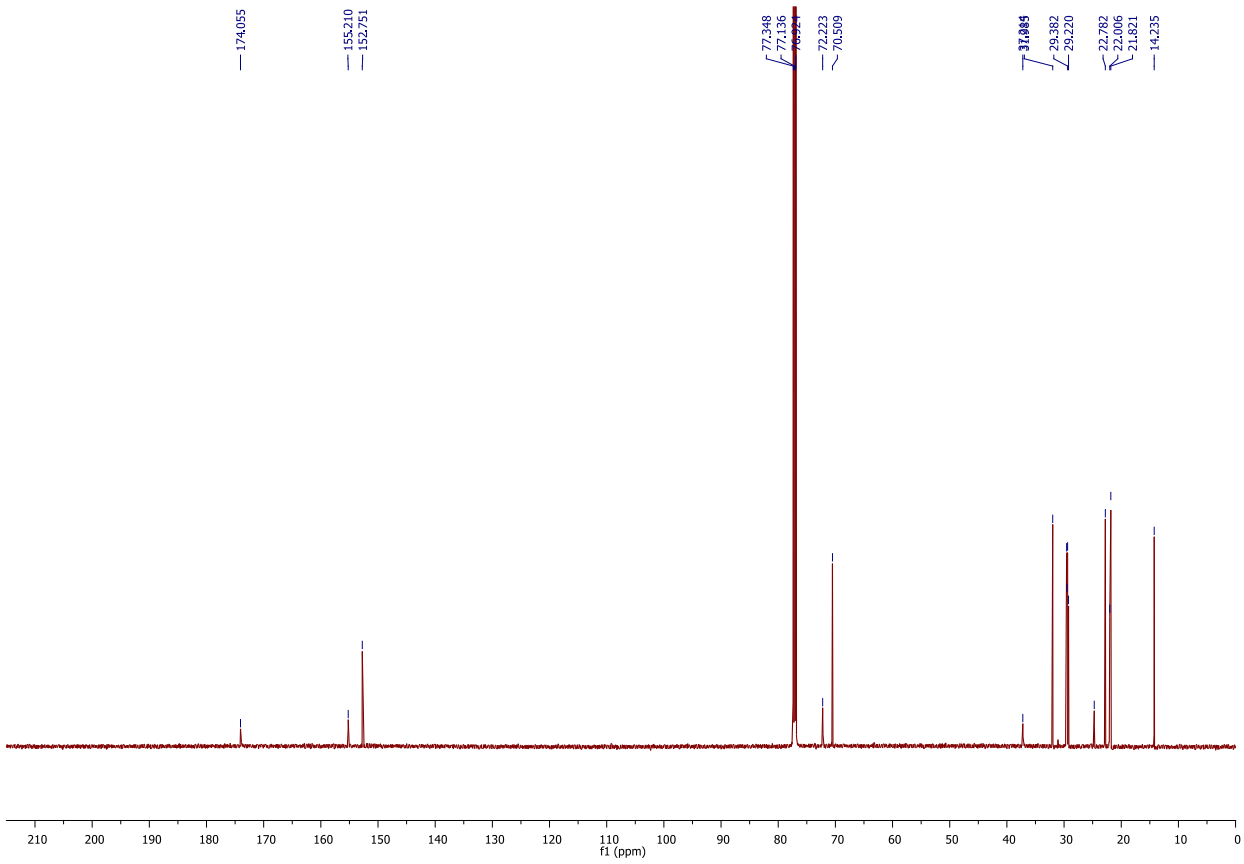


Dipropan-2-yl 1-decanoylhydrazine-1,2-dicarboxylate 48g

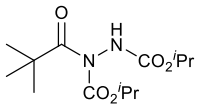


Using Method G, reaction was complete after 72 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-decanoylhydrazine-1,2-dicarboxylate **48g** as a colourless oil (304 mg, 0.85 mmol, 85%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.58 (br s, NH, 1H), 5.03 (septet, *J* = 6.5 Hz, 1H), 4.97 (septet, *J* = 6.5 Hz, 1H), 2.96-2.84 (m, 2H), 1.69-1.62 (m, 2H), 1.37-1.15 (m, 24H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0 (C), 155.2 (C), 152.8 (C), 72.2 (CH), 70.5 (CH), 37.2 (CH_2), 32.0 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 24.7 (CH_2), 22.8 (CH_2), 22.0 (CH_3), 21.8 (CH_3), 14.2 (CH_3); IR (thin film) 3323, 2982, 2924, 2855, 1737, 1720 cm^{-1}; LRMS (FAB) 381 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_{18}H_{34}N_2NaO_5$ $[M+Na]^+$ 381.2365, observed 381.2365.



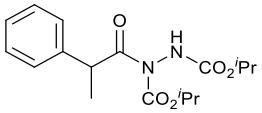


Dipropan-2-yl 1-(2,2-dimethylpropanoyl)hydrazine-1,2-dicarboxylate 48i[11]



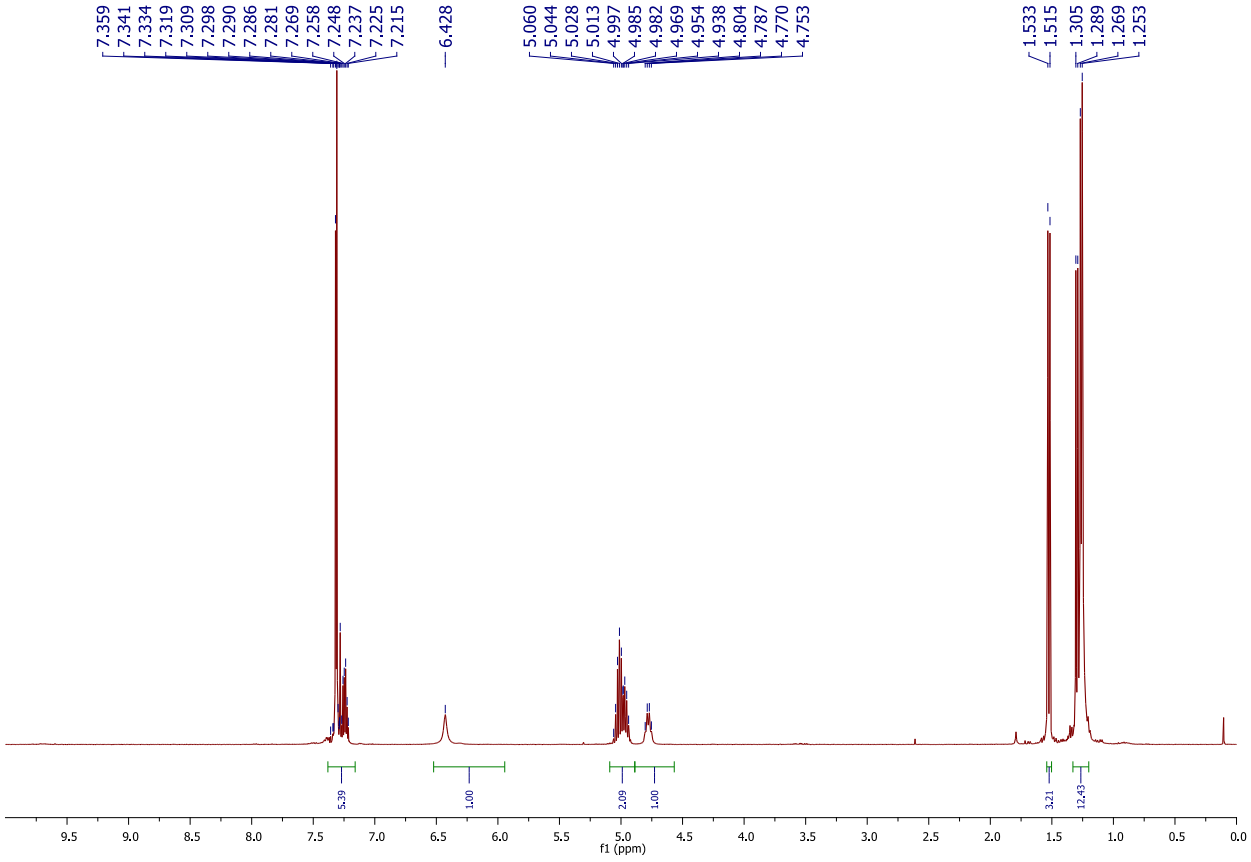
Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-(2,2-dimethylpropanoyl)hydrazine-1,2-dicarboxylate **48i** as a colourless oil (199 mg, 0.69 mmol, 69%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.58 (br s, NH, 1H), 5.04 (septet, J = 6.5 Hz, 1H), 4.99 (septet, J = 6.5 Hz, 1H), 1.33-1.18 (m, 21H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.9 (C), 155.8 (C), 153.4 (C), 72.4 (CH), 70.7 (CH), 42.2 (C), 27.6 (CH_3), 22.0 (CH_3), 21.8 (CH_3); IR (thin film) 3293, 2982, 2937, 1777, 1734, 1721 cm^{-1}; LRMS (FAB) 311 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_{13}H_{24}N_2O_5Na$ $[M+Na]^+$ 311.1583, observed 311.1588.

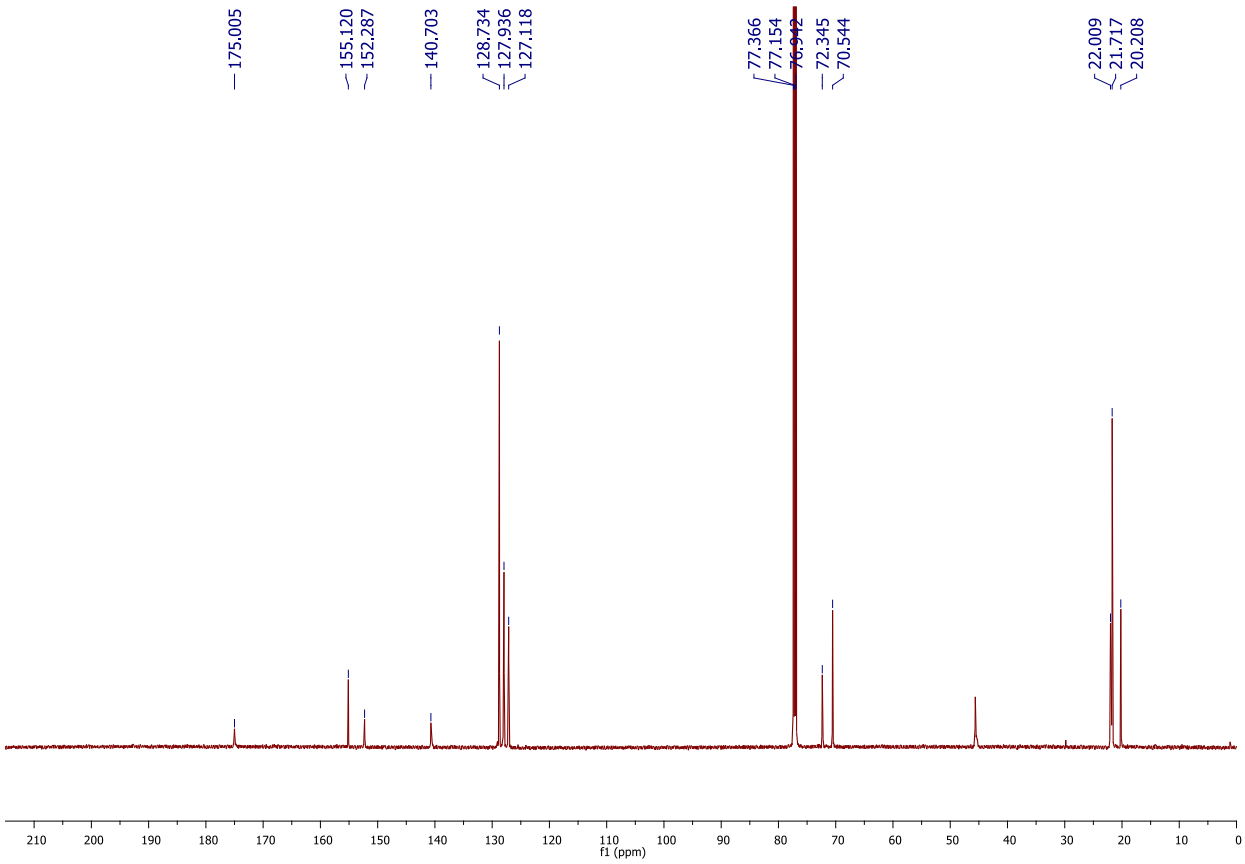
Dipropan-2-yl 1-(2-phenylpropanoyl)hydrazine-1,2-dicarboxylate 48j



Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-(2-phenylpropanoyl)hydrazine-1,2-dicarboxylate **48j** as

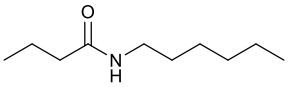
a colourless oil (239 mg, 0.71 mmol, 71%): ^{1}H NMR (400 MHz, $CDCl_3$, 55 °C) δ 7.33-7.20 (m, 5H), 6.42 (br s, NH, 1H), 5.01 (septet, *J* = 6.5 Hz, 1H), 4.98 (septet, *J* = 6.5 Hz, 1H), 4.77 (q, J = 7.0 Hz, 1H), 1.52 (d, *J* = 7.0 Hz, 1H), 1.32-1.21 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.0 (C), 155.1 (C), 152.3 (C), 140.7 (C), 128.7 (CH), 128.0 (CH), 127.1 (CH), 72.3 (CH), 70.5 (CH), 45.1 (CH), 22.0 (CH_3), 21.8 (CH_3), 20.2 (CH_3); IR (thin film) 3312, 2982, 2935, 1785, 1736, 1717 cm^{-1}; LRMS (ES) 335 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{17}H_{23}N_2O_5$ $[M-H]^-$ 335.1685, observed 335.1689.





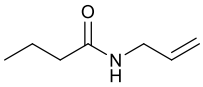
Typical procedure for the synthesis of amides 49a-c from acyl hydrazide 48a - Method H
To a solution of dipropan-2-yl 1-butanoylhydrazine-1,2-dicarboxylate **48a** (1 mmol) in CH_2Cl_2 (2 mL) was added amine (2.5 mmol) and the reaction mixture stirred at 300 rpm at 21 °C for 16 h. The solvent was removed *in vacuo* and the crude residue purified as described below.

***N*-Hexylbutanamide 49a**[11]



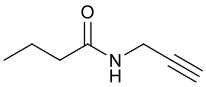
Using Method H. Purification by column chromatography (20-60% EtOAc/petrol) gave *N*-hexylbutanamide **49a** as a colourless oil (164 mg, 0.96 mmol, 96%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.45-5.35 (m, NH, 1H), 3.26 (q, *J* = 7.0 Hz, 2H), 2.16 (t, *J* = 7.5 Hz, 2H), 1.68 (sextet, *J* = 7.5 Hz, 2H), 1.51 (quintet, *J* = 7.0 Hz, 2H), 1.36-1.24 (m, 6H), 1.00 (t, *J* = 7.5 Hz, 3H). 0.95 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.9 (C), 39.6 (CH_2), 38.9 (CH_2), 31.5 (CH_2), 29.7 (CH_2), 26.6 (CH_2), 22.6 (CH_2), 19.3 (CH_2), 14.1 (CH_3), 13.8 (CH_3); IR (thin film) 3290, 3083, 2959, 2929, 2872, 1643, 1550 cm^{-1}; LRMS (CI) 172 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{10}H_{22}NO$ $[M+H]^+$ 172.1701, observed 172.1698.

***N*-(Prop-2-en-1-yl)butanamide 49b**[11]

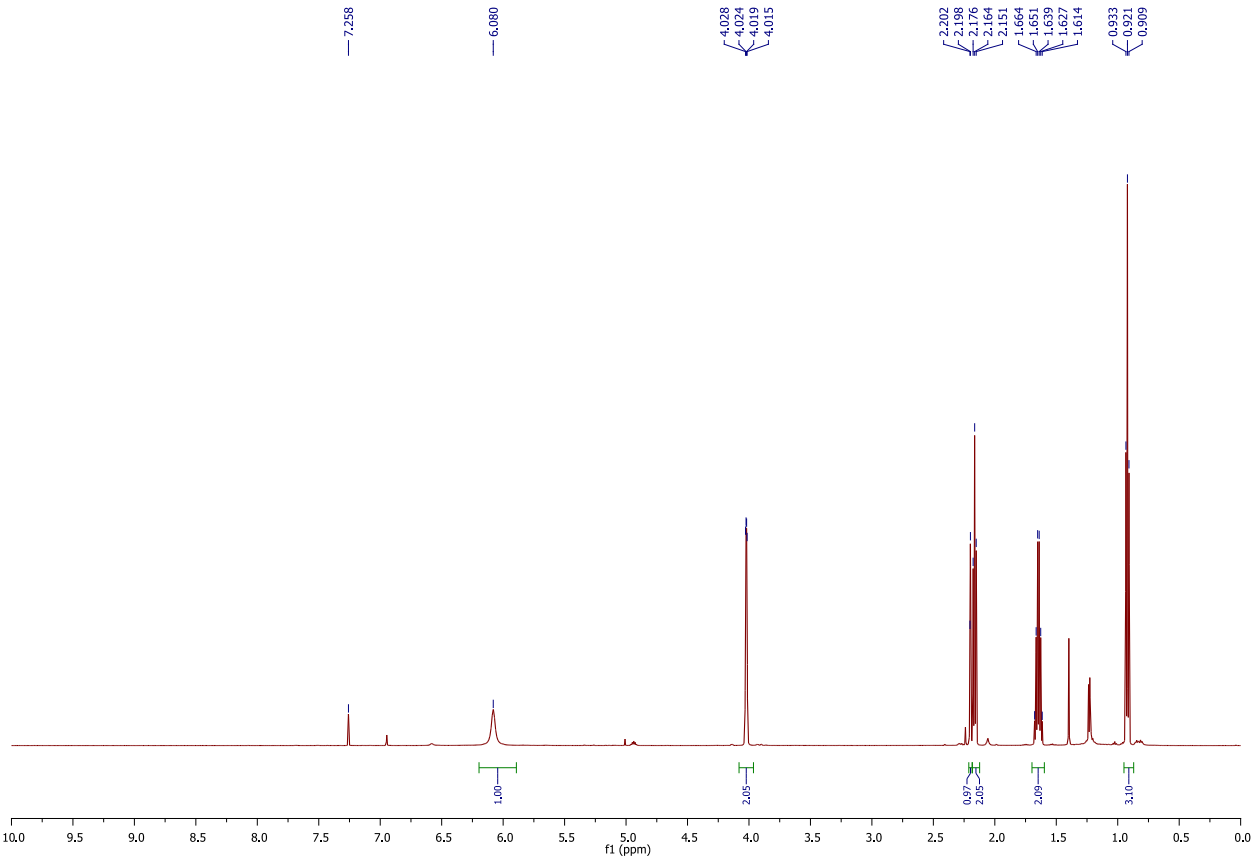


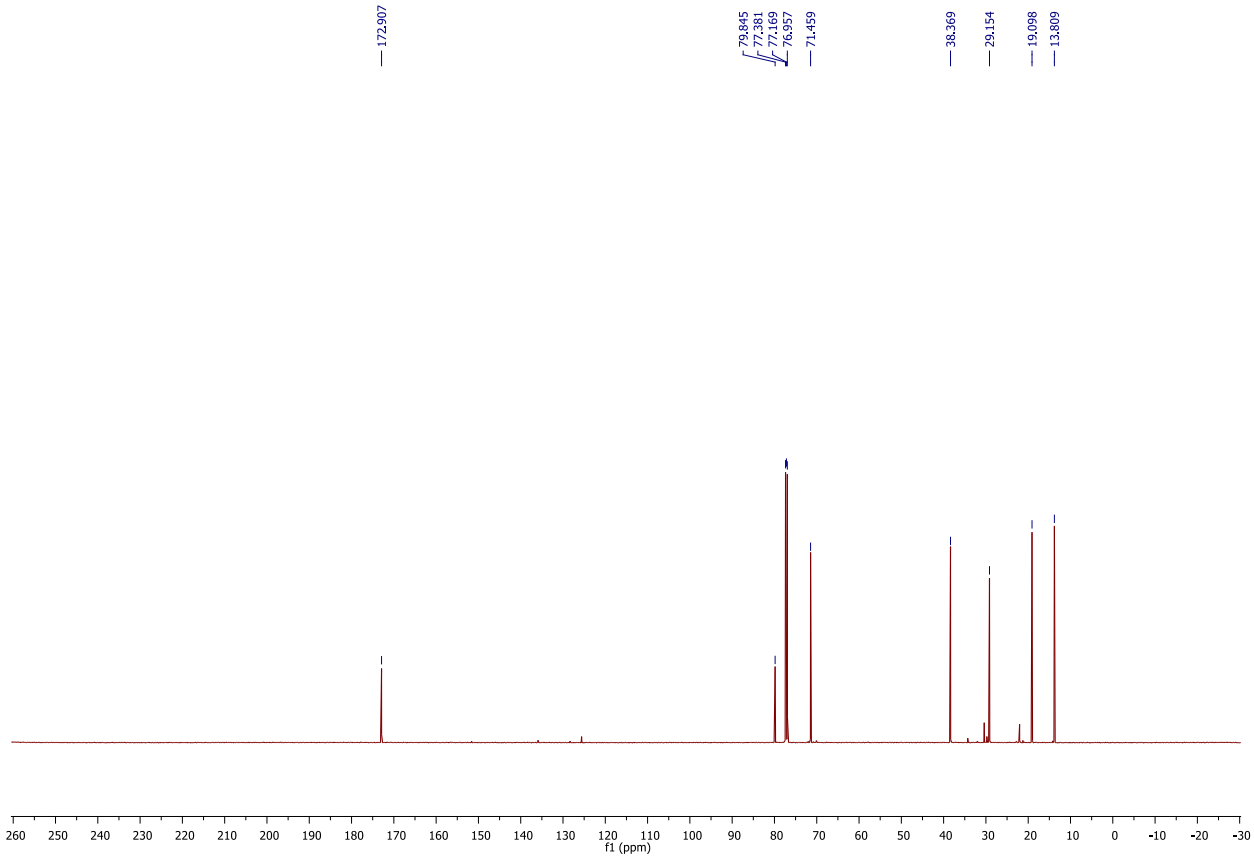
Using Method H. Purification by column chromatography (20-60% EtOAc/petrol) gave *N*-(prop-2-en-1-yl)butanamide **49b** as a colourless oil (121 mg, 0.95 mmol, 95%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.83 (ddt, *J* = 17.0, 11.5, 6.0 Hz, 1H), 5.64-5.56 (m, NH, 1H), 5.08 (dq, *J* = 17.0, 1.5 Hz, 1H), 4.99 (dq, *J* = 11.5, 1.5 Hz, 1H), 3.88 (tt, *J* = 6.0, 1.5 Hz, 2H), 2.17 (t, *J* = 7.5 Hz, 2H), 1.67 (sextet, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0 (C), 134.5 (CH), 116.4 (CH_2), 42.0 (CH_2), 38.8 (CH_2), 19.3 (CH_2), 13.9 (CH_3); IR (thin film) 3290, 3083, 2964, 2930, 2874, 1643, 1548 cm^{-1}; LRMS (EI) 127 (100, $[M]^{+\cdot}$); HRMS (EI) calcd for $C_7H_{13}NO$ $[M]^{+\cdot}$ 127.0992, observed 127.0995.

***N*-(Prop-2-yn-1-yl)butyramide 49c**[12]

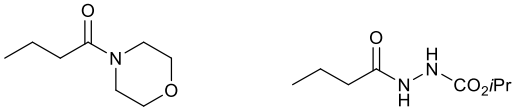


Using Method H. Purification by column chromatography (20-30% Et_2O/petrol) gave *N*-(prop-2-yn-1-yl)butyramide **49c** as an orange oil (123 mg, 0.98 mmol, 98%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.20-6.11 (m, NH, 1H), 4.02 (dd, *J* = 7.5, 4.5 Hz, 2H), 2.19 (t, *J* = 4.5, 1H), 2.17 (t, *J* = 7.5 Hz, 2H), 1.64 (sextet, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0 (C), 79.9 (C), 71.5 (CH), 38.4 (CH_2), 29.2 (CH_2), 19.1 (CH_2), 13.8 (CH_3); IR (thin film) 3067, 2956, 2927, 2864, 1640, 1532 cm^{-1}; LRMS (CI) 126 (100, $[M+H]^{+}$); HRMS (EI) calcd for $C_7H_{12}NO$ $[M+H]^{+}$ 126.0913, observed 126.0911.



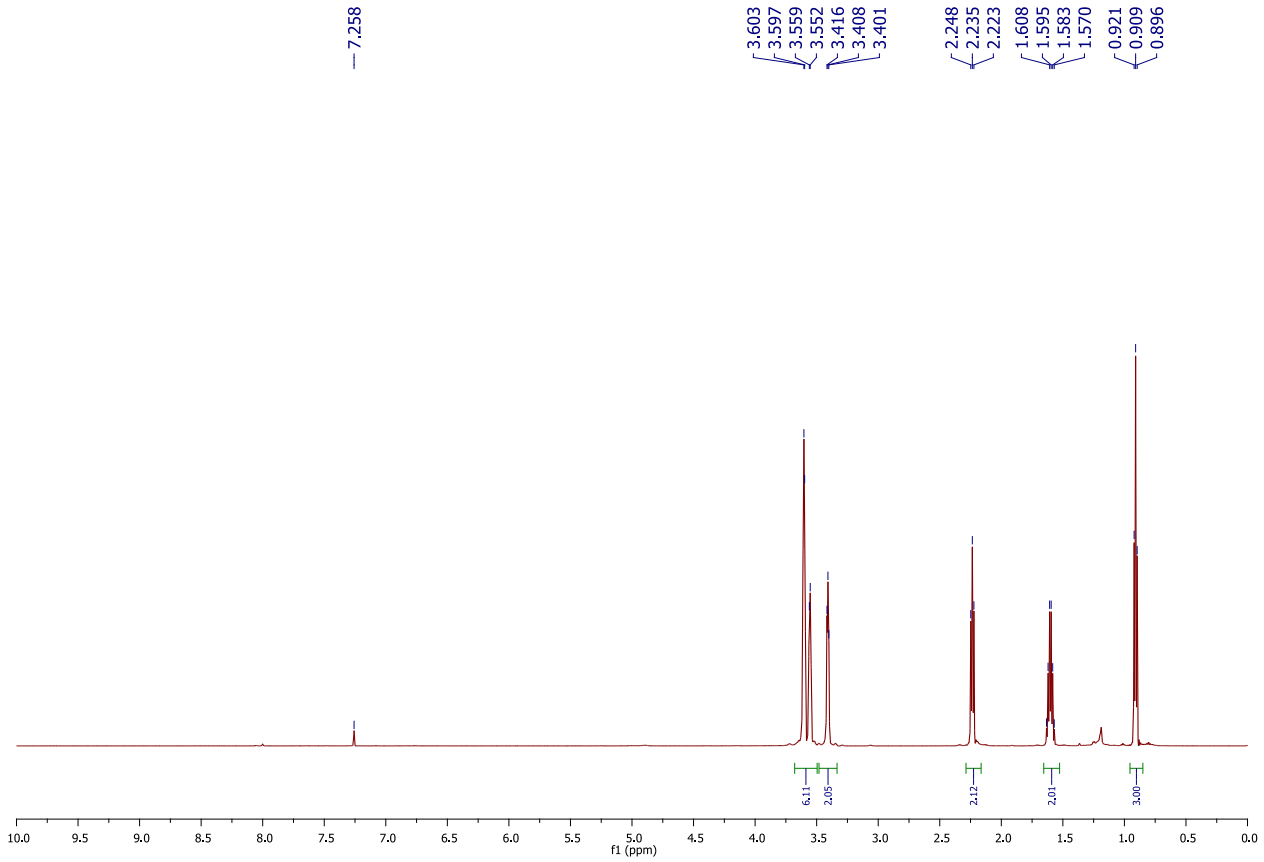


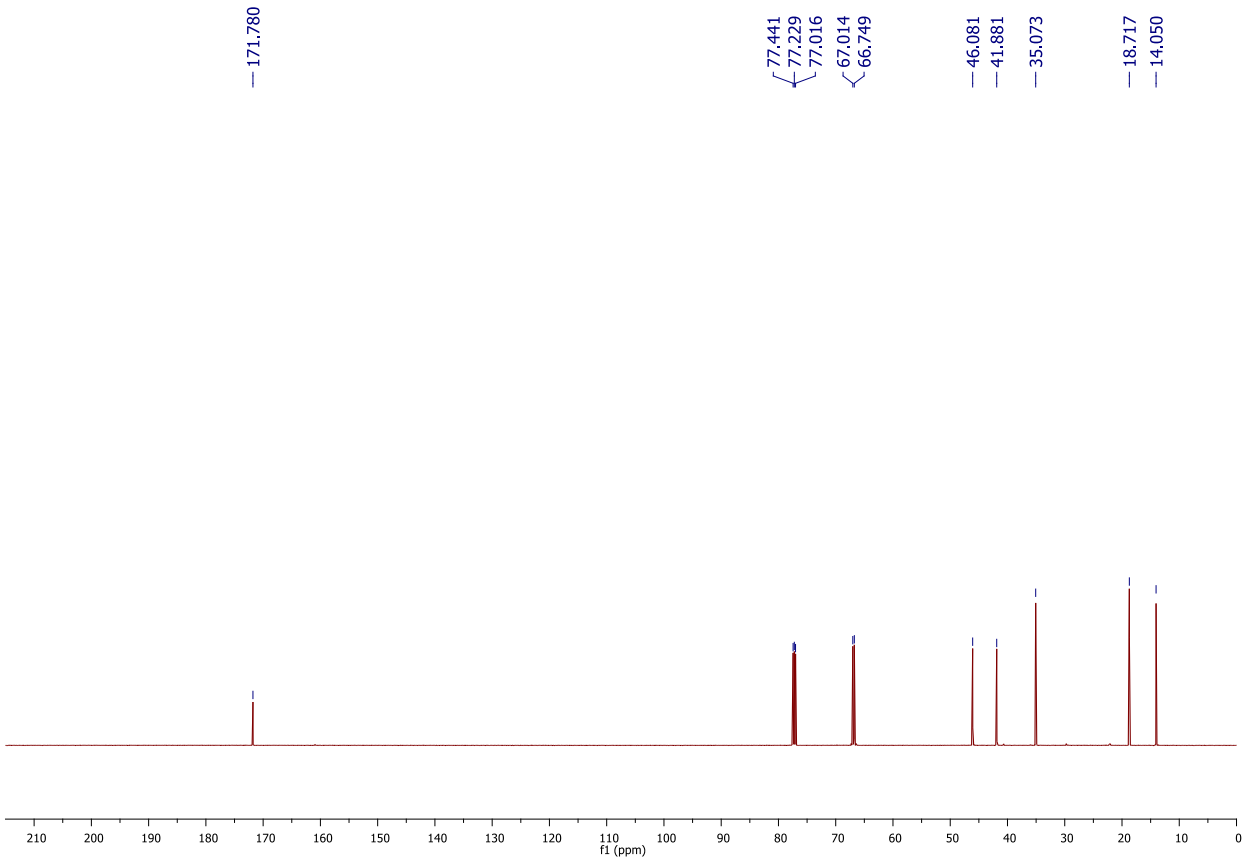
_N_-Morpholinobutan-1-one 49d[13] and isopropyl butyrylcarbamate 51



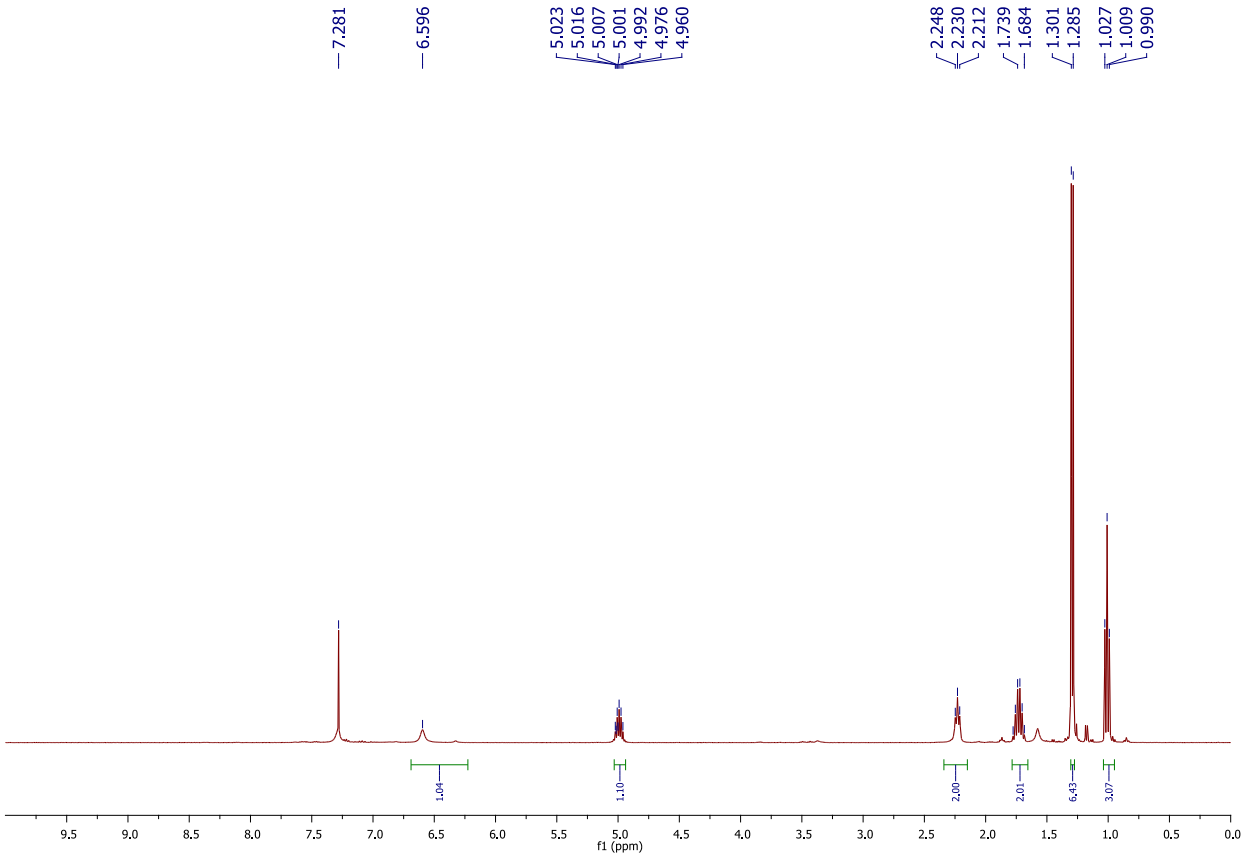
Using Method H. Purification by column chromatography (15-30% Et_2O/Petrol) gave *N*-morpholinobutan-1-one **49d** as an orange oil (30 mg, 0.19 mmol, 19%) and isopropyl butyrylcarbamate **51** (113 mg, 0.60 mmol, 60%).

