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 m (200-400 mesh) silica gel. 1H NMR spectra were recorded at 300 MHz, 400 MHz, 500 MHz and 600 MHz and 13C 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 1H and 13C 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 13C 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

To a stirring solution of (±)-citronellal (771 mg, 902 µL, 5.00 mmol) in CH2Cl2 (20 mL) was added dropwise a solution of m-CPBA (1.04 g, 6.00 mmol) in CH2Cl2 (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. K2CO3 (3 × 30 mL), dried (MgSO4) 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%): 1H NMR (600 MHz, CDCl3) 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$_2$Na [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$_2$Cl$_2$ (40 mL), and a solution of KBr (1.48 g, 0.013 mol) in H$_2$O (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$_2$Cl$_2$ (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$_2$S$_2$O$_3$ (50 mL) and H$_2$O (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 C₅H₁₃O [M+H]^+ 87.0804, observed 87.0809; [α]D = +35.0 (c 2.04, Acetone, 22.0 °C), Lit. [α]D = +35.5 (c 2.50, Acetone, 20.0 °C).

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

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 H₂O (100 mL), extracted with Et₂O (3 × 100 mL), the combined organics washed with sat. NaCl (100 mL), dried (MgSO₄) 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-[(tertbutyldimethylsilyl)oxy]-propionic acid ethyl ester (4.42 g, 18.2 mmol) in Et₂O (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 H₂O (3 mL). After warming to 21 °C and stirring for 90 min, finely ground Na₂SO₄ and MgSO₄ were added and the suspension stirred for 15 min, then filtered through a short plug of Celite and silica, eluting with Et₂O. 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%): ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) δ 204.3 (CH), 73.8 (CH), 25.7 (CH₃), 18.5 (CH₃), 18.2 (CH₃), -4.8 (CH₃), -4.8 (CH₃); IR (thin film) 2952, 2931, 2859, 1742 cm⁻¹; [α]D = -11.0 (c 2.51, CHCl₃, 22.0 °C), Lit. [α]D = -11.1 (c 1.50, CHCl₃, 20.0 °C).

Ethenesulfonic acid pentafluorophenyl ester 14

Pentafluorophenol (11.5 g, 62.5 mmol) and NEt₃ (19 mL, 137.5 mmol) in CH₂Cl₂ (20 mL) was added dropwise over 1 h to a solution at of 2-chloroethane sulfonyl chloride (10.13 g, 62.5 mmol) in CH₂Cl₂ (100 mL) at -78°C. The mixture was allowed to warm slowly to 21 °C and diluted with CH₂Cl₂ (100 mL) and washed with H₂O (100 mL), 2M HCl (2 × 100 mL) and sat. NaHCO₃ (2 × 100 mL), dried (MgSO₄) and the solvent removed in vacuo. Purification by column chromatography on silica gel (10% Et₂O/petrol) gave ethenesulfonic acid pentafluorophenyl ester 14 as a white solid (13.72 g, 50 mmol, 81%): ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 H₂O - Method B**

To a solution of ethenesulfonic acid pentafluorophenyl ester 14 (1 mmol) in H₂O (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**

Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH₂Cl₂/petrol) gave 3-oxo-hexane-1-sulfonic acid pentafluorophenyl ester 15a as an off-white crystalline solid: ¹H NMR (300 MHz, CDCl₃) 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): ¹³C NMR (75 MHz, CDCl₃) δ 204.9 (C), 47.0 (CH₂), 44.6 (CH₂), 35.9 (CH₂), 17.2 (CH₂), 13.6 (CH₃). IR (neat) 2964, 1716 cm⁻¹; LRMS (CI) 364 (100, [M+NH₄]⁺); HRMS (ES) calcd for C₁₂H₁₅F₅NO₄S [M+NH₄]⁺ 364.0636; observed 364.0636.

**4-Methyl-3-oxo-pentane-1-sulfonic acid pentafluorophenyl ester 15b**

Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH₂Cl₂/petrol) gave 4-methyl-3-oxo-pentane-1-sulfonic acid pentafluorophenyl ester 15b as a as a colourless oil: ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ 208.7 (C), 47.2 (CH₂), 41.0 (CH), 33.7 (CH₂), 18.1 (CH₃); IR (neat) 2976, 1716 cm⁻¹; LRMS (CI) 364 (100, [M+NH₄]⁺); HRMS (ES) calcd for C₁₂H₁₅F₅NO₄S [M+NH₄]⁺ 364.0636; observed 364.0635.

**5-Methyl-3-oxo-hexane-1-sulfonic acid pentafluorophenyl ester 15c**

Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH₂Cl₂/petrol) gave 5-methyl-3-oxo-hexane-1-sulfonic acid pentafluorophenyl ester 15c as an off-white crystalline solid: m.p. 56-59 °C; ¹H NMR (300
20
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+ 14

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reaction was complete after 

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2
reaction was complete after 

CH
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2H), 2.40 (d, J = 6.9, 2H), 2.18 (septet, J = 6.7, 1H), 0.95 (d, J = 6.6, 6H); P C NMR (100 MHz, CDCl3) δ 204.7 (C), 51.6 (CH2), 46.9 (CH2), 36.4 (CH2), 24.7 (CH), 22.5 (CH3); IR (neat) 2964, 1720 cm⁻¹; LRMS (CI) 378 (100, [M+NH4]+); HRMS (ES) calcd for C13H15F3NO4S [M+NH4]+ 378.0793; observed 378.0796.

3-Oxo-octane-1-sulfonic acid pentafluorophenyl ester 15d

Using Methods A and B, reaction was complete after 3 h and 6 h, respectively. Purification by flash column chromatography (20-70% CH2Cl2/petrol) gave 3-oxo-octane-1-sulfonic acid pentafluorophenyl ester 15d as white crystals: m.p. 45-47 °C; ¹H NMR (500 MHz, CDCl3) 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); P C NMR (100 MHz, CDCl3) δ 204.7 (C), 51.6 (CH2), 46.9 (CH2), 36.4 (CH2), 24.7 (CH), 22.5 (CH3); IR (neat) 2964, 1720 cm⁻¹; LRMS (CI) 378 (100, [M+NH4]+); HRMS (ES) calcd for C13H15F3NO4S [M+NH4]+ 378.0793; observed 378.0796.

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

Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH2Cl2/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, CDCl3) 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); P C NMR (100 MHz, CDCl3) δ 208.1 (C), 50.7 (CH), 47.1 (CH2), 34.0 (CH2), 28.4 (CH2), 25.6 (CH2), 25.5 (CH2); IR (neat) 2934, 2855, 1706 cm⁻¹; LRMS (CI) 404 (100%, [M+NH4]+); HRMS (ES) calcd for C15H15F3NO4S [M+NH4]+ 404.0949; observed 404.0949.

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

Using Methods A and B, reaction was complete after 1 h and 3 h, respectively. Purification by flash column chromatography (20-70% CH2Cl2/petrol) gave 4-ethyl-3-oxo-octane-1-sulfonic acid pentafluorophenyl ester 15f as a as a colourless oil: ¹H NMR (400 MHz, CDCl3) 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); P C NMR (100 MHz, CDCl3) δ 208.9 (C), 54.0 (CH), 47.1 (CH2), 35.6 (CH2), 31.0 (CH2), 29.8 (CH2), 24.7 (CH2), 22.8 (CH2), 14.0 (CH3), 11.8 (CH3); 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$_5$O$_4$S [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$_2$Cl$_2$/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$_{23}$F$_5$O$_4$S [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$_2$Cl$_2$/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$_5$O$_4$S [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$_2$Cl$_2$/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$_{18}$H$_{13}$F$_5$O$_4$S [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\(_5\)O\(_4\)S [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\(_2\)Cl\(_2\) (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 \textit{in vacuo} and the crude residue purified by flash column chromatography (30-60% CH\(_2\)Cl\(_2\)/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\(_5\)O\(_4\)S\(_2\) [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 CH₂Cl₂ (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

Using Method C. Purification by flash column chromatography (60% CH₂Cl₂/petrol to neat CH₂Cl₂) afforded 1-hexylsulfanyl-hexan-3-one 22a as a colourless oil: ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) δ 209.8 (C), 45.1 (CH), 42.9 (CH₂), 32.6 (CH₂), 31.5 (CH₂), 29.6 (CH₂), 28.6 (CH₂), 25.9 (CH₂), 22.6 (CH₂), 17.3 (CH₂), 14.1 (CH₃), 13.8 (CH₃); IR (thin film) 2959, 2927, 1714 cm⁻¹; LRMS (CI) 217 (100, [M+H]⁺); HRMS (CI) calcd for C₁₂H₂₅OS [M+H]⁺ 217.1626; observed 217.1621.
1-(4-Methyl-benzylsulfanyl)-hexan-3-one 22b

Using Method C. Purification by flash column chromatography (60% CH₂Cl₂/petrol to neat CH₂Cl₂) afforded 1-(4-methyl-benzylsulfanyl)-hexan-3-one 22b as a colourless oil: ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) δ 209.6 (C), 136.8 (C), 129.3 (CH), 128.8 (CH), 45.0 (CH₂), 42.5 (CH₂), 36.5 (CH₂), 25.3 (CH₂), 21.1 (CH), 17.3 (CH₃), 13.8 (CH₃); IR (thin film) 2962, 2928, 2871, 1712, 1535, 1516 cm⁻¹; LRMS (CI) 237 (100, [M+H]+); HRMS (CI) calcd for C₁₄H₂₁OS [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 Et₂O (20 mL), washed with sat. LiCl (3 × 20 mL), sat. NaHCO₃ (3 × 20 mL), 2M HCl (3 × 20 mL), dried (MgSO₄) and the solvent removed in vacuo to afford the desired sulfonamide.

