Dioxygen mediated hydroacylation of vinyl sulfonates and sulfones on water

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General Experimental

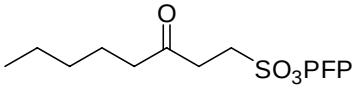
All reagents were purchased from Aldrich or AlfaAesar and were used as received without further purification. All reactions were carried out with HPLC gradient grade water (demineralised) purchased from Fisher Scientific. All reactions were carried out in carousel tubes (15 cm × 2 cm) equipped with an octagon-shaped magnetic stirrer bar (12.7 mm × 3 mm). Where described below petrol refers to petroleum ether (40-60). All reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel plates (254μm). Flash column chromatography was carried out with Kiesegel 60M 0.04/0.063mm (200-400 mesh) silica gel. ^{1}H NMR spectra were recorded at 300 MHz, 400 MHz, 500 MHz and 600 MHz and ^{13}C NMR at 75 MHz, 100 MHz, 125 MHz and 150 MHz on a Bruker AMX300, AMX400, AMX500 and AMX600 at ambient temperature in $CDCl_3$ as described below. The chemical shifts (δ) for ^{1}H and ^{13}C are quoted relative to residual signals of the solvent on the ppm scale. Coupling constants (*J* values) are reported in Hertz (Hz). 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. Melting points were measured with a Gallenkamp apparatus and are uncorrected. Due to the broadness of the ^{13}C NMR signals in the pentafluorophenyl moiety these peaks have not been assigned.

Spectral data for compounds **1a, 3a, 3b, 3c, 3e** and **3f** agrees with that previously reported.[1]

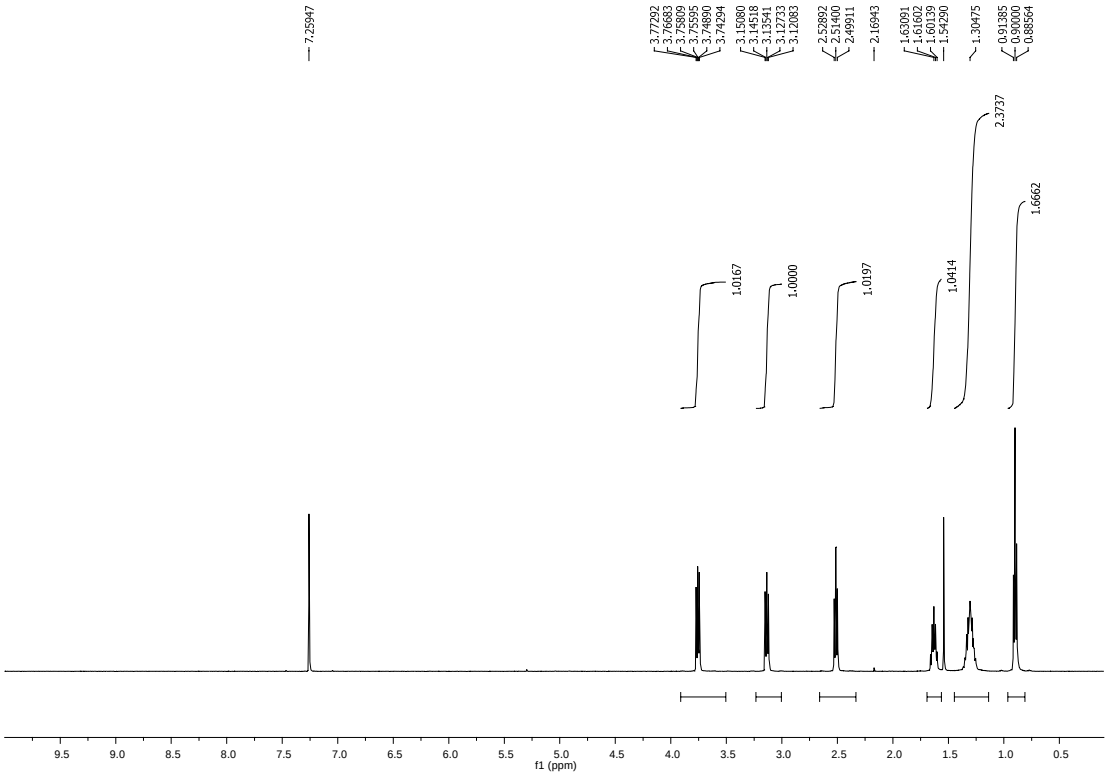
Typical procedure for the synthesis of *β*-keto-pentafluorophenyl-sulfonates

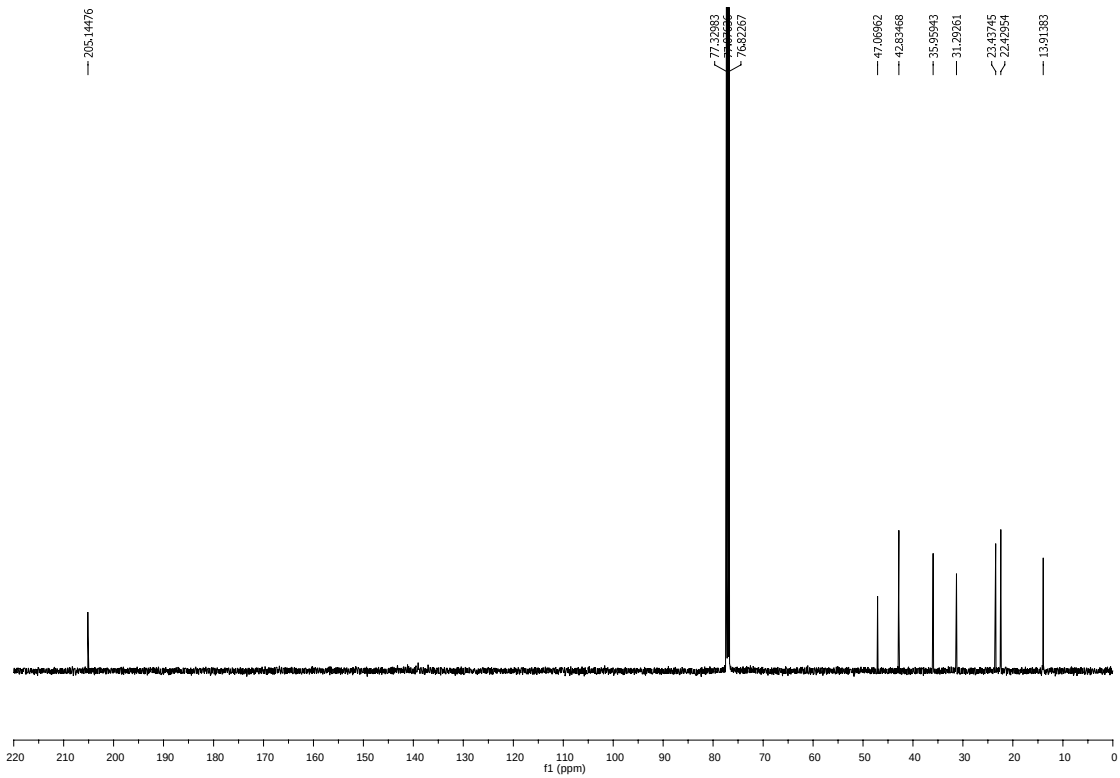
Aldehyde (2 mmol) was added to a solution of ethenesulfonic acid pentafluorophenyl ester (1 mmol) on H_2O (500 μL) and the reaction mixture stirred at 300 rpm at 21 °C until the time specified (see text in paper). The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with H_2O (50 mL), dried ($MgSO_4$), the solvent removed *in vacuo* and purified as described below to afford the desired ketone sulfonate ester.

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

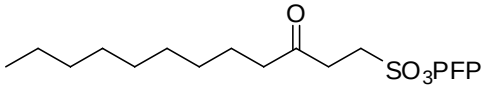


Reaction was complete after 6 h. Purification by column chromatography (30-70% CH_2Cl_2/petrol) and recrystallisation (petrol) gave 3-oxo-octane-1-sulfonic acid pentafluorophenyl ester as white crystals (281 mg, 0.75 mmol, 75%): m.p. 45-47 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (m, 2H), 3.13 (m, 2H), 2.51 (t, *J* = 7.5 Hz, 2H), 2.16 (quintet, *J* = 7.5 Hz, 2H), 1.30 (m, 4H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.1 (s), 47.1 (t), 42.8 (t), 40.0 (t), 31.3 (t), 23.4 (t), 22.4 (t), 13.9 (q); IR (solid) 2937, 2871, 1721, 1520, 1388, 1183 cm^{-1}; LRMS (CI) 375 (100, $[M+H]^+$), 191 (23), 285 (25), 127 (66); HRMS (CI) calcd for $C_{14}H_{16}F_5O_4S$ $[M+H]^+$ 375.06895; observed 375.06852.