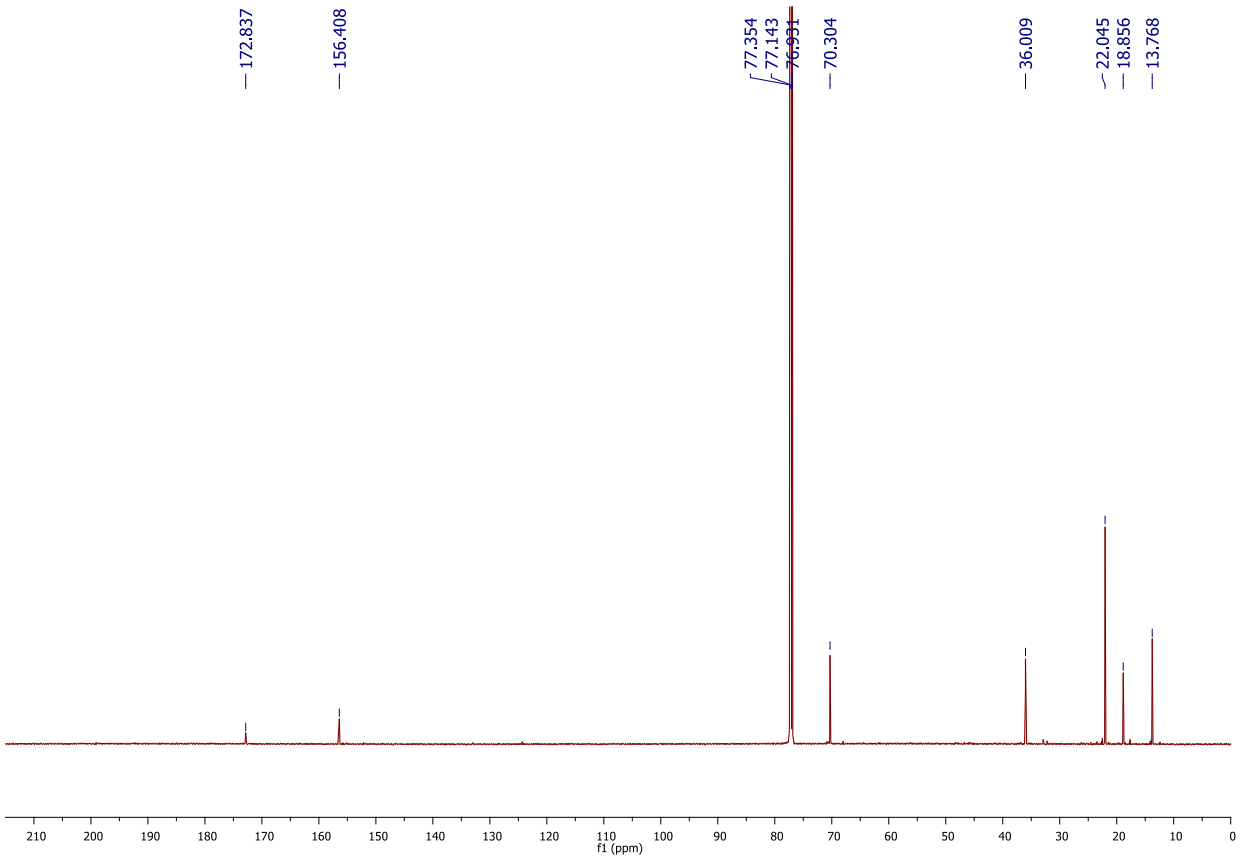
Data for *N*-morpholinobutan-1-one **49d**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.64-3.54 (m, 6H), 3.44-3.38 (m, 2H), 2.24 (t, *J* = 7.5, 2H), 1.58 (sextet, *J* = 7.5, 2H), 0.91 (t, *J* = 7.5, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8 (C), 67.0 (CH_2), 66.8 (CH_2), 46.1 (CH_2), 41.9 (CH_2), 35.1 (CH_2), 18.7 (CH_2), 14.1 (CH_3); IR (thin film) 3290, 3262, 2967, 2926, 1628 cm^{-1}; LRMS (CI) 158 (100, $[M+H]^+$); HRMS (CI) calcd for $C_8H_{16}NO_2$ $[M+H]^+$ 158.1176, observed 158.1174.



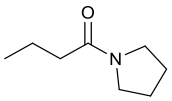


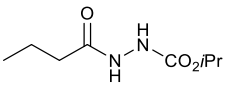
Data for isopropyl butyrylcarbamate **51**: ^{1}H NMR (400 MHz, $CDCl_3$, 55 °C) δ 6.60 (br s, NH, 1H), 5.00 (septet, *J* = 6.5 Hz, 1H), 2.23 (t, *J* = 7.5 Hz, 2H), 1.73 (sextet, *J* = 7.5 Hz, 2H), 1.29 (d, *J* = 6.5 Hz, 6H), 1.01 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8 (C), 156.4 (C), 70.3 (CH), 36.0 (CH_2), 22.0 (CH_3), 18.9 (CH_2), 13.8 (CH_3); IR (thin film) 3305, 2977, 2875, 1712, 1697, 1672 cm^{-1}; LRMS (CI) 189 (100, $[M+H]^+$); HRMS (CI) calcd for $C_8H_{17}N_2O_3$ $[M+H]^+$ 189.1161, observed 189.1170.





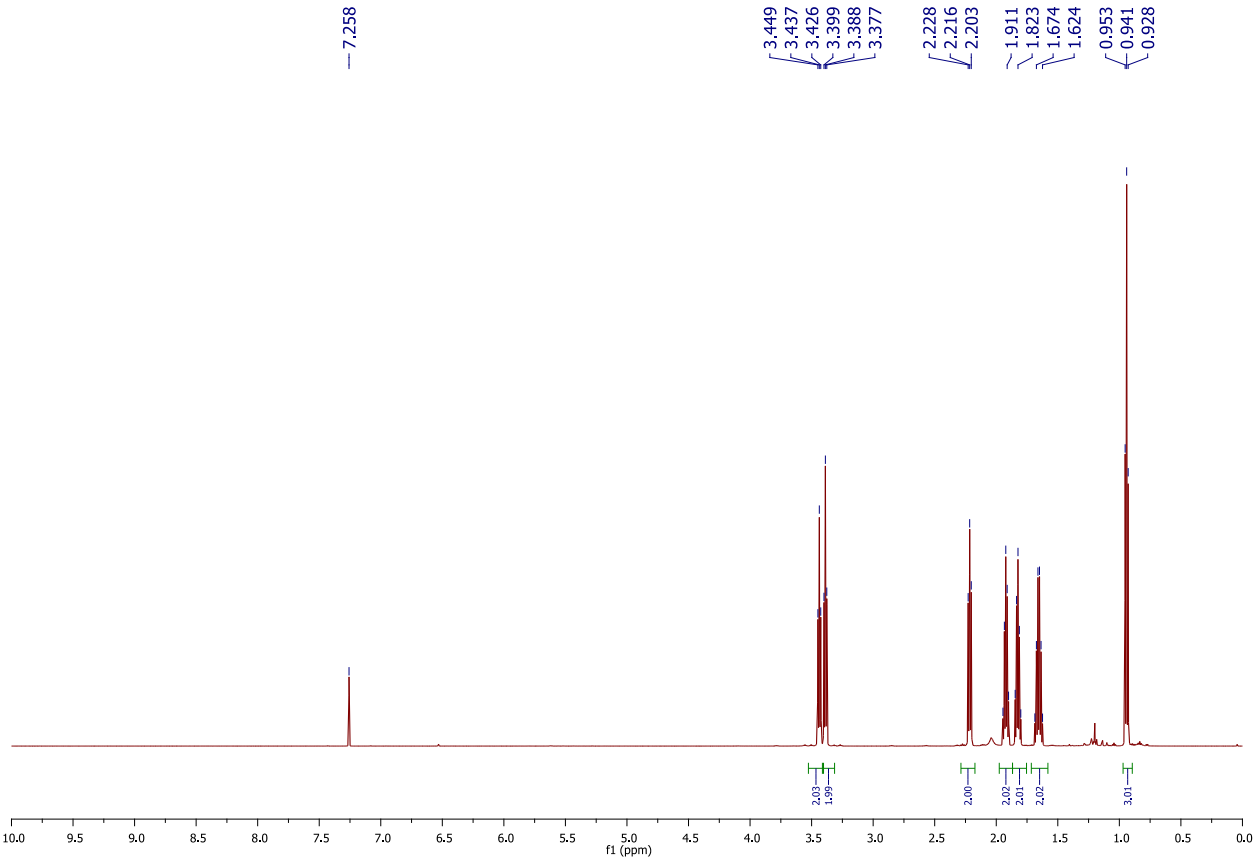
_N_-(Pyrrolidin-1-yl)butan-1-one 49e[14] and isopropyl butyrylcarbamate 51

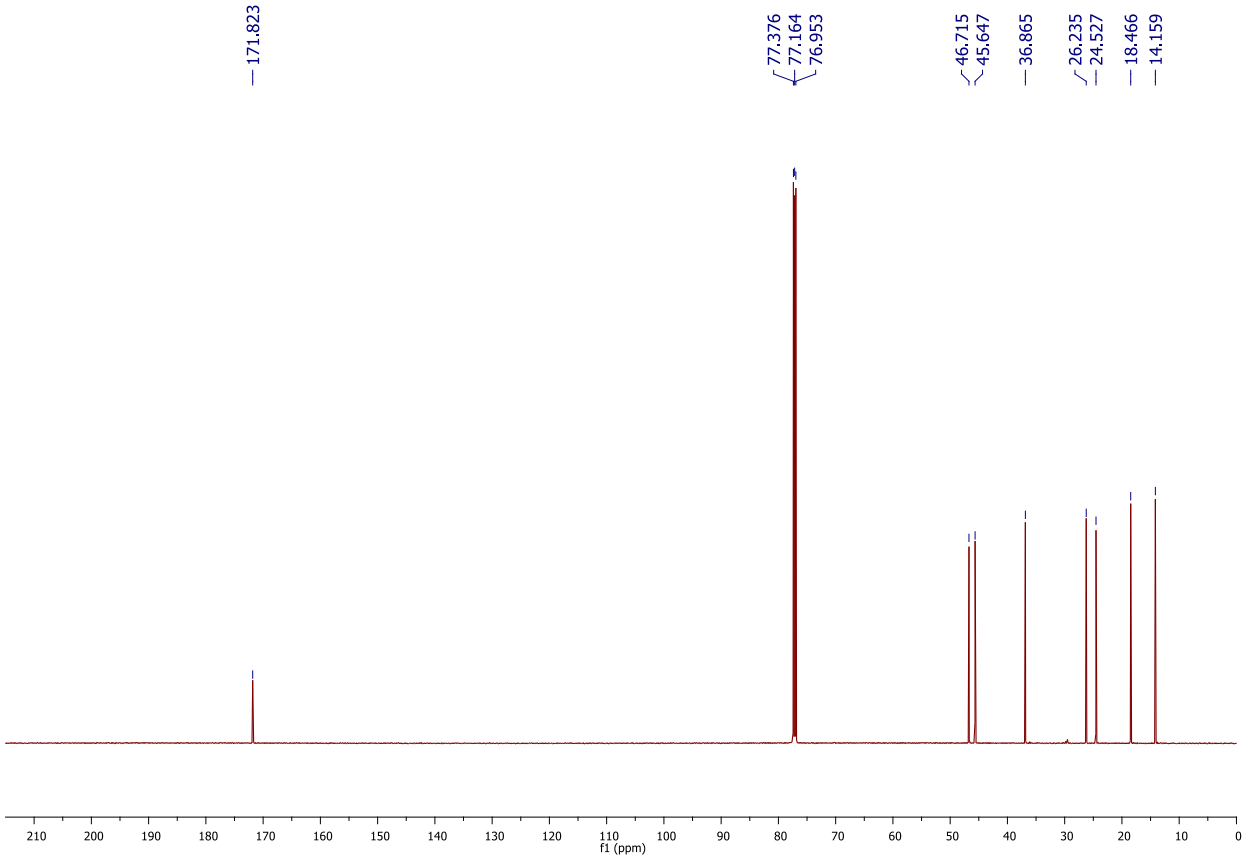




Using Method H. Purification by column chromatography (30-80% Et_2O/petrol) gave *N*-(pyrrolidin-1-yl)butan-1-one **49e** as a colourless oil (35 mg, 0.25 mmol, 25%) and isopropyl butyrylcarbamate **51** (107 mg, 0.57 mmol, 57%).

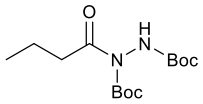
Data for *N*-(pyrrolidin-1-yl)butan-1-one **49e**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.44 (t, *J* = 7.0 Hz, 2H), 3.39 (t, *J* = 7.0 Hz, 2H), 2.22 (t, *J* = 7.5 Hz, 2H), 1.92 (quintet, *J* = 6.5 Hz, 2H), 1.82 (quintet, *J* = 6.5 Hz, 2H), 1.64 (sextet, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.8 (C), 46.7 (CH_2), 45.6 (CH_2), 36.9 (CH_2), 26.2 (CH_2), 24.5 (CH_2), 18.5 (CH_2), 14.2 (CH_3); IR (thin film) 3280, 3258, 2962, 1632 cm^{-1}.



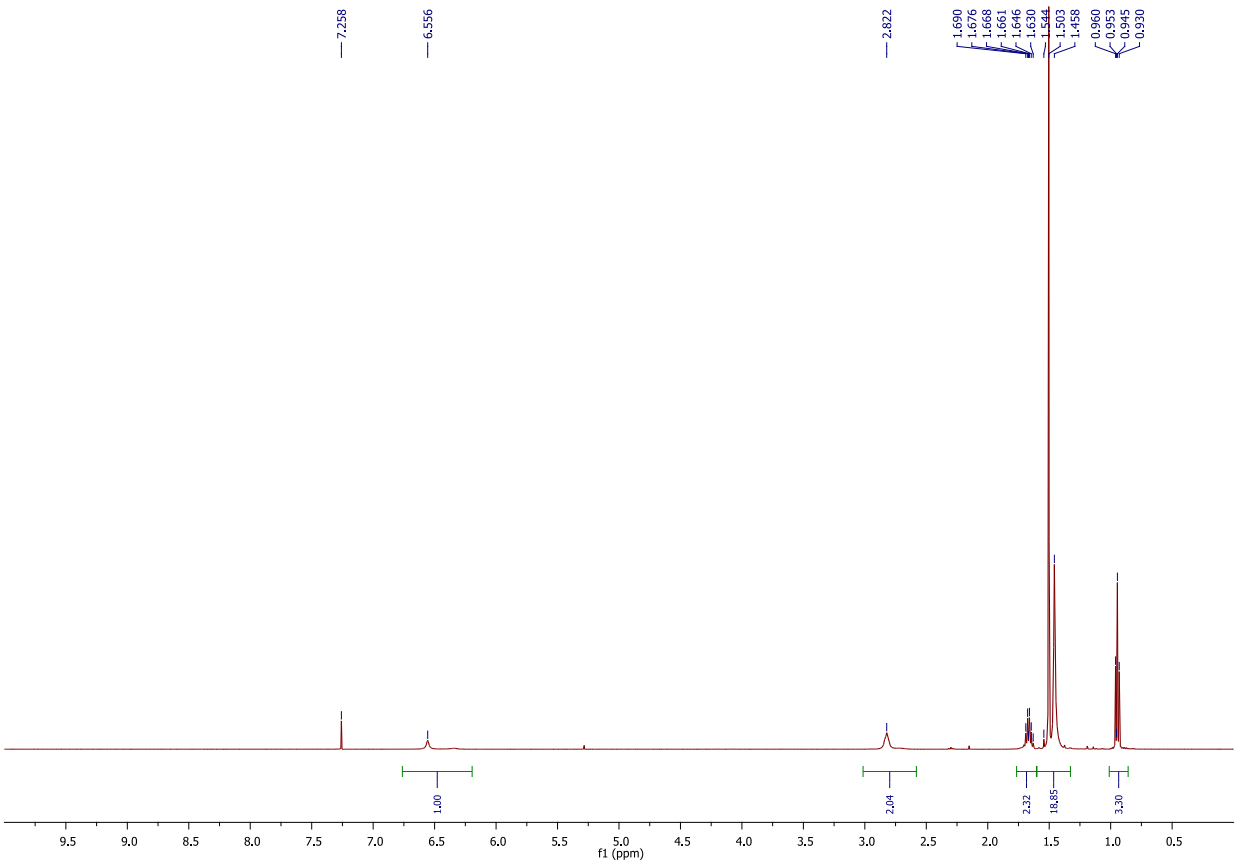


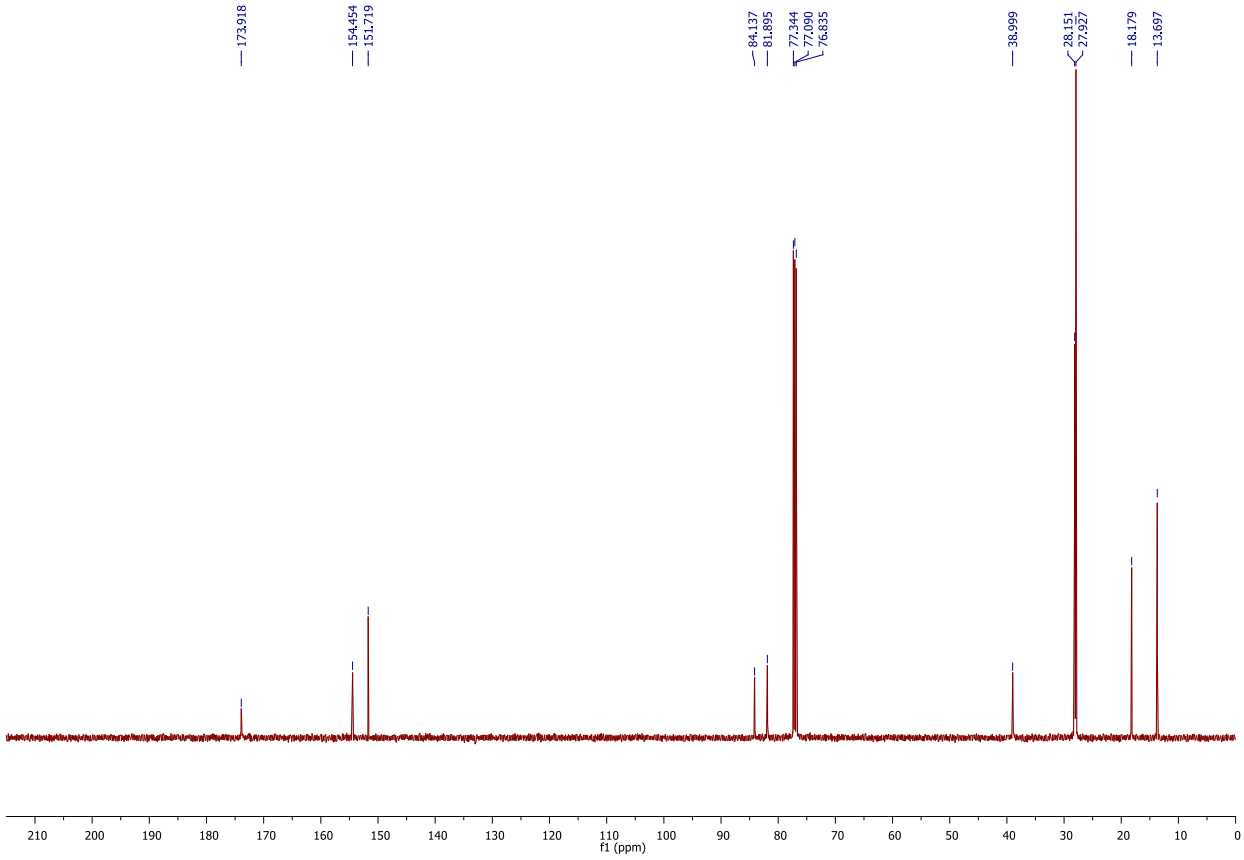
Data for isopropyl butyrylcarbamate **51**: Data matched that as described above.

Di-*tert*-butyl 1-butyrylhydrazine-1,2-dicarboxylate 52



Using Method G, reaction was complete after 120 h. Purification by column chromatography (15-30% Et_2O/Petrol) gave di-*tert*-butyl 1-butyrylhydrazine-1,2-dicarboxylate **52** as a colourless oil (187 mg, 0.62 mmol, 62%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (br s, NH, 1H), 2.84-2.80 (m, 2H), 1.66 (sextet, *J* = 6.5, 2H), 1.50 (s, 18H), 0.95 (t, *J* = 6.5, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.9 (C), 154.5 (C), 151.7 (C), 84.1 (C), 81.9 (C), 39.0 (CH_2), 28.2 (CH_3), 27.9 (CH_3), 18.2 (CH_2), 13.7 (CH_3); IR (thin film) 3343, 2970, 2937, 1733, 1711 cm^{-1}; LRMS (ES) 301 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{14}H_{25}N_2O_5$ $[M-H]^-$ 301.1763, observed 301.1764.

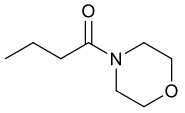




Typical procedure for the synthesis of amides 49d-e from acyl hydrazide 52 - Method I

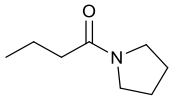
To a solution of di-*tert*-butyl 1-butyrylhydrazine-1,2-dicarboxylate **52** (1 mmol) in CH_2Cl_2 (2 mL) was added amine (2.5 mmol) and the reaction mixture stirred at 300 rpm at 21 °C for 16 h. The solvent was removed *in vacuo* and the crude residue purified as described below.

***N*-Morpholinobutan-1-one 49d**[13]



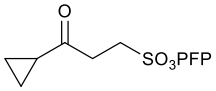
Using Method I. Purification by column chromatography (15-30% Et_2O/Petrol) gave *N*-morpholinobutan-1-one **49d** as an orange oil (93 mg, 0.59 mmol, 59%). Data matched that as described above.

_N_-(Pyrrolidin-1-yl)butan-1-one 49e[14]



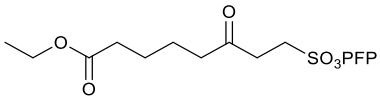
Using Method I. Purification by column chromatography (30-80% Et_2O/petrol) gave *N*-(pyrrolidin-1-yl)butan-1-one **49e** as a colourless oil (106 mg, 0.75 mmol, 75%). Data matched that as described above.

3-Cyclopropyl-3-oxo-propane-1-sulfonic acid pentafluorophenyl ester 15k[6]

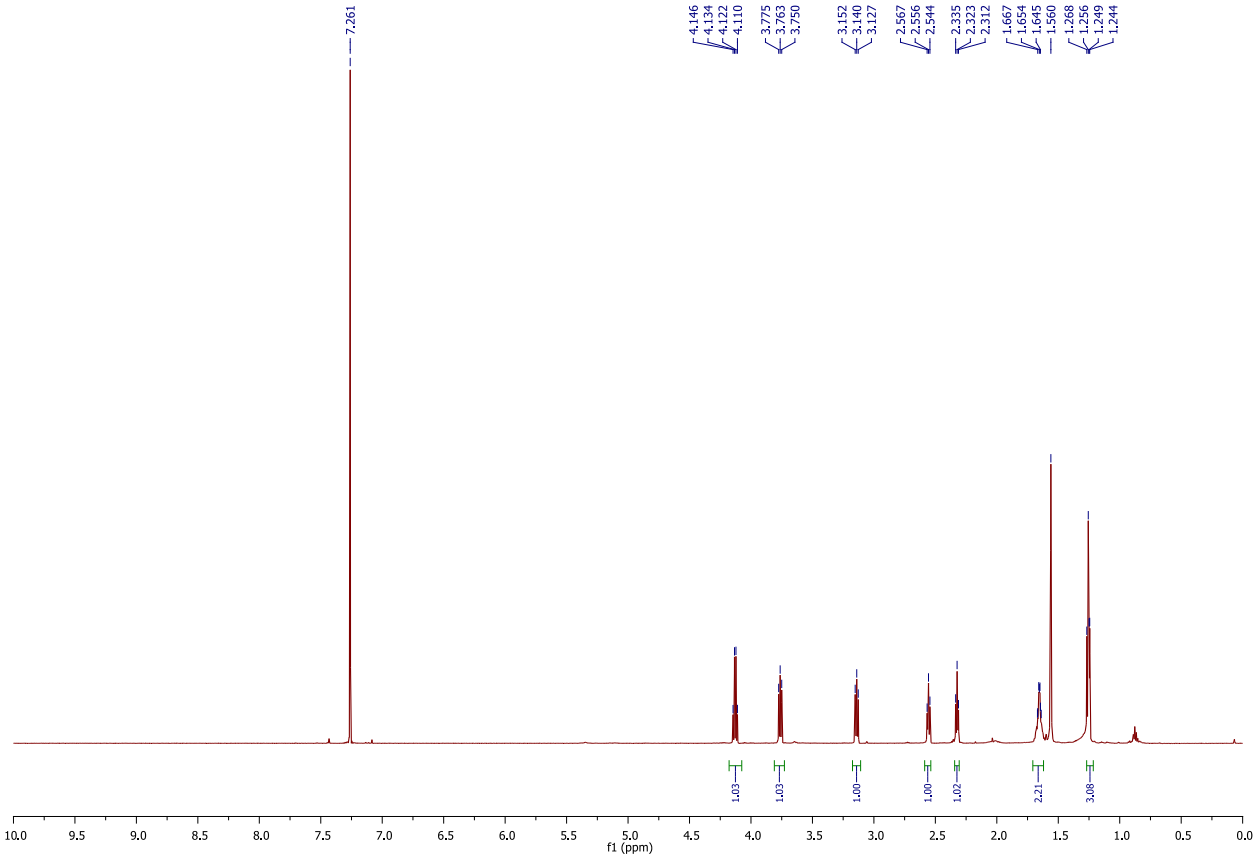


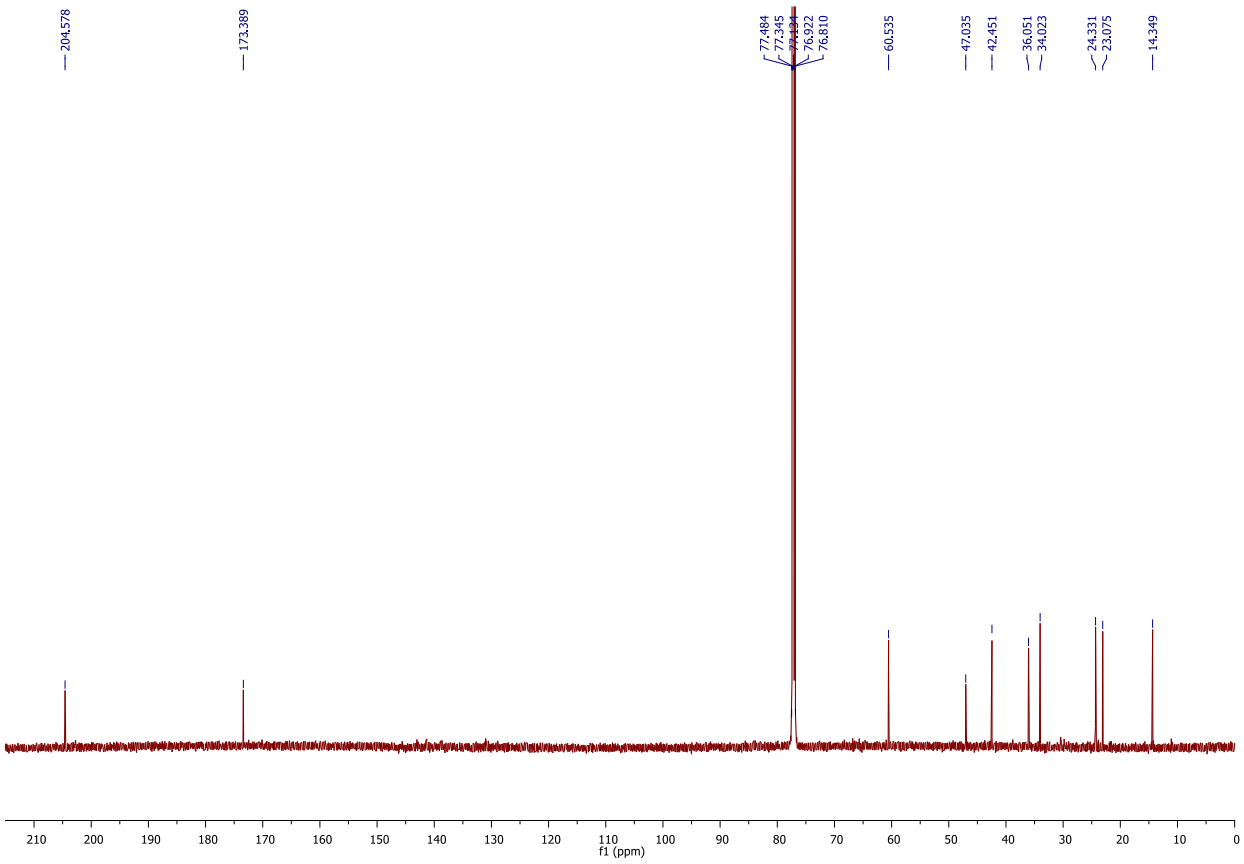
Using Method B, reaction was complete after 3 h. Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave 3-cyclopropyl-3-oxo-propane-1-sulfonic acid pentafluorophenyl ester **15k** as an off-white solid (219 mg, 0.64 mmol, 64%): m.p. 52-54 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82-3.74 (m, 2H), 3.38-3.31 (m, 2H), 2.02 (tt, *J* = 4.5, 7.8, 1H), 1.18-1.12 (m, 2H), 1.06-0.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.9 (C), 47.1 (CH_2), 36.5 (CH_2), 20.7 (CH), 11.8 (CH_2); IR (neat) 2927, 1702 cm^{-1}; LRMS (CI) 362 (100, $[M+NH_4]^+$); HRMS (ES) calcd for $C_{12}H_9F_5NO_4S$ $[M+NH_4]^+$. 362.0480; observed 362.0484.