N-Hexyl-3-oxohexane-1-sulfonamide 23a

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; ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 207.1 (C), 46.6 (CH₂), 44.8 (CH₂), 43.4 (CH₂), 36.5 (CH₂), 33.3 (CH₂), 30.2 (CH₂), 26.3 (CH₂), 22.5 (CH₂), 17.2 (CH₂), 14.0 (CH₃), 13.7 (CH₃); IR (solid) 3288, 2957, 2930, 2859, 1703, 1312, 1136 cm⁻¹; LRMS (CI) 264 (45, [M+H]+), 102 (100); HRMS (CI) calcd for C₁₂H₂₀NO₃S [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; ¹H NMR (400 MHz, CDCl₃) 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), 1.14 (m, 6H), 3.56 (m, 4H), 3.32-3.27 (m, 4H), 3.11 (m, 4H), 2.37-2.32 (m, 2H), 2.08-2.02 (m, 2H), 1.93-1.87 (m, 2H), 1.39 (m, 2H), 1.27 (m, 2H), 1.13 (m, 2H), 0.95 (t, J = 7.0 Hz, 3H); LRMS (CI) 292 (100, [M+H]+); HRMS (CI) calcd for C₂₀H₂₆NO₄S [M+H]+ 294.1689, observed 294.1690.
Hz, 2H), 0.93 (t, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 206.8 (C), 66.5 (CH₂), 45.7 (CH₂), 44.8 (CH₂), 42.6 (CH₂), 35.5 (CH₂), 17.2 (CH₂), 13.7 (CH₃); IR (solid) 2964, 2926, 2860, 1716, 1344, 1157 cm⁻¹; LRMS (Cl) 250 (20, [M+H]⁺), 163 (35), 99 (100); HRMS (Cl) calcd for C₁₀H₂₀NO₄S [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$_3$S [M+H]$^+$ 236.1320, observed 236.1325.
2-Hexyl-3-propyl-1,2-thiazolidine 1,1-dioxide 26

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. NaHCO₃ (3 × 100 mL) and 2M HCl (3 × 100 mL), dried (MgSO₄) and the solvent removed in vacuo. The crude residue was purified by column chromatography (50% Et₂O/petrol) to afford 2-hexyl-3-propyl-isothiazolidine 1,1-dioxide 26 as a colourless oil (41 mg, 0.17 mmol, 87%): ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 58.1 (CH), 46.5 (CH₂), 43.8 (CH₂), 36.0 (CH₂), 31.5 (CH₂), 28.6 (CH₂), 26.7 (CH₂), 25.0 (CH₂), 22.6 (CH₂), 17.8 (CH₂), 14.1 (CH₃), 14.1 (CH₃); IR (thin film) 2957, 2930, 2872, 1305, 1134 cm⁻¹; LRMS (CI) 248 (60, [M+H]+), 204 (100); HRMS (CI) calcd for C₁₂H₂₆NO₂S [M+H]⁺ 248.1684, observed 248.1686.

S13
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 CH₂Cl₂ (2 mL) was bubbled through NH₃ (g) for 45 min at 0 °C. Then the reaction mixture was diluted with CH₂Cl₂ (20 mL), washed with 2M HCl (3 x 20 mL) and sat. K₂CO₃ (3 x 20 mL), dried (MgSO₄) 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, CDCl₃) 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); \(^1^3^C\) NMR (100 MHz, CDCl₃) δ 184.9 (C), 44.0 (CH₂), 37.5 (CH₂), 36.8 (CH₂), 18.9 (CH₂), 13.7 (CH₃); IR (solid) 2966, 2929, 2872, 1617, 1326, 1144 cm⁻¹; LRMS (CI) 162 (100, [M+H]+); HRMS (CI) calcd for C₆H₁₂NO₂S [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 CH₂Cl₂ (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 Et₂O (50 mL), washed with sat. NaHCO₃ (3 × 100 mL), dried (MgSO₄) 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%): ^1H NMR (600 MHz, CDCl₃) 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); ^13C NMR (150 MHz, CDCl₃) δ 82.6 (CH), 45.7 (CH₂), 37.2 (CH₂), 29.6 (CH₂), 18.5 (CH₂), 13.6 (CH₃); IR (thin film) 2963, 2877, 1340, 1157 cm⁻¹; LRMS (CI) 165 (100, [M+H]+); HRMS (CI) calcd for C₆H₁₃O₃S [M+H]+ 165.0585, observed 165.0587.
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 CH₂Cl₂ to 5% CH₃OH/CH₂Cl₂) to give dimethyl (3-oxohexyl)phosphonate 31a, dimethyl (2-oxoethyl)phosphonate 32 and dimethyl [2-(1,4-dioxan-2-yl)ethyl]phosphonate 33.

Data for dimethyl (3-oxohexyl)phosphonate 31a: ¹H NMR (500 MHz, CDCl₃) δ 3.70 (d, J_H-P = 11.0 Hz, 6H), 2.67 (dt, J_H-P = 15.5 and J = 7.5 Hz, 2H), 2.38 (t, J = 7.5 Hz, 2H), 2.00 (dt, J_H-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); ¹³C NMR (125 MHz, CDCl₃) δ 208.1 (d, J_C-P = 14.0 Hz, C), 52.5 (d, J_C-P = 6.5 Hz, CH₃), 44.6 (CH₂), 35.3 (d, J_C-P = 4.0 Hz, CH₂), 18.3 (d, J_C-P = 143.0 Hz, CH₂), 17.3 (CH₂), 13.7 (CH₃); IR (thin film) 2960, 1715, 1245 cm⁻¹; LRMS (CI) 209 (100, [M+H]+); HRMS (CI) calcd for C₈H₁₈O₄P [M+H]⁺ 209.0943, observed 209.0947.

Hydroacylation of dimethyl vinyl phosphonate with n-butanal in 1,4-dioxane at 20 °C⁸,⁹
Data for dimethyl (2-oxoethyl)phosphate\textsuperscript{1} 32: \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 9.68 (td, \(J = 3.0\) Hz, \(J_{H,P} = 1.5\) Hz, 1H), 3.81 (d, \(J_{H,P} = 11.5\) Hz, 6H), 3.10 (dd, \(J_{H,P} = 22.0\) and \(J = 3.0\) Hz, 2H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 192.6 (d, \(J = 6.5\) Hz, CH), 53.1 (d, \(J_{C,P} = 6.5\) Hz, CH\(_2\)), 42.1 (d, \(J_{C,P} = 128.0\) Hz, CH\(_2\)); IR (thin film) 2954, 2859, 1720, 1240 cm\(^{-1}\); LRMS (CI) 153 (100, [M+H]\textsuperscript{+}); HRMS (CI) calcd for C\(_4\)H\(_8\)O\(_4\)P [M+H]\textsuperscript{+} 153.0317, observed 153.0318.

Data for dimethyl [2-(1,4-dioxan-2-yl)ethyl]phosphate\textsuperscript{30}: \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) \(\delta\) 3.80-3.69 (m, 10H), 3.62-3.53 (m, 2H), 2.37 (dd, \(J = 11.5\), 10.0 Hz, 1H), 1.82-1.62 (m, 3H); \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}) \(\delta\) 74.7 (d, \(J = 6.5\) Hz, CH\(_2\)), 53.1 (d, \(J_{C,P} = 6.5\) Hz, CH\(_3\)), 42.1 (d, \(J_{C,P} = 6.5\) Hz, CH\(_2\)), 24.4 (d, \(J_{C,P} = 14.5\) Hz, CH\(_2\)), 20.2 (d, \(J_{C,P} = 142.0\) Hz, CH\(_2\)); IR (thin film) 2957, 2853, 1244 cm\(^{-1}\); LRMS (FAB) 247 (100, [M+Na]\textsuperscript{+}); HRMS (FAB) calcd for C\(_8\)H\(_{17}\)NaO\(_3\)P [M+Na]\textsuperscript{+} 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-dioxan (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)phosphate 31a\textsuperscript{9}**

\[
\text{Me}_2\text{P(OCH}_2\text{CH}_2\text{C(OH)CH}_2\text{OH)}
\]

Using Method E. Purification by column chromatography (neat CH\(_2\)Cl\(_2\) to 2.5% MeOH/CH\(_2\)Cl\(_2\)) gave dimethyl (3-oxohexyl)phosphate 31a as a colourless oil (146 mg, 0.70 mmol, 70%). Data matched that as described above.