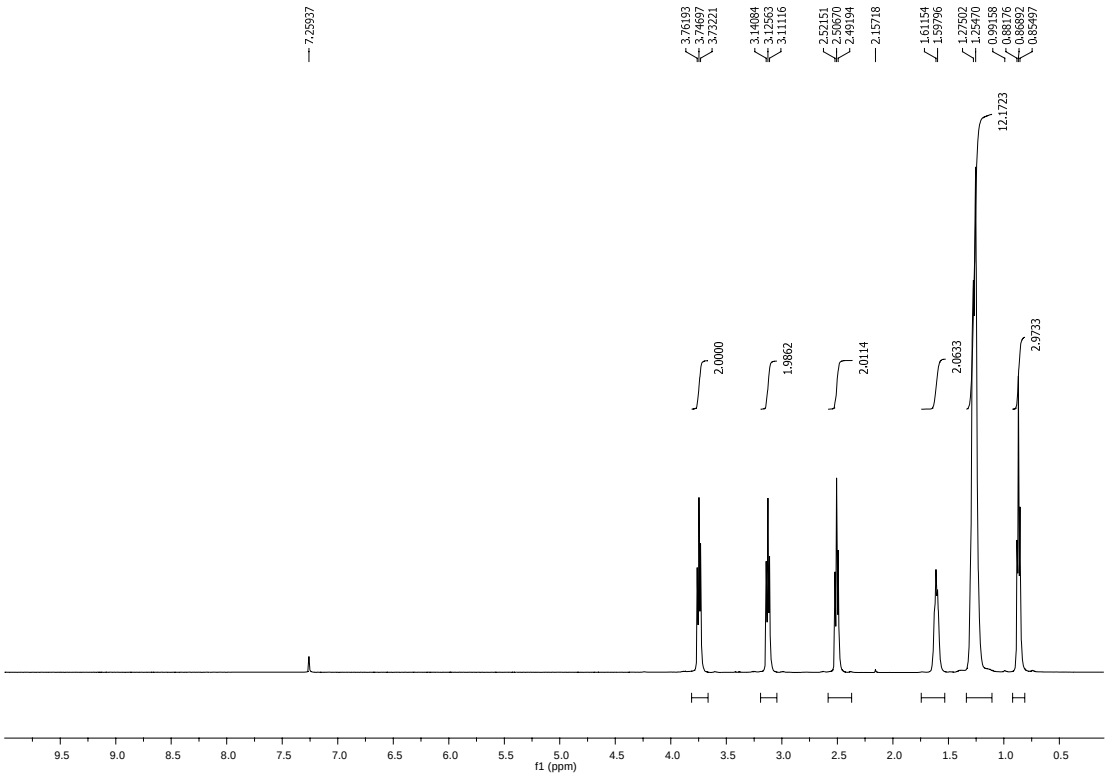




3-Oxo-dodecane-1-sulfonic acid pentafluorophenyl ester



Reaction was complete after 6 h. Purification by column chromatography (30-70% CH_2Cl_2/petrol) and recrystallisation (petrol) gave 3-oxo-dodecane-1-sulfonic acid pentafluorophenyl ester as white crystals (267 mg, 0.62 mmol, 62%): m.p. 68-70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.75 (m, 2H), 3.13 (m, 2H), 2.51 (t, J = 7.5 Hz, 2H), 1.61 (quintet, J = 7.5 Hz, 2H), 1.30-1.20 (m, 12H), 0.87 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.1 (s), 47.0 (t), 42.8 (t), 35.9 (t), 31.9 (t), 29.6 (t), 29.4 (t), 29.3 (t), 29.1 (t), 23.7 (t), 22.7 (t), 14.1 (q); IR (solid) 2954, 2918, 2849, 1710, 1518, 1378, 1178 cm^{-1}; LRMS (CI) 431 (100, $[M+H]^+$), 183 (37); HRMS (CI) calcd for $C_{18}H_{24}F_5O_4S$ $[M+H]^+$ 431.13100; observed 431.12897.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1.61154
1.59796
1.27502
1.25970
0.99158
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2.0000
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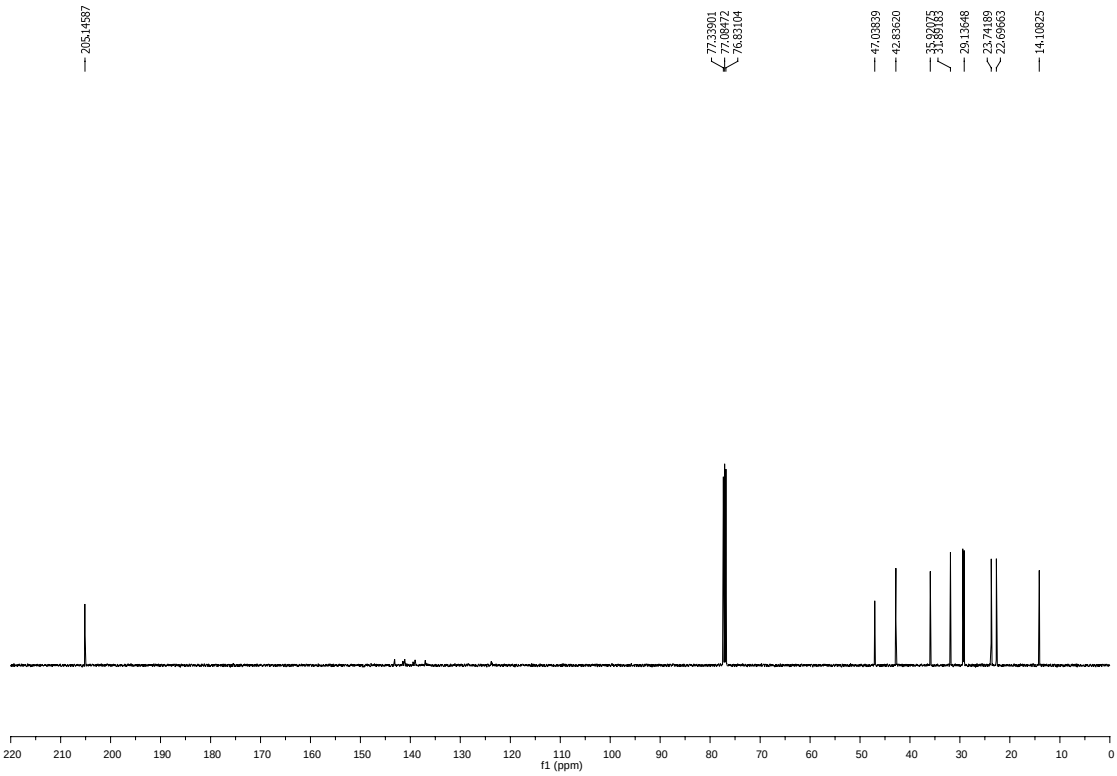
2.0114
2.0633
2.9733
f1 (ppm)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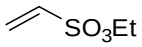
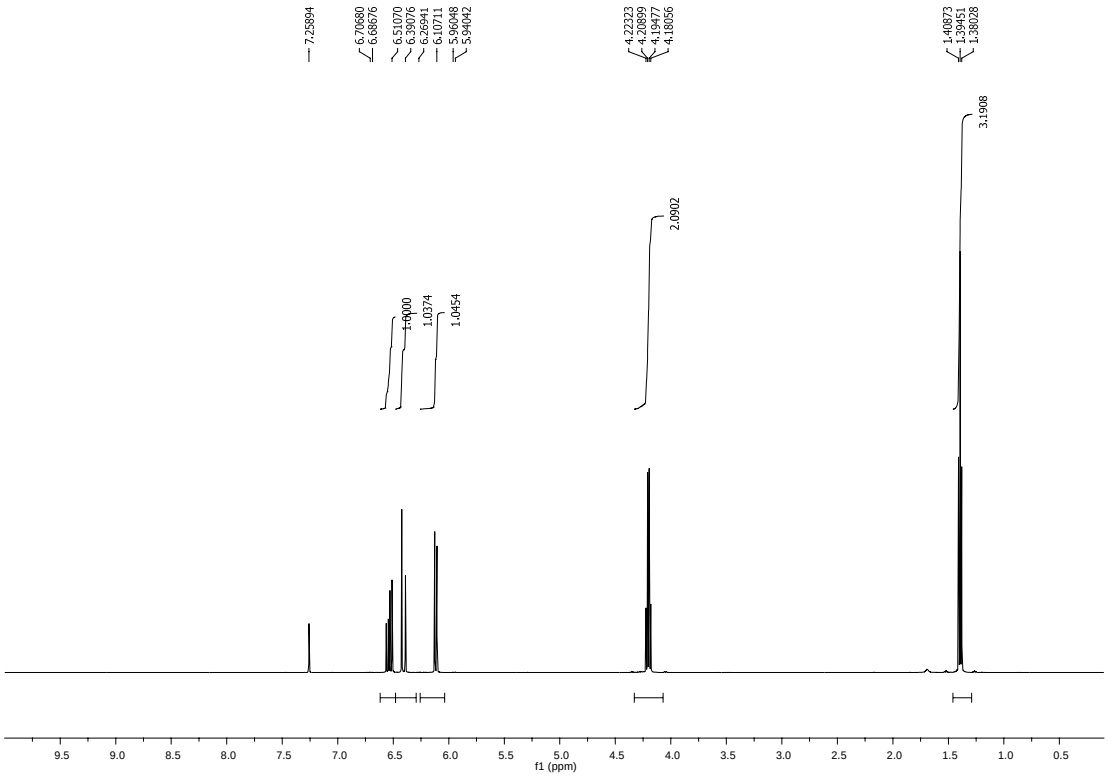
22.69663
14.10825
f1 (ppm)