Ethyl 6-oxo-8-((pentafluorophenyl)sulfonate)octanoate 15l

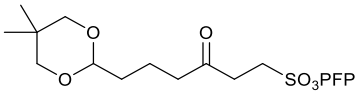


Using Method B, reaction was complete after 3 h. Purification by flash column chromatography (20-95% CH_2Cl_2/petrol) gave ethyl 6-oxo-8-((pentafluorophenoxy)sulfonyl)octanoate **15l** as an oil (294 mg, 0.68 mmol, 68%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.12 (q, *J* = 7.0 Hz, 2H), 3.77-3.75 (m, 2H), 3.15-3.12 (m, 2H), 2.56 (t, *J* = 7.0 Hz, 2H), 2.32 (t, *J* = 7.0 Hz, 2H), 1.70-1.59 (m, 2H), 1.25 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.6 (C), 173.4 (C), 60.5 (CH_2), 47.0 (CH_2), 42.5 (CH_2), 36.1 (CH_2), 34.0 (CH_2), 24.3 (CH_2), 23.1 (CH_2), 14.4 (CH_3); IR (neat) 2928, 2849, 1726, 1520 cm^{-1}; LRMS (CI) 433 (20, $[M+H]^+$), 387 (100); HRMS (CI) calcd for $C_{16}H_{18}F_5O_6S$ $[M+H]^+$ 433.0744; observed 433.0743.

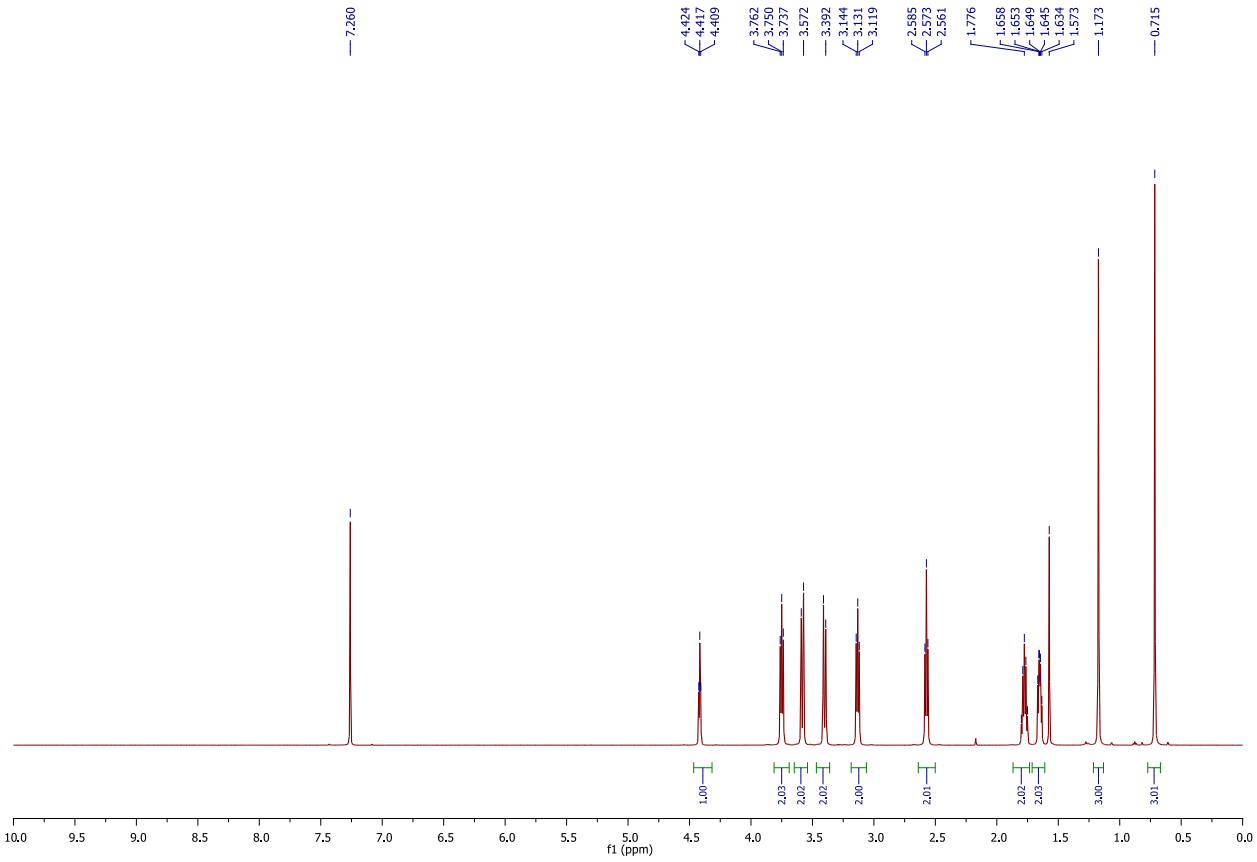


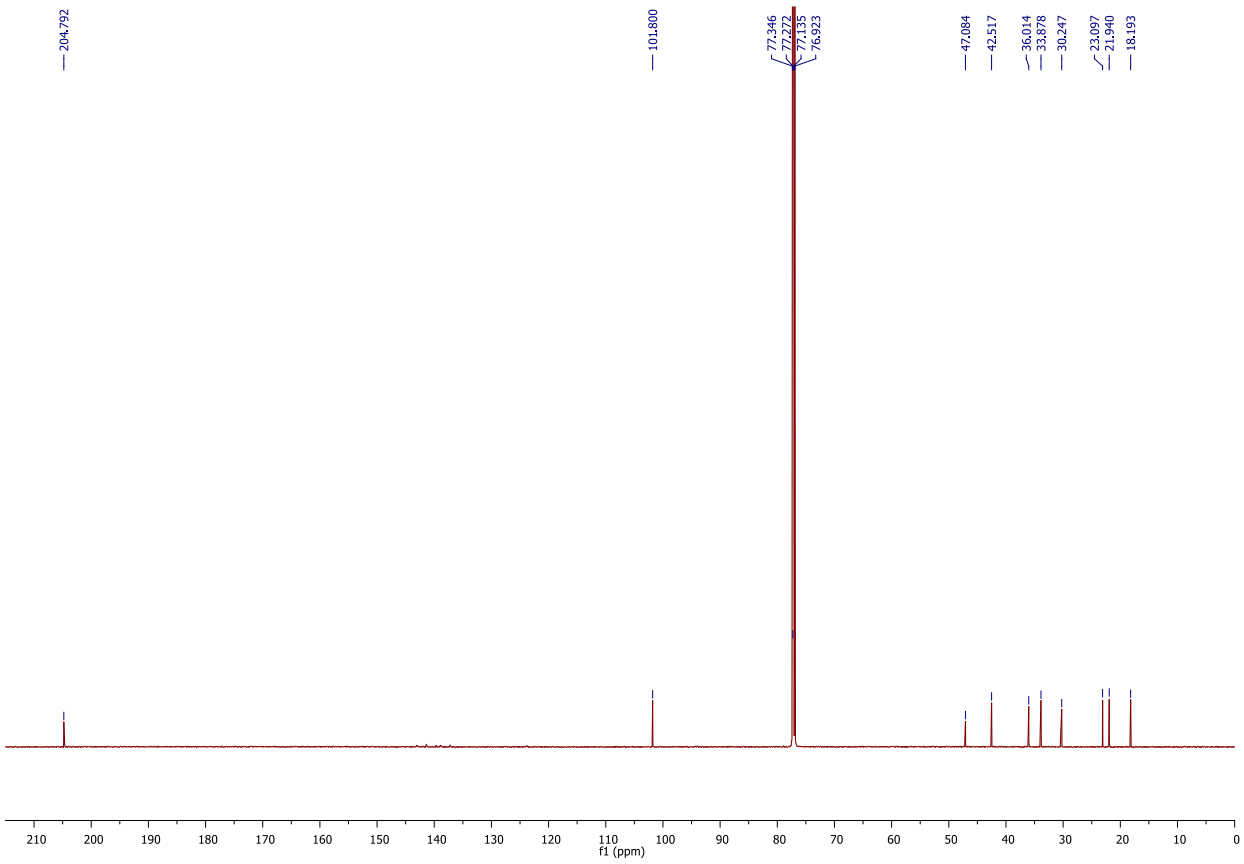


6-(5,5-Dimethyl-1,3-dioxan-2-yl)-3-oxohexane-1-sulfonate acid pentafluorophenyl ester 15m

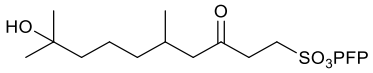


Using Method B, reaction was complete after 6 h. Purification by flash column chromatography (20-95% CH_2Cl_2/petrol) gave 6-(5,5-dimethyl-1,3-dioxan-2-yl)-3-oxohexane-1-sulfonate acid pentafluorophenyl ester **15m** as an oil (285 mg, 0.62 mmol, 62%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.42 (t, *J* = 4.5 Hz, 1H), 3.77-3.75 (m, 2H), 3.58 (d, *J* = 11.0 Hz, 2H), 3.40 (d, *J* = 11.0 Hz, 2H), 3.14-3.11 (m, 2H), 2.57 (t, *J* = 7.0 Hz, 2H), 1.80-1.75 (m, 2H), 1.67-1.62 (m, 2H), 1.17 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.8 (C), 101.8 (CH), 47.1 (CH_2), 42.5 (CH_2), 36.0 (CH_2), 33.9 (CH_2), 30.2 (C), 23.1 (CH_3), 22.0 (CH_3), 18.2 (CH_2); IR (neat) 2953, 2857, 1718, 1520 cm^{-1}; LRMS (CI) 461 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{18}H_{22}F_5O_6S$ $[M+H]^+$ 461.1052; observed 461.1058.

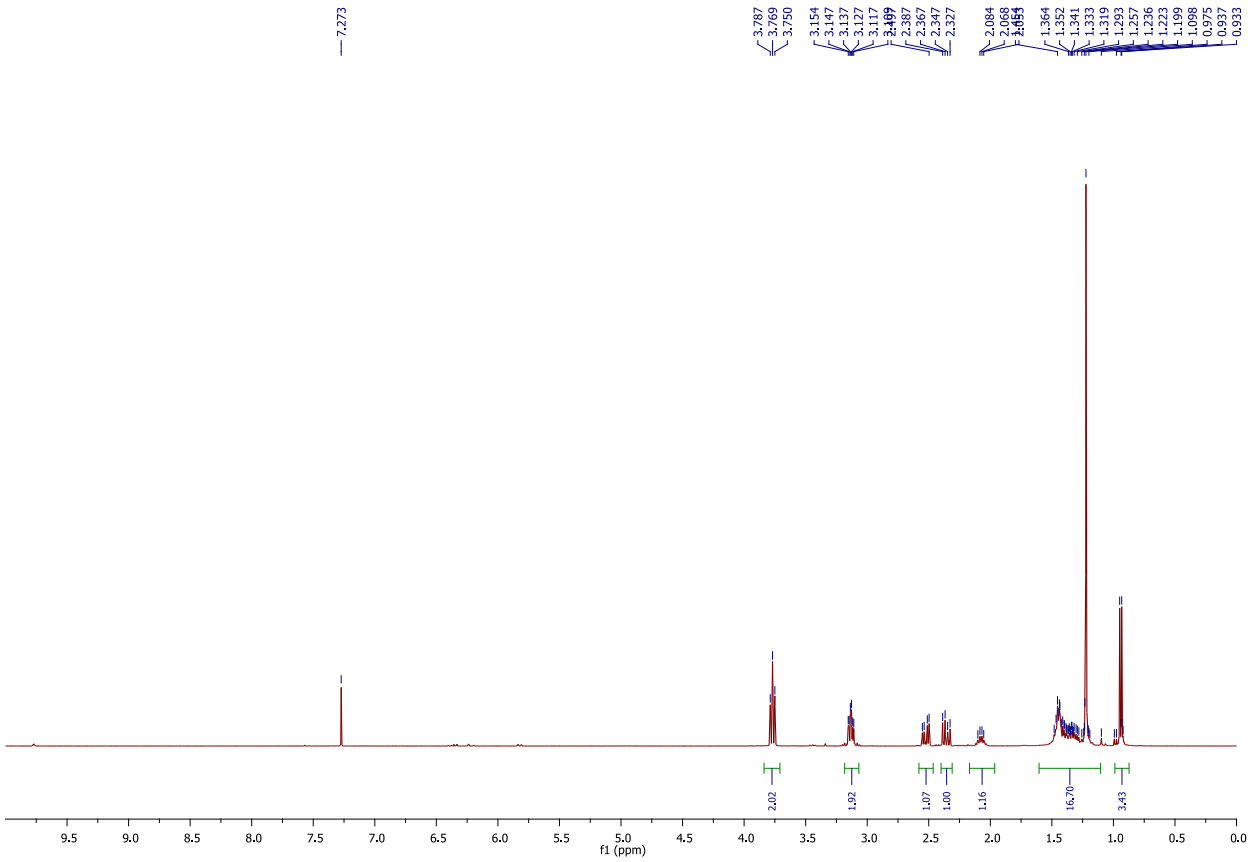


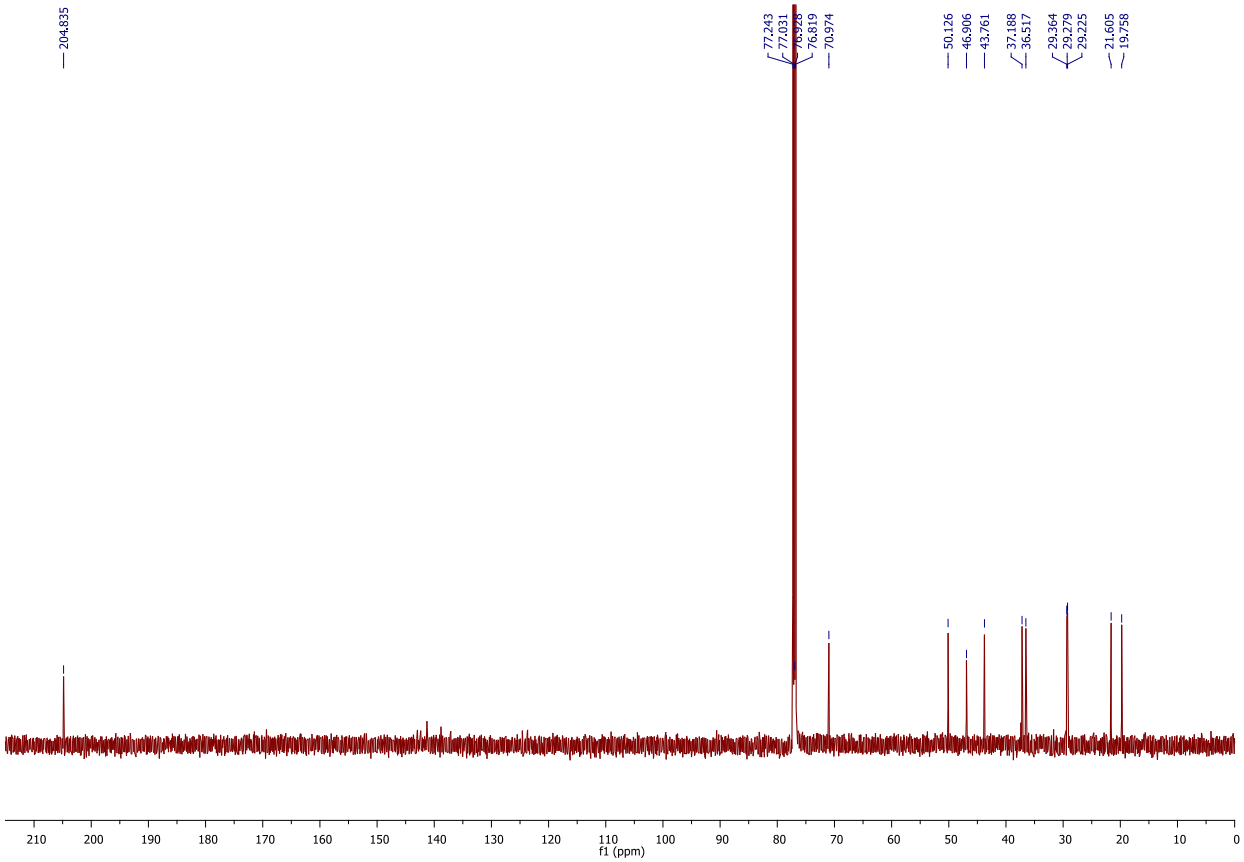


9-Hydroxy-5,9-dimethyl-3-oxodecane-1-sulfonate acid pentafluorophenyl ester 15n

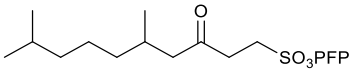


Using Method B, reaction was complete after 6 h. Purification by flash column chromatography (20% EtOAc/petrol) gave 9-hydroxy-5,9-dimethyl-3-oxodecane-1-sulfonate sulfonate acid pentafluorophenyl ester **15n** as an oil (361 mg, 0.81 mmol, 81%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.79-3.75 (m, 2H), 3.15-3.11 (m, 2H), 2.53 (dd, *J* = 16.0, 6.0 Hz, 1H), 2.35 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.11-2.04 (m, 1H), 1.50-1.19 (m, 13H), 0.93 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.9 (C), 71.0 (C), 50.1 (CH_2), 46.9 (CH_2), 43.8 (CH_2), 37.2 (CH_2), 36.5 (CH_2), 29.4 (CH_3), 29.3 (CH_3), 29.2 (CH), 21.6 (CH_2), 19.8 (CH_3); IR (neat) 3417, 2968, 1718, 1518, 1383 cm^{-1}; LRMS (FAB) 469 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_{18}H_{23}F_5O_5SNa$ $[M+Na]^+$ 469.1084; observed 461.1090.

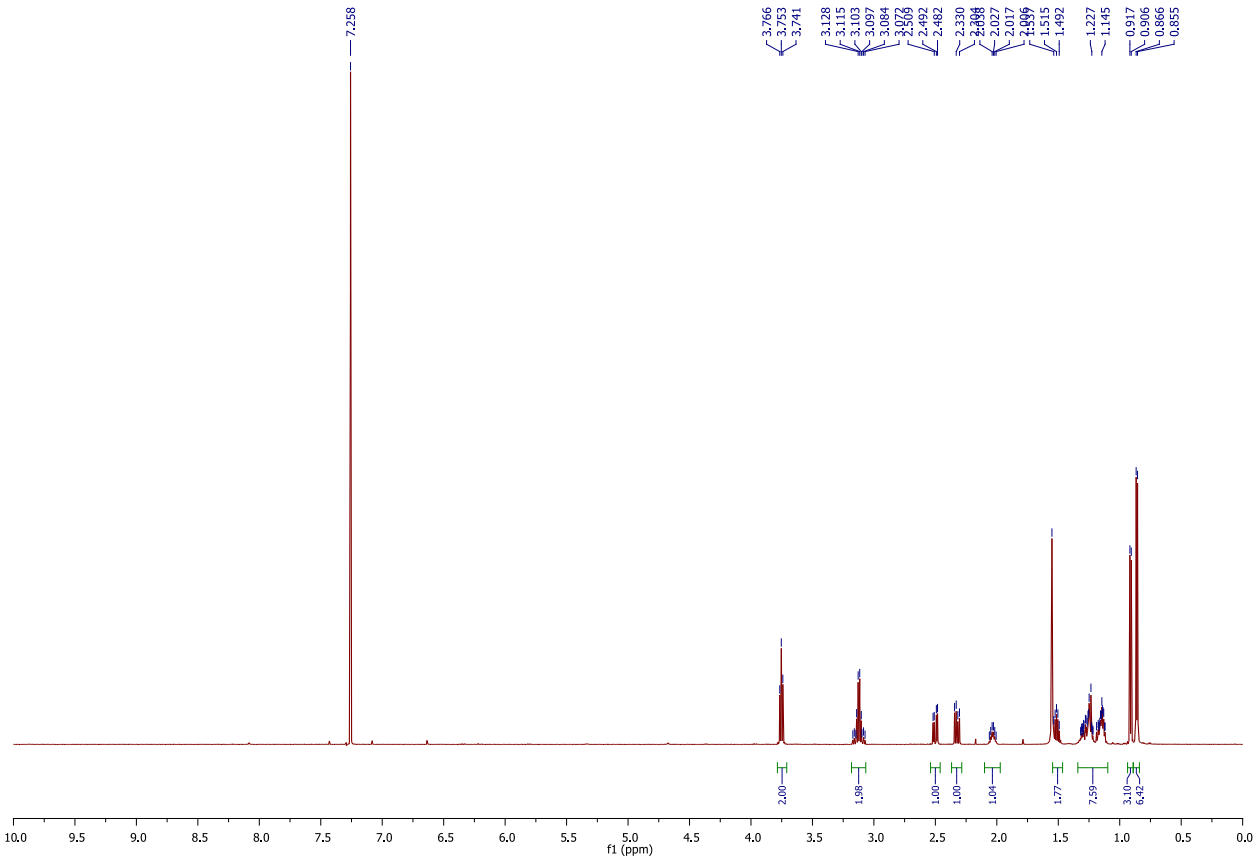

7.273
3.787
3.769
3.750
3.154
3.147
3.137
3.127
3.117
2.387
2.367
2.347
2.327
2.084
2.068
1.364
1.352
1.341
1.333
1.319
1.293
1.257
1.236
1.223
1.199
1.098
0.975
0.937
0.933
2.02
1.92
1.07
1.00
1.16
16.70
3.43
f1 (ppm)

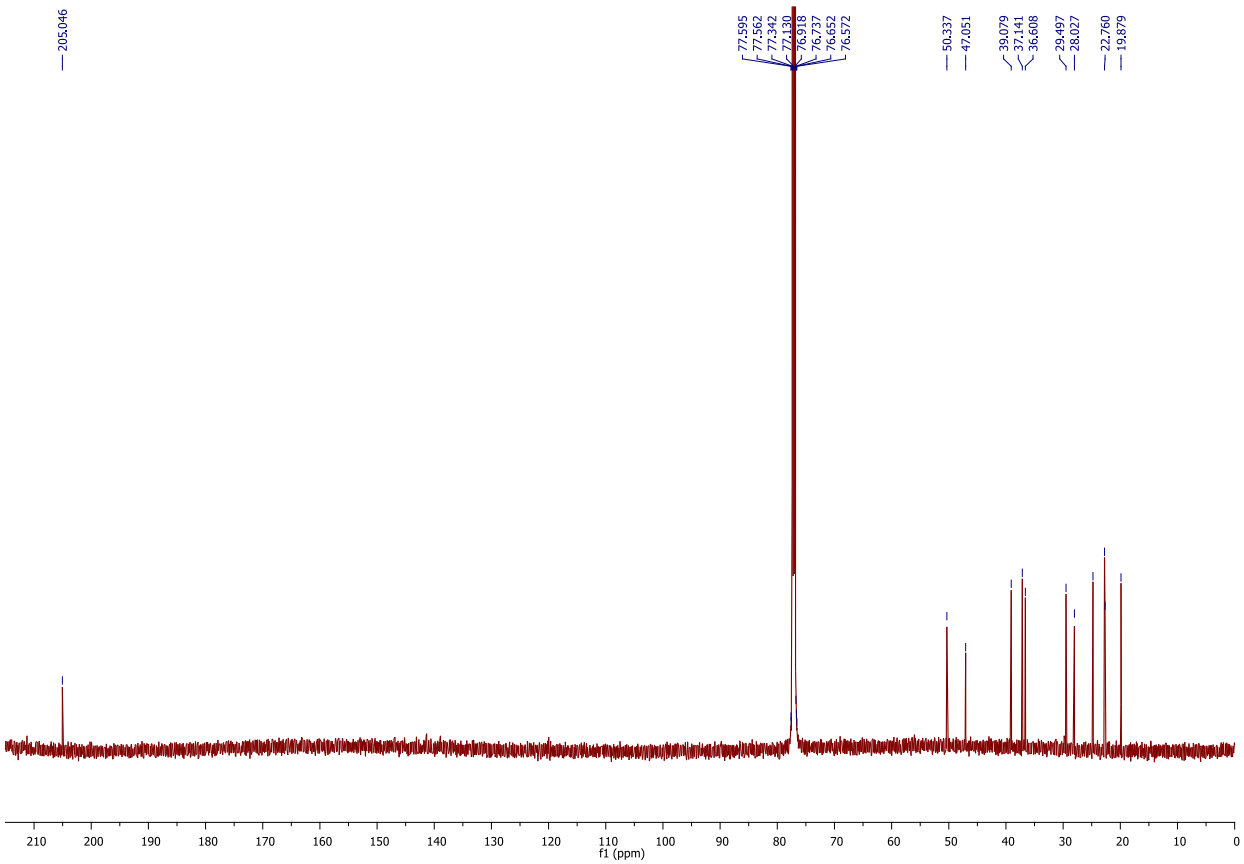


5,9-Dimethyl-3-oxodecane-1-sulfonate acid pentafluorophenyl ester 15r

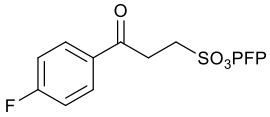


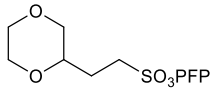
Using Method B, reaction was complete after 6 h. Purification by flash column chromatography (20-95% CH_2Cl_2/petrol) gave 5,9-dimethyl-3-oxodecane-1-sulfonate sulfonate acid pentafluorophenyl ester **15r** as a white solid (284 mg, 0.66 mmol, 66%): m.p. 49-51 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.75 (t, *J* = 7.5 Hz, 2H), 3.14-3.11 (m, 2H), 2.50 (dd, *J* = 16.0, 5.5 Hz, 1H), 3.32 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.06-2.01 (m, 1H), 1.51 (septet, *J* = 6.5 Hz, 1H), 1.36-1.12 (m, 4H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 205.1 (C), 50.3 (CH_2), 47.1 (CH_2), 39.1 (CH_2), 37.1 (CH_2), 36.6 (CH_2), 29.5 (CH), 28.0 (CH), 24.8 (CH_2), 22.8 (CH_3), 22.7 (CH_3), 19.9 (CH_3); IR (solid) 3417, 2959, 1720, 1516, 1380 cm^{-1}; LRMS (CI) 431 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{18}H_{24}F_5O_4S$ $[M+H]^+$ 431.1315; observed 431.1319.