**Dimethyl (4-methyl-3-oxopentyl)phosphate 31b**

\[
\text{Me}_2\text{P(OCH}_2\text{CH}_2\text{CH(OH)CH}_2\text{CH}_3)}
\]

Using Method E. Purification by column chromatography (neat CH\(_2\)Cl\(_2\) to 2.5% MeOH/CH\(_2\)Cl\(_2\)) gave dimethyl (4-methyl-3-oxopentyl)phosphate 31b as a colourless oil (83 mg, 0.40 mmol, 40%): \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) \(\delta\) 3.73 (d, \(J_{H,P} = 11.0\) Hz, 6H), 2.75 (dt, \(J_{H,P} = 15.5\) and \(J = 7.0\) Hz, 2H), 2.31 (septet, \(J = 7.0\) Hz, 1H), 2.03 (dt, \(J_{H,P} = 18.0\) and \(J = 7.0\) Hz, 2H), 1.11 (d, \(J = 7.0\) Hz, 6H); \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}) \(\delta\) 212.0 (d, \(J_{C,P} = 14.0\) Hz, C), 52.5 (d, \(J_{C,P} = 6.5\) Hz, CH\(_3\)), 40.9 (CH\(_3\)), 33.0 (d, \(J_{C,P} = 4.0\) Hz, CH\(_2\)), 18.4 (CH\(_3\)), 18.3 (d, \(J_{C,P} = 144.0\) Hz, CH\(_2\)); IR (thin film) 2965, 2853, 1713, 1242 cm\(^{-1}\); LRMS (EI) 208 (20, [M]\textsuperscript{+}), 165 (100); HRMS (EI) calcd for C\(_8\)H\(_{17}\)O\(_4\)P [M]\textsuperscript{+} 208.0859, observed 208.0863.
Dimethyl (5-methyl-3-oxohexyl)phosphonate 31c\(^9\)

Using Method E. Purification by column chromatography (neat CH\(_2\)Cl\(_2\) to 2.5% MeOH/CH\(_2\)Cl\(_2\)) gave (dimethyl (5-methyl-3-oxohexyl)phosphonate 31c as a colourless oil (144 mg, 0.65 mmol, 65%): \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 3.74 (d, \(J\)\(_{H-P}\) = 11.0 Hz, 6H), 2.69 (dt, \(J\)\(_{H-P}\) = 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, \(J\)\(_{H-P}\) = 18.0 and \(J\) = 7.5 Hz, 2H), 0.89 (d, \(J\) = 7.0 Hz, 6H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 208.3 (d, \(J\)\(_{C-P}\) = 14.0 Hz, C), 52.4 (d, \(J\)\(_{C-P}\) = 6.5 Hz, CH\(_3\)), 51.6 (CH\(_2\)), 35.7 (d, \(J\)\(_{C-P}\) = 4.0 Hz, CH\(_2\)), 24.7 (CH), 22.5 (CH\(_3\)), 18.2 (d, \(J\)\(_{C-P}\) = 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\(_9\)H\(_{19}\)O\(_4\)PNa [M+Na]\(^+\) 245.0919, observed 245.0915.

Dimethyl (3-oxooctyl)phosphonate 31d\(^9\)

Using Method E. Purification by column chromatography (neat CH\(_2\)Cl\(_2\) to 2.5% MeOH/CH\(_2\)Cl\(_2\)) gave dimethyl (3-oxooctyl)phosphonate 31d as a colourless oil (170 mg, 0.72 mmol, 72%): \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 3.74 (d, \(J\)\(_{H-P}\) = 11.0 Hz, 6H), 2.72 (dt, \(J\)\(_{H-P}\) = 15.5 and \(J\) = 7.5 Hz, 2H),
2.43 (t, J = 7.5 Hz, 2H), 2.00 (dt, $J_{H-P} = 18.0$ 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$_3$) $\delta$ 208.3 (d, $J_{C-P} = 14.0$ Hz C), 52.4 (d, $J_{C-P} = 6.5$ Hz, CH$_3$), 42.6 (CH$_2$), 35.2 (d, $J_{C-P} = 4.0$ Hz, CH$_2$), 31.4 (CH$_2$), 23.5 (CH$_2$), 22.4 (CH$_2$), 18.2 (d, $J_{C-P} = 143.0$ 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$_4$PNa [M+Na]$^+$ 259.1076, observed 259.1070.

Dimethyl (3-cyclohexyl-3-oxopropyl)phosphonate 31e

Using Method E. Purification by column chromatography (neat CH$_2$Cl$_2$ to 2.5% MeOH/CH$_2$Cl$_2$) gave dimethyl (3-cyclohexyl-3-oxopropyl)phosphonate 31e as a colourless oil (149 mg, 0.60 mmol, 60%): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.74 (d, $J_{H-P} = 11.0$ Hz, 6H), 2.75 (dt, $J_{H-P} = 15.5$ and $J = 7.5$ Hz, 2H), 2.36 (tt, $J = 11.0$, 3.0 Hz, 1H), 2.00 (dt, $J_{H-P} = 18.0$ and $J = 7.5$ Hz, 2H), 1.87-1.18 (m, 10H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 211.1 (d, $J_{C-P} = 144.0$ Hz, C), 52.4 (d, $J_{C-P} = 6.5$ Hz, CH$_3$), 50.7 (CH), 33.2 (d, $J_{C-P} = 4.0$ Hz, CH$_2$), 28.5 (CH$_2$), 25.8 (CH$_2$), 25.6 (CH$_2$), 18.2 (d, $J_{C-P} = 143.0$ Hz, CH$_2$); IR (thin film) 2930, 2854, 1709, 1243 cm$^{-1}$; LRMS (EI) 248 (100, [M]$^+$); HRMS (EI) calcd for C$_{11}$H$_{21}$O$_4$P [M]$^+$ 248.1172, observed 248.1176.

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

Using Method E. Purification by column chromatography (neat CH$_2$Cl$_2$ to 2.5% MeOH/CH$_2$Cl$_2$) gave dimethyl (4-ethyl-3-oxooctyl)phosphonate 31f as a colourless oil (137 mg, 0.52 mmol, 52%): $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 3.73 (d, $J_{H-P} = 11.0$ Hz, 6H), 2.71 (dt, $J_{H-P} = 11.5$ and $J = 7.5$ Hz, 2H), 2.43-2.38 (m, 1H), 2.02 (dt, $J_{H-P} = 18.0$ 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$_3$) $\delta$ 212.0 (d, $J_{C-P} = 14.0$ Hz, C), 53.9 (CH), 52.5 (d, $J_{C-P} = 6.5$ Hz, CH$_3$), 35.0 (d, $J_{C-P} = 4.0$ Hz, CH$_2$), 31.2 (CH$_2$), 29.7 (CH$_2$), 24.8 (CH$_2$), 22.9 (CH$_2$), 18.6 (d, $J_{C-P} = 144.0$ 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$_4$P [M]$^+$ 264.1485, observed 264.1489.
Using Method E. Purification by column chromatography (neat CH$_2$Cl$_2$ to 2.5% MeOH/CH$_2$Cl$_2$) gave dimethyl (3-oxododecyl)phosphonate 31g as a colourless oil (161 mg, 0.55 mmol, 55%): $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 3.73 (d, $J_{H-P}$ = 11.0 Hz, 6H), 2.71 (dt, $J_{H-P}$ = 11.5 and $J$ = 7.5 Hz, 2H), 2.42 (t, $J$ = 7.5 Hz, 6H), 2.02 (dt, $J_{H-P}$ = 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$_3$) $\delta$ 208.4 (d, $J_{C-P}$ = 14.0 Hz, C), 52.5 (d, $J_{C-P}$ = 6.5 Hz, CH$_3$), 42.8 (CH$_2$), 35.3 (d, $J_{C-P}$ = 4.0 Hz, CH$_2$), 32.0 (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, $J_{C-P}$ = 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$_4$P [M+H]$^+$ 293.1882, observed 293.1890.
Dimethyl (3-oxobutyl)phosphonate 31h

Using Method E. Purification by column chromatography (neat CH₂Cl₂ to 2.5% MeOH/CH₂Cl₂) gave dimethyl (3-oxobutyl)phosphonate 31h as a colourless oil (122 mg, 0.68 mmol, 68%): ¹H NMR (600 MHz, CDCl₃) δ 3.74 (d, J_H-P = 11.0 Hz, 6H), 2.76 (dt, J_H-P = 15.5 and J = 7.5 Hz, 2H), 2.18 (s, 3H), 2.02 (dt, J_H-P = 18.0 and J = 7.5 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 205.7 (d, J_C-P = 14.0 Hz, C), 52.5 (d, J_C-P = 6.5 Hz, CH₃), 36.2 (d, J_C-P = 4.0 Hz, CH₂), 29.7 (CH₃), 18.2 (d, J_C-P = 143.0 Hz, CH₂); IR (thin film) 2958, 1717, 1239 cm⁻¹; LRMS (EI) 180 (5, [M]+), 110 (100); HRMS (EI) calcd for C₆H₁₃O₄P [M]+ 180.0546, observed 180.0548.

Dimethyl (3,3-dimethylbutyl)phosphonate 9

Using Method E. Purification by column chromatography (neat CH₂Cl₂ to 2.5% CH₃OH/CH₂Cl₂) to give dimethyl (3,3-dimethylbutyl)phosphonate as a colourless oil (89 mg, 0.46 mmol, 46%): ¹H NMR (600 MHz, CDCl₃) δ 3.75 (d, J_H-P = 11.0 Hz, 6H), 1.74-1.67 (m, 2H), 1.50-1.46 (m, 2H), 0.89 (s, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 52.4 (d, J_C-P = 6.5 Hz, CH₃), 35.7 (d, J_C-P = 4.0 Hz, 9H).
Hz, CH₂), 30.4 (d, J_C-P = 18.0 Hz, C), 28.7 (CH₃), 20.1 (d, J_C-P = 140.0 Hz, CH₂); IR (thin film) 2955, 2868, 1245 cm⁻¹; LRMS (CI) 195 (100, [M+H]+); HRMS (CI) calcd for C₈H₂O₃P [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 36a¹⁰

Using Method F, reaction was complete after 3 days. Purification by column chromatography (10-30% Et₂O/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, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) δ 203.8 (C), 171.8 (C), 168.9 (C), 53.8 (CH), 52.7 (CH₂), 52.0 (CH₃), 44.6 (CH₂), 32.1 (CH₂), 16.8 (CH₂), 13.4 (CH₃); IR (thin film) 2959, 2880, 1734, 1717 cm⁻¹; LRMS (CI) 217 (100, [M+H]+), 185 (27); HRMS (CI) calcd for C₁₀H₁₇O₅ [M+H]+ 217.1076, observed 217.1072.