Ethenesulfonic acid ethyl ester



A solution of EtOH (5.6 g, 7.2 mmol, 123 mmol) and NEt_3 (18.7 g, 25.6 mL, 184 mmol) in CH_2Cl_2 (100 mL) was added dropwise over 1 h to a solution at of 2-chloroethane-1-sulfonyl chloride (10 g, 61.3 mmol) in CH_2Cl_2 (100 mL) at -15 °C. The reaction mixture was allowed to warm to 21 °C, diluted with CH_2Cl_2 (100 mL), washed with sat. $NaHCO_3$ (2 × 250 mL) and the solvent removed *in vacuo*. The reaction mixture was diluted with Et_2O, washed with 2M HCl (2 × 250 mL) and sat. NaCl (250 mL), dried ($MgSO_4$) and the solvent removed *in vacuo* to afford ethenesulfonic acid ethyl ester as a colourless oil (6.6 g, 48 mmol, 79%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.55 (dd, J = 10.0, 16.5 Hz, 1H), 6.40 (d, J = 16.5 Hz, 1H), 6.11 (d, J = 10.0 Hz, 1H), 4.21 (q, J = 7.0 Hz, 2H), 1.39 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.8 (d), 130.0 (t), 67.2 (t), 15.0 (q); IR (thin film) 3068, 2990, 1614, 1351, 1168 cm^{-1}; LRMS (CI) 137 (26, $[M+H]^+$), 109 (100); HRMS (CI) calcd for $C_4H_9O_3S$ $[M+H]^+$ 137.02724; observed 137.02729.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6.39076
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1.0000
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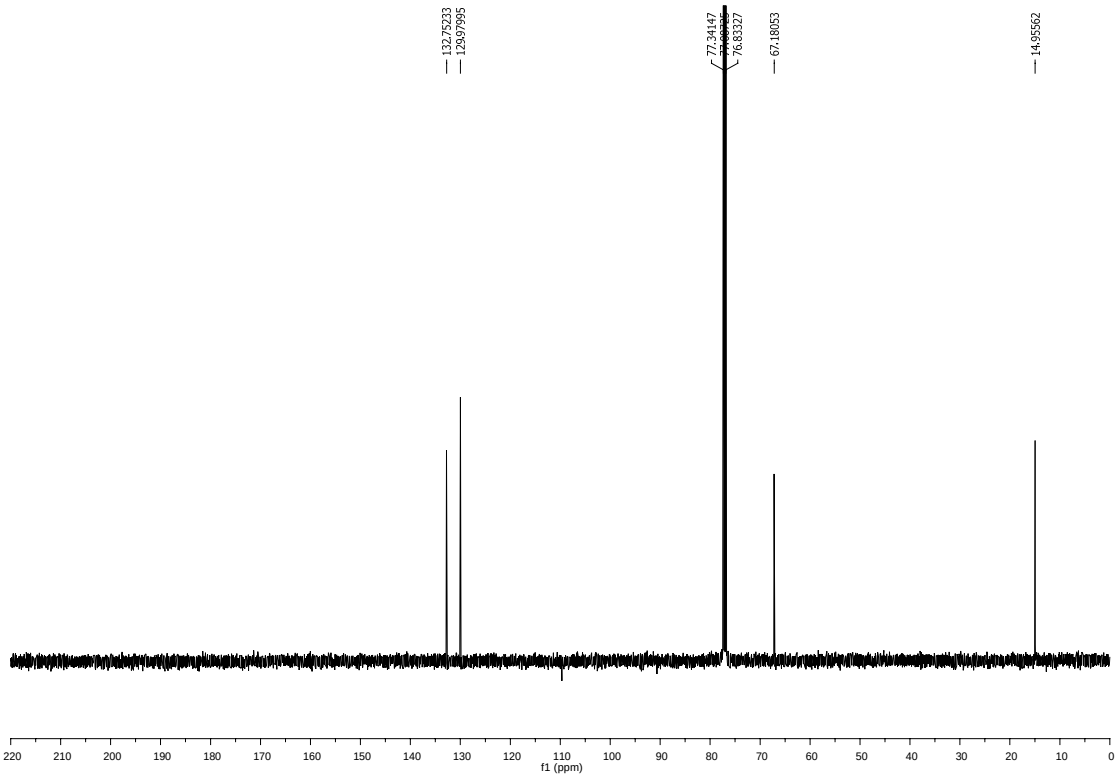
f1 (ppm)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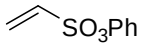
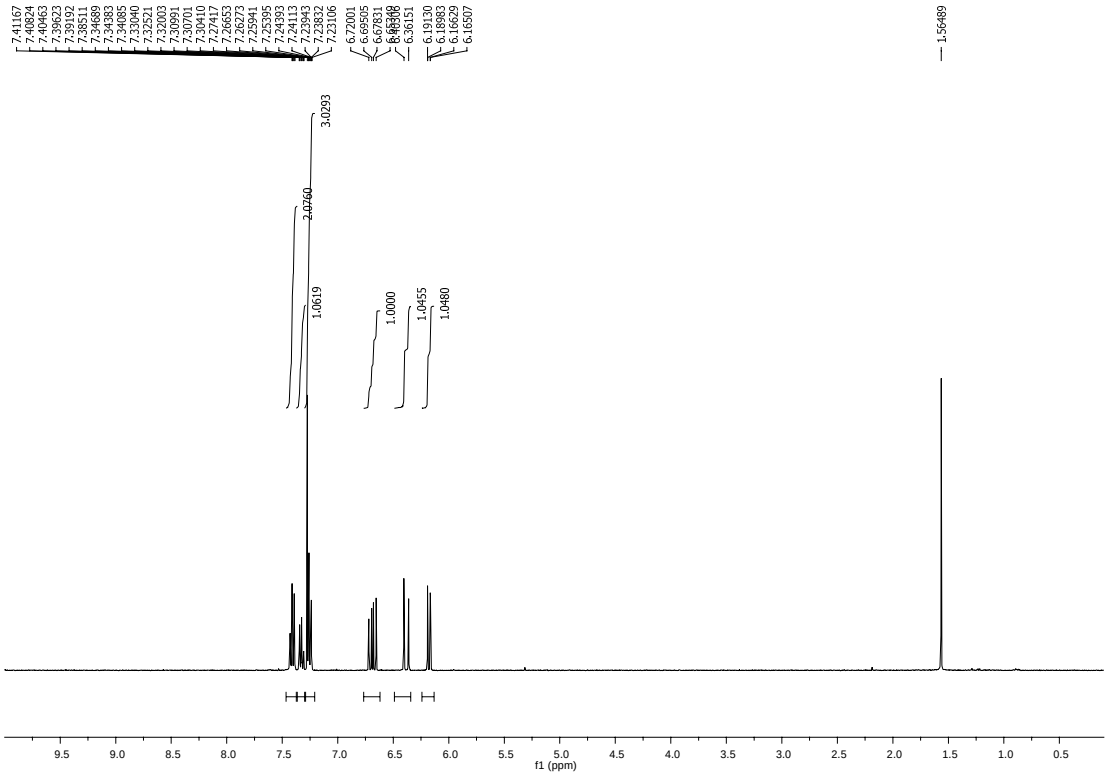
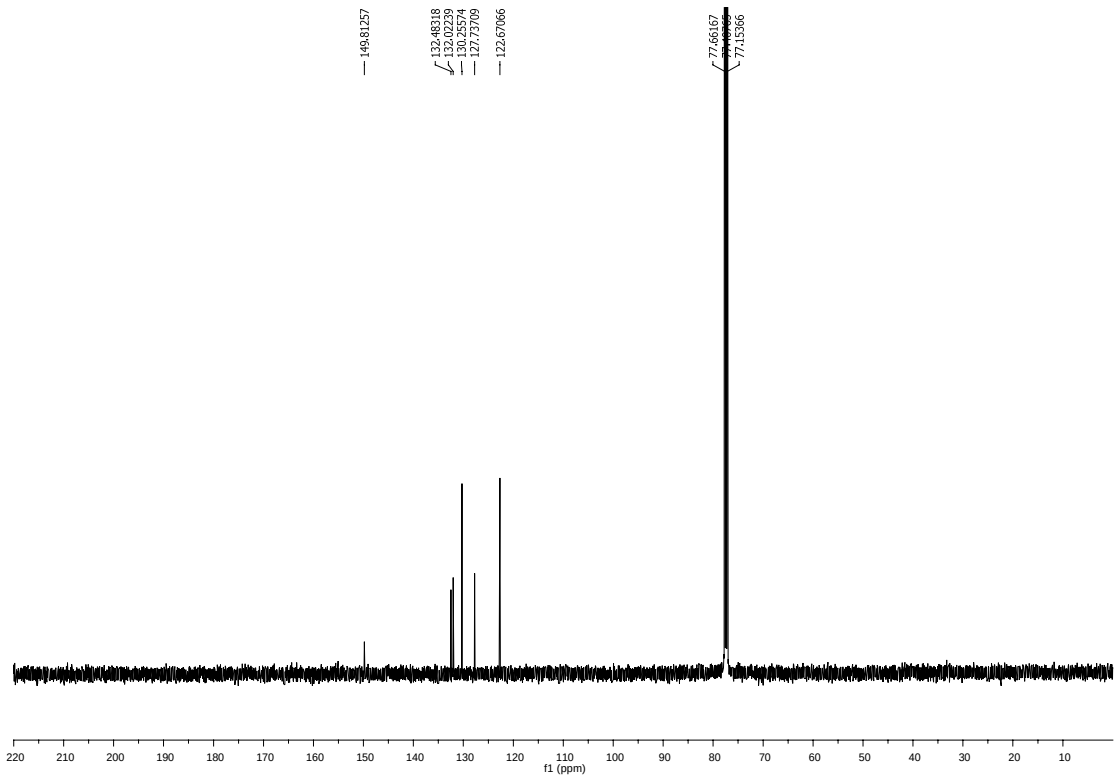
f1 (ppm)

Ethenesulfonic acid phenyl ester



A solution of NEt_3 (31.2 g, 43 mL, 307 mmol) in CH_2Cl_2 (100 mL) was added dropwise over 1 h to a solution at of 2-chloroethane-1-sulfonyl chloride (10 g, 61.3 mmol) and phenol (6.9 g, 74 mmol) in CH_2Cl_2 (100 mL) at -15 °C. The reaction mixture was allowed to warm to 21 °C, the solvent removed *in vacuo*, the crude residue diluted with Et_2O (200 mL), washed with 2M HCl (2 × 250 mL), sat. $NaHCO_3$ (2 × 250 mL) and sat. NaCl (250 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. Purification by column chromatography (20-30% Et_2O/petrol) gave ethenesulfonic acid phenyl ester as a white solid (8.4 g, 50 mmol, 82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.39 (m, 2H), 7.35-7.30 (m, 1H), 7.26-7.23 (m, 2H), 6.69 (dd, *J* = 16.5, 10.0 Hz, 1H), 6.38 (dd, *J* = 16.5, 0.5 Hz, 1H), 6.18 (d, *J* = 10.0, 0.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5 (s), 132.2 (s), 131.7 (t), 129.9 (d), 127.4 (d), 122.3 (d); IR (solid) 3065, 1586, 1487, 1359, 1140 cm^{-1}; LRMS (CI) 184 (45, $[M+H]^+$), 94 (100); HRMS (CI) calcd for $C_8H_8O_3S$ $[M+H]^+$ 184.01886; observed 184.01904.