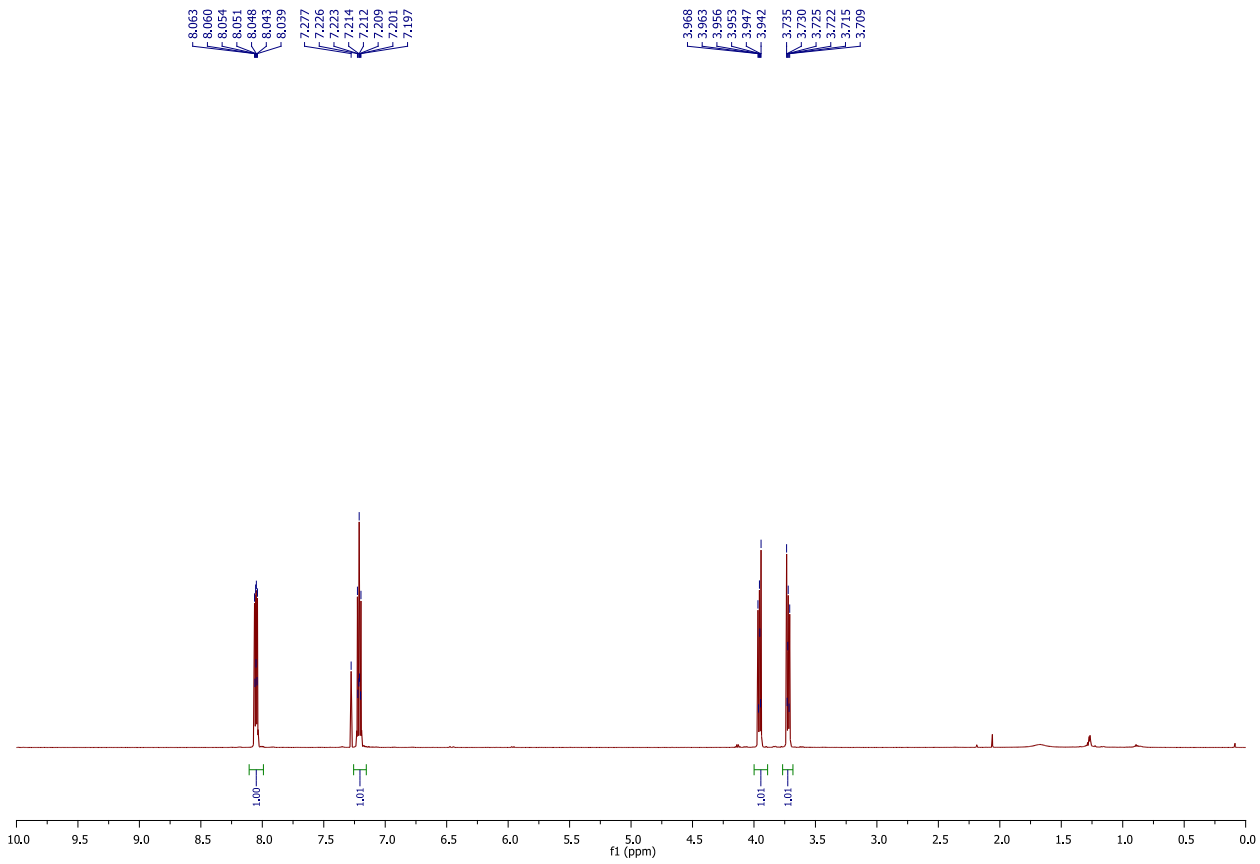
3-(4-Fluorophenyl)-3-oxopropane-1-sulfonate acid pentafluorophenyl ester 15u and 2-(1,4-dioxan-2-yl)ethane-1--sulfonate acid pentafluorophenyl ester

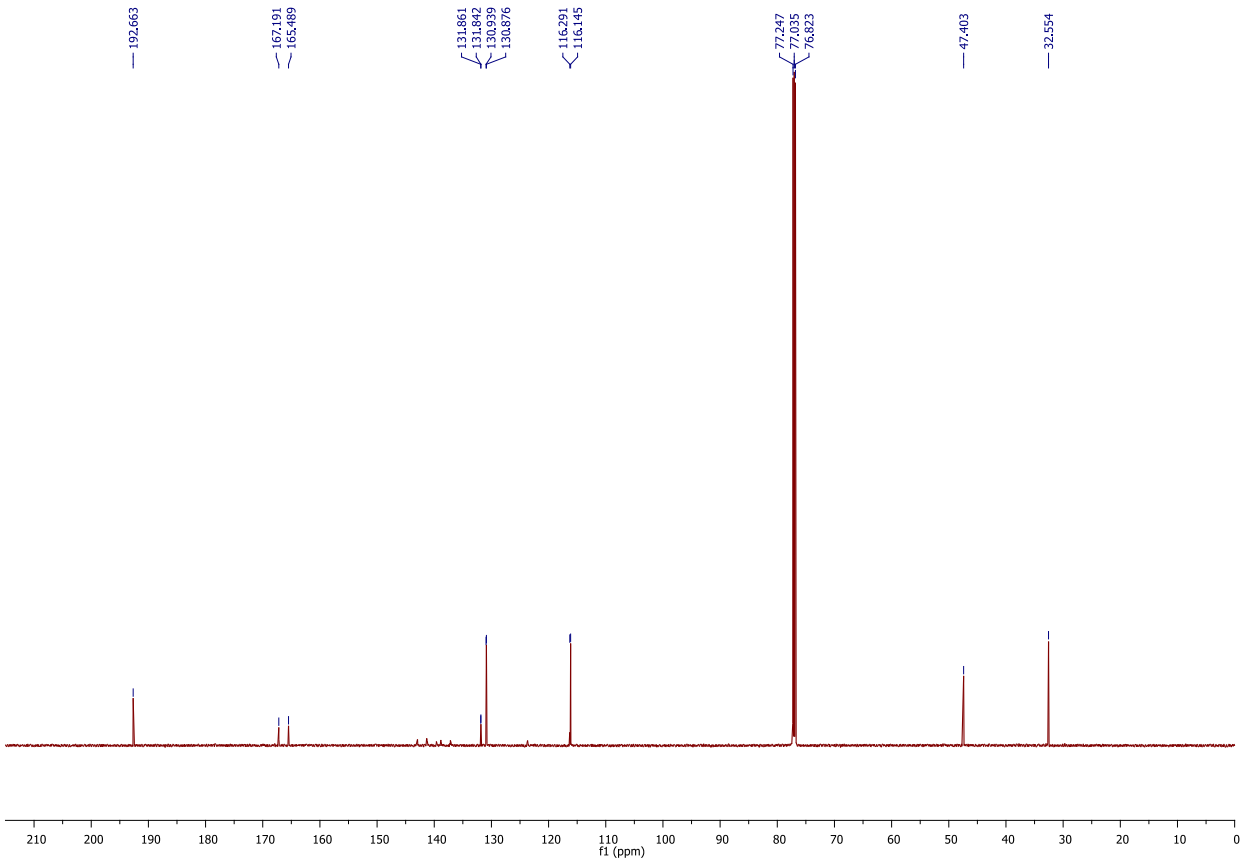




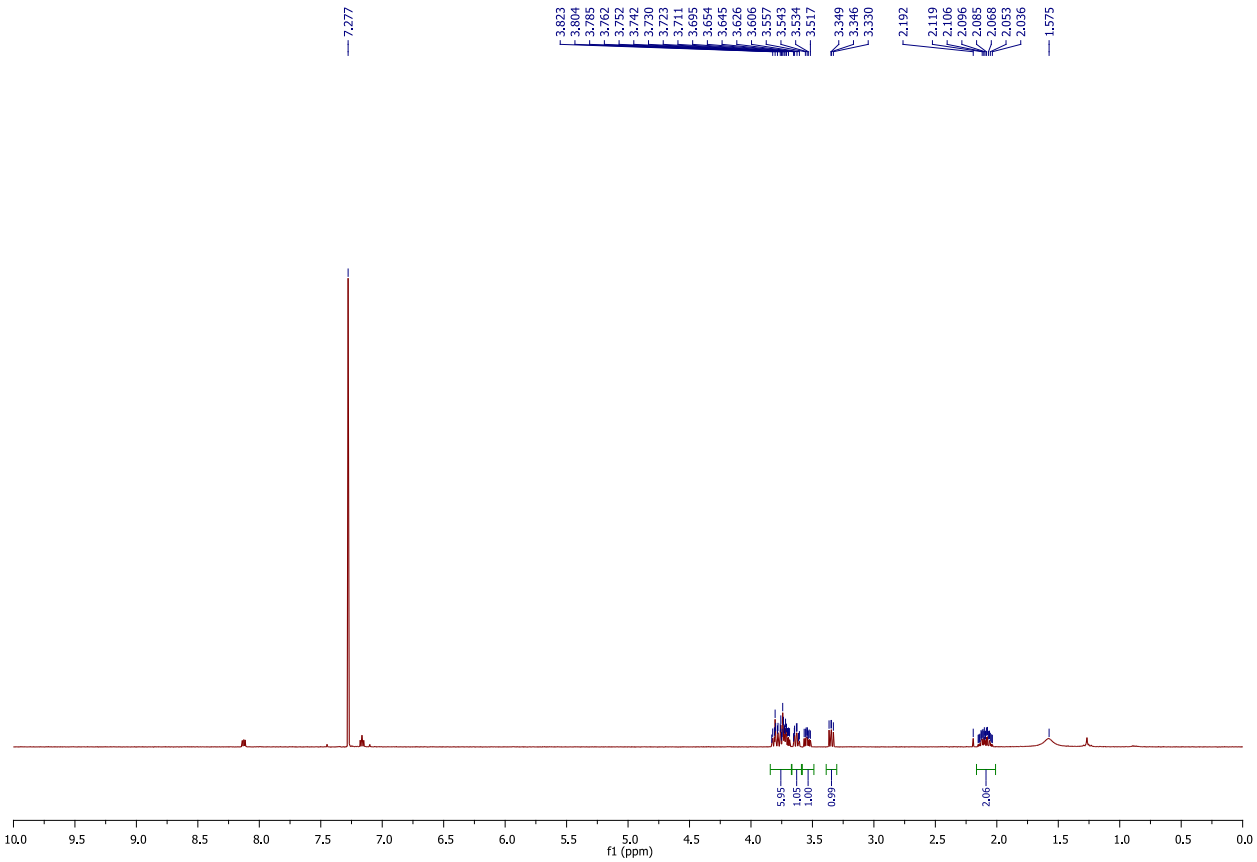
Using Method B, reaction was complete after 6 h. Purification by flash column chromatography (5% Et_2O/petrol) gave 3-(4-fluorophenyl)-3-oxopropane-1-sulfonate sulfonate acid pentafluorophenyl ester **15u** as a white solid (40 mg, 0.10 mmol, 10%) and 2-(1,4-dioxan-2-yl)ethane-1--sulfonate acid pentafluorophenyl ester as an oil (145 mg, 0.40 mmol, 40%)

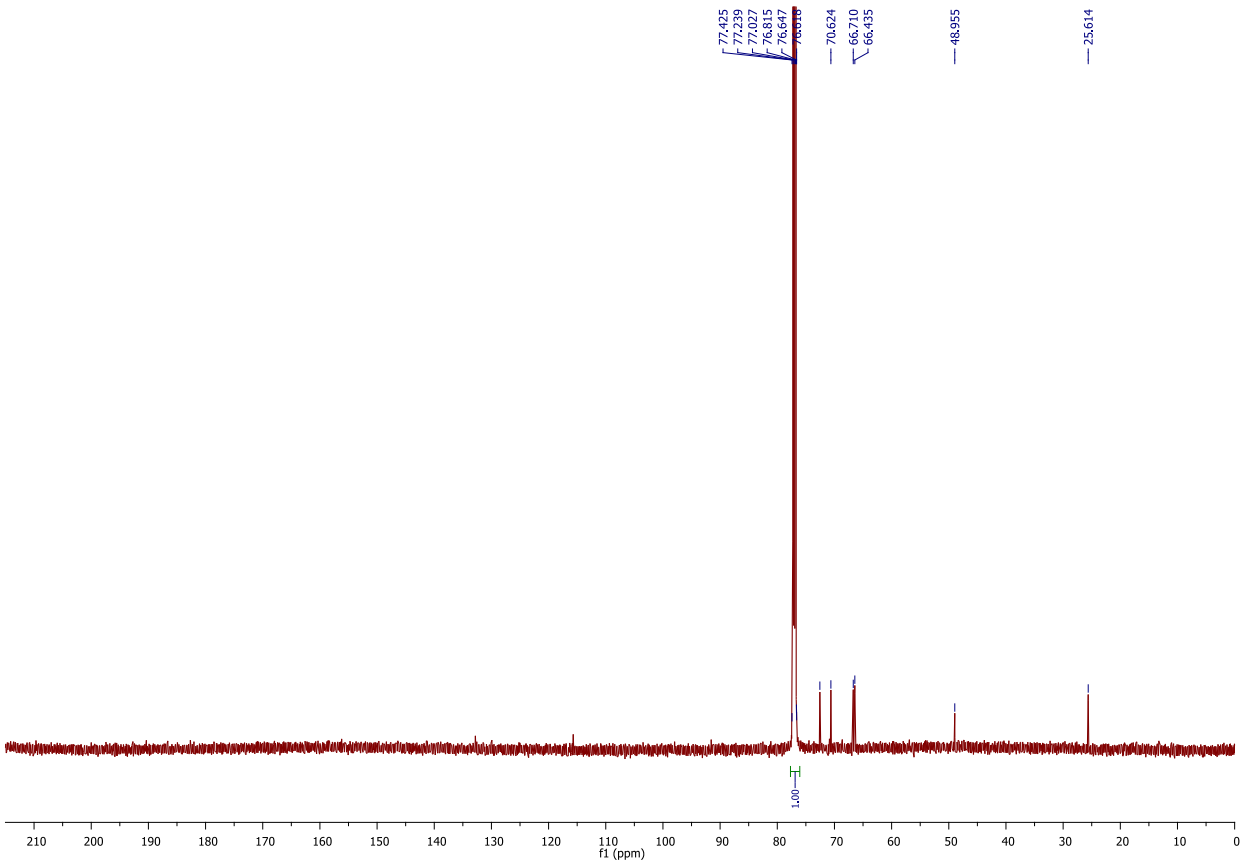
Data for 3-(4-fluorophenyl)-3-oxopropane-1-sulfonate sulfonate acid pentafluorophenyl ester **15u**: m.p. 102-105 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05-8.03 (m, 2H), 7.22-7.19 (m, 2H), 3.96-3.94 (m, 2H), 3.75-7.71 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.7 (C), 166.3 (d, $J_{C\text{-}F}$ = 255.0 Hz, C), 138.8 (C), 137.1 (d, $J_{C\text{-}F}$ = 13.5 Hz, CH), 116.2 (d, $J_{C\text{-}F}$ = 22.5 Hz, CH), 47.4 (CH_2), 32.6 (CH_2); IR (solid) 3069, 2960, 1684, 1381 cm^{-1}; LRMS (CI) 399 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{15}H_9F_6O_4S$ $[M+H]^+$ 399.0126; observed 399.0120.



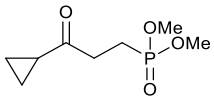


Data for 2-(1,4-dioxan-2-yl)ethane-1--sulfonate acid pentafluorophenyl ester: m.p. 102-105 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.83-3.69 (m, 6H), 3.66-3.60 (m, 1H), 3.55 (ddd, *J* = 16.0, 10.0, 6.0, 1H), 3.35 (dd, *J* = 11.5, 10.0 Hz, 1H), 2.15-2.03 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 72.6 (CH), 70.6 (CH_2), 66.7 (CH_2), 66.4 (CH_2), 49.0 (CH_2), 25.6 (CH_2); IR (neat) 3069, 2960, 1684, 1381 cm^{-1}; LRMS (FAB) 385 (100, $[M+Na]^+$); HRMS (CI) calcd for $C_{12}H_{11}F_5O_5SNa$ $[M+Na]^+$ 385.0145; observed 385.0152.



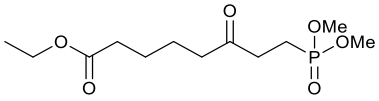


Dimethyl (3-cyclopropyl-3-oxopropyl)phosphonate 31k[9]



Using Method E. Purification by column chromatography (neat CH_2Cl_2-2.5% MeOH/CH_2Cl_2) gave dimethyl (3-cyclopropyl-3-oxopropyl)phosphonate **31k** as a colourless oil (117 mg, 0.57 mmol, 57%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.75 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.91-2.87 (m, 2H), 2.08-2.02 (m, 2H), 1.95-1.92 (m, 1H), 1.06-1.03 (m, 2H), 0.94-0.90 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.0 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 52.5 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 35.8 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 20.4 (CH), 18.3 (d, $J_{C\text{-}P}$ = 143.0 Hz, CH_2), 11.1 (CH_2); IR (thin film) 2962, 1699, 1238 cm^{-1}; LRMS (FAB) 229 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_8H_{15}O_4PNa$ $[M+Na]^+$ 229.0606, observed 229.0601.

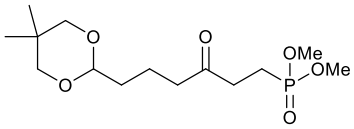
Ethyl 8-(dimethoxyphosphoryl)-6-oxooctanoate 31l[9]



Using Method E. Purification by column chromatography (neat CH_2Cl_2-4% MeOH/CH_2Cl_2) gave ethyl 8-(dimethoxyphosphoryl)-6-oxooctanoate **31l** as a colourless oil (197 mg, 0.67 mmol, 67%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.10 (q, J = 7.0 Hz, 2H), 3.71 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.69

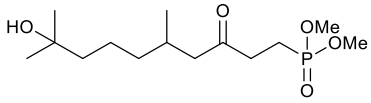
(dt, J_{H-P} = 15.5 and J = 7.5 Hz, 2H), 2.45-2.42 (m, 2H), 2.30-2.27 (m, 2H), 2.04-1.98 (m, 2H), 1.61-1.58 (m, 4H), 1.23 (t, J = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.7 (d, J_{C-P} = 14.0 Hz, C), 173.5 (C) 60.5 (CH_2), 52.5 (d, J_{C-P} = 6.0 Hz, CH_3), 42.3 (CH_2), 35.4 (d, J_{C-P} = 3.0 Hz, CH_2), 34.1 (CH_2), 24.5 (CH_2), 23.2 (CH_2), 18.3 (d, J_{C-P} = 144.0 Hz, CH_2), 14.3 (CH_3); IR (thin film) 2955, 1730, 1717, 1244 cm^{-1}; LRMS (ES) 317 (100, $[M+Na]^+$); HRMS (ES) calcd for $C_{12}H_{23}O_6PNa$ $[M+Na]^+$ 317.1130, observed 317.1120.

Dimethyl [6-(5,5-dimethyl-1,3-dioxan-2-yl)-3-oxohexyl]phosphonate 31m[9]



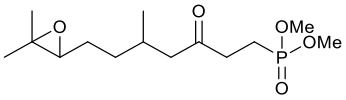
Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 2.5% MeOH/CH_2Cl_2) gave dimethyl [6-(5,5-dimethyl-1,3-dioxan-2-yl)-3-oxohexyl]phosphonate **31m** as a colourless oil (228 mg, 0.71 mmol, 71%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.40 (t, J = 5.0 Hz, 1H), 3.73 (d, J_{H-P} = 11.0 Hz, 6H), 3.57 (d, J = 10.0 Hz, 2H), 3.40 (d, J = 11.0 Hz, 2H), 2.70 (dt, J_{H-P} = 15.5 and J = 7.5 Hz, 2H), 2.47 (t, J = 7.0 Hz, 2H), 2.02 (dt, J_{H-P} = 18.0 and J = 7.5 Hz, 2H), 1.78-1.60 (m, 4H), 1.17 (s, 3H), 0.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7 (d, J_{C-P} = 14.0 Hz, C), 101.9 (CH), 77.2 (CH_2), 52.4 (d, J_{C-P} = 6.0 Hz, CH_3), 42.3 (CH_2), 35.2 (d, J_{C-P} = 4.0 Hz, CH_2), 34.1 (CH_2), 30.1 (C), 23.1 (CH_3), 21.9 (CH_3), 18.4 (CH_2), 18.3 (d, J_{C-P} = 144.0 Hz, CH_2); IR (thin film) 2955, 2850, 1717, 1244 cm^{-1}; LRMS (EI) 321 (15, $[M-H]^{+\cdot}$), 219 (65), 115 (100); HRMS (EI) calcd for $C_{14}H_{26}O_6P$ $[M-H]^{+\cdot}$ 321.1461, observed 321.1465.

Dimethyl (9-hydroxy-5,9-dimethyl-3-oxodecyl)phosphonate 31n[9]



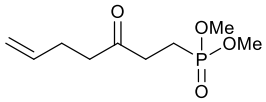
Using Method E. Purification by column chromatography (neat CH_2Cl_2 to 7.5% MeOH/CH_2Cl_2) gave dimethyl (9-hydroxy-5,9-dimethyl-3-oxodecyl)phosphonate **31n** as a colourless oil (228 mg, 0.74 mmol, 74%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.74 (d, J_{H-P} = 11.0 Hz, 3H), 3.74 (d, J_{H-P} = 11.0 Hz, 3H), 2.75-2.65 (m, 2H), 2.43 (dd, J = 16.0, 6.0 Hz, 1H), 2.26 (dd, J = 16.0, 8.0 Hz, 1H), 2.03 (dt, J_{H-P} = 18.0 and J = 8.0 Hz, 2H), 1.48-1.14 (m, 14H), 0.91 (d, J = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.0 (d, J_{C-P} = 14.0 Hz, C), 70.9 (C), 52.5 (d, J_{C-P} = 6.5 Hz, CH_3), 52.4 (d, J_{C-P} = 6.5 Hz, CH_3), 50.0 (CH_2), 43.8 (CH_2), 37.3 (CH_2), 35.8 (d, J_{C-P} = 4.0 Hz, CH_2), 29.4 (CH_3), 29.3 (CH_3), 29.2 (CH), 21.6 (CH_2), 19.9 (CH_3), 18.1 (d, J_{C-P} = 143.0 Hz, CH_2); IR (thin film) 3409, 2960, 2928, 2848, 1715, 1238 cm^{-1}; LRMS (FAB) 331 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_{14}H_{29}O_5PNa$ $[M+Na]^+$ 331.1650, observed 331.1653.

Dimethyl [7-(3,3-dimethyloxiran-2-yl)-5-methyl-3-oxoheptyl]phosphonate 31o[9]



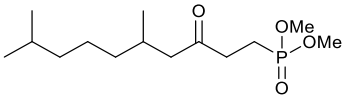
Using Method E. Purification by column chromatography (neat CH_2Cl_2-3% MeOH/CH_2Cl_2) gave dimethyl [7-(3,3-dimethyloxiran-2-yl)-5-methyl-3-oxoheptyl]phosphonate **31o** as a 1:1 mixture of diastereoisomers (A and B) as a colourless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.71 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.71-2.64 (m, 3H), 2.44-2.38 (m, 1H), 2.28-2.23 (m, 1H), 2.06-1.98 (m, 3H), 1.56-1.21 (m, 10H), 0.88 (d, J = 7.0 Hz, 3H of diastereoisomer A, 1.5H), 0.88 (d, J = 7.0 Hz, 3H of diastereoisomer A, 1.5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.7 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 207.7 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 64.4 (CH), 58.5 (C), 58.4 (C), 52.6 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 50.0 (CH_2), 49.9 (CH_2), 36.0 (CH_2), 35.9 (CH_2), 33.5 (CH_2), 29.2 (CH), 29.1 (CH), 26.6 (CH_2), 26.5 (CH_2), 25.0 (CH_3), 19.8 (CH_3), 19.8 (CH_3), 18.8 (CH_3), 18.7 (CH_3), 18.2 (d, $J_{C\text{-}P}$ = 143.0 Hz, CH_2); IR (thin film) 2958, 2927, 1716, 1248 cm^{-1}; LRMS (CI) 307 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{14}H_{28}O_5P$ $[M+H]^+$ 307.1674, observed 307.1683.

Dimethyl (3-oxohept-6-en-1-yl)phosphonate 31p[9]



Using Method E. Purification by column chromatography (neat CH_2Cl_2-4% CH_3OH/CH_2Cl_2) gave dimethyl (3-oxohept-6-en-1-yl)phosphonate **31p** as a colourless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.80 (ddt, J = 17.0, 10.0, 6.5 Hz, 1H), 5.04 (dq, J = 17.0, 1.5 Hz, 1H), 5.00 (dq, J = 10.0, 1.5 Hz, 1H), 3.74 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.75-2.71 (m, 2H), 2.55 (t, J = 7.5 Hz, 2H), 2.37-2.33 (m, 2H), 2.07-2.02 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.3 (d, $J_{C\text{-}P}$ = 13.5 Hz, C), 136.8 (CH), 115.5 (CH_2), 52.5 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 41.6 (CH_2), 35.4 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_2), 27.7 (CH_2), 18.0 (d, $J_{C\text{-}P}$ = 144.0 Hz, CH_2); IR (thin film) 2956, 1716, 1642, 1237 cm^{-1}; LRMS (EI) 220 (24, $[M]^{+\cdot}$), 165 (100); HRMS (EI) calcd for $C_9H_{17}O_4P$ $[M]^{+\cdot}$ 220.0859, observed 220.0853.

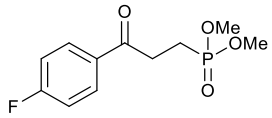
Dimethyl (5,9-dimethyl-3-oxodecyl)phosphonate 31r[9]



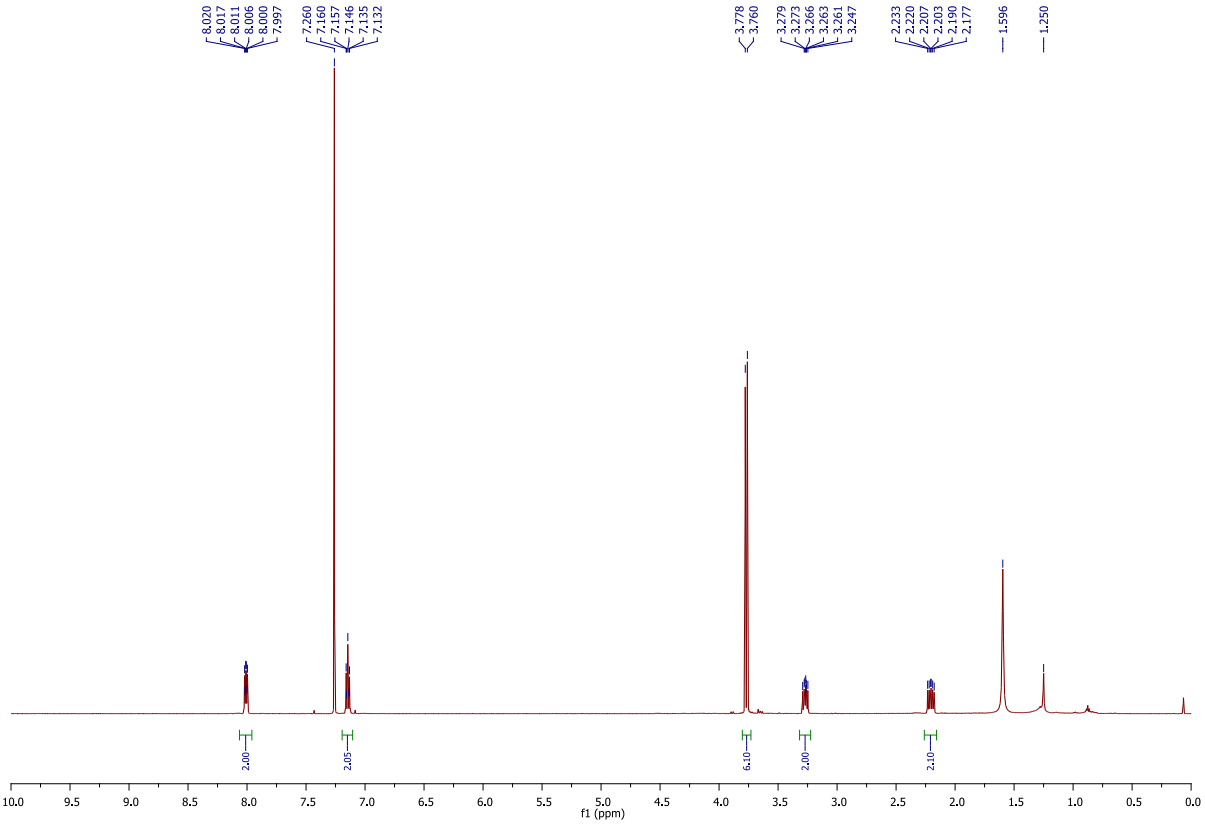
Using Method E. Purification by column chromatography (neat CH_2Cl_2-4% MeOH/CH_2Cl_2) gave dimethyl (5,9-dimethyl-3-oxodecyl)phosphonate **31r** as a colourless oil (198 mg, 0.68 mmol, 68%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.72 (d, $J_{H\text{-}P}$ = 11.0 Hz, 6H), 2.74-2.64 (m, 2H), 2.40 (dd, J = 16.0, 5.5 Hz, 1H), 2.22 (dd, J = 16.0, 8.0 Hz, 1H), 2.05-1.96 (m, 3H), 1.49 nonet, J = 6.5 Hz, 1H), 1.32-1.08 (m, 6H), 0.87 (d, J = 6.5 Hz, 3H), 0.84 (d, J = 6.5 Hz, 3H), 0.84 (d, J = 6.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.2 (d, $J_{C\text{-}P}$ = 14.0 Hz, C), 52.5 (d, $J_{C\text{-}P}$ = 6.5 Hz, CH_3), 50.3 (CH_2), 39.1 (CH_2), 37.2 (CH_2), 35.9 (d, $J_{C\text{-}P}$ = 4.0 Hz, CH_2), 29.5 (CH), 28.0 (CH), 24.8 (CH_2), 22.8 (CH_3), 22.7 (CH_3), 19.9 (CH_3), 18.3 (d, $J_{C\text{-}P}$ = 143.0 Hz, CH_2); IR (thin film) 2955,

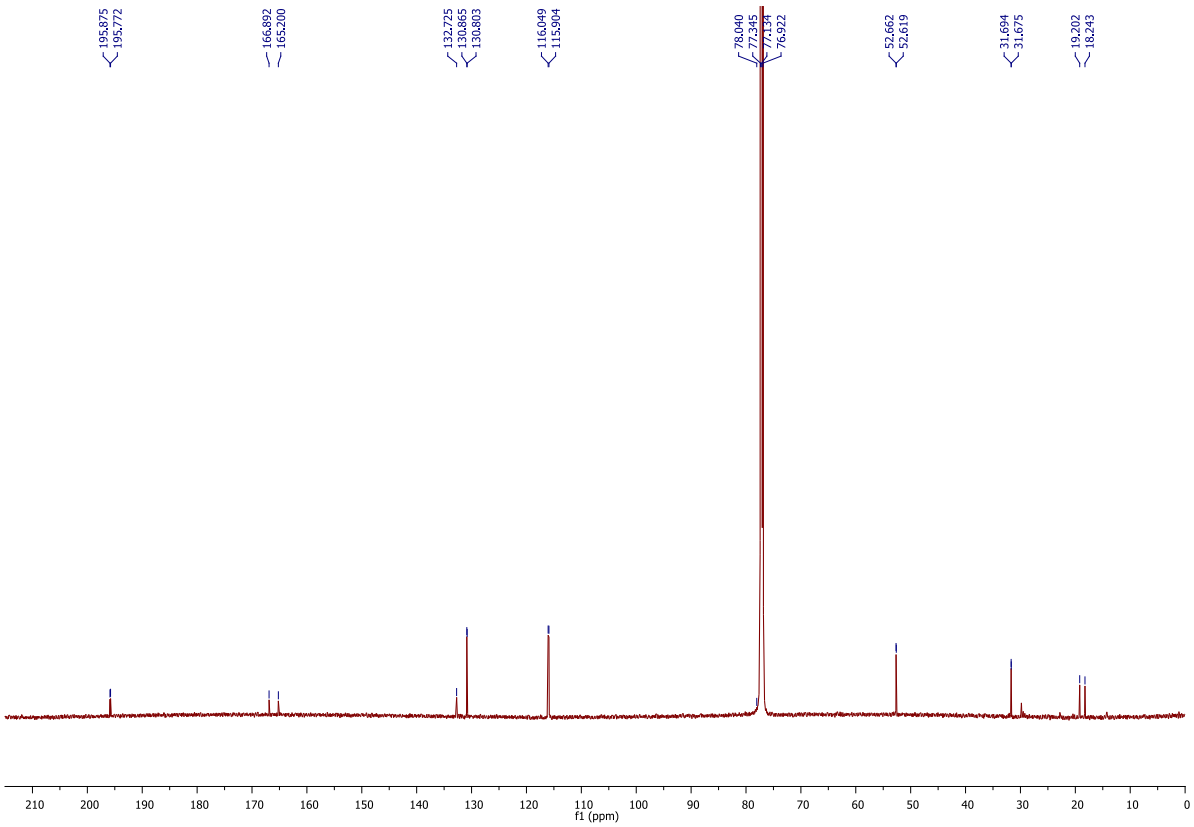
2928, 1716 cm^{-1}; LRMS (CI) 293 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{14}H_{30}O_4P$ $[M+H]^+$ 293.1882, observed 293.1884.