2-Butyryl-succinic acid diethyl ester 42¹⁰

Using Method F, reaction was complete after 4 days. Purification by column chromatography (10-20% Et₂O/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, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 204.0 (C), 171.4 (C), 168.5 (C), 61.8 (CH₂), 61.0 (CH₂), 54.0 (CH), 44.6 (CH₂), 32.4 (CH₂), 16.8 (CH₂), 14.1 (CH₃), 14.0 (CH₃), 13.5 (CH₃); IR (thin film) 2967, 2881, 1736, 1719 cm⁻¹; LRMS (CI) 245 (60, [M+H]+), 199 (100); HRMS (CI) calcd for C₁₂H₂₁O₅ [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% Et₂O/petrol) gave 2-isobutyryl-succinic acid dimethyl ester 36b as a colourless oil (45 mg, 0.21 mmol, 21%). Only the $^1$H NMR peaks for 2-isobutyryl-succinic acid dimethyl ester 36b have been assigned as it predominates: $^1$H NMR (600 MHz, CDCl₃) δ 4.20 (dd, $J = 8.0$ and 6.5 Hz, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 1.14 (d, $J = 7.0$ Hz, 3H); $^{13}$C NMR (150 MHz, CDCl₃) δ 203.4 (C), 169.1 (C), 52.0 (CH), 52.8 (CH), 52.1 (CH₂), 50.2 (CH₃), 39.7 (CH₂), 32.3 (CH), 18.6 (CH₃), 17.8 (CH₃); 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% Et₂O/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 $^1$H NMR peaks for 2-(3-methyl-butyryl)-succinic acid dimethyl ester have been assigned as it predominates: $^1$H NMR (600 MHz, CDCl₃) 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), 2.58 (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, CDCl₃) δ 203.4 (C), 171.8 (C), 168.9 (C), 54.2 (CH), 52.7 (CH₃), 52.1 (CH₂), 51.5 (CH₂), 32.1 (CH₂), 24.1 (CH), 22.5 (CH₃), 22.2 (CH₃); IR (thin film) 2957, 1738, 1719 cm⁻¹; LRMS (EI) 230 (15, [M+H]^+), 199 (100); HRMS (EI) calcd for C₁₀H₁₇O₅ [M]^+ 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% Et₂O/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 $^1$H NMR peaks for 2-hexanoyl-succinic acid dimethyl ester have been assigned as it predominates: $^1$H NMR (400 MHz, CDCl₃) 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, CDCl₃) δ 207.8 (C), 171.8 (C), 54.7 (CH), 32.1 (CH₂), 24.1 (CH), 22.5 (CH₃), 21.8 (CH₃), 18.6 (CH₃), 17.8 (CH₃); IR (thin film) 2957, 2886, 1736, 1714 cm⁻¹; LRMS (EI) 230 (15, [M+H]^+), 199 (100); HRMS (EI) calcd for C₁₀H₁₇O₅ [M]^+ 230.1149, observed 230.1143.
M\text{Hz, CDCl}_3 \delta 204.0 \text{ (C)}, 171.9 \text{ (C)}, 169.0 \text{ (C)}, 53.8 \text{ (CH}_3\text{)}, 52.8 \text{ (CH}_3\text{)}, 52.1 \text{ (CH)}, 42.8 \text{ (CH}_2\text{)}, 32.2 \text{ (CH}_2\text{)}, 31.1 \text{ (CH}_2\text{)}, 23.1 \text{ (CH}_2\text{)}, 22.4 \text{ (CH}_2\text{)}, 13.9 \text{ (CH}_3\text{)}; \text{IR (thin film)} 2959, 2934, 1738, 1720 \text{ cm}^{-1}; \text{LRMS (CI)} 245 \text{ (15, [M+H]}^+)\text{), 213 (85), 99 (100); HRMS (CI) calcd for C_{12}H_{23}O_5 [M+H]^+ 245.1389, observed 245.1382.

**2-Cyclohexanecarbonyl-succinic acid dimethyl ester 36e**

![Diagram](image)

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 \textsuperscript{1}H NMR peaks for 2-cyclohexanecarbonyl-succinic acid dimethyl ester have been assigned as it predominates: \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) \delta 3.95 \text{ (dd, } J = 8.0, 6.5 \text{ Hz, 1H)}, 3.75 \text{ (s, 3H)}, 3.65 \text{ (s, 3H)}, 2.96 \text{ (dd, } J = 17.5, 8.0 \text{ Hz, 1H)}, 2.84 \text{ (dd, } J = 17.5, 6.5 \text{ Hz, 1H}), 2.68 \text{ (tt, } J = 11.0, 3.5 \text{ Hz, 1H}), 2.03-1.97 \text{ (m, 1H)}, 1.84-1.77 \text{ (m, 3H)}, 1.72-1.67 \text{ (m, 1H)}, 1.47-1.40 \text{ (m, 1H)}, 1.35-1.19 \text{ (m, 4H)}; \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}) \delta 207.0 \text{ (C)}, 171.8 \text{ (C)}, 169.1 \text{ (C)}, 52.8 \text{ (CH)}, 52.1 \text{ (CH}_3\text{)}, 50.6 \text{ (CH)}, 32.3 \text{ (CH}_2\text{)}, 28.9 \text{ (CH}_2\text{)}, 27.9 \text{ (CH}_2\text{)}, 25.8 \text{ (CH}_2\text{)}, 25.7 \text{ (CH}_2\text{)}, 25.3 \text{ (CH}_2\text{)}; \text{IR (thin film)} 2934, 2855, 1740, 1711 \text{ cm}^{-1}; \text{LRMS (ES\textsuperscript{+}) 255 (70, [M-H]\textsuperscript{+}), 208 (100); HRMS (ES\textsuperscript{+}) calcd for C_{13}H_{19}O_5 [M-H]^- 255.1232, observed 255.1234.

**2-(2-Ethyl-hexanoyl)-succinic acid dimethyl ester 36f**

![Diagram](image)

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 \textsuperscript{1}H NMR peaks for 2-(2-ethyl-hexanoyl)-succinic acid dimethyl ester have been assigned as it predominates: \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \delta 4.14 \text{ (m, 1H)}, 3.78-3.68 \text{ (m, 6H)}, 2.95-2.73 \text{ (m, 3H)}, 1.74-1.61 \text{ (m, 2H)}, 1.55-1.20 \text{ (m, 6H)}, 0.96-0.80 \text{ (m, 6H)}; \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}) \delta 206.7 \text{ (C)}, 206.6 \text{ (C)}, 171.8 \text{ (C)}, 171.8 \text{ (C)}, 168.9 \text{ (C)}, 168.8 \text{ (C)}, 54.4 \text{ (CH)}, 54.3 \text{ (CH)}, 52.7 \text{ (CH)}, 52.6 \text{ (CH}_2\text{)}, 52.5 \text{ (CH)}, 52.1 \text{ (CH}_3\text{)}, 31.9 \text{ (CH}_2\text{)}, 31.9 \text{ (CH}_2\text{)}, 31.0 \text{ (CH}_2\text{)}, 29.6 \text{ (CH}_2\text{)}, 29.5 \text{ (CH}_2\text{)}, 29.3 \text{ (CH}_2\text{)}, 24.6 \text{ (CH}_2\text{)}, 23.5 \text{ (CH}_2\text{)}, 22.8 \text{ (CH}_2\text{)}, 13.9 \text{ (CH}_3\text{)}, 11.7 \text{ (CH}_3\text{)}, 11.4 \text{ (CH}_3\text{)}; \text{IR (thin film)} 2957, 2932, 1740, 1717 \text{ cm}^{-1}; \text{LRMS (ES\textsuperscript{+}) 271 (100, [M-H]\textsuperscript{+}); HRMS (ES\textsuperscript{+}) calcd for C_{14}H_{23}O_5 [M-H]^- 271.1545, observed 271.1558.
2-Decanoyl-succinic acid dimethyl ester 36g\textsuperscript{10}

Using Method F, reaction was complete after 9 days. Purification by column chromatography (10-30% Et\textsubscript{2}O/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 \textsuperscript{1}H NMR peaks for 2-decanoyl-succinic acid dimethyl ester have been assigned as it predominates: \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{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); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) δ 204.0 (C), 171.9 (C), 167.0 (C), 53.8 (CH), 52.7 (CH\textsubscript{3}), 52.0 (CH\textsubscript{3}), 42.8 (CH\textsubscript{2}), 32.2 (CH\textsubscript{2}), 31.9 (CH\textsubscript{2}), 29.4 (CH\textsubscript{2}), 29.3 (CH\textsubscript{2}), 29.0 (CH\textsubscript{2}), 23.4 (CH\textsubscript{2}), 22.7 (CH\textsubscript{2}), 14.1 (CH\textsubscript{3}); IR (thin film) 2959, 2926, 2856, 1742, 1720 cm\textsuperscript{-1}; LRMS (ES\textsuperscript{+}) 299 (100, [M-H]); HRMS (ES\textsuperscript{+}) calcd for C\textsubscript{16}H\textsubscript{27}O\textsubscript{5} [M-H]\textsuperscript{+} 299.1858, observed 299.1860.