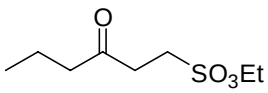




Typical procedure for the synthesis of *β*-keto-ethyl/phenyl-sulfonates

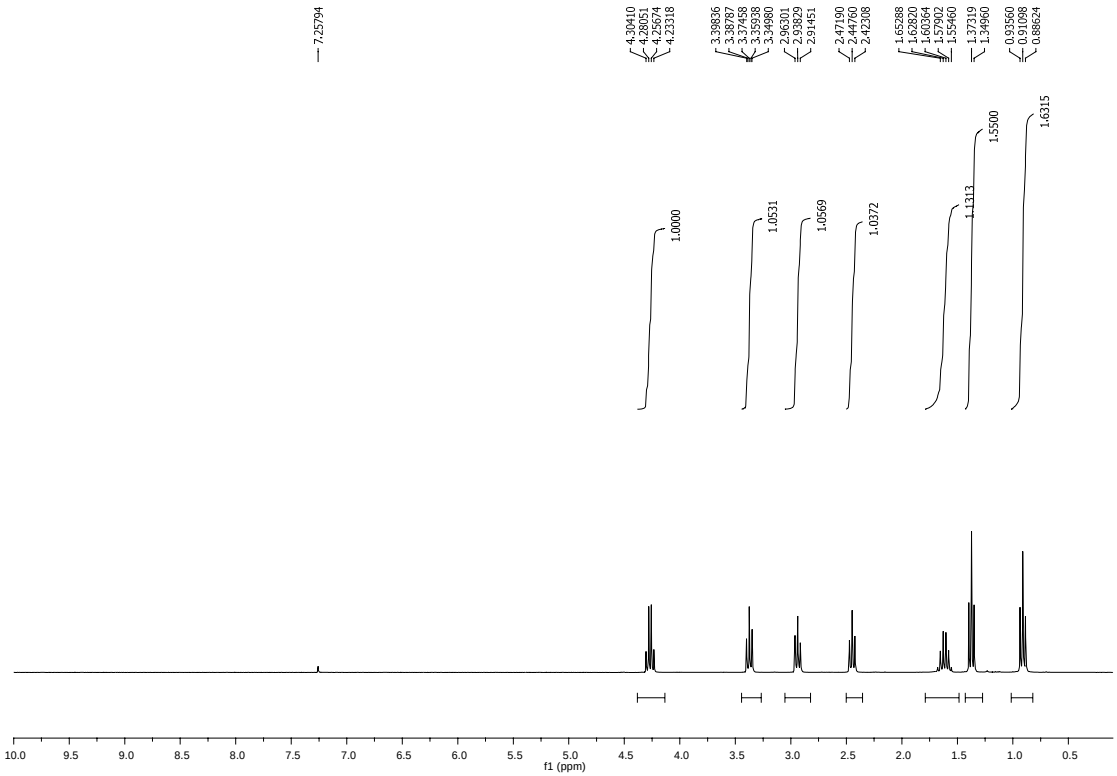
Aldehyde (5 mmol) was added to a solution of alkene (1 mmol) on H_2O (500 μL) and the reaction mixture stirred at 300 rpm at 21 °C in a stoppered vessel. The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with H_2O (50 mL), dried ($MgSO_4$), the solvent removed *in vacuo* and purified as described below to afford the desired ketone sulfonate ester.

3-Oxo-hexane-1-sulfonic acid ethyl ester



Reaction was complete after 96 h. Purification by column chromatography (20-60% EtOAc/petrol) gave 3-oxo-hexane-1-sulfonic acid ethyl ester as a yellow oil (114 mg, 0.55 mmol, 55%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.27 (q, J = 7.0 Hz, 2H), 3.36 (m, 2H), 2.91 (m, 2H), 2.44 (t, J = 7.0 Hz, 2H), 1.60 (sextet, J = 7.0 Hz, 2H), 1.37 (t, J = 7.0 Hz, 3H), 0.91 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.1 (s), 66.7 (t), 44.7 (t),

44.3 (t), 36.0 (t), 17.1 (t), 15.0 (q), 13.6 (q); IR (thin film) 2964, 2873, 1716, 1350, 1168 cm^{-1}; LRMS (CI) 209 (100, $[M+H]^+$), 163 (22); HRMS (CI) calcd for $C_8H_{17}O_4S$ $[M+H]^+$ 209.08475; observed 209.08504.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2.91451
2.47190
2.44760
2.42208
1.65288
1.62820
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1.57902
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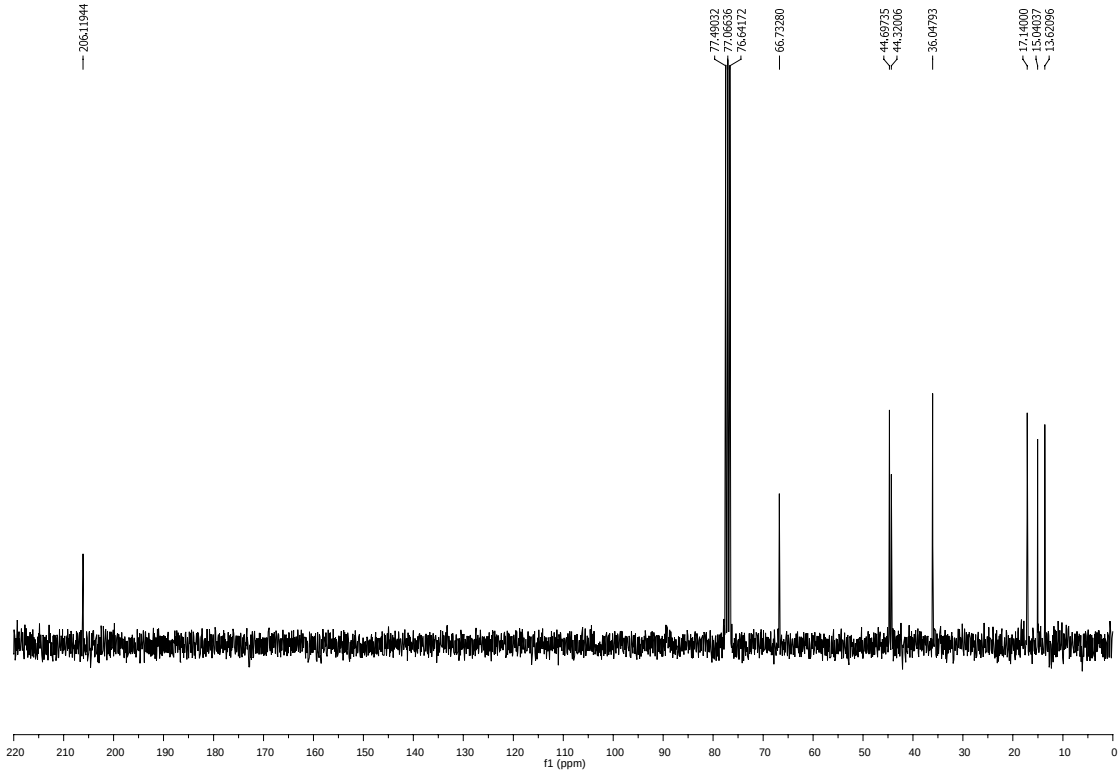
f1 (ppm)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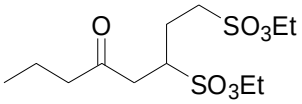
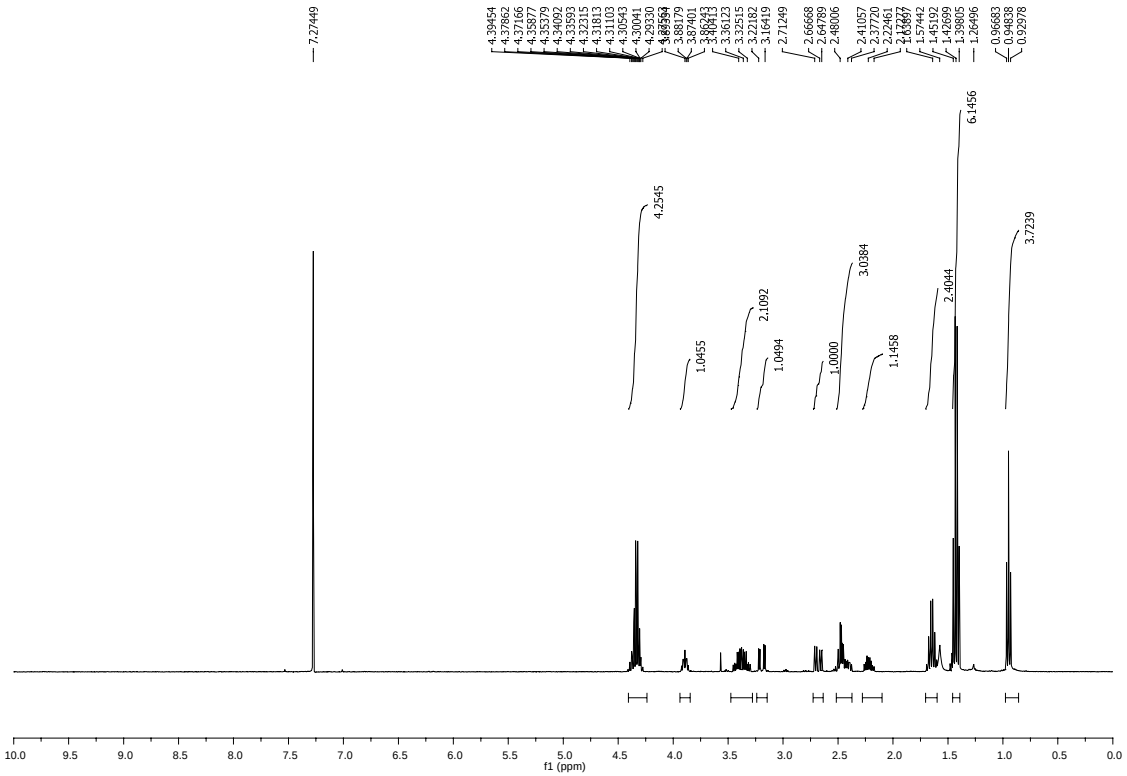
f1 (ppm)