Dimethyl (3-(4-fluorophenyl)-3-oxopropyl)phosphonate 31u

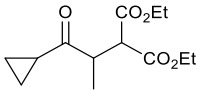


Using Method E. Purification by column chromatography (neat CH_2Cl_2-4% MeOH/CH_2Cl_2) gave dimethyl (3-(4-fluorophenyl)-3-oxopropyl)phosphonate **31u** as a colourless oil (70 mg, 0.27 mmol, 27%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (dd, J = 5.5, 9.0 Hz, 2H), 7.15 (t, J = 9.0 Hz, 2H), 3.72 (d, J_{H-P} = 11.0 Hz, 6H), 3.30-3.24 (m, 2H), 2.24-2.17 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.8 (d, J_{C-P} = 15.0 Hz, C), 166.9 (d, J_{C-F} = 253.5 Hz, C), 132.7 (d, J_{C-F} = 3.5 Hz, C), 130.8 (d, J_{C-F} = 8.5 Hz, CH), 115.0 (d, J_{C-F} = 22.0 Hz, CH), 52.6 (d, J_{C-P} = 6.5 Hz, CH_3), 31.7 (d, J_{C-P} = 3.5 Hz, CH_2), 18.7 (d, J_{C-P} = 142.5 Hz, CH_2); IR (thin film) 2956, 2926, 2853, 1688, 1599 cm^{-1}; LRMS (CI) 261 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{11}H_{15}O_4PF$ $[M+H]^+$ 261.0614, observed 261.0620.

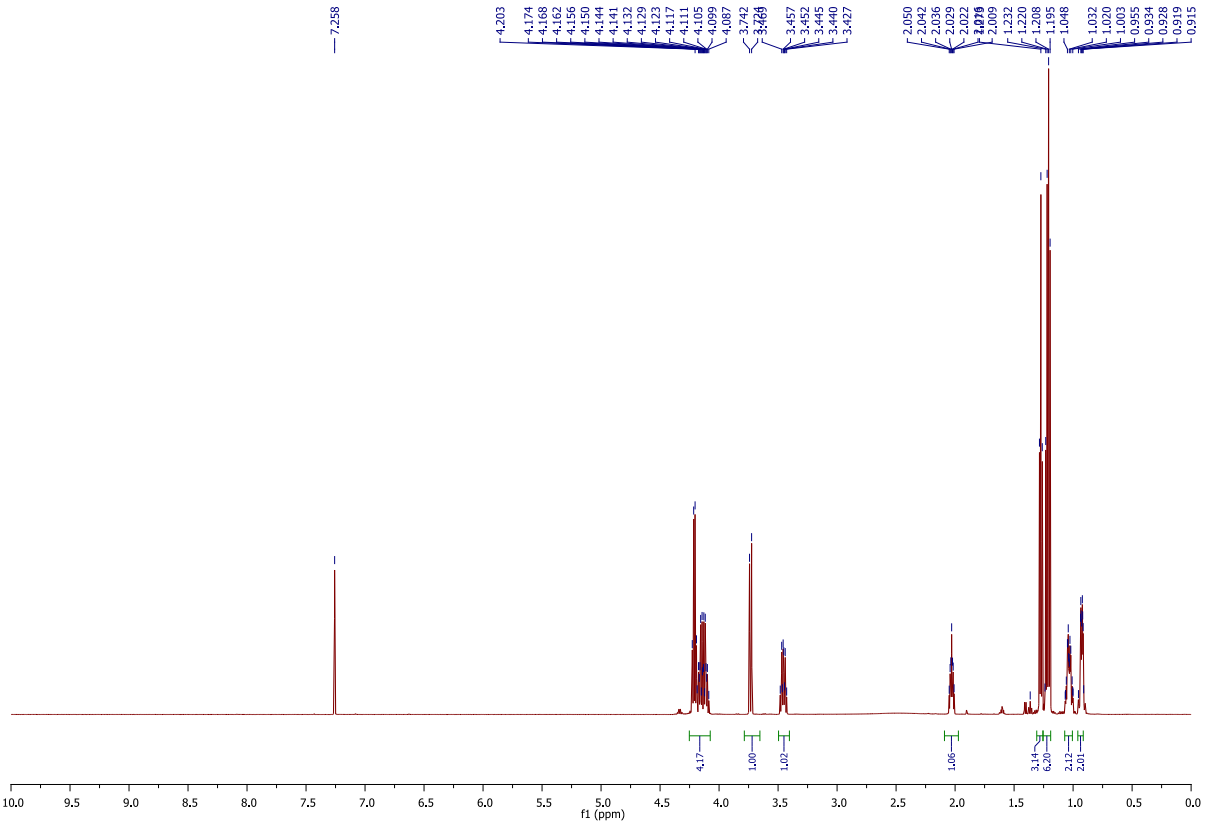


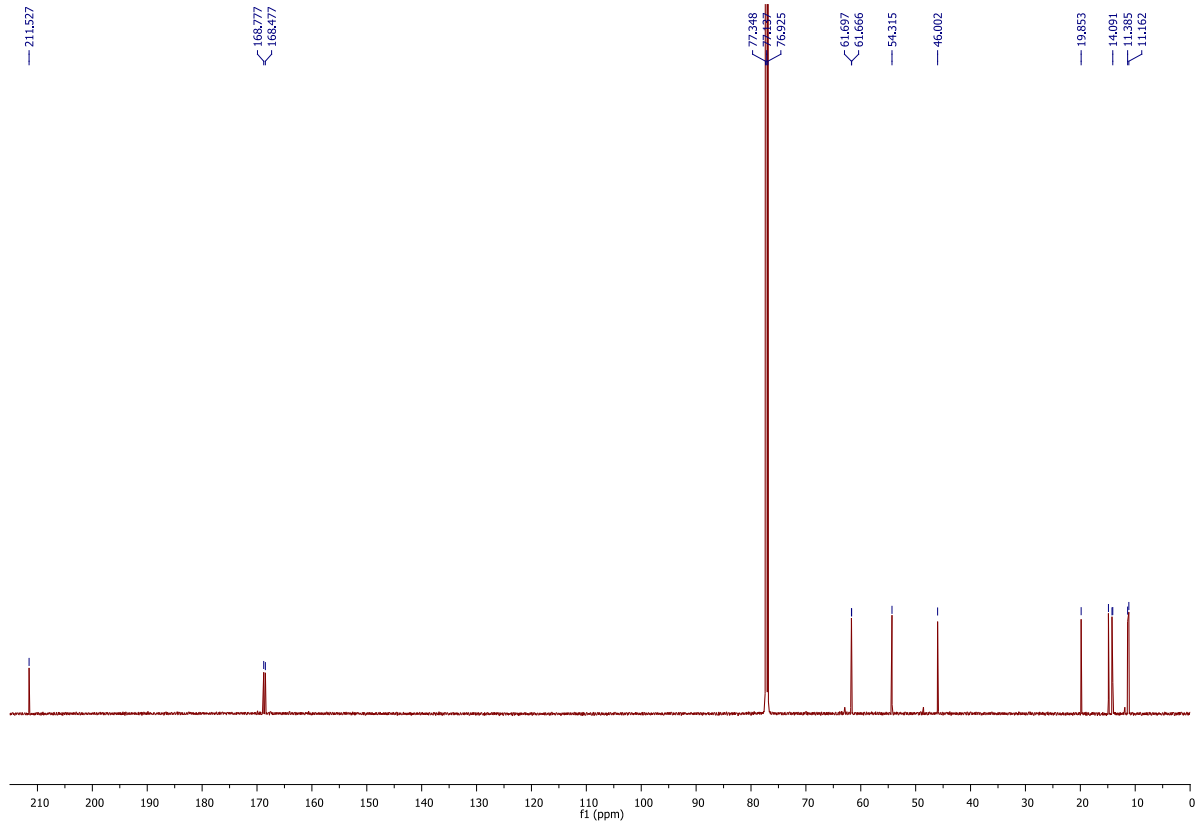


2-(1-Cyclopropyl-1-oxopropan-2-yl)-malonic acid diethyl ester 44k

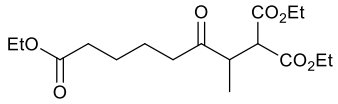


Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-30% Et_2O/petrol) gave 2-(1-cyclopropyl-1-oxopropan-2-yl)-malonic acid diethyl ester **44k** as a colourless oil (159 mg, 0.62 mmol, 62%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.23-4.09 (m, 4H), 3.73 (d, *J* = 10.5 Hz, 1H), 3.44 (dq, *J* = 10.5, 7.0 Hz, 1H), 2.05-2.00 (m, 1H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.07-1.00 (m, 2H), 0.94-0.91 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.5 (C), 168.8 (C), 168.5 (C), 62.0 (CH_2), 61.7 (CH_2), 54.3 (CH), 46.0 (CH), 19.9 (CH), 19.9 (CH_3), 14.9 (CH_3), 14.2 (CH_3), 11.4 (CH_2), 11.2 (CH_2); IR (thin film) 2982, 2937, 1748, 1730, 1698 cm^{-1}; LRMS (ES) 255 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{13}H_{19}O_5$ $[M-H]^-$ 255.1232, observed 255.1230.

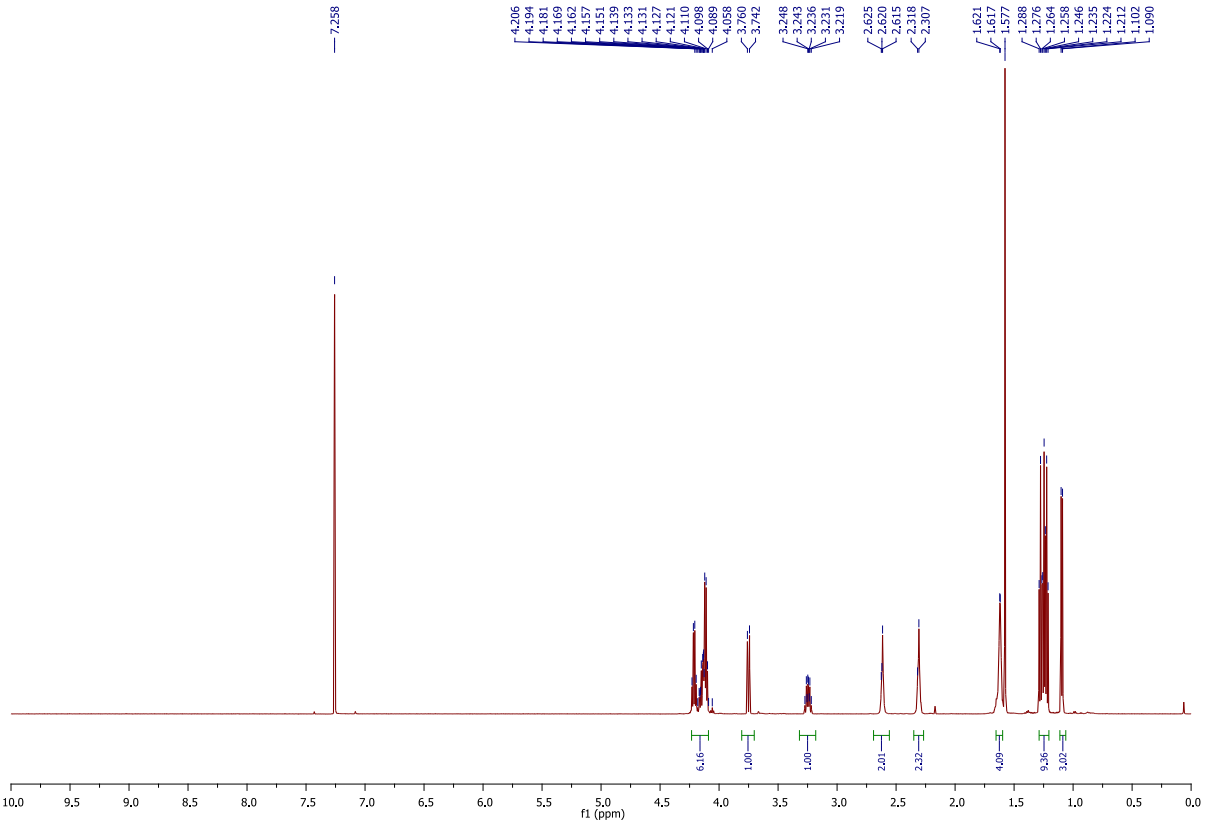


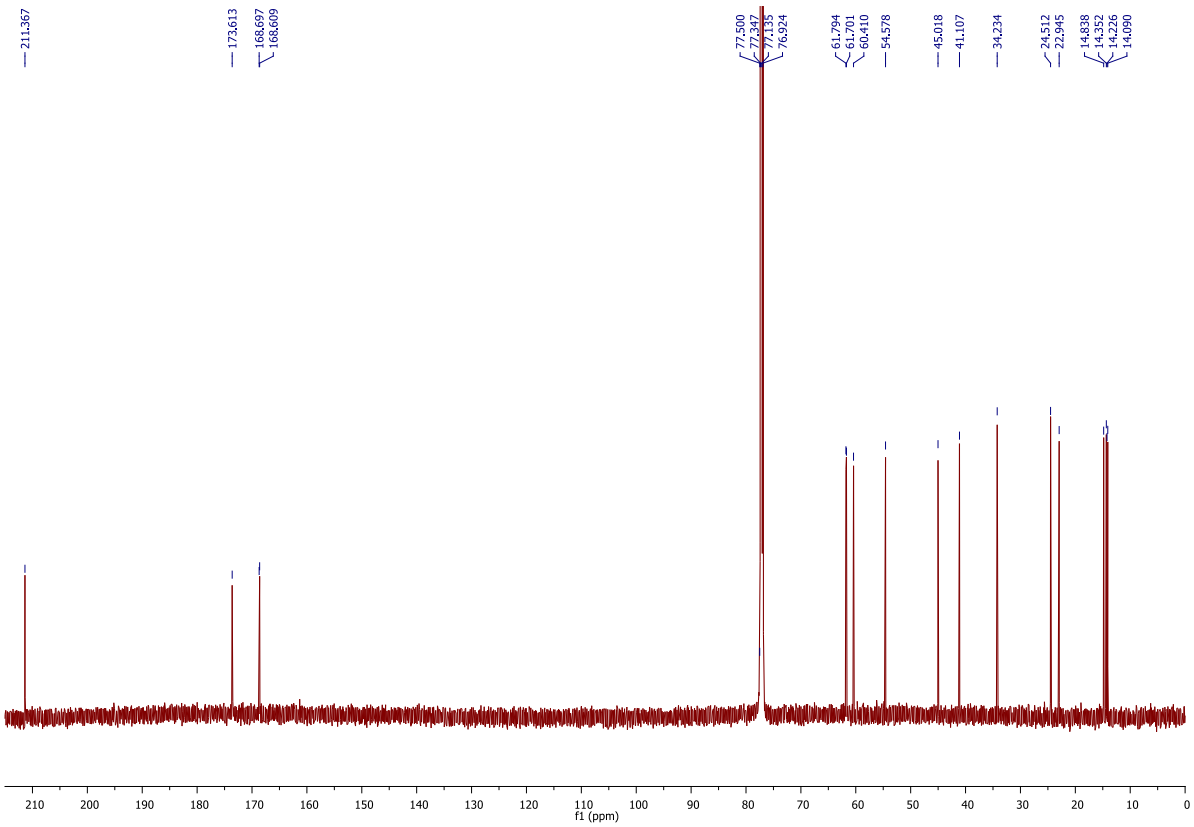


Triethyl 2-methyl-3-oxoheptane-1,1,7-tricarboxylate 44l

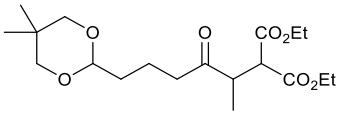


Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-40% Et_2O/petrol) gave triethyl 2-methyl-3-oxoheptane-1,1,7-tricarboxylate **44l** as a colourless oil (244 mg, 0.71 mmol, 71%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.24-4.07 (m, 6H), 3.74 (d, *J* = 10.5 Hz, 1H), 3.25 (dq, *J* = 10.5, 7.0 Hz, 1H), 2.63-2.60 (m, 2H), 2.33-2.29 (m, 2H), 1.65-1.58 (m, 4H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.09 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.4 (C), 173.6 (C), 168.7 (C), 168.6 (C), 61.8 (CH_2), 61.7 (CH_2), 60.4 (CH_2), 54.6 (CH), 45.0 (CH), 41.1 (CH_2), 34.2 (CH_2), 24.5 (CH_2), 23.0 (CH_2), 14.8 (CH_3), 14.4 (CH_3), 14.2 (CH_3), 14.1 (CH_3); IR (thin film) 2980, 2940, 1745, 1732, 1699 cm^{-1}; LRMS (ES) 343 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{17}H_{27}O_7$ $[M-H]^-$ 343.1835, observed 343.1838.

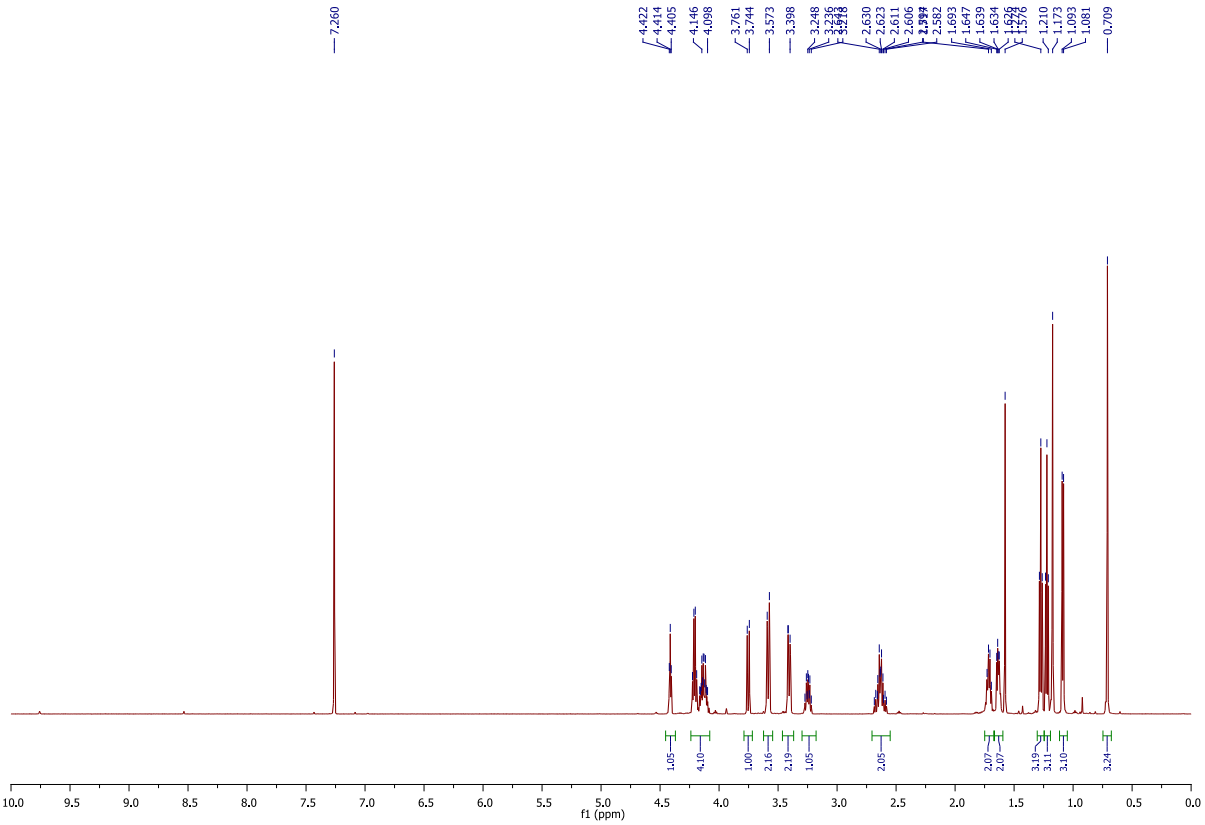


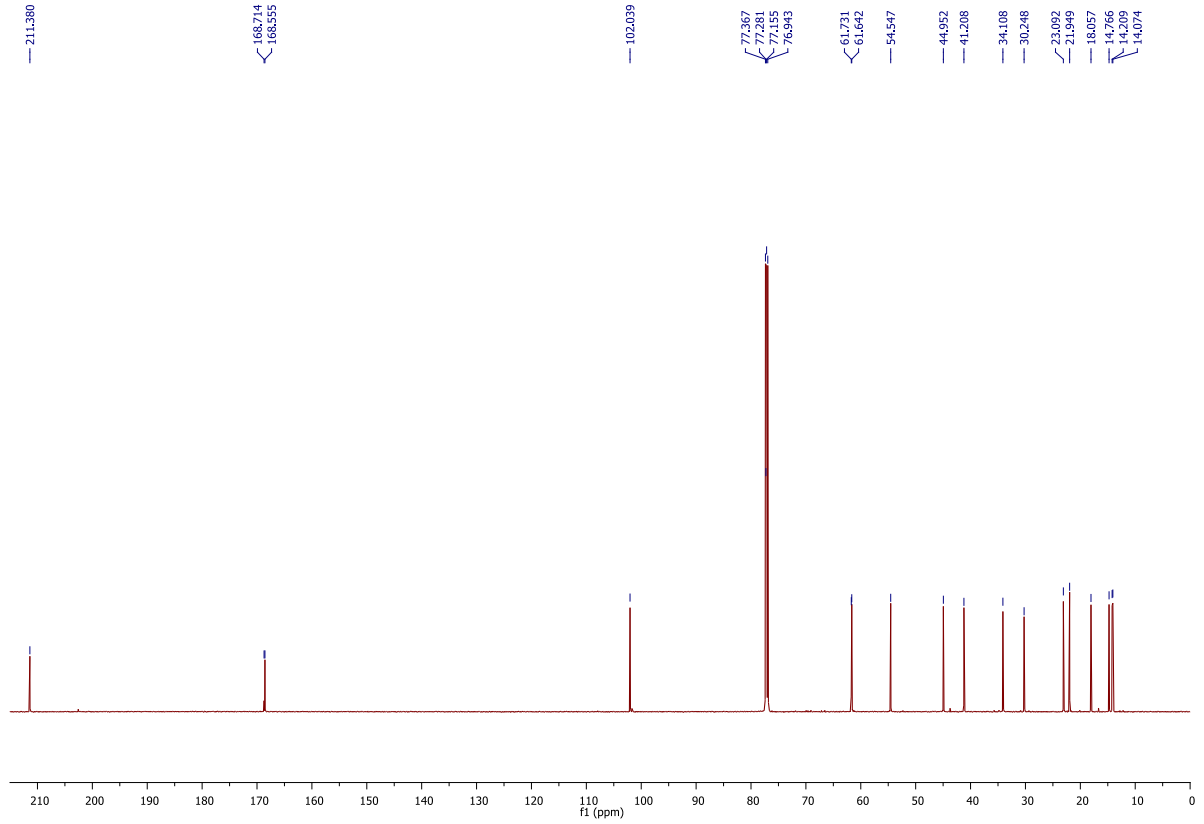


2-(6-(5,5-Dimethyl-1,3-dioxan-2-yl)-3-oxohexan-2-yl)-malonic acid diethyl ester 44m

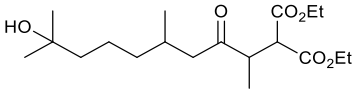


Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-40% Et_2O/petrol) gave 2-(6-(5,5-dimethyl-1,3-dioxan-2-yl)-3-oxohexan-2-yl)- malonic acid diethyl ester **44m** as a colourless oil (249 mg, 0.67 mmol, 67%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.53 (t, *J* = 4.5 Hz, 1H), 4.25-4.09 (m, 4H), 3.75 (d, *J* = 10.5 Hz, 1H), 3.58 (d, *J* = 10.5 Hz, 2H), 3.40 (dd, *J* = 10.5, 2.0 Hz, 2H), 3.25 (dq, *J* = 10.5, 7.0 Hz, 1H), 2.69-2.58 (m, 2H), 1.74-1.68 (m, 2H), 1.66-1.61 (m, 2H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.17 (s, 3H), 1.09 (d, *J* = 7.0 Hz, 3H), 0.71 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.4 (C), 168.7 (C), 168.6 (C), 102.0 (CH), 61.7 (CH_2), 61.6 (CH_2), 54.5 (CH), 45.0 (CH), 41.2 (CH_2), 34.1 (CH_2), 30.2 (C), 23.1 (CH_3), 22.0 (CH_3), 18.1 (CH_2), 14.8 (CH_3), 14.2 (CH_3), 14.1 (CH_3); IR (thin film) 2954, 2845, 1748, 1731, 1717 cm^{-1}; LRMS (ES) 371 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{19}H_{31}O_7$ $[M-H]^-$ 371.2070, observed 371.2077.

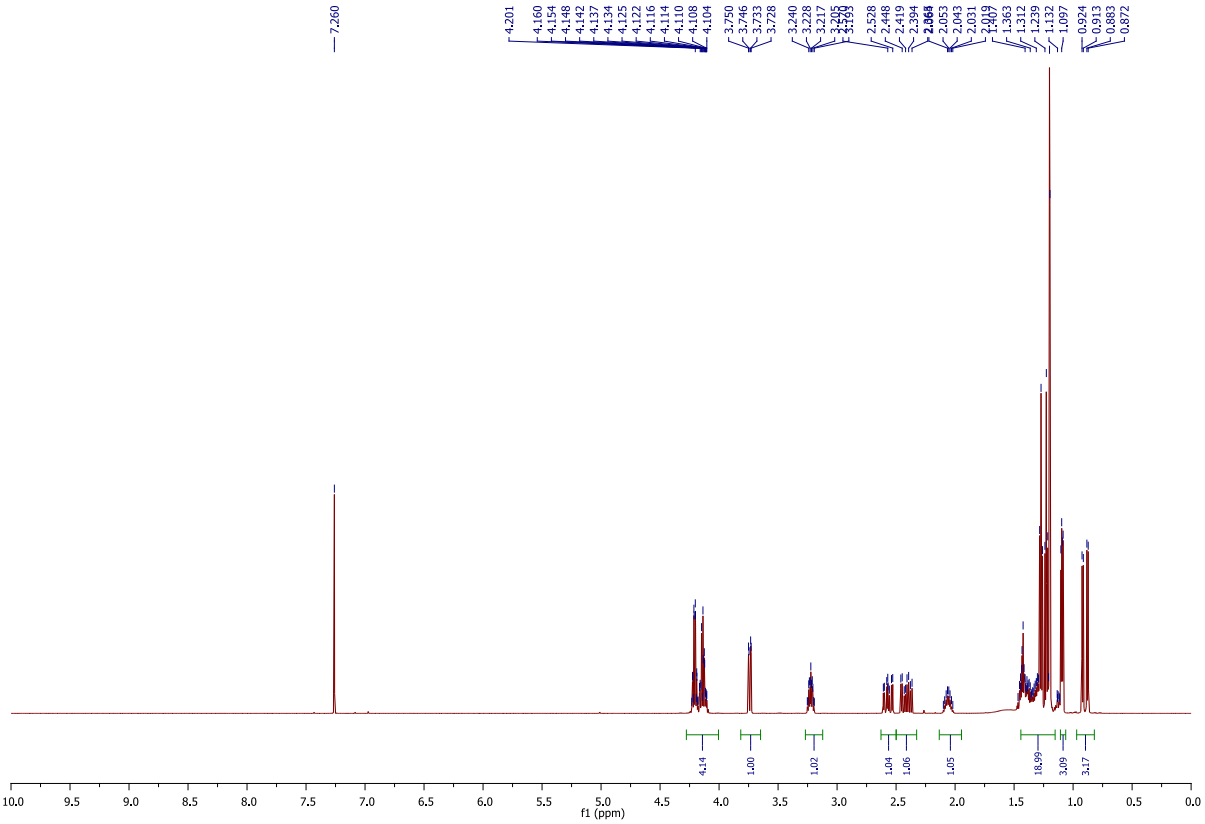


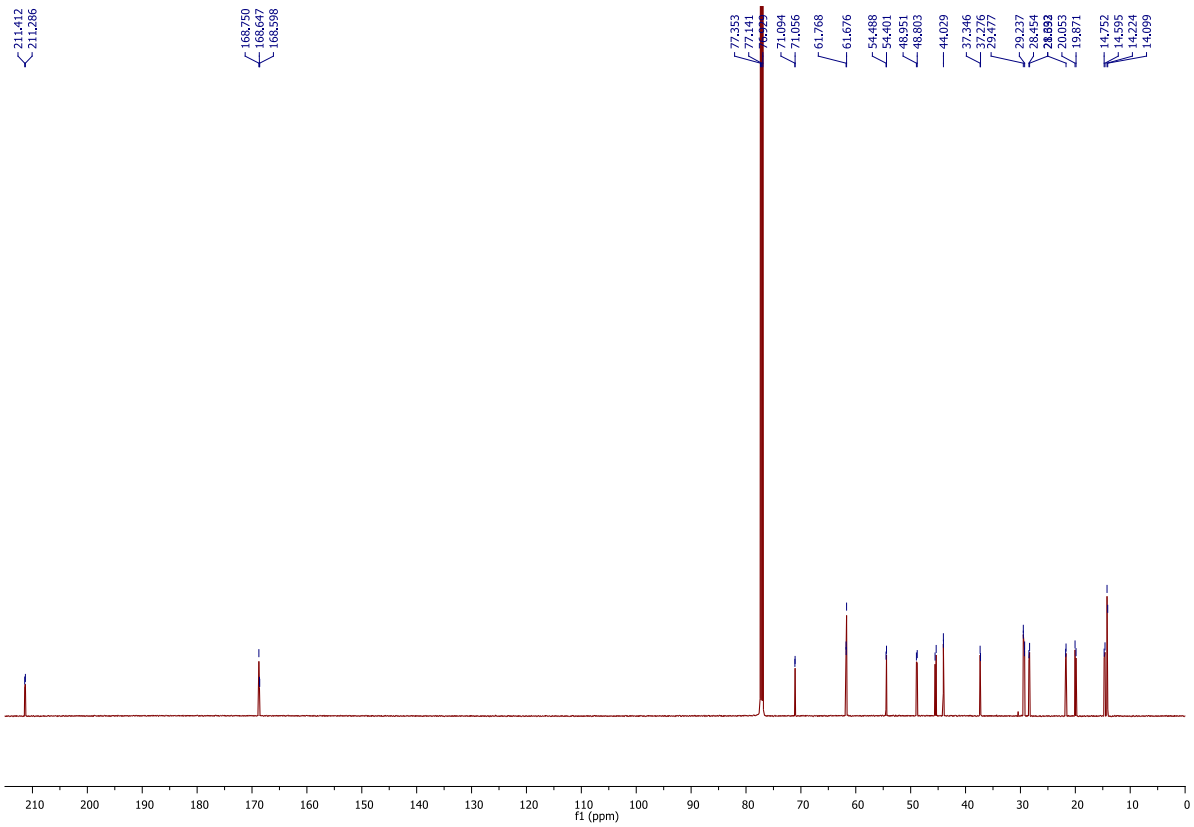


2-(9-Hydroxy-5,9-dimethyl-3-oxodecan-2-yl)-malonic acid diethyl ester 44n

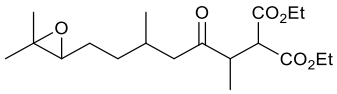


Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-40% Et_2O/petrol) gave 2-(9-hydroxy-5,9-dimethyl-3-oxodecan-2-yl)-malonic acid diethyl ester **44n** as a colourless oil (243 mg, 0.68 mmol, 68%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.23-4.11 (m, 4H), 3.75 (app. dd, *J* = 10.5, 2.5 Hz, 1H), 3.25-3.18 (m, 1H), 2.56 (app. ddd, *J* = 24.0, 17.5, 5.5 Hz, 1H), 2.41 (app. ddd, *J* = 31.0, 17.5, 7.0 Hz, 1H), 2.07-2.01 (m, 1H), 1.48-1.20 (m, 18H), 1.11-1.08 (m, 3H), 0.93-0.87 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.4 (C), 211.3 (C), 168.8 (C), 168.7 (C), 168.6 (C), 71.1 (C), 71.1 (C), 61.8 (CH_2), 61.7 (CH_2), 61.7 (CH_2), 54.5 (CH), 54.4 (CH), 49.0 (CH_2), 48.8 (CH_2), 45.6 (CH), 45.4 (CH), 44.0 (CH_2), 44.0 (CH_2), 37.4 (CH_2), 37.3 (CH_2), 29.5 (CH_3), 29.5 (CH_3), 29.3 (CH_3), 29.2 (CH_3), 28.5 (CH_3), 28.3 (CH_3), 20.1 (CH), 19.9 (CH), 14.8 (CH_3), 14.6 (CH_3), 14.2 (CH_3), 14.1 (CH_3); IR (thin film) 3541, 2970, 2937, 1748, 1730, 1715 cm^{-1}; LRMS (ES) 357 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{19}H_{33}O_6$ $[M-H]^-$ 357.2277, observed 357.2277.