2-(1-Methyl-2-oxo-pentyl)-malonic acid diethyl ester 44a\textsuperscript{10}

Using Method F, reaction was complete after 3 days. Purification by column chromatography (10-30% Et\textsubscript{2}O/petrol) gave 2-(1-methyl-2-oxo-pentyl)-malonic acid diethyl ester 44a as a colourless oil (181 mg, 0.70 mmol, 70%): \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{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); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) δ 211.7 (C), 168.7 (C), 168.1 (C), 168.0 (C), 167.9 (C), 167.8 (C), 167.3 (C), 167.2 (C), 166.8 (C), 166.7 (C), 163.7 (C), 157.3 (C), 156.3 (C), 156.2 (C), 155.6 (C), 155.5 (C), 154.5 (C), 54.5 (CH), 45.0 (CH), 43.4 (CH\textsubscript{2}), 16.9 (CH\textsubscript{2}), 14.7 (CH\textsubscript{3}), 14.2 (CH\textsubscript{3}), 14.0 (CH\textsubscript{3}), 13.8 (CH\textsubscript{3}); IR (thin film) 2967, 2933, 1759, 1733, 1715 cm\textsuperscript{-1}; LRMS (CI) 259 (15, [M+H]\textsuperscript{+}), 213 (100); HRMS (CI) calcd for C\textsubscript{13}H\textsubscript{23}O\textsubscript{5} [M+H]\textsuperscript{+} 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\textsubscript{2}O/petrol) gave 2-(4-methyl-3-oxo-pentyl)-malonic acid diethyl ester 44b as a colourless oil (108 mg, 0.42 mmol, 42%): \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{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); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) δ 215.4 (C), 168.8 (C), 168.4 (C), 61.6 (CH\textsubscript{2}), 61.6 (CH\textsubscript{2}), 54.7 (CH), 43.7 (CH), 39.5 (CH), 18.9 (CH\textsubscript{3}), 18.2 (CH\textsubscript{3}), 15.1 (CH\textsubscript{3}), 14.2 (CH\textsubscript{3}), 14.1 (CH\textsubscript{3}); IR (thin film)
2977, 2939, 1751, 1734, 1714 cm⁻¹; LRMS (ES) 281 (100, [M+Na]⁺); HRMS (ES) calcd for C₁₃H₂₂O₅Na [M+Na]⁺ 281.1365, observed 281.1360.
Using Method F, reaction was complete after 3 days. Purification by column chromatography (5-20% Et₂O/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, CDCl₃) \(\delta\) 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, CDCl₃) \(\delta\) 211.1 (C), 168.6 (C), 168.5 (C), 61.6 (CH₂), 61.5 (CH₂), 54.3 (CH), 50.3 (CH₂), 45.3 (CH), 23.8 (CH), 22.6 (CH₃), 22.4 (CH₃), 14.5 (CH₃), 14.1 (CH₃), 14.0 (CH₃); IR (thin film) 2960, 2870, 1746, 1733, 1713 cm⁻¹; LRMS (EI) 272 (10, [M]⁺), 227 (85), 189 (100); HRMS (EI) calcd for C₁₄H₂₄O₅ [M]⁺ 272.1618, observed 272.1621.

2-(1,4-Dimethyl-2-oxo-pentyl)-malonic acid diethyl ester 44c
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\(_2\)O/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\(_3\)) \(\delta\) 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); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 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\(_3\)); IR (thin film) 2963, 2935, 1749, 1732, 1709 cm\(^{-1}\); LRMS (ESI) 287 (12, [M+H]\(^{+}\)), 241 (85), 230 (70), 187 (100); HRMS (ESI) calcd for C\(_{15}\)H\(_{23}\)O\(_3\) [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\(_2\)O/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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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 (ESI\(^{+}\)) 321 (100, [M+Na]\(^{+}\)); HRMS (ESI\(^{+}\)) calcd for C\(_{16}\)H\(_{26}\)O\(_3\)Na [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\(_2\)O/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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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
(CH₂), 22.8 (CH₂), 24.6 (CH₂), 23.0 (CH₂), 22.9 (CH₂), 22.8 (CH₂), 14.5 (CH₃), 14.4 (CH₃), 14.1 (CH₃), 14.0 (CH₃), 14.0 (CH₃), 12.1 (CH₃), 11.4 (CH₃); IR (thin film) 2962, 2934, 2875, 1753, 1734, 1710 cm⁻¹; LRMS (ESI) 337 (100, [M+Na]⁺), 269 (30); HRMS (ESI) calcd for C₁₇H₃₀O₅Na [M+Na]⁺ 337.1991, observed 337.2011.

2-(1-Methyl-2-oxo-undecyl)-malonic acid diethyl ester 44g¹⁰

Using Method F, reaction was complete after 6 days. Purification by column chromatography (5-20% Et₂O/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, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) δ 211.8 (C), 168.7 (C), 168.6 (C), 61.7 (CH₂), 61.6 (CH₂), 54.5 (CH), 45.0 (CH), 41.5 (CH₂), 31.9 (CH₂), 29.5 (CH₂), 29.3 (CH₂), 29.3 (CH₂), 23.5 (CH₂), 22.7 (CH₂), 14.8 (CH₃), 14.1 (CH₃), 14.1 (CH₃), 14.0 (CH₃); IR (thin film) 2927, 2855, 1750, 1717 cm⁻¹; LRMS (ESI) 365 (100, [M+Na]⁺), 283 (30); HRMS (ESI) calcd for C₁₉H₃₄O₅Na [M+Na]⁺ 365.2318, observed 365.2304.

2-(1-Ethoxy-2-oxo-pentyl)-malonic acid diethyl ester 46a¹⁰

Using Method F, reaction was complete after 7 days. Purification by column chromatography (5-20% Et₂O/petrol) gave 2-(1-ethoxy-2-oxo-pentyl)-malonic acid dimethyl 46a as a colourless oil: ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) δ 209.5 (C), 167.0 (C), 167.0 (C), 82.4 (CH), 67.8 (CH₂), 61.8 (CH₂), 61.7 (CH₂), 54.5 (CH), 41.1 (CH₂), 16.5 (CH₂), 15.4 (CH₃), 14.1 (CH₃), 14.0 (CH₃), 13.8 (CH₃); IR (thin film) 2978, 2934, 2873, 1744, 1724 cm⁻¹; LRMS (Cl) 289 (100, [M+H]⁺), 243 (40), 217 (47); HRMS (Cl) calcd for C₁₄H₂₅O₆ [M+H]⁺ 289.1651, observed 289.1648.

2-(1-Ethoxy-4-methyl-2-oxo-pentyl)-malonic acid diethyl ester 46c¹⁰

Using Method F, reaction was complete after 5 days. Purification by column chromatography (5-20% Et₂O/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, CDCl₃) 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$_3$) $\delta$ 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, 1736 (C), 339.1784. LRMS (CI) 303 (5, [M+H]$^+$), 285 (10), 211 (100); HRMS (ESI) calcd for C$_{12}$H$_{24}$O$_3$Na [M+Na]$^+$ 339.1780, observed 339.1780.

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$_2$O/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$_3$) $\delta$ 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$_3$) $\delta$ 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$_3$); IR (thin film) 2978, 2959, 2932, 1750, 1736 cm$^{-1}$; LRMS (ESI$^+$) 339 (100, [M+Na]$^+$); HRMS (ESI$^+$) calcd for C$_{16}$H$_{28}$O$_6$Na [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$_2$O/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$_3$) $\delta$ 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$_3$) $\delta$ 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 (ESI$^+$) 351 (100, [M+Na]$^+$); HRMS (ES$^+$) calcd for C$_{17}$H$_{26}$O$_6$Na [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$_2$O/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\(_3\)) \(\delta 4.35\) (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\(_3\)) \(\delta 209.7\) (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, \([\text{M}+\text{Na}]^+\)); HRMS (ES\(^+\)) calcd for C\(_{20}\)H\(_{36}\)O\(_6\)Na \([\text{M}+\text{Na}]^+\) 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\(_2\)O (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-butanoilhydrazine-1,2-dicarboxylate 48a**

\[\text{C}_6\text{H}_{18}\text{O}_5\]

Using Method G, reaction was complete after 24 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave diropan-2-yl 1-butanoilhydrazine-1,2-dicarboxylate \(48a\) as a colourless oil (249 mg, 0.91 mmol, 91%); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 6.58\) (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\(_3\)) \(\delta 173.9\) (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, \([\text{M}+\text{H}]^+\)); HRMS (CI) calcd for C\(_{12}\)H\(_{22}\)N\(_2\)O\(_5\) \([\text{M}+\text{H}]^+\) 275.1607, observed 275.1609.

**Dipropan-2-yl 1-(2-methylpropanoyl)hydrazine-1,2-dicarboxylate 48b**

\[\text{C}_6\text{H}_{18}\text{O}_5\]

Using Method G, reaction was complete after 48 h. Purification by column chromatography (10-40% EtOAc/Petrol) gave diropan-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\(_3\)) \(\delta 6.76\) (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\(_3\)) \(\delta 178.4\) (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, \([\text{M}+\text{H}]^+\)); HRMS (CI) calcd for C\(_{12}\)H\(_{22}\)N\(_2\)O\(_5\) \([\text{M}+\text{H}]^+\) 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 (Cl) 289 (100, [M+H]$^+$); HRMS (Cl) calcd for C$_{13}$H$_{25}$N$_2$O$_5$ [M+H]$^+$ 289.1764, observed 289.1760.
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%): \( ^1H \text{NMR} \) (600 MHz, CDCl\(_3\)) \( \delta \) 6.70 (br s, NH, 1H), 5.01 (septet, \( J = 6.5 \text{ Hz} \), 1H), 4.94 (septet, \( J = 6.5 \text{ Hz} \), 1H), 2.87-2.75 (m, 2H), 1.64 (t, \( J = 7.0 \text{ Hz} \), 2H), 1.32-1.17 (m, 16H), 0.86 (t, \( J = 7.0 \text{ Hz} \), 3H); \( ^13C \text{NMR} \) (125 MHz, CDCl\(_3\)) \( \delta \) 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\(_2\)O\(_5\) [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%): \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) \( \delta \) 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); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \( \delta \) 177.2 (C), 155.3 (C), 152.8 (C), 72.0 (CH), 70.1 (CH), 44.1 (CH), 29.4 (CH\textsubscript{2}), 25.8 (CH\textsubscript{2}), 25.6 (CH\textsubscript{2}), 21.9 (CH\textsubscript{3}), 21.7 (CH\textsubscript{3}); IR (thin film) 3318, 2983, 2933, 2856, 1726, 1719 cm\textsuperscript{-1}; LRMS (ES) 313 (100, [M-H]\textsuperscript{-}); HRMS (ES) calcd for C\textsubscript{15}H\textsubscript{25}N\textsubscript{2}O\textsubscript{5} [M-H]\textsuperscript{-} 313.1763, observed 313.1765.