5-Oxo-octane-1,3-disulfonic acid diethyl ester



^{1}H NMR (400 MHz, $CDCl_3$) δ 4.45-4.28 (m, 4H), 3.90 (m, 1H), 3.38 (dddd, *J* = 20.0, 5.5 Hz, 2H), 3.20 (dd, *J* = 18.5, 4.5 Hz, 1H), 2.68 (dd, *J* = 18.5, 7.5 Hz, 1H), 2.50-2.36 (m, 3H), 2.23 (m, 1H), 1.65 (app sextet, *J* = 8.0 Hz, 2H), 1.47 (m, 6H), 0.95 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.7 (s), 67.3 (t), 66.8 (t), 53.9 (d), 47.5 (t), 45.0 (t), 42.2 (t), 24.5 (t), 17.2 (t), 15.2 (q), 15.2 (q), 13.7 (q); IR (thin film) 2934, 1716, 1344, 1166 cm^{-1}; LRMS (CI) 345 (15, $[M+H]^+$), 235 (100); HRMS (CI) calcd for $C_{15}H_{25}O_7S_2$ $[M+H]^+$ 345.1042; observed 345.1036.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3.86243
3.40413
3.36123
3.32515
3.22182
3.16419
2.71249
2.66868
2.64789
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2.41057
2.37720
2.22461
1.57442
1.45192
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1.39865
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0.96683
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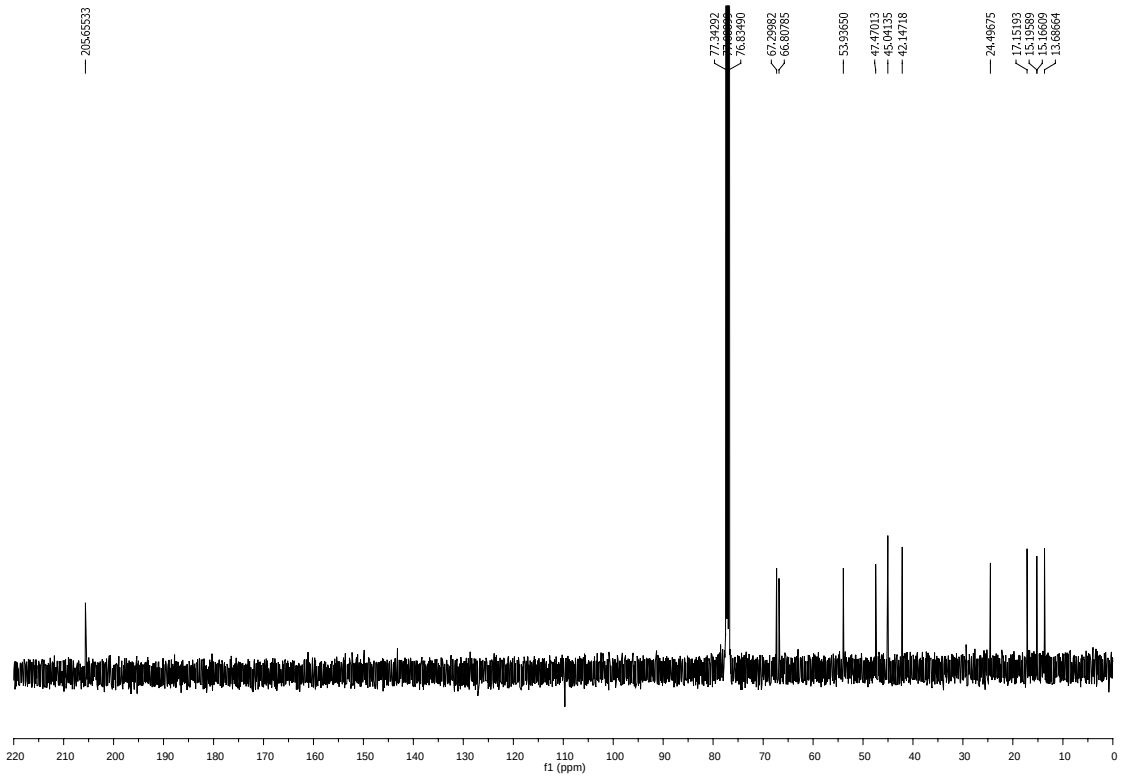
f1 (ppm)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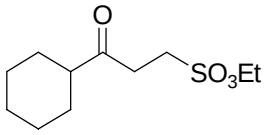
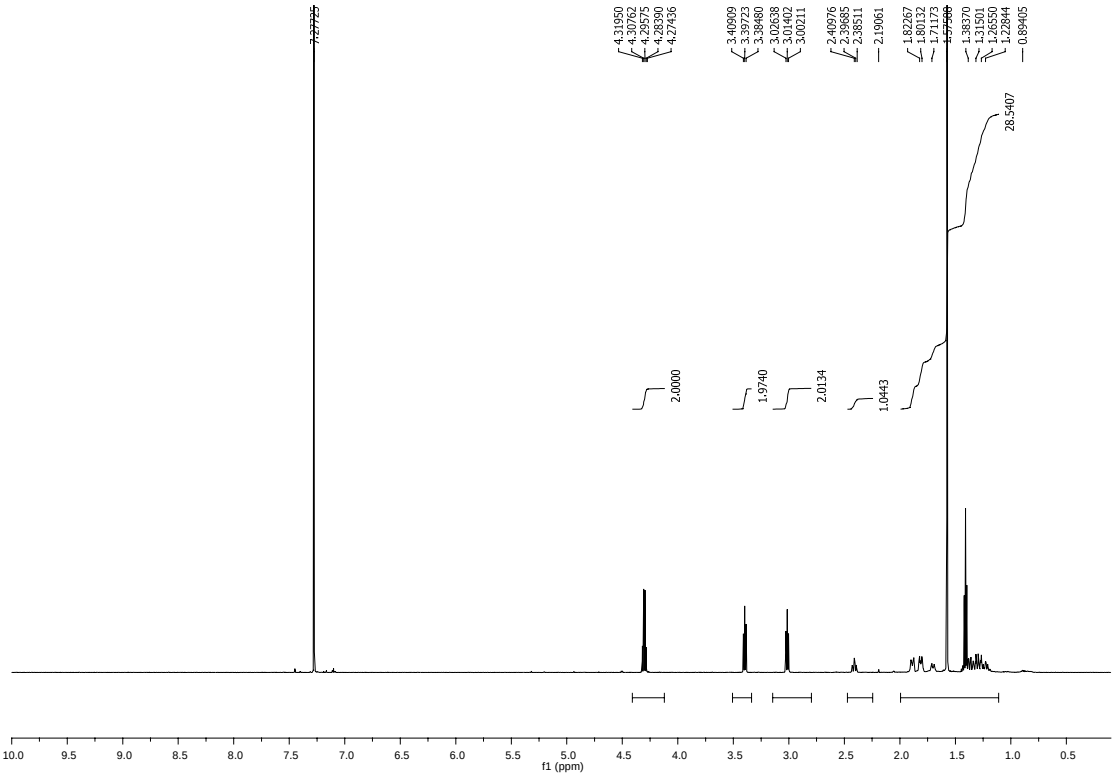
f1 (ppm)