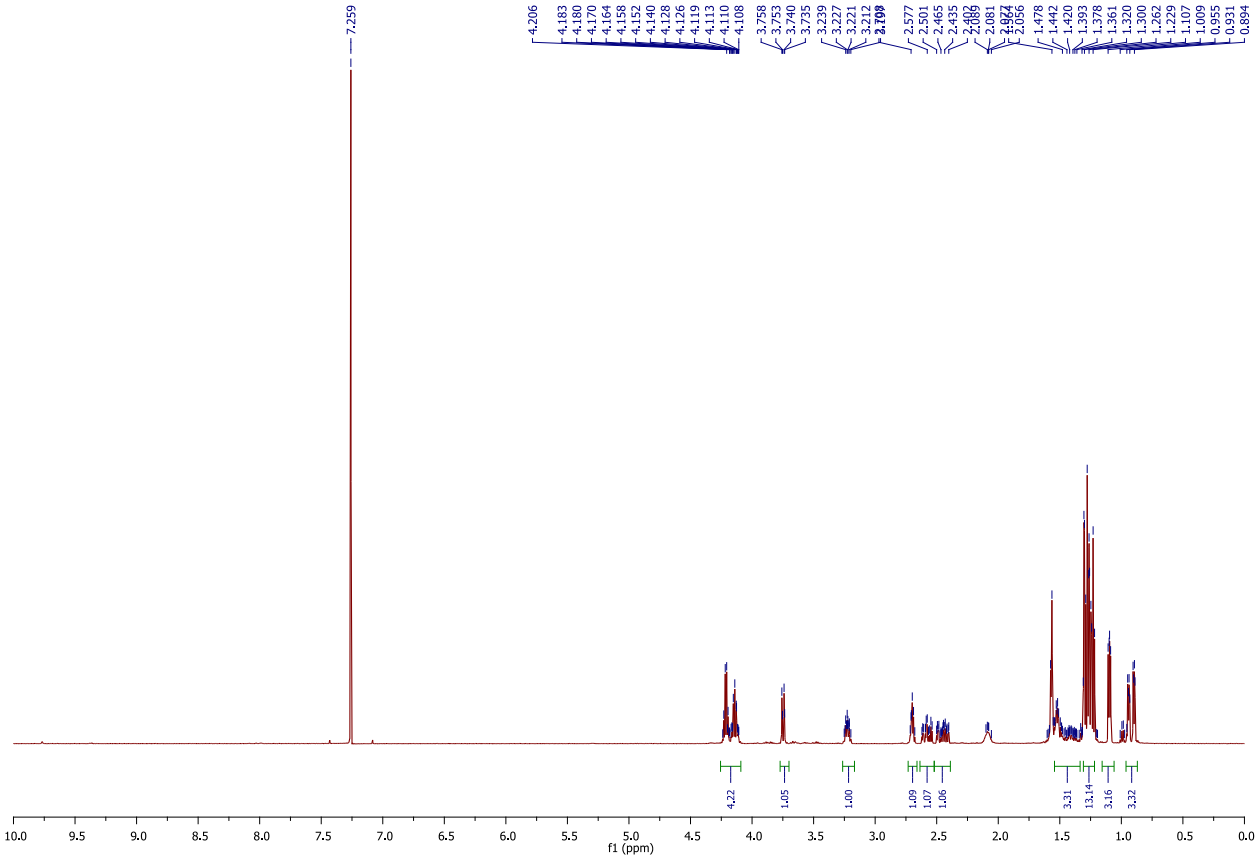


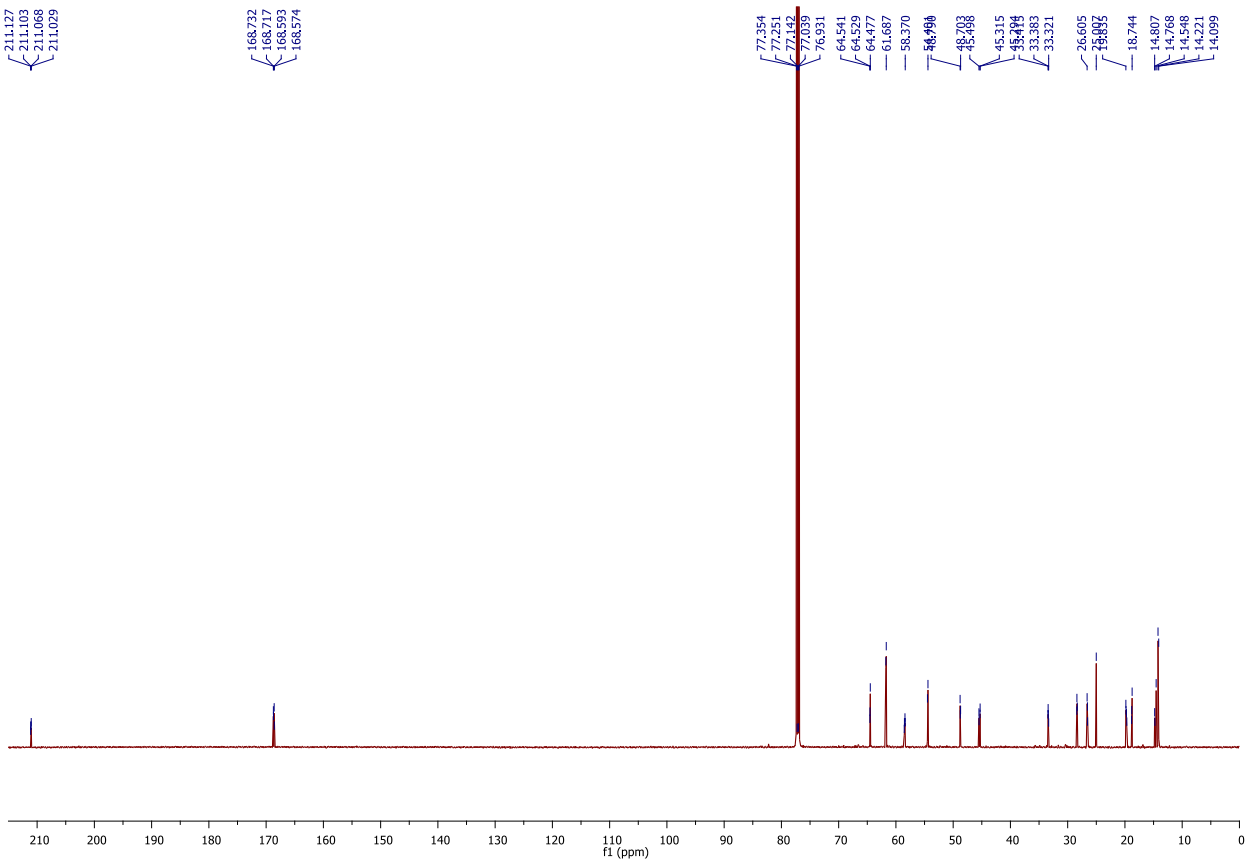


2-(7-(3,3-Dimethyloxiran-2-yl)-5-methyl-3-oxoheptan-2-yl)-malonic acid diethyl ester 44o

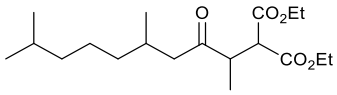


Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-40% Et_2O/petrol) gave 2-(7-(3,3-dimethyloxiran-2-yl)-5-methyl-3-oxoheptan-2-yl)-malonic acid diethyl ester **44o** as a colourless oil (214 mg, 0.60 mmol, 60%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.23-4.10 (m, 4H), 3.76-3.73 (m, 1H), 3.25-3.21 (m, 1H), 2.72-2.68 (m, 1H), 2.62-2.54 (m, 1H), 2.50-2.41 (m, 1H), 2.12-2.07 (m, 1H), 1.59-1.35 (m, 3H), 1.30-1.19 (m, 13H), 1.11-1.08 (m, 3H), 0.93-0.88 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.1 (C), 211.1 (C), 211.0 (C), 168.7 (CH), 168.7 (C), 168.6 (C), 168.6 (C), 64.5 (CH), 64.5 (CH), 64.5 (CH), 61.8 (CH_2), 61.7 (CH_2), 58.5 (C), 58.5 (C), 58.4 (C), 58.4 (C), 54.5 (CH), 54.4 (CH), 48.8 (CH_2), 48.8 (CH_2), 48.7 (CH_2), 45.5 (CH), 45.5 (CH), 45.3 (CH), 45.3 (CH), 33.4 (CH_2), 33.4 (CH_2), 33.4 (CH_2), 33.3 (CH_2), 28.4 (CH_3), 28.4 (CH_3), 28.3 (CH_3), 26.6 (CH_2), 26.6 (CH_2), 26.5 (CH_2), 25.0 (CH_3), 19.8 (CH), 19.8 (CH), 19.8 (CH), 19.7 (CH), 18.8 (CH), 18.8 (CH), 18.8 (CH), 14.8 (CH_3), 14.8 (CH_3), 14.6 (CH_3), 14.2 (CH_3), 14.1 (CH_3); IR (thin film) 2968, 2929, 2877, 1748, 1732, 1717 cm^{-1}; LRMS (CI) 357 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{19}H_{33}O_6$ $[M+H]^+$ 357.2272, observed 357.2271.

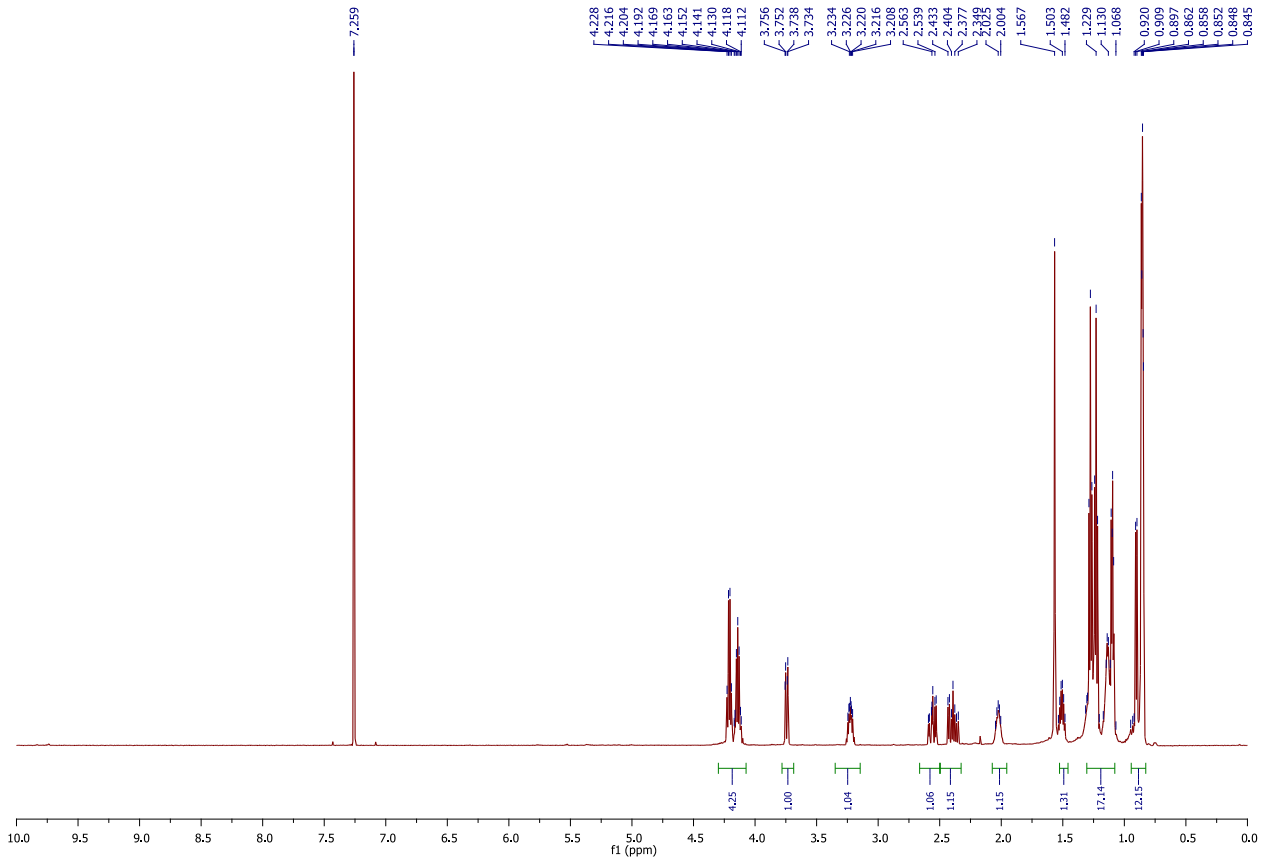


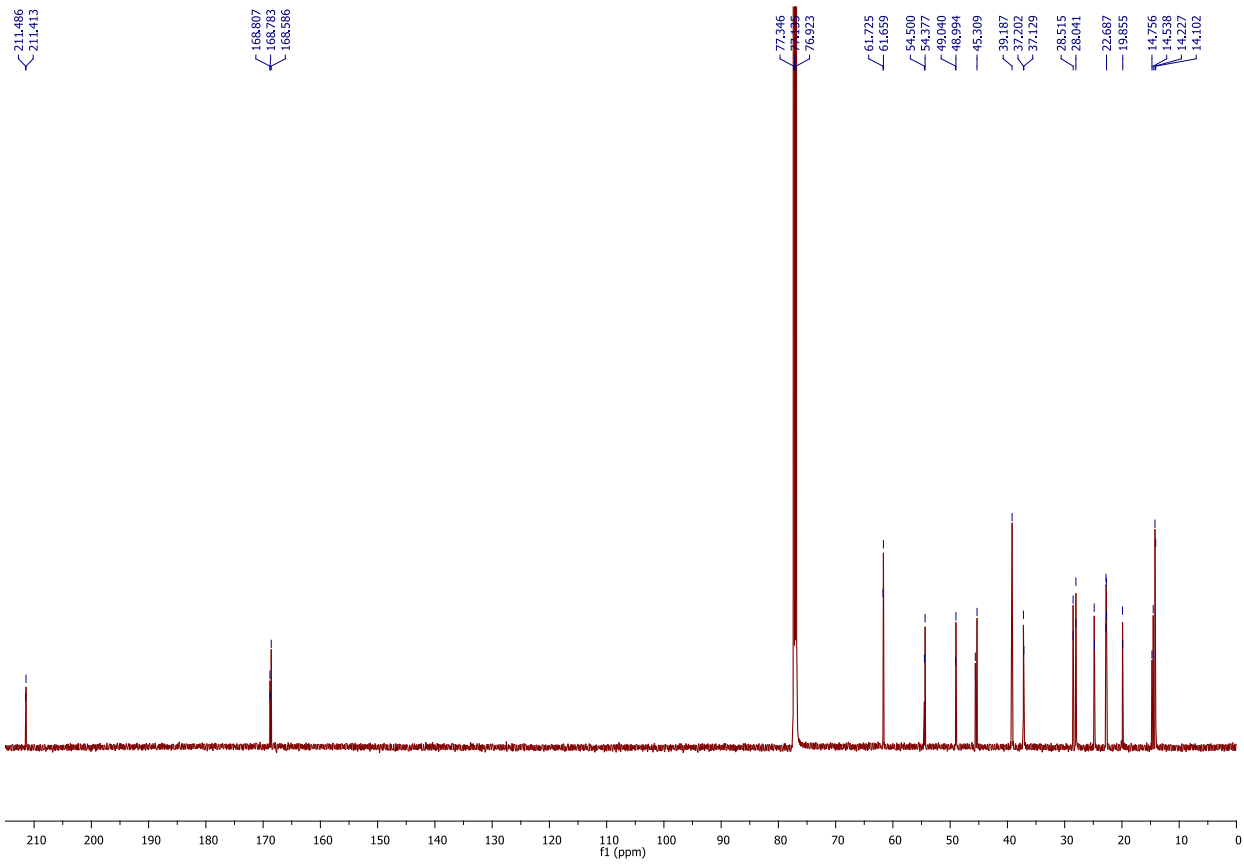


2-(5,9-Dimethyl-3-oxodecan-2-yl)-malonic acid diethyl ester 44r

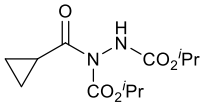


Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-40% Et_2O/petrol) gave 2-(5,9-dimethyl-3-oxodecan-2-yl)-malonic acid diethyl ester **44r** as a colourless oil (209 mg, 0.61 mmol, 61%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.24-4.11 (m, 4H), 3.74 (app. dd, *J* = 10.5, 2.5 Hz, 1H), 3.26-3.19 (m, 1H), 2.56 (app. ddd, *J* = 24.0, 17.5, 5.5 Hz, 1H), 2.39 (app. ddd, *J* = 31.5, 17.5, 7.0 Hz, 1H), 2.05-2.00 (m, 1H), 1.58-1.45 (m, 1H), 1.32-1.06 (m, 12H), 0.93-0.84 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.5 (C), 211.4 (C), 168.8 (C), 168.8 (C), 168.6 (C), 61.7 (CH_2), 61.7 (CH_2), 54.5 (CH), 54.4 (CH), 49.0 (CH_2), 49.0 (CH_2), 45.6 (CH), 45.3 (CH), 39.2 (CH_2), 37.2 (CH_2), 37.1 (CH_2), 28.5 (CH), 28.1 (CH), 28.0 (CH), 24.8 (CH_2), 24.8 (CH_2), 22.8 (CH_3), 22.8 (CH_3), 22.7 (CH_3), 22.7 (CH_3), 19.9 (CH_3), 19.9 (CH_3), 14.8 (CH_3), 14.5 (CH_3), 14.2 (CH_3), 14.1 (CH_3); IR (thin film) 2956, 2930, 1750, 1734, 1716 cm^{-1}; LRMS (ES) 341 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{19}H_{33}O_5$ $[M-H]^-$ 341.2328, observed 341.2329.

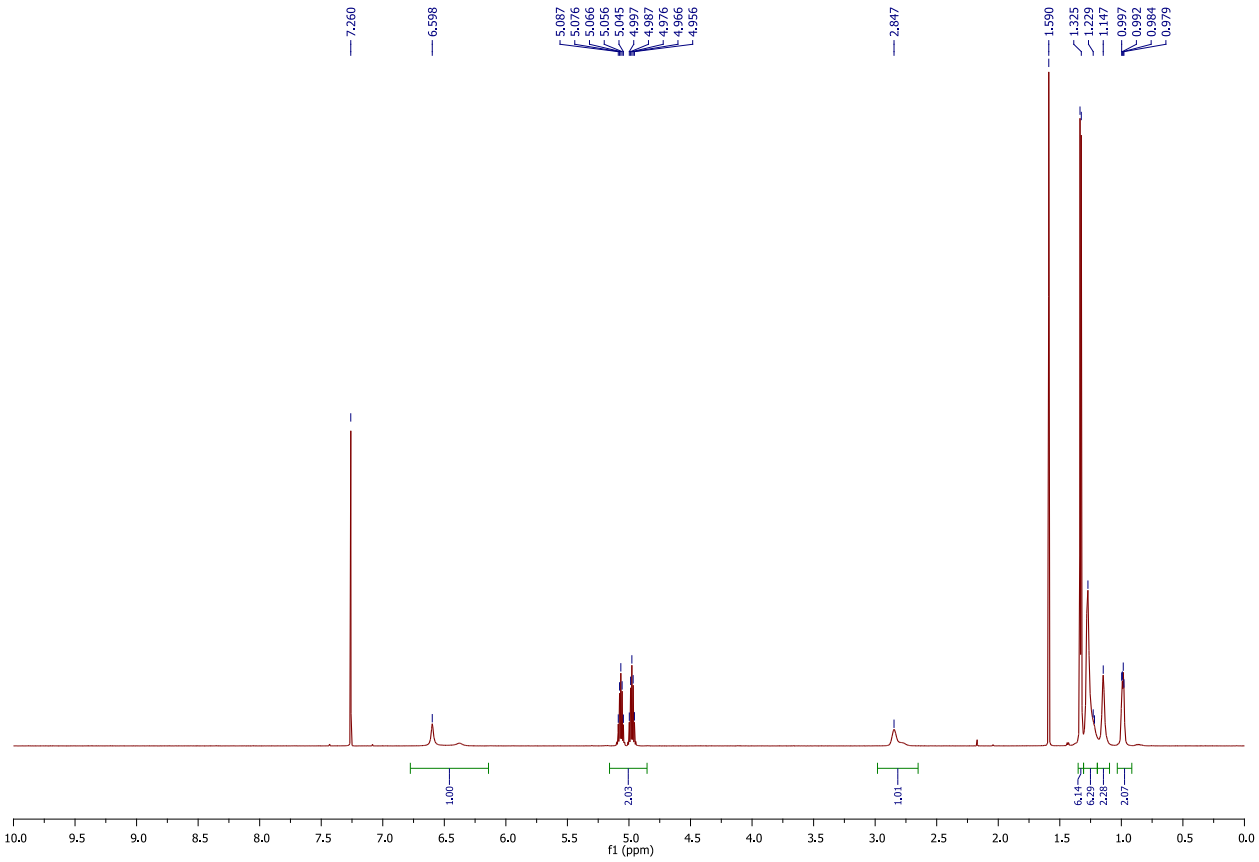


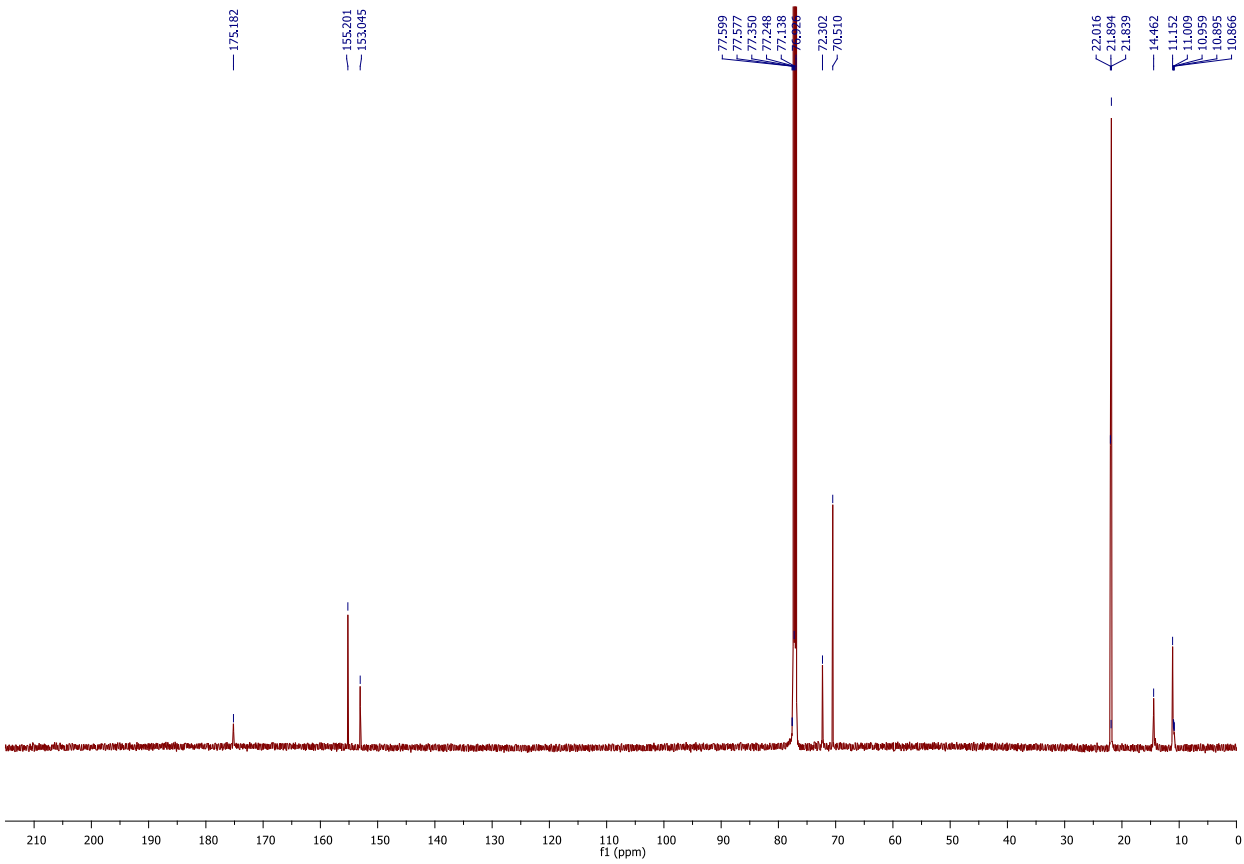


Dipropan-2-yl 1-(cyclopropanecarbonyl)hydrazine-1,2-dicarboxylate 48k

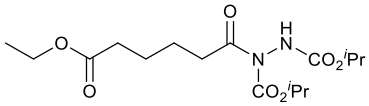


Using Method G, reaction was complete after 24 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-(cyclopropanecarbonyl)hydrazine-1,2-dicarboxylate **48k** as a colourless oil (237 mg, 0.87 mmol, 87%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.60 (br s, NH, 1H), 5.05 (septet, J = 6.5 Hz, 1H), 4.97 (septet, J = 6.5 Hz, 1H), 2.90-2.71 (m, 1H), 1.34-1.22 (m, 12H), 1.18-1.12 (m, 2H), 1.01-0.96 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.2 (C), 155.2 (C), 153.0 (C), 72.3 (CH), 70.5 (CH), 22.0 (CH_3), 21.8 (CH_3), 14.5 (CH), 11.2 (CH_2); IR (thin film) 3314, 2984, 2939, 1734, 1720 cm^{-1}; LRMS (ES) 271 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{12}H_{19}N_2O_5$ $[M-H]^-$ 271.1294, observed 271.1293.



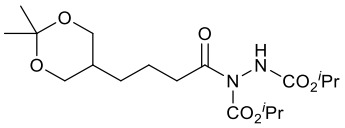


Dipropan-2-yl 1-(6-ethoxy-6-oxohexanoyl)hydrazine-1,2-dicarboxylate 48l[11]



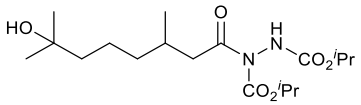
Using Method G, reaction was complete after 96 h. Purification by column chromatography (10-20% EtOAc/Petrol) gave dipropan-2-yl 1-(6-ethoxy-6-oxohexanoyl)hydrazine-1,2-dicarboxylate **48l** as a colourless oil (288 mg, 0.80 mmol, 80%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.56 (br s, NH, 1H), 5.03 (septet, *J* = 6.0 Hz, 1H), 4.97 (septet, *J* = 6.0 Hz, 1H), 4.10 (q, *J* = 7.0 Hz, 2H), 2.97-2.82 (m, 2H), 2.32 (t, *J* = 7.0 Hz, 2H), 1.73-1.65 (m, 4H), 1.32-1.23 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.5 (C), 173.4 (C), 155.2 (C), 152.7 (C), 72.3 (CH), 70.6 (CH), 60.4 (CH_2), 36.8 (CH_2), 34.2 (CH_2), 24.4 (CH_2), 24.2 (CH_2) 22.0 (CH_3), 21.8 (CH_3), 14.4 (CH_3); IR (thin film) 3321, 2982, 1788, 1727, 1725 cm^{-1}; LRMS (ES$^-$) 359 (100, [M-H]$^-$); HRMS (ES$^-$) calcd for $C_{16}H_{27}N_2O_7$ [M-H]$^-$ 359.1818, observed 359.1826.