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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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 diropan-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$_3$) $\delta$ 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$_3$) $\delta$ 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$_2$NaO$_5$ [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 diropan-2-yl 1-decanoylhydrazine-1,2-dicarboxylate 48g as a colourless oil (304 mg, 0.85 mmol, 85%): $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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$_2$NaO$_5$ [M+Na]$^+$ 381.2365, observed 381.2365.
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$_2$O$_5$Na [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$_2$O$_5$ [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$_2$Cl$_2$ (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**

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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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]+); HRMS (EI) calcd for C\(_7\)H\(_{13}\)NO [M]+ 127.0992, observed 127.0995.

N-(Prop-2-yn-1-yl)butyramide 49c\(^{12}\)

Using Method H. Purification by column chromatography (20-30% Et\(_2\)O/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\(_3\)) \(\delta\) 6.20-6.11 (m, NH, 1H), 4.02 (dd, \(J = 7.5, 4.5\) Hz, 2H), 2.19 (t, \(J = 4.5, 1\)H), 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\(_3\)) \(\delta\) 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\(_7\)H\(_{12}\)NO [M+H]+ 126.0913, observed 126.0911.
Using Method H. Purification by column chromatography (15-30% Et₂O/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: ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) δ 171.8 (C), 67.0 (CH₂), 66.8 (CH₂), 46.1 (CH₂), 41.9 (CH₂), 35.1 (CH₂), 18.7 (CH₂), 14.1 (CH₃); IR (thin film) 3290, 3262, 2967, 2926, 1628 cm⁻¹; LRMS (CI) 158 (100, [M+H]⁺); HRMS (CI) calcd for C₈H₁₆NO₂ [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 (Cl) 189 (100, [M+H]$^+$); HRMS (Cl) calcd for C$_8$H$_{17}$N$_2$O$_3$ [M+H]$^+$ 189.1161, observed 189.1170.
Using Method H. Purification by column chromatography (30-80% Et₂O/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, CDCl₃) $\delta$ 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, CDCl₃) $\delta$ 171.8 (C), 46.7 (CH₂), 45.6 (CH₂), 36.9 (CH₂), 26.2 (CH₂), 24.5 (CH₂), 18.5 (CH₂), 14.2 (CH₃); 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$_2$O/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$_3$) $\delta$ 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$_3$) $\delta$ 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$_2$O$_5$ [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$_2$Cl$_2$ (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$_2$O/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**

Using Method I. Purification by column chromatography (30-80% Et₂O/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**

Using Method B, reaction was complete after 3 h. Purification by flash column chromatography (20-70% CH₂Cl₂/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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) δ 204.9 (C), 47.1 (CH₂), 36.5 (CH₂), 20.7 (CH), 11.8 (CH₂); IR (neat) 2927, 1702 cm⁻¹; LRMS (CI) 362 (100, [M+NH₄]⁺); HRMS (ES) calcd for C₁₂H₉F₅NO₄S [M+NH₄]⁺ 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% CH₂Cl₂/petrol) gave ethyl 6-oxo-8-((pentafluorophenoxy)sulfonyl)octanoate 15l as an oil (294 mg, 0.68 mmol, 68%): ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 204.6 (C), 173.4 (C), 60.5 (CH₂), 47.0 (CH₂), 42.5 (CH₂), 36.1 (CH₂), 34.0 (CH₂), 24.3 (CH₂), 23.1 (CH₂), 14.4 (CH₃); IR (neat) 2928, 2849, 1726, 1520 cm⁻¹; LRMS (CI) 433 (20, [M+H]+), 387 (100); HRMS (CI) calcd for C₁₆H₁₈F₅O₆S [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% CH₂Cl₂/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%): ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 204.8 (C), 101.8 (CH), 47.1 (CH₂), 42.5 (CH₂), 36.0 (CH₂), 33.9 (CH₂), 30.2 (C), 23.1 (CH₃), 22.0 (CH₃), 18.2 (CH₂); IR (neat) 2953, 2857, 1718, 1520 cm⁻¹; LRMS (CI) 461 (100, [M+H]⁺); HRMS (CI) calcd for C₁₈H₂₂F₅O₆S [M+H]⁺ 461.1052; observed 461.1058.
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$_3$) $\delta$ 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$_3$) $\delta$ 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$_5$O$_5$SNa [M+Na]$^+$ 469.1084; observed 461.1090.
Using Method B, reaction was complete after 6 h. Purification by flash column chromatography (20-95% CH₂Cl₂/petrol) gave 5,9-dimethyl-3-oxodecane-1-sulfonate acid pentafluorophenyl ester 15r as a white solid (284 mg, 0.66 mmol, 66%): m.p. 49-51 °C; ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 205.1 (C), 50.3 (CH₂), 47.1 (CH₂), 39.1 (CH₂), 37.1 (CH₂), 36.6 (CH₂), 29.5 (CH), 28.0 (CH), 24.8 (CH₂), 22.8 (CH₃), 22.7 (CH₃), 19.9 (CH₃); IR (solid) 3417, 2959, 1720, 1516, 1380 cm⁻¹; LRMS (CI) 431 (100, [M+H]+); HRMS (CI) calcd for C₁₈H₂₄F₅O₄S [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% Et₂O/petrol) gave 3-(4-fluorophenyl)-3-oxopropane-1-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 acid pentafluorophenyl ester 15u: m.p. 102-105 °C; ¹H NMR (600 MHz, CDCl₃) δ 8.05-8.03 (m, 2H), 7.22-7.19 (m, 2H), 3.96-3.94 (m, 2H), 3.75-3.71 (m, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 192.7 (C), 166.3 (d, J_C-F = 255.0 Hz, C), 138.8 (C), 137.1 (d, J_C-F = 13.5 Hz, CH), 116.2 (d, J_C-F = 22.5 Hz, CH), 47.4 (CH₂), 32.6 (CH₂); IR (solid) 3069, 2960, 1684, 1381 cm⁻¹; LRMS (CI) 399 (100, [M+H]⁺); HRMS (CI) calcd for C₁₅H₈F₆O₄S [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$_5$O$_5$SNa [M+Na]$^+$ 385.0145; observed 385.0152.
Dimethyl (3-cyclopropyl-3-oxopropyl)phosphonate 31k

Using Method E. Purification by column chromatography (neat CH₂Cl₂-2.5% MeOH/CH₂Cl₂) gave dimethyl (3-cyclopropyl-3-oxopropyl)phosphonate 31k as a colourless oil (117 mg, 0.57 mmol, 57%): ¹H NMR (600 MHz, CDCl₃) δ 3.75 (d, J_H-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); ¹³C NMR (150 MHz, CDCl₃) δ 208.0 (d, J_C-P = 14.0 Hz, C), 52.5 (d, J_C-P = 6.5 Hz, CH₃), 35.8 (d, J_C-P = 4.0 Hz, CH₂), 20.4 (CH), 18.3 (d, J_C-P = 143.0 Hz, CH₂), 11.1 (CH₂); IR (thin film) 2962, 1699, 1238 cm⁻¹; LRMS (FAB) 229 (100, [M+Na]⁺); HRMS (FAB) calcd for C₈H₁₅O₄PNa [M+Na]⁺ 229.0606, observed 229.0601.

Ethyl 8-(dimethoxyphosphoryl)-6-oxooctanoate 31l

Using Method E. Purification by column chromatography (neat CH₂Cl₂-4% MeOH/CH₂Cl₂) gave ethyl 8-(dimethoxyphosphoryl)-6-oxooctanoate 31l as a colourless oil (197 mg, 0.67 mmol, 67%): ¹H NMR (600 MHz, CDCl₃) δ 4.10 (q, J = 7.0 Hz, 2H), 3.71 (d, J_H-P = 11.0 Hz, 6H), 2.69
Using Method E. Purification by column chromatography (neat CH₂Cl₂ to 2.5% MeOH/CH₂Cl₂) 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%): ¹H NMR (400 MHz, CDCl₃) δ 4.40 (t, J = 5.0 Hz, 1H), 3.73 (d, J₃₋₆ = 11.0 Hz, 3H), 3.57 (d, J = 10.0 Hz, 2H), 3.40 (d, J = 11.0 Hz, 2H), 2.70 (dt, J₆₋₇ = 15.5 and J₇₋₈ = 18.0 Hz, 2H), 2.47 (t, J = 7.0 Hz, 2H), 2.02 (dt, J₆₋₇ = 18.0 and J = 7.5 Hz, 2H), 1.78-1.60 (m, 4H), 1.17 (s, 3H), 0.71 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 207.7 (d, J₆₋₇ = 144.0 Hz, C), 101.9 (CH), 77.2 (CH₂), 52.4 (d, J₆₋₇ = 6.0 Hz, CH₃), 42.3 (CH₂), 35.2 (d, J₆₋₇ = 4.0 Hz, CH₂), 34.1 (CH₂), 30.1 (C), 23.1 (CH₃), 18.4 (CH₂), 18.3 (d, J₆₋₇ = 144.0 Hz, CH₂); IR (thin film) 2955, 2850, 1717, 1244 cm⁻¹; LRMS (FAB) 321 (15, [M-H]⁺), 219 (65), 115 (100); HRMS (FAB) calcd for C₁₄H₂₀O₅PNa [M+Na]⁺ 331.1461, observed 331.1465.