3-Cyclohexyl-3-oxo-propane-1-sulfonic acid ethyl ester



Reaction was complete after 96 h. Purification by column chromatography (20-60% EtOAc/petrol) gave 3-cyclohexyl-3-oxo-propane-1-sulfonic acid ethyl ester as a colourless oil (129 mg, 0.52 mmol, 52%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.30 (q, J = 7.0 Hz, 2H), 3.40 (m, 2H), 3.01 (m, 2H), 2.41 (tt, J = 11.0, 3.0 Hz, 1H), 1.92-1.86 (m, 2H), 1.84-1.78 (m, 2H), 1.72-1.66 (m, 1H), 1.44-1.18 (m, 8H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 209.2 (s), 66.7 (t), 50.8 (d), 44.4 (t), 34.1 (t), 28.4 (t), 25.7 (t), 25.5 (t), 15.0 (q); IR (thin film) 2930, 2855, 1710, 1352, 1168 cm^{-1}; LRMS (EI) 248 (10, $[M]^{+\cdot}$), 139 (100); HRMS (EI) calcd for $C_{11}H_{20}O_4S$ $[M]^{+\cdot}$ 248.10768; observed 248.10658.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2.40976
2.39685
2.38511
2.19061
1.82267
1.80132
1.71173
1.57388
1.38370
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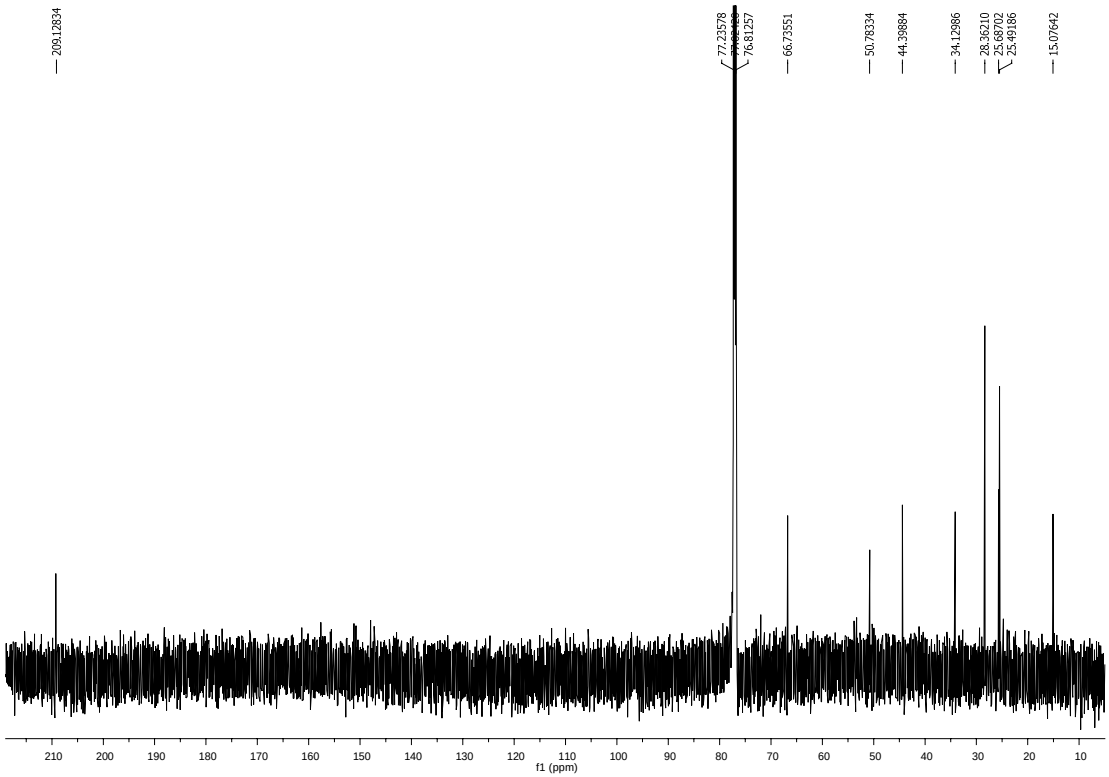
1.0443
f1 (ppm)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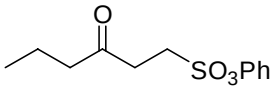
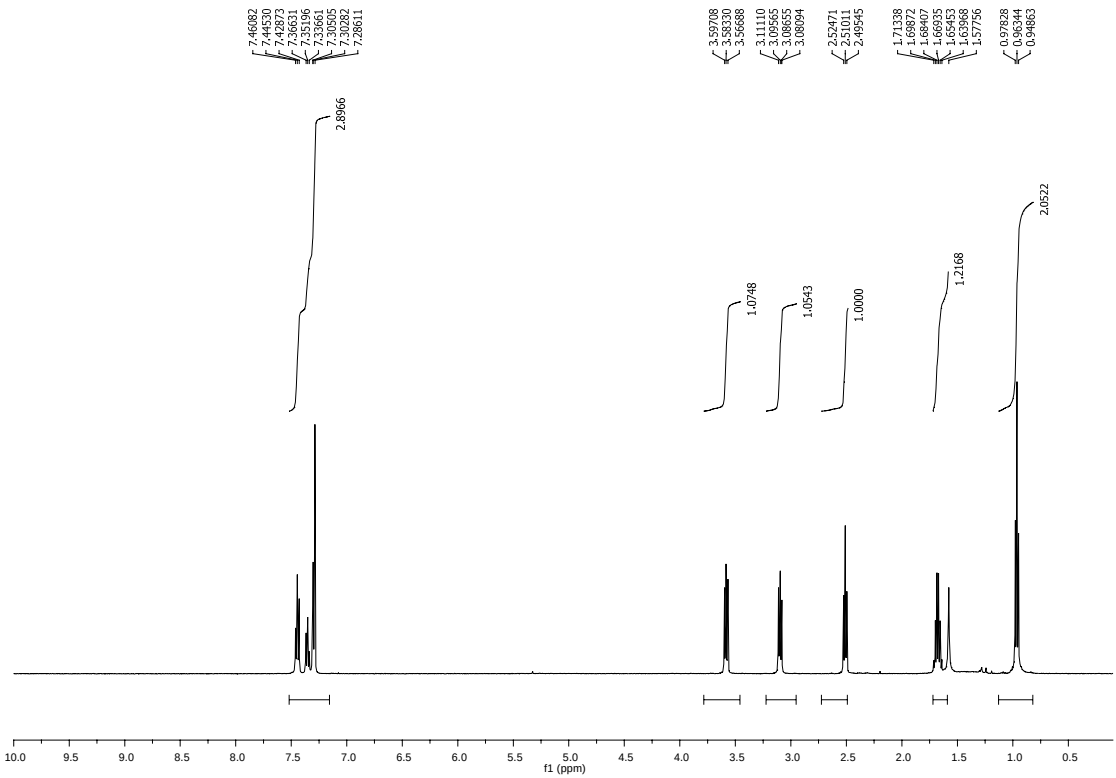
f1 (ppm)