Dipropan-2-yl 1-[4-(5,5-dimethyl-1,3-dioxan-2-yl)butanoyl]hydrazine-1,2-dicarboxylate 48m[11]

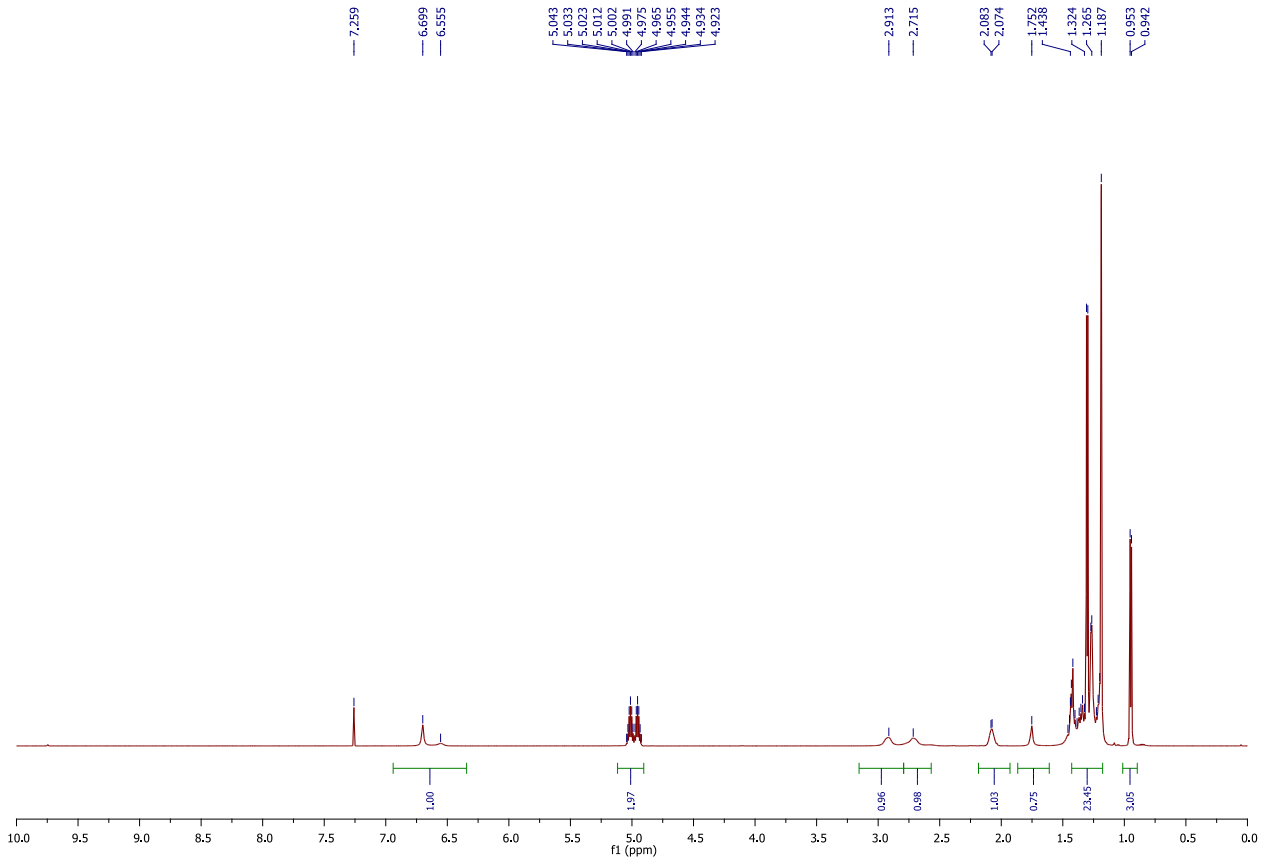


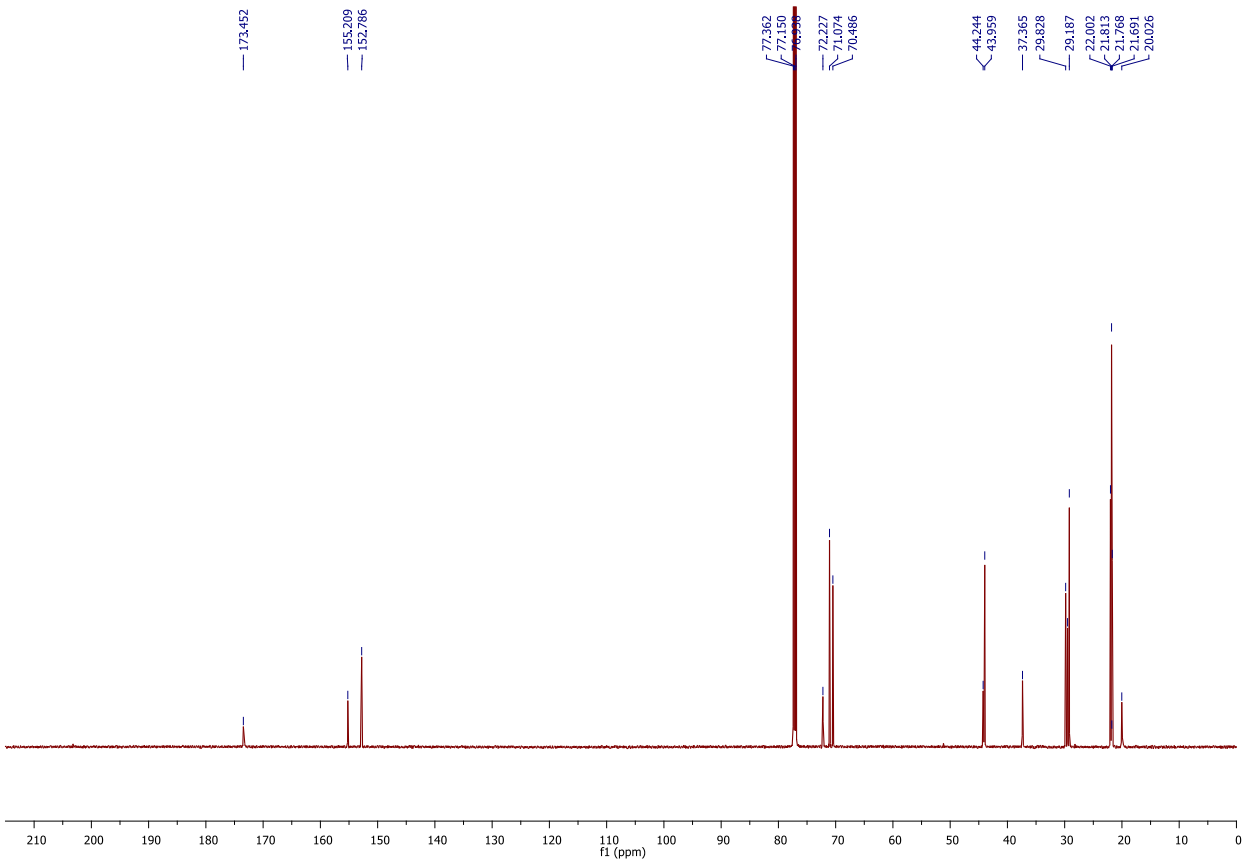
Using Method G, reaction was complete after 24 h. Purification by column chromatography (10-20% EtOAc/Petrol) gave dipropan-2-yl 1-[4-(5,5-dimethyl-1,3-dioxan-2-yl)butanoyl]hydrazine-1,2-dicarboxylate **48m** as a colourless oil (268 mg, 0.69 mmol, 69%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.56 (br s, NH, 1H), 5.03 (septet, *J* = 6.0 Hz, 1H), 4.96 (septet, *J* = 6.0 Hz, 1H), 4.43 (t, *J* = 5.0 Hz, 1H), 3.57 (d, *J* = 10.5 Hz, 2H), 3.40 (d, *J* = 11.0 Hz, 2H), 2.97-2.87 (m, 2H), 1.82-1.77 (m 2H), 1.70-1.67 (m, 2H), 1.32-1.20 (m, 12H), 1.17 (s, 3H), 0.70 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.6 (C), 155.2 (C), 152.7 (C), 101.9 (CH), 77.5 (CH_2), 72.1 (CH), 70.2 (CH), 36.7 (CH_2), 33.9 (CH_2), 30.2 (C), 23.0 (CH_3), 21.9 (CH_3), 21.8 (CH_3), 21.7 (CH_3), 19.2 (CH_2); IR (thin film) 3299, 2955, 2848, 1780, 1738, 1734 cm^{-1}; LRMS (ES$^+$) 411 (100, [M+Na]$^+$); HRMS (ES$^+$) calcd for $C_{18}H_{32}N_2O_7Na$ [M+Na]$^+$ 411.2107, observed 411.2116.

Dipropan-2-yl 1-(7-hydroxy-3,7-dimethyloctanoyl)hydrazine-1,2-dicarboxylate 48n

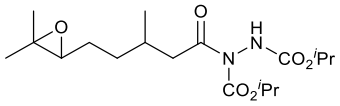


Using Method G, reaction was complete after 24 h. Purification by column chromatography (10-50% EtOAc/petrol) gave dipropan-2-yl 1-(7-hydroxy-3,7-dimethyloctanoyl)hydrazine-1,2-dicarboxylate **48n** as a colourless oil (307 mg, 0.82 mmol, 82%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.69 (br s, NH, 1H), 5.01 (septet, *J* = 6.0 Hz, 1H), 4.95 (septet, *J* = 6.0 Hz, 1H), 2.97-2.90 (m, 1H), 2.80-2.65 (m, 1H), 2.12-2.05 (m, 1H), 1.77-1.71 (m, 1H), 1.48-1.18 (m, 23H), 0.95 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.5 (C), 155.2 (C), 152.8 (C), 72.2 (CH), 71.1 (C), 70.5 (CH), 44.2 (CH_2), 44.0 (CH_2), 37.4 (CH_2), 29.8 (CH_3), 29.5 (CH_3), 29.2 (CH_3), 22.0 (CH_3), 21.8 (CH_3), 21.7 (CH_2), 20.0 (CH); IR (thin film) 3318, 2978, 2938, 1784, 1738, 1723 cm^{-1}; LRMS (ES) 373 (100, [M-H]$^-$); HRMS (ES) calcd for $C_{18}H_{33}N_2O_6$ [M-H]$^-$ 373.2339, observed 373.2328.



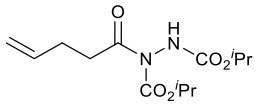


Dipropan-2-yl 1-[5-(3,3-dimethyloxiran-2-yl)-3-methylpentanoyl]hydrazine-1,2-dicarboxylate 48o[11]

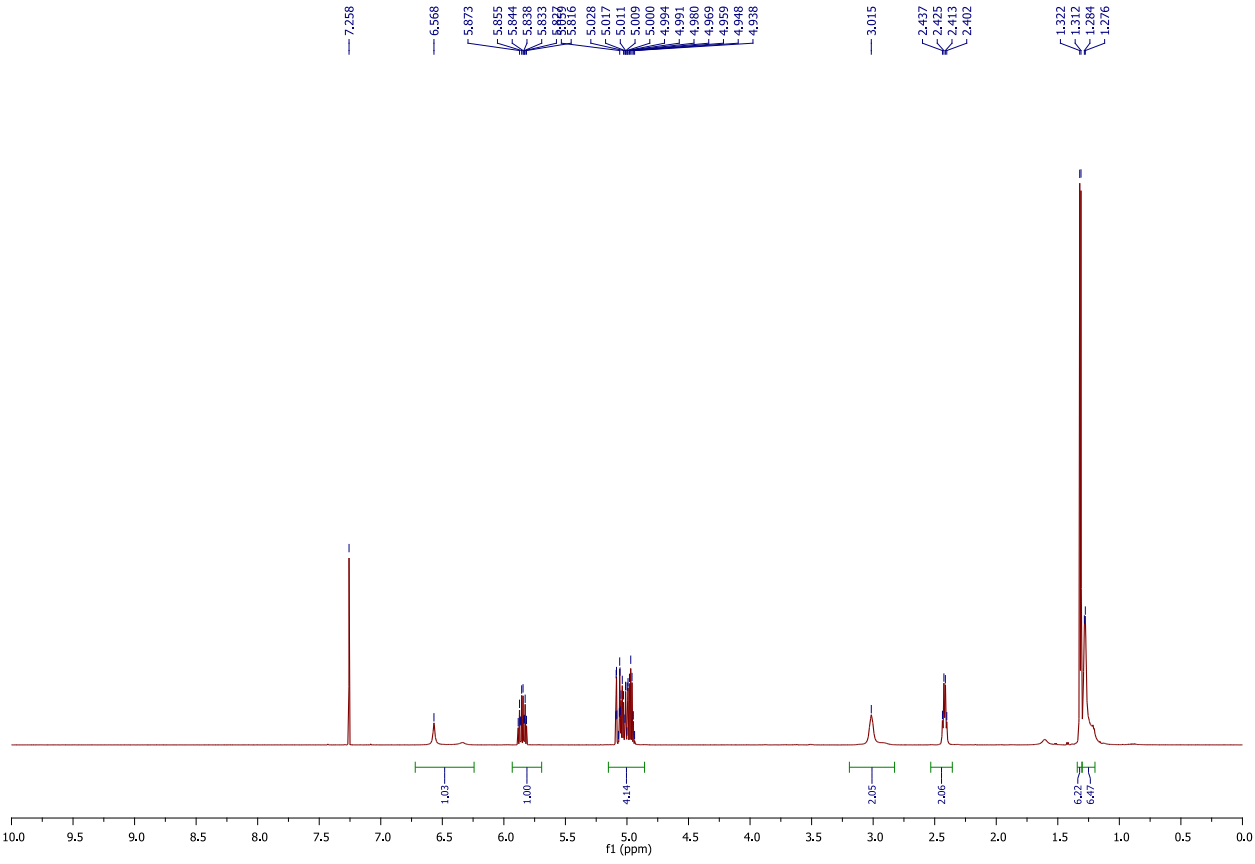


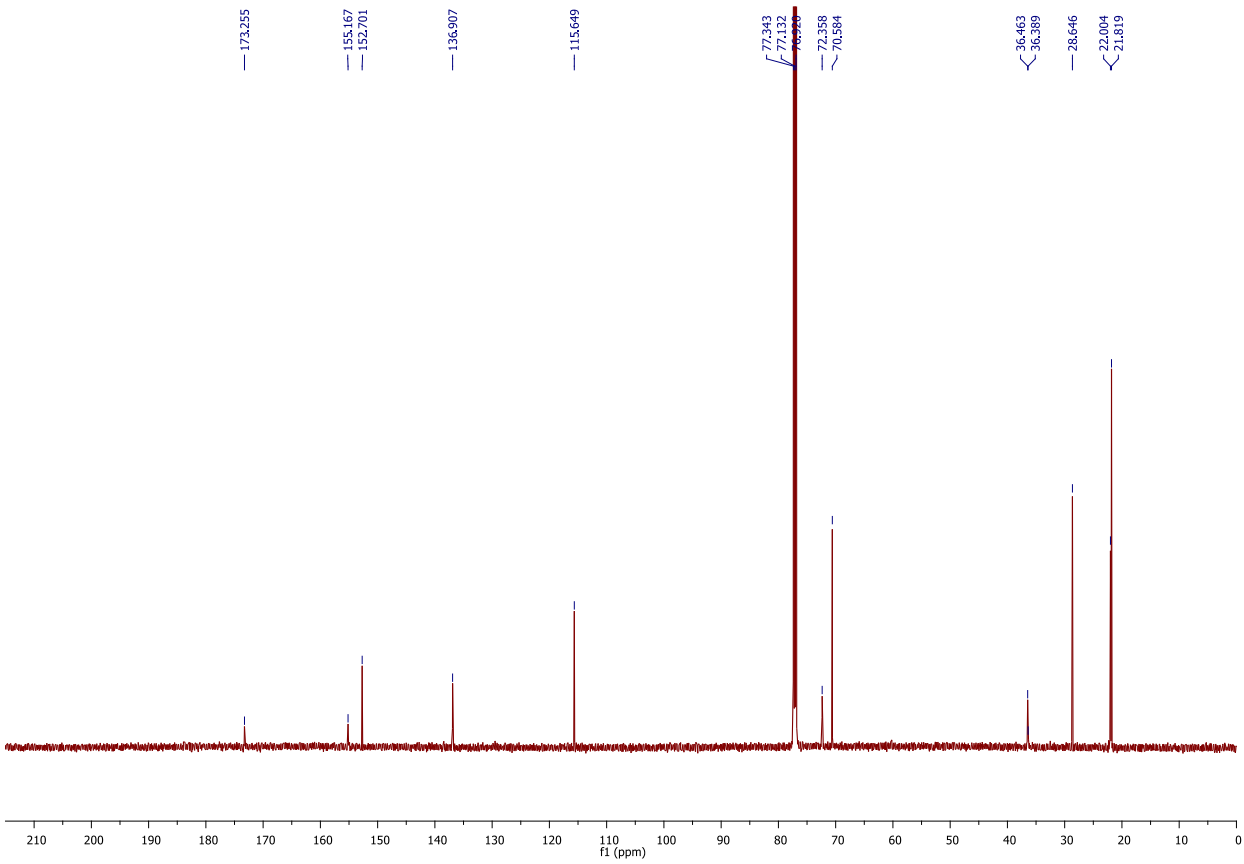
Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-20% EtOAc/Petrol) gave dipropan-2-yl 1-[5-(3,3-dimethyloxiran-2-yl)-3-methylpentanoyl]hydrazine-1,2-dicarboxylate **48o** as a colourless oil (249 mg, 0.67 mmol, 67%) as a 1:1 mixture of diastereoisomers: ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.58 (br s, NH, 1H), 5.02 (septet, *J* = 6.0 Hz, 1H) 4.97 (septet, *J* = 6.5 Hz, 1H), 2.97-2.73 (m, 2H), 2.72-2.68 (m, 1H), 2.11 (m, 1H) 1.62-1.35 (m, 4H), 1.33-1.23 (m, 18H), 0.96 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.2 (C), 155.2 (C), 152.7 (C), 72.3 (CH), 70.6 (CH), 64.6 (CH), 64.4 (CH), 58.5 (C), 58.4 (C), 44.2 (CH_2), 33.5 (CH_2), 33.4 (CH_2), 29.8 (CH), 29.8 (CH), 26.5 (CH_2), 26.5 (CH_2), 25.0 (CH_3), 22.0 (CH_3), 21.8 (CH_3), 19.8 (CH_3), 19.7 (CH_3), 18.8 (CH_3), 18.7 (CH_3); IR (thin film) 3298, 2932, 1788, 1736, 1722, 1104 cm^{-1}; LRMS (ES$^+$) 395 (100, $[M+Na]^+$); HRMS (ES$^+$) calcd for $C_{18}H_{32}N_2O_6Na$ $[M+Na]^+$ 395.2158, observed 395.2150.

Dipropan-2-yl 1-(pent-4-enoyl)hydrazine-1,2-dicarboxylate 48p

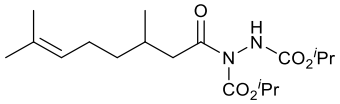


Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-20% EtOAc/petrol) gave dipropan-2-yl 1-(pent-4-enoyl)hydrazine-1,2-dicarboxylate **48p** as a colourless oil (120 mg, 0.42 mmol, 42%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.60 (br s, NH, 1H), 5.85 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 5.09-4.94 (m, 4H), 3.08-2.90 (m, 2H), 2.42 (q, *J* = 7.0 Hz, 2H), 1.31 (d, *J* = 6.5 Hz, 6H), 1.30-1.25 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.3 (C), 155.2 (C), 152.7 (C), 136.9 (CH), 115.6 (CH_2), 72.3 (CH), 70.6 (CH), 36.5 (CH_2), 28.6 (CH_2), 22.0 (CH_3), 21.8 (CH_3); IR (thin film) 3308, 2982, 2941, 1787, 1734, 1718, 1642 cm^{-1}; LRMS (CI) 287 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{13}H_{23}N_2O_5$ $[M+H]^+$ 287.1607, observed 287.1612.

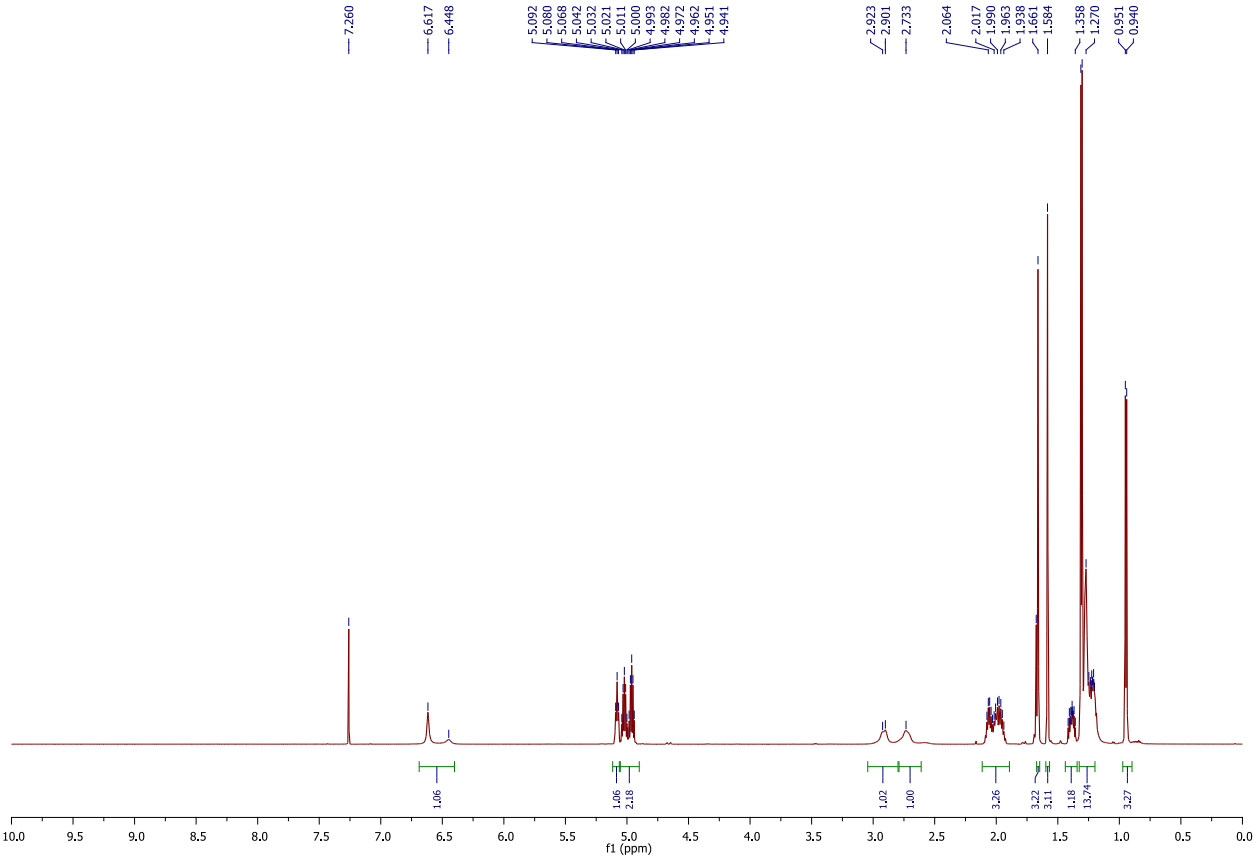


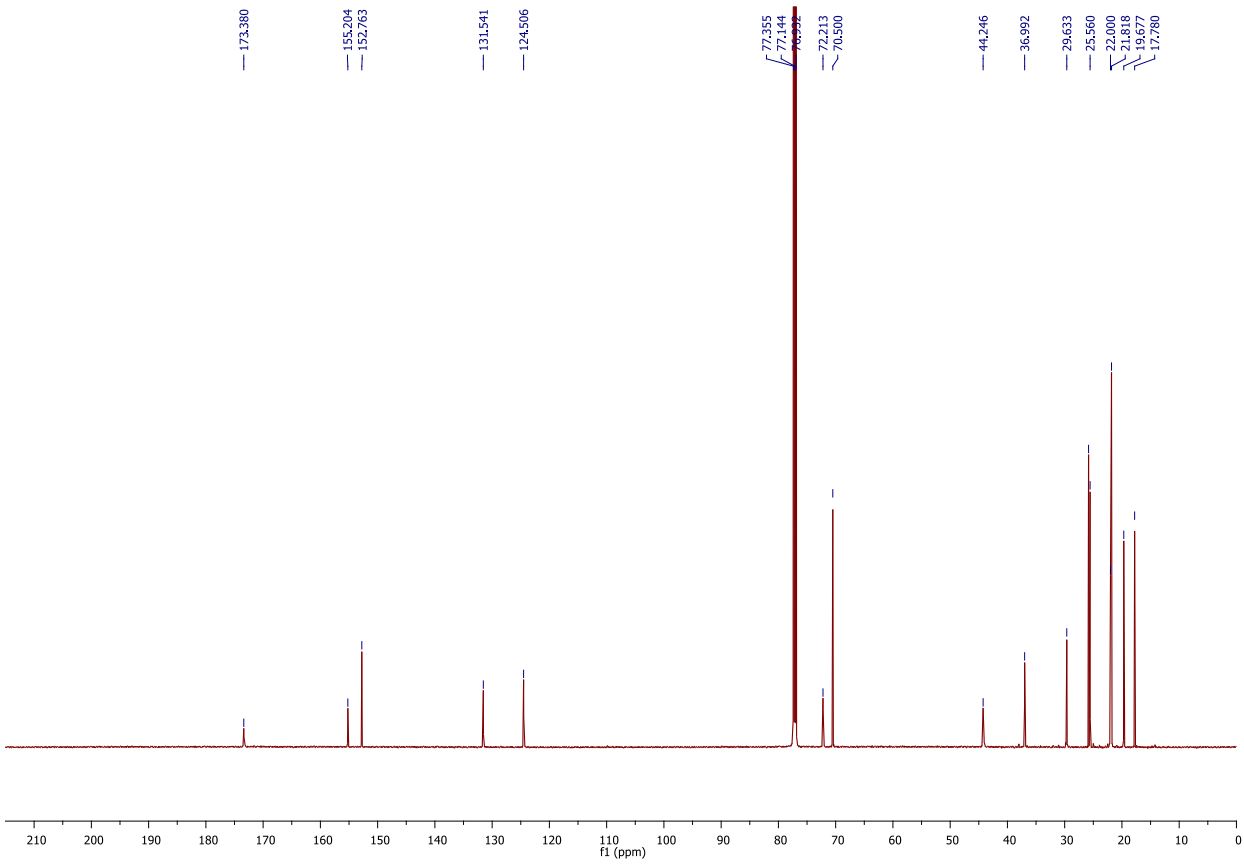


Dipropan-2-yl 1-(3,7-dimethyloct-6-enoyl)hydrazine-1,2-dicarboxylate 48q

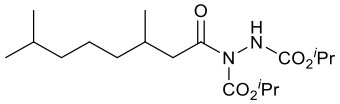


Using Method G, reaction was complete after 24 h. Purification by column chromatography (10-30% EtOAc/petrol) gave dipropan-2-yl 1-(3,7-dimethyloct-6-enoyl)hydrazine-1,2-dicarboxylate **48q** as a colourless oil (192 mg, 0.54 mmol, 54%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.62 (br s, NH, 1H), 5.10-5.06 (m, 1H), 5.02 (septet, *J* = 6.0 Hz, 1H), 4.96 (septet, *J* = 6.0 Hz, 1H), 2.97-2.90 (m, 1H), 2.80-2.65 (m, 1H), 2.09-1.92 (m, 3H), 1.66 (s, 3H), 1.58 (s, 3H), 1.41-1.35 (m, 1H), 1.32-1.18 (m, 13H), 0.95 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.4 (C), 155.2 (C), 152.8 (C), 131.5 (C), 124.5 (CH), 72.2 (CH), 70.5 (CH), 44.2 (CH_2), 37.0 (CH_2), 29.6 (CH_3), 25.8 (CH_3), 25.6 (CH_2), 22.0 (CH_3), 21.8 (CH_3), 19.7 (CH), 17.8 (CH_3); IR (thin film) 3317, 2981, 2928, 1787, 1736, 1720 cm^{-1}; LRMS (ES) 355 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{18}H_{31}N_2O_5$ $[M-H]^-$ 355.2233, observed 355.2233.