Using Method E. Purification by column chromatography (neat CH₂Cl₂ to 7.5% MeOH/CH₂Cl₂) gave dimethyl (9-hydroxy-5,9-dimethyl-3-oxodecyl)phosphonate 31n as a colourless oil (228 mg, 0.74 mmol, 74%): ¹H NMR (600 MHz, CDCl₃) δ 3.74 (d, J₃₋₆ = 11.0 Hz, 3H), 3.74 (d, J₃₋₆ = 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, J₆₋₇ = 18.0 and J = 8.0 Hz, 2H), 1.48-1.14 (m, 14H), 0.91 (d, J = 7.0 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 208.0 (d, J₆₋₇ = 14.0 Hz, C), 70.9 (C), 52.5 (d, J₆₋₇ = 6.5 Hz, CH₃), 52.4 (d, J₆₋₇ = 6.5 Hz, CH₃), 50.0 (CH₂), 43.8 (CH₂), 37.3 (CH₂), 35.8 (d, J₆₋₇ = 4.0 Hz, CH₂), 29.4 (CH₃), 29.3 (CH₃), 29.2 (CH), 21.6 (CH₂), 19.9 (CH₃), 18.1 (d, J₆₋₇ = 143.0 Hz, CH₂); IR (thin film) 3409, 2960, 2928, 2848, 1715, 1238 cm⁻¹; LRMS (FAB) 331 (100, [M+Na]⁺); HRMS (FAB) calcd for C₁₄H₂₉O₅PNa [M+Na]⁺ 331.1650, observed 331.1653.
Dimethyl [7-(3,3-dimethyloxiran-2-yl)-5-methyl-3-oxoheptyl]phosphonate 31o

Using Method E. Purification by column chromatography (neat CH₂Cl₂-3% MeOH/CH₂Cl₂) 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: ¹H NMR (600 MHz, CDCl₃) δ 3.71 (d, J_H-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); ¹³C NMR (150 MHz, CDCl₃) δ 207.7 (d, J_C-P = 14.0 Hz, C), 207.7 (d, J_C-P = 14.0 Hz, C), 64.4 (CH), 58.5 (C), 58.4 (C), 52.6 (d, J_C-P = 6.5 Hz, CH₃), 50.0 (CH₂), 49.9 (CH₂), 36.0 (CH₂), 35.9 (CH₂), 33.5 (CH₂), 29.2 (CH), 29.1 (CH), 26.6 (CH₂), 26.5 (CH₂), 25.0 (CH₃), 19.8 (CH₃), 19.8 (CH₃), 18.8 (CH₃), 18.7 (CH₃), 18.2 (d, J_C-P = 143.0 Hz, CH₂); IR (thin film) 2958, 2927, 1716, 1248 cm⁻¹; LRMS (EI) 307 (100, [M+H]+); HRMS (EI) calcd for C₁₄H₂₈O₅P [M+H]^+ 307.1674, observed 307.1683.

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

Using Method E. Purification by column chromatography (neat CH₂Cl₂-4% CH₃OH/CH₂Cl₂) gave dimethyl (3-oxohept-6-en-1-yl)phosphonate 31p as a colourless oil: ¹H NMR (600 MHz, CDCl₃) 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-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); ¹³C NMR (150 MHz, CDCl₃) δ 207.3 (d, J_C-P = 13.5 Hz, C), 136.8 (CH), 115.5 (CH₂), 52.5 (d, J_C-P = 6.5 Hz, CH₃), 41.6 (CH₂), 35.4 (d, J_C-P = 6.5 Hz, CH₂), 27.7 (CH₂), 18.0 (d, J_C-P = 144.0 Hz, CH₂); IR (thin film) 2956, 1716, 1642, 1237 cm⁻¹; LRMS (EI) 220 (24, [M]+), 165 (100); HRMS (EI) calcd for C₉H₁₇O₃P [M]^+ 220.0859, observed 220.0853.

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

Using Method E. Purification by column chromatography (neat CH₂Cl₂-4% MeOH/CH₂Cl₂) gave dimethyl (5,9-dimethyl-3-oxodecyl)phosphonate 31r as a colourless oil (198 mg, 0.68 mmol, 68%): ¹H NMR (600 MHz, CDCl₃) δ 3.72 (d, J_H-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); ¹³C NMR (150 MHz, CDCl₃) δ 208.2 (d, J_C-P = 14.0 Hz, C), 52.5 (d, J_C-P = 6.5 Hz, CH₃), 50.3 (CH₂), 39.1 (CH₂), 37.2 (CH₂), 35.9 (d, J_C-P = 4.0 Hz, CH₂), 29.5 (CH), 28.0 (CH), 24.8 (CH₂), 22.8 (CH₃), 22.7 (CH₃), 19.9 (CH₃), 18.3 (d, J_C-P = 143.0 Hz, CH₂); IR (thin film) 2955,
2928, 1716 cm\(^{-1}\); LRMS (Cl) 293 (100, [M+H]\(^+\)); HRMS (Cl) calcd for C\(_{14}\)H\(_{30}\)O\(_4\)P [M+H]\(^+\) 293.1882, observed 293.1884.

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

Using Method E. Purification by column chromatography (neat CH\(_2\)Cl\(_2\)-4% MeOH/CH\(_2\)Cl\(_2\)) 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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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\(_2\)), 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 (Cl) 261 (100, [M+H]\(^+\)); HRMS (Cl) calcd for C\(_{11}\)H\(_{15}\)O\(_4\)PF [M+H]\(^+\) 261.0614, observed 261.0620.
Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-30% Et₂O/petrol) gave 2-(1-cyclopropyl-1-oxopropan-2-yl)-malonic acid diethyl ester 44k as a colourless oil (159 mg, 0.62 mmol, 62%): ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 211.5 (C), 168.8 (C), 168.5 (C), 62.0 (CH₂), 61.7 (CH₂), 54.3 (CH), 46.0 (CH), 19.9 (CH), 19.9 (CH₃), 14.9 (CH₃), 14.2 (CH₃), 11.4 (CH₂), 11.2 (CH₂); IR (thin film) 2982, 2937, 1748, 1730, 1698 cm⁻¹; LRMS (ES) 255 (100, [M-H]⁻); HRMS (ES) calcd for C₁₃H₁₉O₅ [M-H]⁻ 255.1232, observed 255.1230.
Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-40% Et₂O/petrol) gave triethyl 2-methyl-3-oxoheptane-1,1,7-tricarboxylate 44l as a colourless oil (244 mg, 0.71 mmol, 71%): ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 211.4 (C), 173.6 (C), 168.7 (C), 168.6 (C), 61.8 (CH₂), 61.7 (CH₂), 60.4 (CH₂), 54.6 (CH), 45.0 (CH), 41.1 (CH₂), 34.2 (CH₂), 24.5 (CH₂), 23.0 (CH₂), 14.8 (CH₃), 14.2 (CH₃), 14.1 (CH₃); IR (thin film) 2980, 2940, 1745, 1732, 1699 cm⁻¹; LRMS (ES) 343 (100, [M-H]⁻); HRMS (ES) calcd for C₁₇H₂₇O₇ [M-H]⁻ 343.1835, observed 343.1838.
Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-40% Et₂O/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%): ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 211.4 (C), 168.7 (C), 168.6 (C), 102.0 (CH), 61.7 (CH₂), 61.6 (CH₂), 54.5 (CH), 45.0 (CH), 41.2 (CH₂), 34.1 (CH₂), 30.2 (C), 23.1 (CH₃), 22.0 (CH₃), 18.1 (CH₂), 14.8 (CH₃), 14.2 (CH₃), 14.1 (CH₃); IR (thin film) 2954, 2845, 1748, 1731, 1717 cm⁻¹; LRMS (ES) 371 (100, [M-H]); HRMS (ES) calcd for C₁₀H₁₉O₇ [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% Et₂O/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%): ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 211.4 (C), 211.3 (C), 168.8 (C), 168.7 (C), 168.6 (C), 71.1 (C), 71.1 (C), 61.8 (CH₂), 61.7 (CH₂), 61.7 (CH₂), 54.5 (CH), 54.4 (CH), 49.0 (CH₂), 48.8 (CH₂), 45.6 (CH), 45.4 (CH), 44.0 (CH₂), 44.0 (CH₂), 37.4 (CH₂), 37.3 (CH₂), 29.5 (CH₃), 29.5 (CH₃), 29.3 (CH₃), 29.2 (CH₃), 28.5 (CH₃), 28.3 (CH₃), 20.1 (CH), 19.9 (CH), 14.8 (CH₃), 14.6 (CH₃), 14.2 (CH₃), 14.1 (CH₃); IR (thin film) 3541, 2970, 2937, 1748, 1730, 1715 cm⁻¹; LRMS (ES) 357 (100, [M-H]⁻); HRMS (ES) calcd for C₁₉H₃₃O₆ [M-H]⁻ 357.2277, observed 357.2277.
Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-40% Et₂O/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\(_3\)) \(\delta\) 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); \(^1^3\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 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), 19.7 (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.
Using Method F, reaction was complete after 5 days. Purification by column chromatography (10-40% Et₂O/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%): ¹H NMR (600 MHz, CDCl₃) 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); ¹³C NMR (150 MHz, CDCl₃) δ 211.5 (C), 211.4 (C), 168.8 (C), 168.8 (C), 168.6 (C), 61.7 (CH₂), 61.7 (CH₂), 54.5 (CH), 54.4 (CH), 49.0 (CH₂), 49.0 (CH₂), 45.6 (CH), 45.3 (CH), 39.2 (CH₂), 37.2 (CH₂), 37.1 (CH₂), 28.5 (CH), 28.1 (CH), 28.0 (CH), 24.8 (CH₂), 24.8 (CH₂), 22.8 (CH₃), 22.8 (CH₃), 22.7 (CH₃), 22.7 (CH₃), 19.9 (CH₃), 19.9 (CH₃), 14.8 (CH₃), 14.5 (CH₃), 14.2 (CH₃), 14.1 (CH₃); IR (thin film) 2956, 2930, 1750, 1734, 1716 cm⁻¹; LRMS (ES) 341 (100, [M-H]⁺); HRMS (ES) calcd for C₁⁹H₃₅O₅ [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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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\(_2\)O\(_5\) [M-H]\(^+\) 271.1294, observed 271.1293.
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$_3$) $\delta$ 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$_3$) $\delta$ 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$_3$) 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$_2$O$_7$ [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