3-Oxo-hexane-1-sulfonic acid phenyl ester



Reaction was complete after 120 h. Purification by column chromatography (50-95% CH_2Cl_2/petrol) and recrystallisation (petrol) gave 3-oxo-hexane-1-sulfonic acid phenyl ester as a white solid (133 mg, 0.52 mmol, 52%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (dt, *J* = 1.0, 7.0 Hz, 2H), 7.32 (dt, *J* = 1.0, 7.0 Hz, 1H), 7.27 (dd, *J* = 1.0, 7.0 Hz, 2H), 3.55 (m, 2H), 3.06 (m, 2H), 2.48 (t, *J* = 7.5 Hz, 2H), 1.65 (sextet, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7 (s), 149.1 (s), 130.1 (d), 127.5 (d), 122.0 (d), 44.9 (t), 44.8 (t), 36.1 (t), 17.3 (t), 13.7 (q); IR (solid) 2964, 2934, 2875, 1718, 1588, 1489, 1370, 1145 cm^{-1}; LRMS (CI) 257 (45, $[M+H]^+$), 163 (100); HRMS (CI) calcd for $C_{12}H_{17}O_4S$ $[M+H]^+$ 257.08475; observed 257.08498.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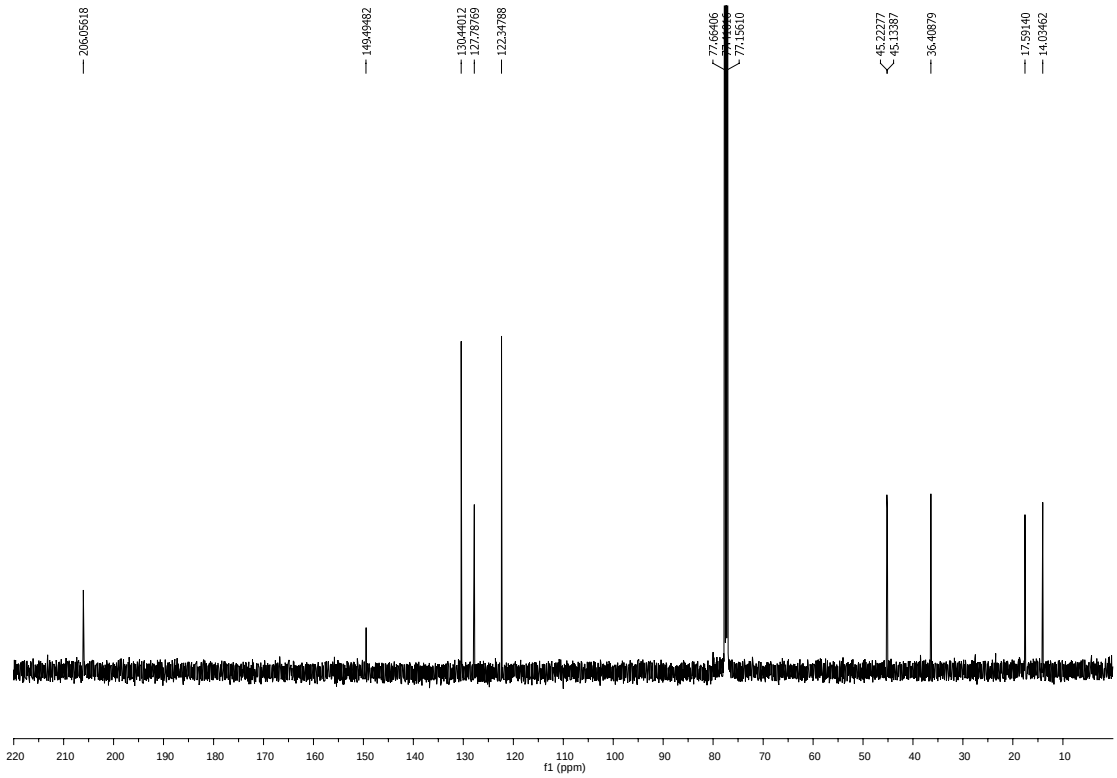
7.44530
7.42873
7.36631
7.35196
7.33661
7.30555
7.30282
7.28611
3.59708
3.58330
3.56688
3.11110
3.09565
3.08655
3.08094
2.52471
2.51011
2.49545
1.71338
1.69872
1.68407
1.66935
1.65453
1.63968
1.57756
0.97828
0.96344
0.94863
2.8966
1.0748
1.0543
1.0000
1.2168
2.0522
f1 (ppm)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127.78769
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77.15610
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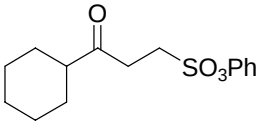
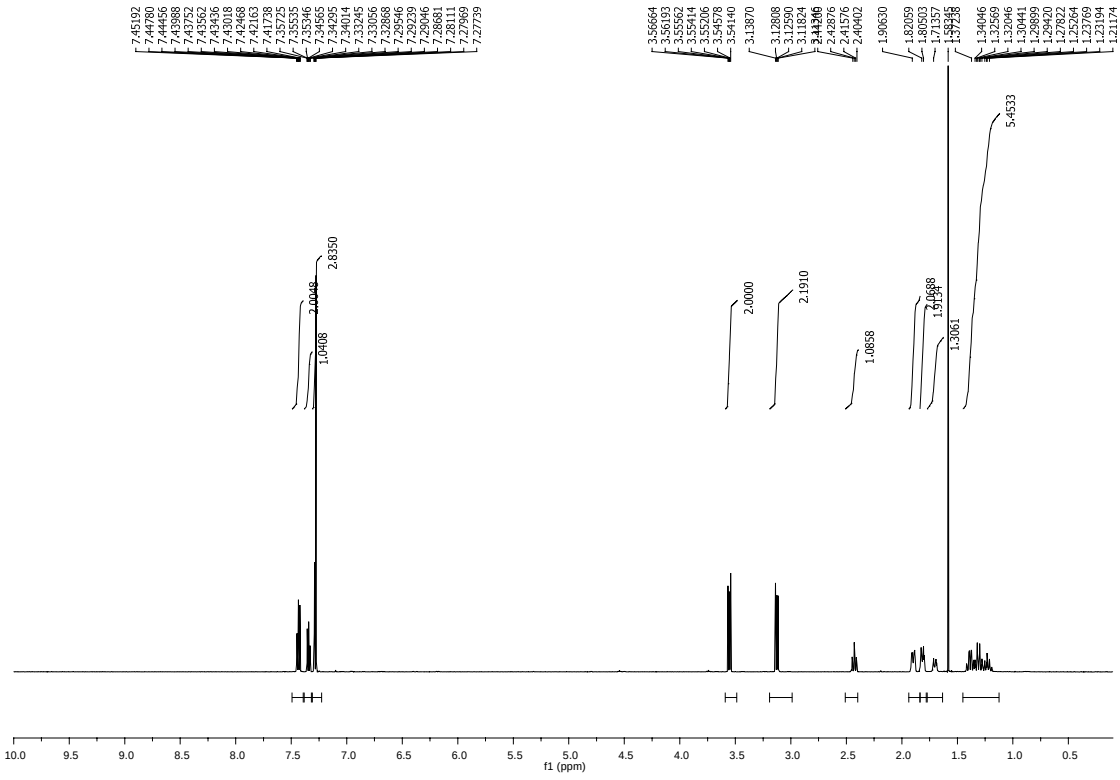
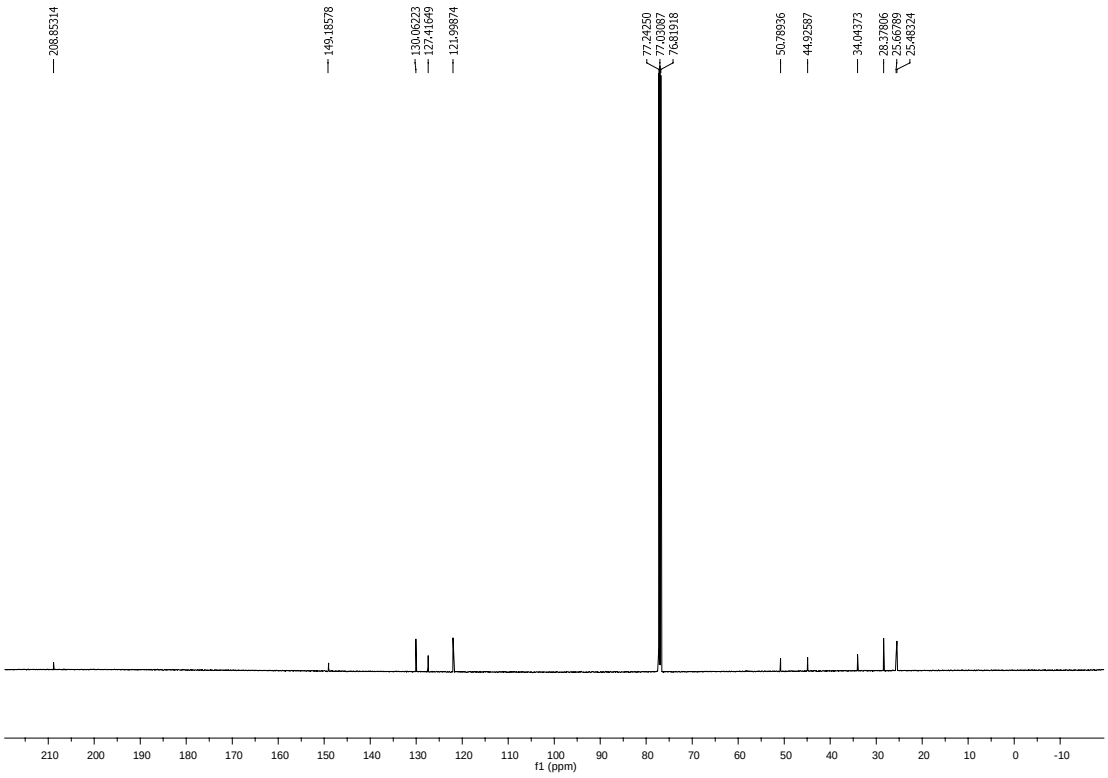
45.13387
36.40879
17.59140
14.03462
f1 (ppm)

3-Cyclohexyl-3-oxo-propane-1-sulfonic acid phenyl ester



Reaction was complete after 120 h. Purification by column chromatography (50-95% CH_2Cl_2/petrol) and recrystallisation (petrol) gave 3-cyclohexyl-3-oxo-propane-1-sulfonic acid phenyl ester as a white solid (169 mg, 0.57 mmol, 57%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47-7.42 (m, 2H), 7.38-7.34 (m, 1H), 7.32-7.28 (m, 2H), 3.59-3.55 (m, 2H), 3.17-3.12 (m, 2H), 2.44 (tt, *J* = 11.0, 3.0 Hz, 1H), 1.92-1.86 (m, 2H), 1.84-1.78 (m, 2H), 1.72-1.66 (m, 1H), 1.44-1.18 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.9 (s), 149.01 (s), 130.1 (d), 127.4 (d), 122.0 (d), 50.8 (d), 44.9 (t), 34.0 (t), 28.4 (t), 25.7 (t), 25.5 (t); IR (solid) 2930, 2855, 1711, 1588, 1488, 1370, 1144 cm^{-1}; LRMS (FAB) 319 (17, $[M+Na]^+$), 297 (18, $[M+H]^+$), 176 (52), 154 (100); HRMS (FAB) calcd for $C_{15}H_{21}O_4S$ $[M+H]^+$ 297.11605; observed 297.11665.