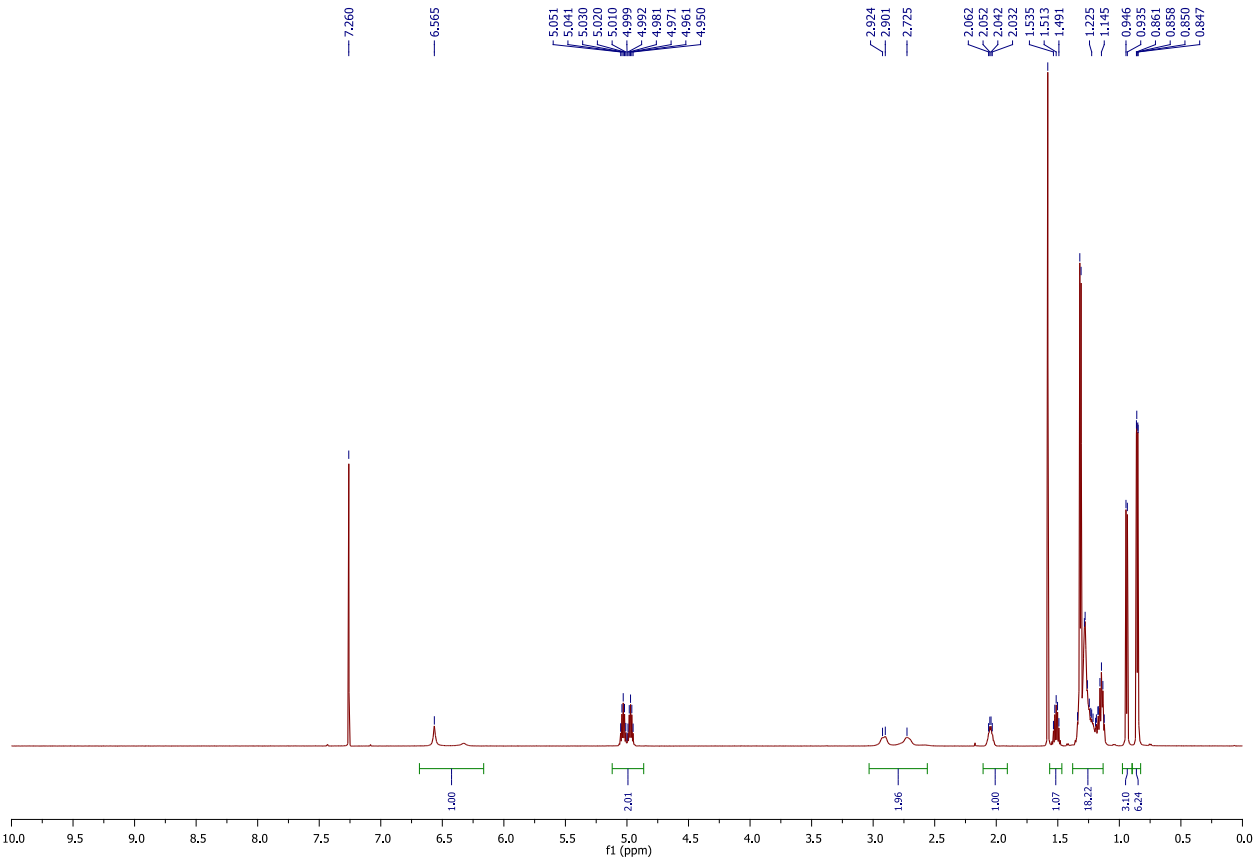


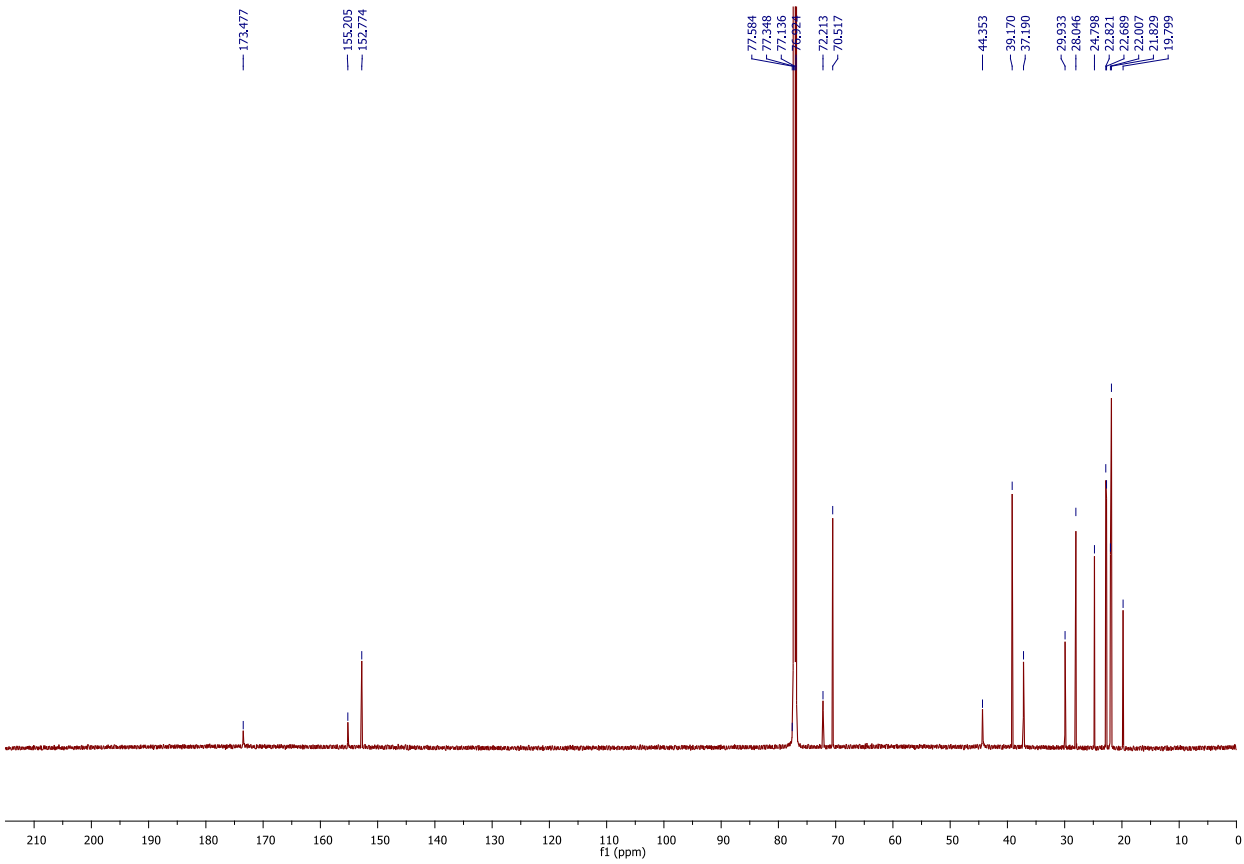


Dipropan-2-yl 1-(3,7-dimethyloctanoyl)hydrazine-1,2-dicarboxylate 48r

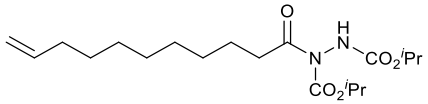


Using Method G, reaction was complete after 24 h. Purification by column chromatography (10-30% EtOAc/petrol) gave dipropan-2-yl 1-(3,7-dimethyloctanoyl)hydrazine-1,2-dicarboxylate **48r** as a colourless oil (311 mg, 0.87 mmol, 87%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.56 (br s, NH, 1H), 5.03 (septet, *J* = 6.0 Hz, 1H), 4.96 (septet, *J* = 6.0 Hz, 1H), 2.97-2.90 (m, 1H), 2.78-2.65 (m, 1H), 2.07-2.03 (m, 1H), 1.51 (septet, *J* = 6.5 Hz, 1H), 1.33-1.12 (m, 18H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.85 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.5 (C), 155.2 (C), 152.8 (C), 72.2 (CH), 70.5 (CH), 44.3 (CH_2), 39.2 (CH_2), 37.2 (CH_2), 29.9 (CH), 28.0 (CH_3), 24.8 (CH_2), 22.8 (CH_3), 22.7 (CH_3), 22.0 (CH_3), 21.8 (CH_3), 19.8 (CH); IR (thin film) 3317, 2956, 2931, 2872, 1788, 1738, 1724 cm^{-1}; LRMS (ES) 357 (100, $[M-H]^-$); HRMS (ES) calcd for $C_{18}H_{33}N_2O_5$ $[M-H]^-$ 357.2389, observed 357.2391.



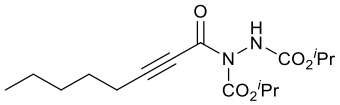


Dipropan-2-yl 1-(undec-10-enoyl)hydrazine-1,2-dicarboxylate 48s[11]



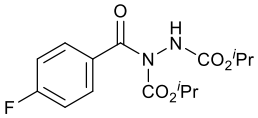
Using Method G, reaction was complete after 72 h. Purification by column chromatography (10-20% EtOAc/Petrol) gave dipropan-2-yl 1-(undec-10-enoyl)hydrazine-1,2-dicarboxylate **48s** as a colourless oil (285 mg, 0.77 mmol, 77%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.63 (br s, NH, 1H), 5.80 (ddt, *J* = 17.0, 10.0, 6.5 Hz 1H), 5.03 (septet, *J* = 6.0 Hz, 1H), 5.01-4.90 (m, 3H), 2.94-2.89 (m, 2H), 2.03 (q, *J* = 7.0 Hz, 2H), 1.65 (quintet, *J* = 6.9 Hz, 2H), 1.38-1.22 (m, 22H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0 (C), 155.2 (C), 152.8 (C), 139.4 (CH), 114.2 (CH_2), 72.2 (CH), 70.5 (CH), 37.2 (CH_2), 33.9 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 24.7 (CH_2), 22.0 (CH_3), 21.8 (CH_3); IR (thin film) 3313, 2981, 2855, 1788, 1736, 1722 cm^{-1}; LRMS (CI) 371 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{19}H_{35}N_2O_5$ $[M+H]^+$ 371.2546, observed 371.2548.

Dipropan-2-yl 1-(oct-2-ynoyl)hydrazine-1,2-dicarboxylate 48t[11]



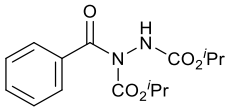
Using Method G, reaction was complete after 72 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-(oct-2-ynoyl)hydrazine-1,2-dicarboxylate **48t** as a colourless oil (179 mg, 0.55 mmol, 55%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.63 (br s, NH, 1H), 5.08 (septet, J = 6.5 Hz, 1H), 4.99 (septet, J = 6.5 Hz, 1H), 2.39 (t, J = 7.0 Hz, 2H), 1.62-1.55 (m, 2H), 1.42-1.22 (m, 16H), 0.90 (t, J = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.7 (C), 152.4 (C), 151.4 (C), 98.8 (C), 74.3 (C), 72.8 (CH), 70.8 (CH), 31.1 (CH_2), 27.3 (CH_2), 22.2 (CH_2), 22.0 (CH_3), 21.8 (CH_3), 19.4 (CH_2), 14.0 (CH_3); IR (thin film) 3314, 2983, 2936, 2873, 2229, 1741, 1724, 1687 cm^{-1}; LRMS (FAB) 349 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_{16}H_{26}N_2O_5Na$ $[M+Na]^+$ 349.1739, observed 349.1733.

Dipropan-2-yl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate 48u[11]



Using Method G, reaction was complete after 96 h. Purification by column chromatography (10-20% EtOAc/Petrol) gave dipropan-2-yl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate **48u** as a colourless oil (245 mg, 0.75 mmol, 75%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76-7.69 (m, 2H), 7.12-7.08 (m, 2H), 6.93 (br s, NH, 1H), 5.00 (septet, J = 6.5 Hz, 1H), 4.90 (septet, J = 6.5 Hz, 1H), 1.30-1.22 (m, 6H), 1.20-1.05 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.3 (C), 165.1 (d, $J_{C\text{-}F}$ = 252 Hz, C), 155.4 (C), 153.0 (C), 131.3 (C), 131.0 (d, $J_{C\text{-}F}$ = 8.0 Hz, CH), 115.5 (d, $J_{C\text{-}F}$ = 21.0 Hz, CH), 72.8 (CH), 70.9 (CH), 22.0 (CH_3), 21.5 (CH_3); IR (thin film) 3313, 2984, 2938, 1734, 1705, 1603, 1507 cm^{-1}; LRMS (FAB) 349 (100, $[M+Na]^+$); HRMS (FAB) calcd for $C_{15}H_{19}N_2O_5FNa$ $[M+Na]^+$ 349.1176, observed 349.1171.

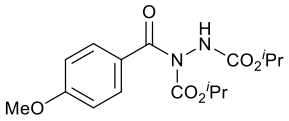
Dipropan-2-yl 1-benzoylhydrazine-1,2-dicarboxylate 48v[11]



Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-20% EtOAc/Petrol) gave dipropan-2-yl 1-benzoylhydrazine-1,2-dicarboxylate **48v** as a white solid (243 mg, 0.79 mmol, 79%): m.p. 98-101 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72-7.59 (m, 2H), 7.52-7.48 (m 1H), 7.43-7.37 (m, 2H), 7.07 (br s, NH, 1H), 5.00 (septet, J = 6.5 Hz, 1H), 4.92-4.84 (m, 1H), 1.31-1.23 (m, 6H), 1.10-1.02 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.3 (C), 155.4 (C), 152.9 (C), 135.2 (C), 131.9 (CH), 128.2 (CH), 128.1 (CH), 72.5 (CH), 70.6 (CH), 21.9 (CH_3), 21.3 (CH_3); IR (thin film) 3265, 2988, 1755, 1738, 1682, 1601, 1519 cm^{-1}; LRMS

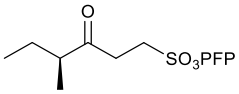
(ES$^-$) 307 (100, [M-H]$^-$); HRMS (ES$^-$) calcd for $C_{15}H_{19}N_2O_5$ [M-H]$^-$ 307.1294, observed 307.1289.

Dipropan-2-yl 1-(4-methoxybenzoyl)hydrazine-1,2-dicarboxylate 48w[11]

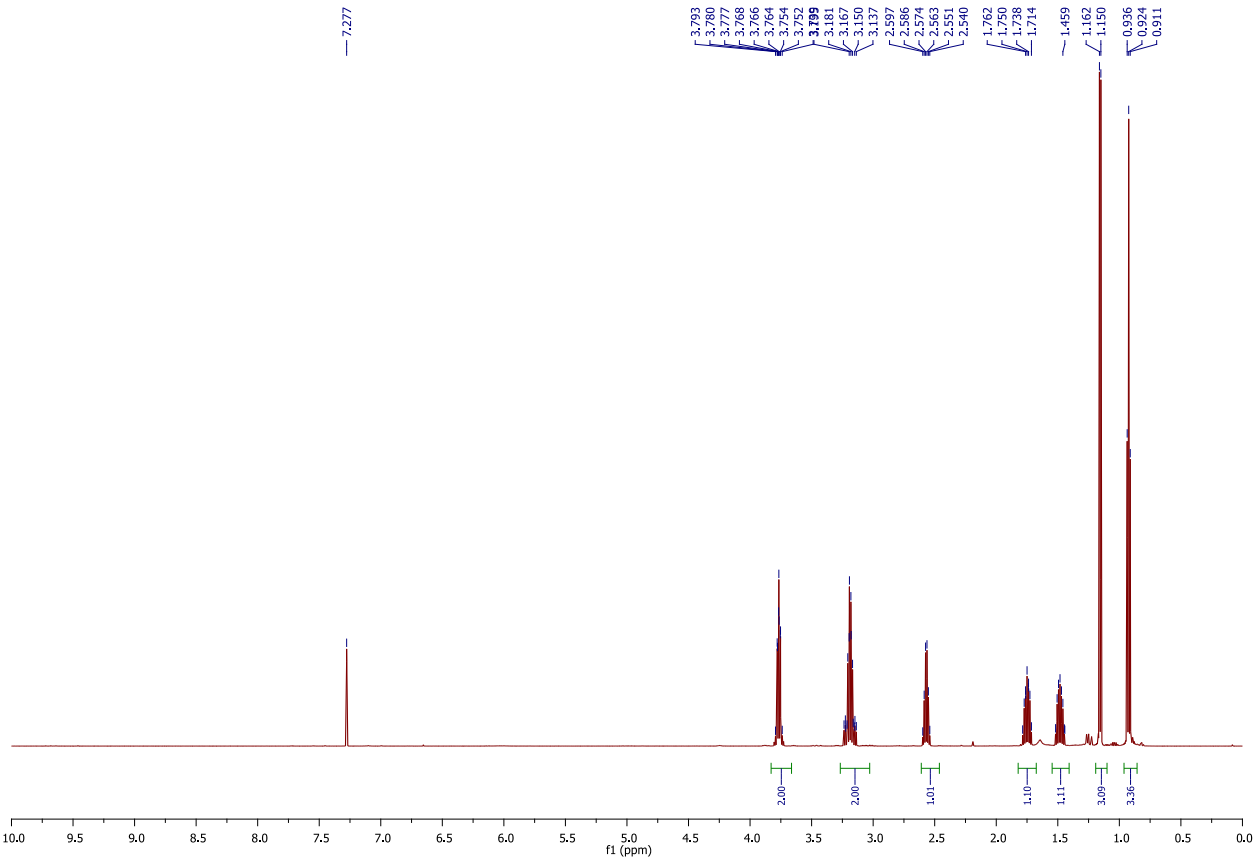


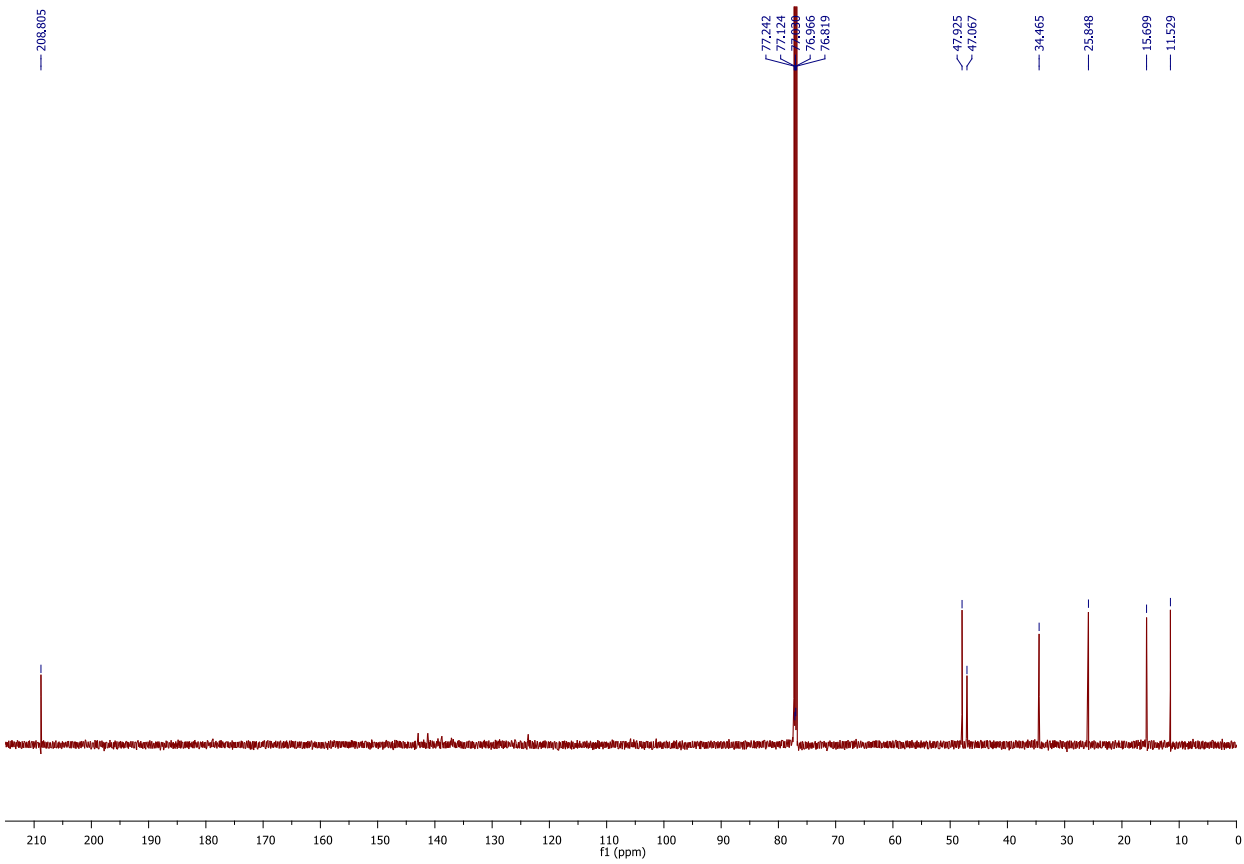
Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-20% EtOAc/Petrol) gave dipropan-2-yl 1-(4-methoxybenzoyl)hydrazine-1,2-dicarboxylate **48w** as a white solid (149 mg, 0.44 mmol, 44%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73-7.60 (m, 2H), 7.12 (br s, NH, 1H) 6.87 (d, *J* = 8.5 Hz, 2H), 4.97 (septet, *J* = 6.5 Hz, 1H), 4.89 (septet, *J* = 6.5 Hz, 1H) 3.82 (s, 3H), 1.29-1.07 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.8 (C), 163.1 (C), 155.5 (C), 153.4 (C), 131.1 (CH), 127.0 (C), 113.5 (CH), 72.4 (CH), 70.6 (CH), 55.6 (CH_3), 22.0 (CH_3), 21.6 (CH_3); IR (thin film) 3309, 2982, 2938, 1733, 1701, 1604, 1579 cm^{-1}; LRMS (ES$^-$) 337 (100, [M-H]$^-$); HRMS (ES$^-$) calcd for $C_{16}H_{21}N_2O_6$ [M-H]$^-$ 337.1400, observed 337.1406.

Pentafluorophenyl (4*S*)-4-methyl-3-oxohexane-1-sulfonate 15x

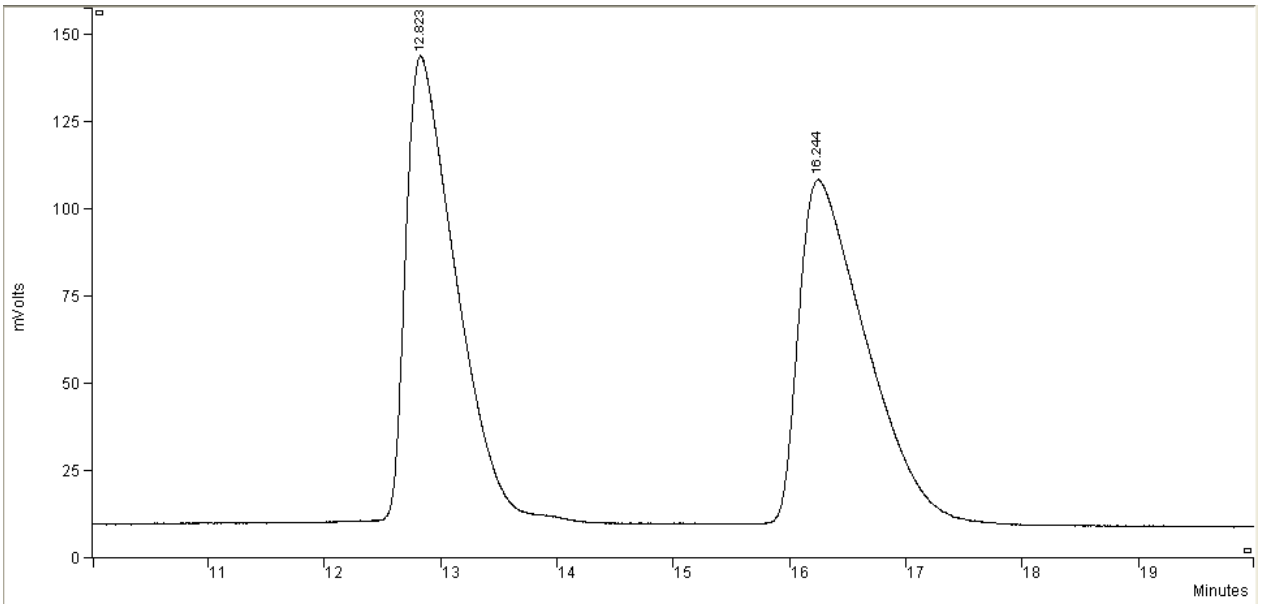


Using Method B, reaction was complete after 3 h Purification by flash column chromatography (20-70% CH_2Cl_2/petrol) gave pentafluorophenyl (4*S*)-4-methyl-3-oxohexane-1-sulfonate **15x** as a colourless oil (317 mg, 0.88 mmol, 88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79-3.73 (m, 2H), 3.24-3.14 (m, 2H), 2.57 (sextet, *J* = 7.5 Hz, 1H), 1.75 (doublet of quintets, *J* = 14.0 and 7.5 Hz, 1H), 1.48 (doublet of quintets, *J* = 14.0 and 7.5 Hz, 1H), 1.16 (d, *J* = 7.5 Hz, 3H), 0.92 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.8 (C), 47.9 (CH), 47.1 (CH_2), 34.5 (CH_2), 25.9 (CH_2), 15.7 (CH_3), 11.5 (CH_3); IR (solid) 2970, 2940, 1716, 1516, 1384, 1184 cm^{-1}; LRMS (CI) 361 (100, [M+H]$^+$); HRMS (CI) calcd for $C_{13}H_{14}F_5O_4S$ [M+H]$^+$ 361.0533, observed 361.0526; $[\alpha]_D$ = +9.76 (*c* 18.9, CHCl3, 23.5 °C); HPLC conditions: CHIRALCEL-OD column, hexane:*i*-PrOH 97:3, 1.2 mL/min, t_R (minor) = 12.8 min, t_R (major) = 16.3 min, 97%ee.

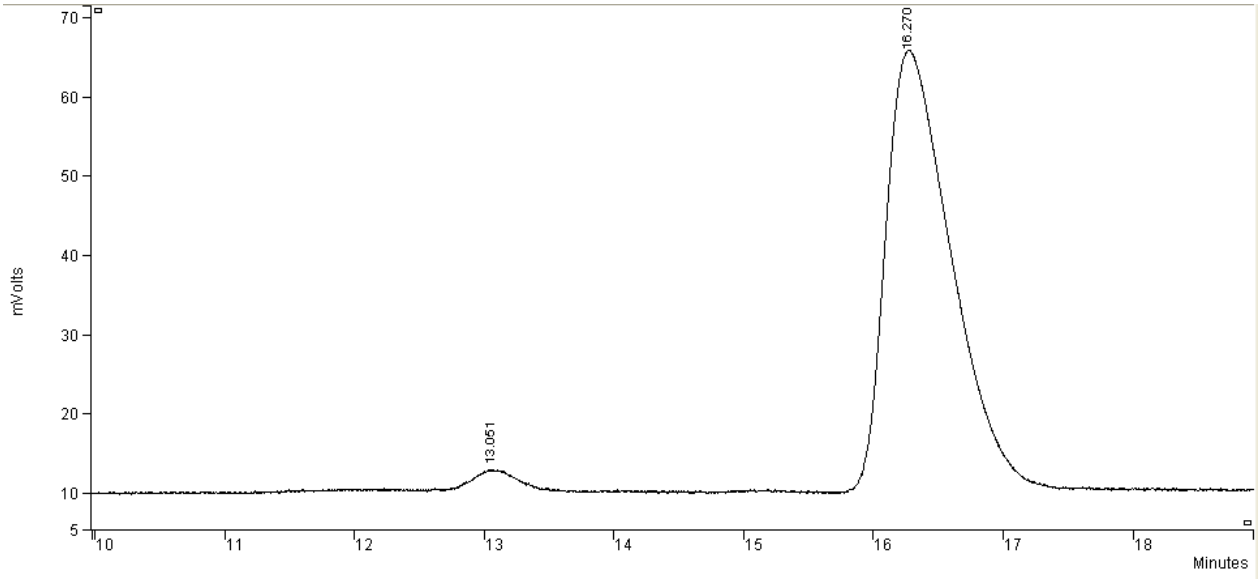




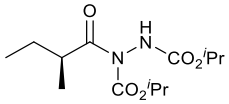
HPLC trace for pentafluorophenyl (4*rac*)-4-methyl-3-oxohexane-1-sulfonate **15x**



HPLC trace for pentafluorophenyl (4*S*)-4-methyl-3-oxohexane-1-sulfonate **15x**

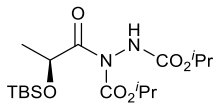


Dipropan-2-yl 1-[(*S*)-2-methylbutanoyl]hydrazine-1,2-dicarboxylate 48x[11]



Using Method G, reaction was complete after 24 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave dipropan-2-yl 1-[(*S*)-2-methylbutanoyl]hydrazine-1,2-dicarboxylate **48x** as a colourless oil (254 mg, 0.88 mmol, 88%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65 (br s, NH, 1H), 5.05 (septet, *J* = 6.5 Hz, 1H), 4.97 (septet, *J* = 6.5 Hz, 1H), 3.55-3.47 (m, 1H), 1.80 (doublet of quintets, *J* = 14.5, 7.5 Hz, 1H), 1.46 (doublet of quintets, *J* = 14.5, 7.0 Hz, 1H), 1.34-1.17 (m, 15H), 0.93 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0 (C), 155.3 (C), 152.7 (C), 72.2 (CH), 70.4 (CH), 41.0 (CH), 27.1 (CH_2), 22.0 (CH_3), 21.8 (CH_3), 16.9 (CH_3), 11.7 (CH_3); IR (thin film) 3313, 2981, 2938, 1736, 1718 cm^{-1}; LRMS (CI) 289 (100, $[M+H]^+$); HRMS (CI) calcd for $C_{13}H_{25}N_2O_5$ $[M+H]^+$ 289.1764, observed 289.1757; $[\alpha]_D$ = +20.0 (*c* 0.48, $CHCl_3$, 20.0 °C); HPLC conditions: CHIRALCEL-OD column, hexane:*i*-PrOH 99:1, 0.6 mL/min, t_R (major) = 36.8 min, t_R (minor) = 42.9 min, 98%ee.

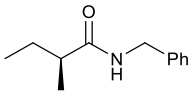
Dipropan-2-yl 1-α(S)-2-(*tert*-butyldimethysilyloxy)propanoyl]hydrazine-1,2-dicarboxylate 48y[11]



Using Method G, reaction was complete after 96 h. Purification by column chromatography (5-10% EtOAc/Petrol) gave dipropan-2-yl 1-[(S)-2-(tert-butyldimethysilyloxy)propanoyl]hydrazine-1,2-dicarboxylate **48y** as a colourless oil (238 mg, 0.61 mmol, 61%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.60 (br s, NH, 1H), 5.38 (q, *J* = 6.5 Hz, 1H), 5.04 (septet, *J* = 6.5 Hz, 1H), 4.98-4.92

(m, 1H), 1.47-1.40 (m, 3H), 1.34-1.17 (m, 12H), 0.91 (s, 9H), 0.09 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.7 (C), 155.1 (C), 152.6 (C), 72.5 (CH), 70.7 (CH), 69.5 (CH), 25.9 (CH_3), 22.0 (CH_3), 22.0 (CH_3), 21.8 (CH_3), 21.8 (CH_3), 21.6 (CH_3), 18.5 (C), –4.7 (CH_3), –5.1 (CH_3); IR (thin film) 3309, 2931, 2858, 1788, 1741, 1727 cm^{-1}; LRMS (ES$^+$) 413 (100, $[M+Na]^+$); HRMS (ES$^+$) calcd for $C_{17}H_{34}N_2O_6NaSi$ $[M+Na]^+$ 413.2084, observed 413.2069. $[\alpha]_D$ = +22.7 (*c* 0.55, $CHCl_3$, 20.0 °C); HPLC conditions: CHIRALCEL-OD column, hexane:*i*-PrOH 99:1, 0.6 mL/min, t_R (major) = 19.8 min, t_R (minor) = 30.1 min, 99%ee.

(*S*)-*N*-Benzyl-2-methylbutanamide 53[11,15,16]



Using Method H. Purification by column chromatography (50% Et_2O/petrol) gave (*S*)-*N*-benzyl-2-methylbutanamide **53** as an oil (86% yield, determined by integration of crude ^{1}H NMR relative to pentachlrorbenzene as internal standard) as a colourless oil: $[\alpha]_D$ = +16.0 (*c* 1.08, Acetone, 20.0 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.32 (m, 2H), 7.29-7.25 (m, 3H), 5.70-5.62 (m, NH, 1H), 4.49-4.42 (m, 2H), 2.12 (sextet, *J* = 7.0 Hz, 2H), 1.74-1.66 (m, 1H), 1.45 (ddq, *J* = 14.5, 13.5, 7.5 Hz, 1H), 1.16 (d, *J* = 7.5 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.4 (C), 138.6 (C), 128.8 (CH), 127.9 (CH), 127.6 (CH), 43.6 (CH_2), 43.4 (CH), 27.5 (CH_2), 17.7 (CH_3), 12.1 (CH_3); IR (thin film) 3282, 2965, 2929, 2876, 1646, 1548 cm^{-1}; LRMS (CI) 192 (100, $[M+H]^+$); HRMS (EI) calcd for $C_{12}H_{18}NO$ $[M+H]^+$ 192.1388, observed 192.1392; Data agrees with that reported by Yamakawa[15] and Gago.[16]

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