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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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\(_2\)O\(_7\)Na [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\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 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\(_2\)O\(_6\) [M-H]\(^-\) 373.2339, observed 373.2328.
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$_3$) $\delta$ 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$_3$) $\delta$ 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, 1104 cm$^{-1}$; LRMS (ES$^+$) 395 (100, [M+Na]$^+$); HRMS (ES$^+$) calcd for C$_{18}$H$_{32}$N$_2$O$_6$Na [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 diropan-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 (Cl) 287 (100, [M+H]$^+$); HRMS (Cl) calcd for C$_{13}$H$_{23}$N$_2$O$_5$ [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\(_2\)O\(_5\) [M-H] \(^{+}\) 355.2233, observed 355.2233.
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$_3$) $\delta$ 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$_3$) $\delta$ 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$_2$O$_5$ [M-H$^-$] 357.2389, observed 357.2391.
Dipropan-2-yl 1-(undec-10-enoyl)hydrazine-1,2-dicarboxylate 48s

Using Method G, reaction was complete after 72 h. Purification by column chromatography (10-20% EtOAc/Petrol) gave diropan-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$_2$O$_5$ [M+H]$^+$ 371.2546, observed 371.2548.
Dipropan-2-yl 1-(oct-2-ynoyl)hydrazine-1,2-dicarboxylate 48t\textsuperscript{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\textsubscript{3}) \( \delta \) 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\textsubscript{3}) \( \delta \) 154.7 (C), 152.4 (C), 151.4 (C), 98.8 (C), 74.3 (C), 72.8 (CH), 70.8 (CH), 31.1 (CH\textsubscript{2}), 27.3 (CH\textsubscript{2}), 22.2 (CH\textsubscript{2}), 22.0 (CH\textsubscript{3}), 21.8 (CH\textsubscript{3}), 19.4 (CH\textsubscript{2}), 14.0 (CH\textsubscript{3}); IR (thin film) 3314, 2983, 2936, 2873, 2229, 1741, 1724, 1687 cm\textsuperscript{-1}; LRMS (FAB) 349 (100, [M+Na]\textsuperscript{+}); HRMS (FAB) calcd for C\textsubscript{16}H\textsubscript{26}N\textsubscript{2}O\textsubscript{5}Na [M+Na]\textsuperscript{+} 349.1739, observed 349.1733.

Dipropan-2-yl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate 48u\textsuperscript{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\textsubscript{3}) \( \delta \) 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\textsubscript{3}) \( \delta \) 170.3 (C), 165.1 (d, \( J_{C-F} = 252 \) Hz, C), 155.4 (C), 153.0 (C), 131.3 (C), 131.0 (d, \( J_{C-F} = 8.0 \) Hz, CH), 115.5 (d, \( J_{C-F} = 21.0 \) Hz, CH), 72.8 (CH), 70.9 (CH), 22.0 (CH\textsubscript{3}), 21.5 (CH\textsubscript{3}); IR (thin film) 3314, 2983, 2938, 1734, 1705, 1603, 1507 cm\textsuperscript{-1}; LRMS (FAB) 349 (100, [M+Na]\textsuperscript{+}); HRMS (FAB) calcd for C\textsubscript{15}H\textsubscript{19}N\textsubscript{2}O\textsubscript{5}FNa [M+Na]\textsuperscript{+} 349.1176, observed 349.1171.

Dipropan-2-yl 1-benzoylhydrazine-1,2-dicarboxylate 48v\textsuperscript{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\textsubscript{3}) \( \delta \) 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\textsubscript{3}) \( \delta \) 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\textsubscript{3}), 21.3 (CH\textsubscript{3}); IR (thin film) 3265, 2988, 1755, 1738, 1682, 1601, 1519 cm\textsuperscript{-1}; LRMS
(ES') 307 (100, [M-H]); HRMS (ES') calcd for C_{15}H_{19}N_{2}O_{5} [M-H] 307.1294, observed 307.1289.

**Dipropan-2-yl 1-(4-methoxybenzoyl)hydrazine-1,2-dicarboxylate 48w**

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%): ^1H NMR (600 MHz, CDCl₃) 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); ^13C NMR (150 MHz, CDCl₃) 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 (CH₃), 22.0 (CH₃), 21.6 (CH₃); 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_{2}O_{6} [M-H] 337.1400, observed 337.1406.

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

Using Method B, reaction was complete after 3 h. Purification by flash column chromatography (20-70% CH₂Cl₂/petrol) gave pentafluorophenyl (4S)-4-methyl-3-oxohexane-1-sulfonate 15x as a colourless oil (317 mg, 0.88 mmol, 88%): ^1H NMR (400 MHz, CDCl₃) 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); ^13C NMR (150 MHz, CDCl₃) δ 208.8 (C), 47.9 (CH), 47.1 (CH₂), 34.5 (CH₂), 25.9 (CH₂), 15.7 (CH₃), 11.5 (CH₃); IR (solid) 2970, 2940, 1716, 1516, 1384, 1184 cm⁻¹; LRMS (Cl) 361 (100, [M+H]⁺); HRMS (Cl) calcd for C_{13}H_{14}F₅O₄S [M+H]⁺ 361.0533, observed 361.0526; [α]D = +9.76 (c 18.9, CHCl₃, 23.5 °C); HPLC conditions: CHIRALCEL-OD column, hexane:i-PrOH 97:3, 1.2 mL/min, tᵣ (minor) = 12.8 min, tᵣ (major) = 16.3 min, 97%ee.
HPLC trace for pentafluorophenyl (4rac)-4-methyl-3-oxohexane-1-sulfonate 15x
HPLC trace for pentafluorophenyl (4S)-4-methyl-3-oxohexane-1-sulfonate 15x

Dipropan-2-yl 1-[(S)-2-methylbutanoyl]hydrazine-1,2-dicarboxylate 48x\textsuperscript{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%): \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{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); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) δ 178.0 (C), 155.3 (C), 152.7 (C), 72.2 (CH), 70.4 (CH), 41.0 (CH), 27.1 (CH\textsubscript{2}), 22.0 (CH\textsubscript{3}), 21.8 (CH\textsubscript{3}), 16.9 (CH\textsubscript{3}), 11.7 (CH\textsubscript{3}); IR (thin film) 3313, 2981, 2938, 1736, 1718 cm\textsuperscript{-1}; LRMS (CI) 289 (100, [M+H]\textsuperscript{+}); HRMS (CI) calcd for C\textsubscript{13}H\textsubscript{25}N\textsubscript{2}O\textsubscript{5} [M+H]\textsuperscript{+} 289.1764, observed 289.1757; [\textalpha]\textsubscript{D} = +20.0 (c 0.48, CHCl\textsubscript{3}, 20.0 °C); HPLC conditions: CHIRALCEL-OD column, hexane:i-PrOH 99:1, 0.6 mL/min, t\textsubscript{R} (major) = 36.8 min, t\textsubscript{R} (minor) = 42.9 min, 98%ee.

Dipropan-2-yl 1-α(S)-2-(tert-butyldimethylsilyloxy)propanoyl]hydrazine-1,2-dicarboxylate 48y\textsuperscript{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-butyldimethylsilyloxy)propanoyl]hydrazine-1,2-dicarboxylate 48y as a colourless oil (238 mg, 0.61 mmol, 61%): \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{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
(S)-N-Benzyl-2-methylbutanamide 53\textsuperscript{11,15,16}

Using Method H. Purification by column chromatography (50% Et\textsubscript{2}O/petrol) gave (S)-N-benzyl-2-methylbutanamide 53 as an oil (86% yield, determined by integration of crude \textsuperscript{1}H NMR relative to pentachlorobenzene as internal standard) as a colourless oil: [\alpha]_{D}^{25} = +16.0 (c 1.08, Acetone, 20.0 °C); \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}) \(\delta\) 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); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 176.4 (C), 155.1 (C), 152.6 (C), 72.5 (CH), 70.7 (CH), 69.5 (CH), 43.4 (CH), 27.5 (CH\textsubscript{2}), 17.7 (CH\textsubscript{3}), 12.1 (CH\textsubscript{3}); IR (thin film) 3282, 2965, 2929, 2876, 1646, 1548 cm\textsuperscript{-1}; LRMS (CI) 192 (100, [M+H]\textsuperscript{+}); HRMS (EI) calcd for C\textsubscript{12}H\textsubscript{18}NO [M+H]\textsuperscript{+} 192.1388, observed 192.1392; Data agrees with that reported by Yamakawa\textsuperscript{15} and Gago.\textsuperscript{16}

References