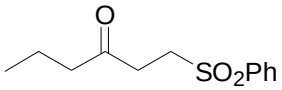




Typical procedure for the synthesis of *β*-keto-sulfones

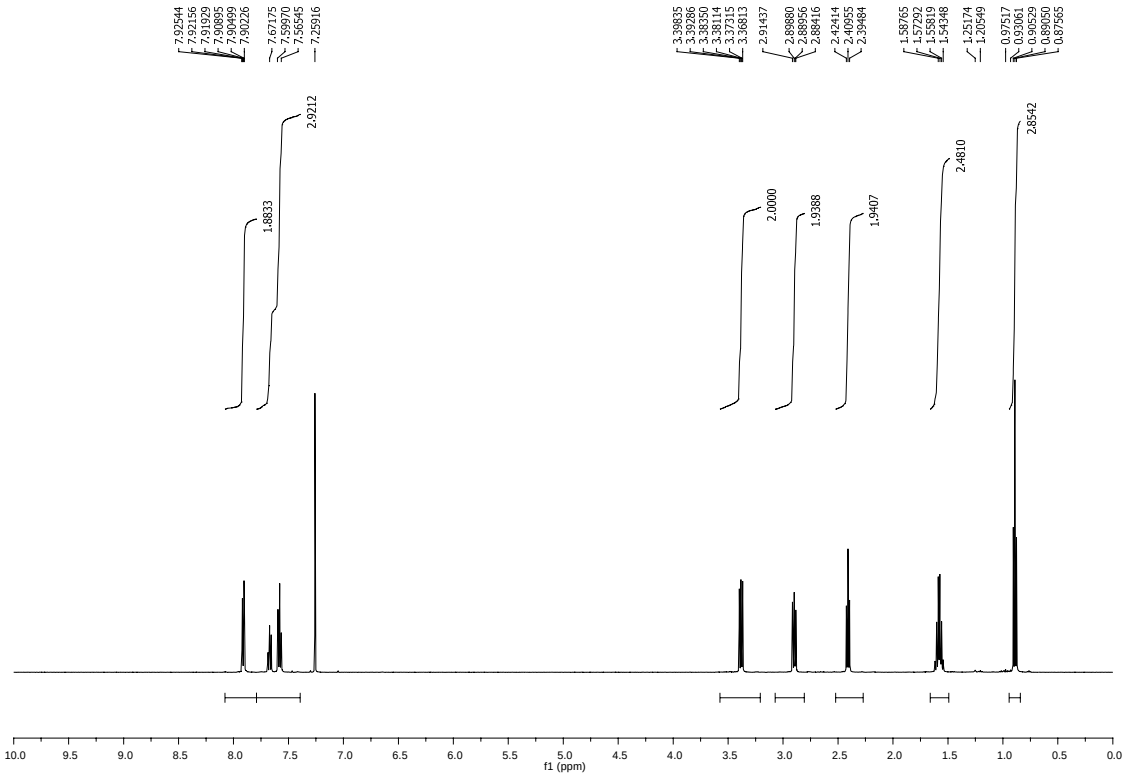
Aldehyde (5 mmol) was added to a solution of alkene (1 mmol) on H_2O (500 μL) and the reaction mixture stirred at 300 rpm at 60 °C with an attached condenser for 24 h. The solvent was removed *in vacuo* and purified as described below to afford the desired *β*-keto-sulfonate.

1-Benzenesulfonyl-hexan-3-one



Purification by column chromatography (10-30% EtOAc/petrol) gave 1-benzenesulfonyl-hexan-3-one as a yellow oil (134 mg, 0.56 mmol, 56%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (m, 2H), 7.66 (m, 1H), 7.58 (m, 2H), 3.38 (m 2H), 2.89 (m, 2H), 2.40 (t, J = 7.5, 2H), 1.58 (sextet, J = 7.5, 2H), 0.90 (t, J = 7.5, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2 (s), 139.1 (s), 134.0 (d), 129.5 (d), 128.0 (d), 50.6 (t), 44.8 (t), 35.0 (t), 17.2 (t), 13.7 (q);

IR (thin film) 2965, 1716, 1308, 1150 cm^{-1}; LRMS (CI) 258 (100, $[M+NH_4]^+$), 116 (56); HRMS (ES) calcd for $C_{12}H_{20}NO_3S$ $[M+NH_4]^+$ 258.1158; observed 258.1160.


7.92544
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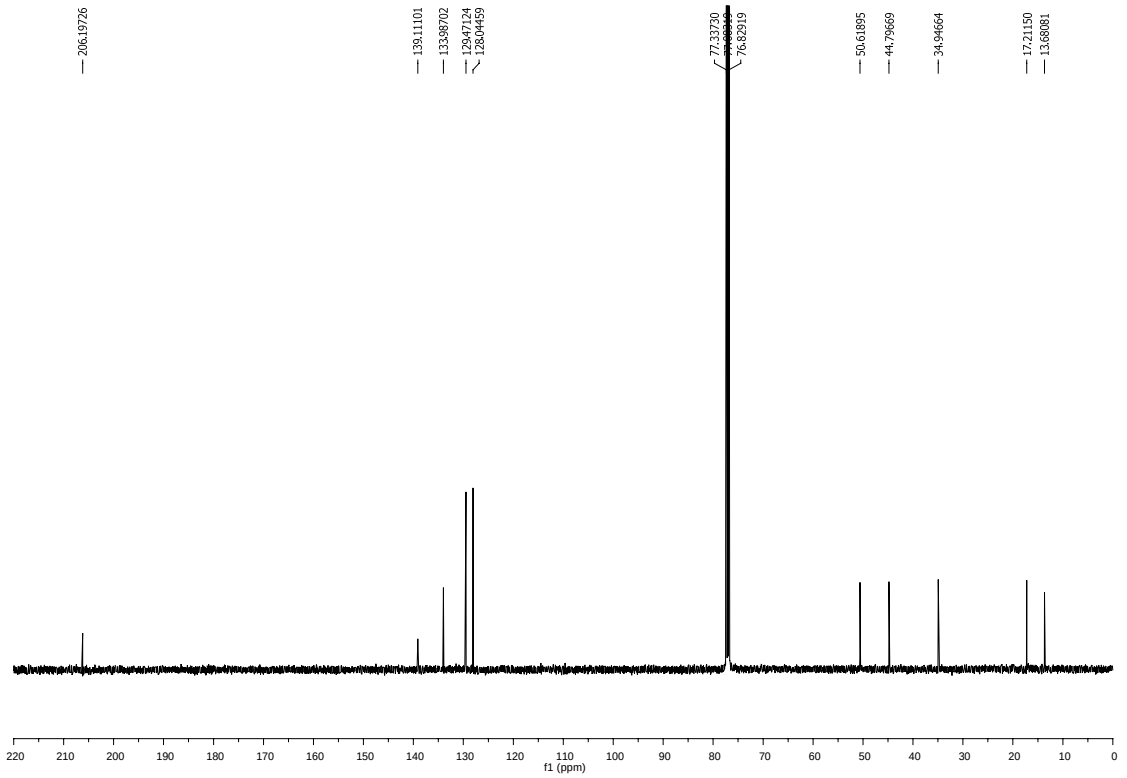
7.90699
7.90226
7.67175
7.59970
7.56545
7.25916
3.39835
3.39286
3.38350
3.38114
3.37315
3.36813
2.91437
2.89880
2.88956
2.88416
2.42414
2.40855
2.39464
1.58765
1.57292
1.55819
1.54348
1.25174
1.20549
0.97517
0.93061
0.90529
0.89650
0.87565
2.9212
1.8833
2.0000
1.9388
1.9407
2.4810
2.8542
f1 (ppm)


206.19726
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133.98702
129.47124
128.04459
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77.08316
76.82919
50.61895
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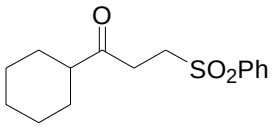
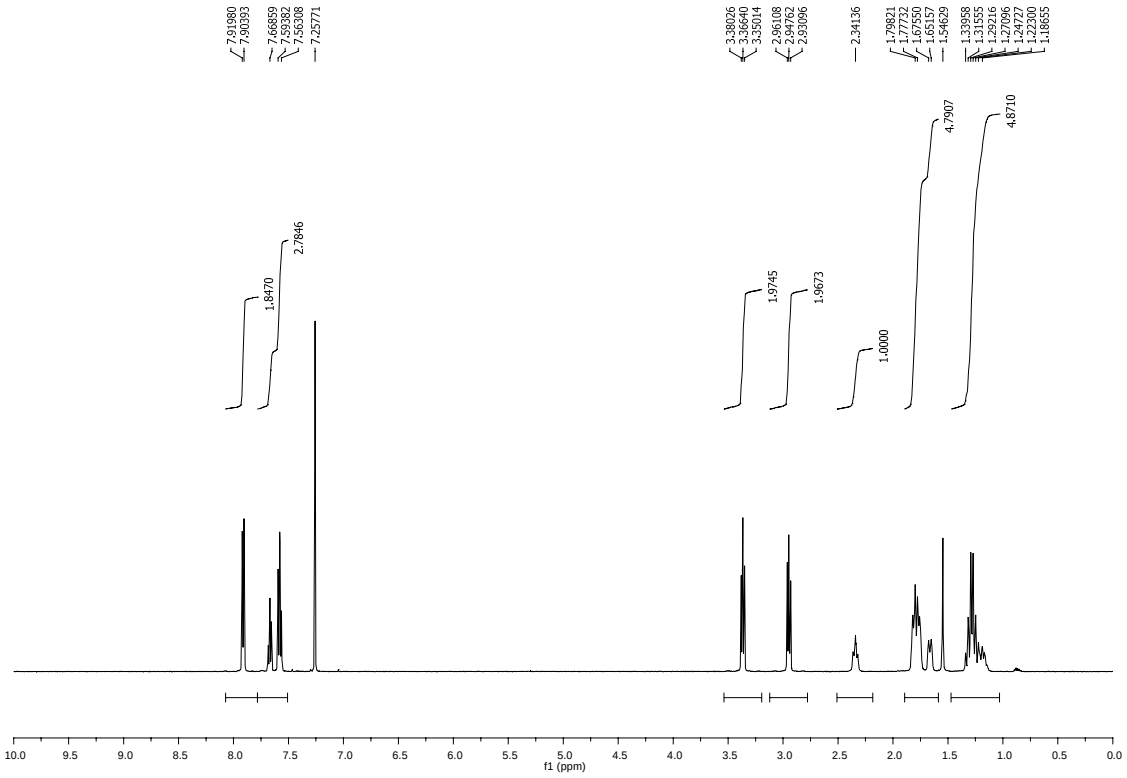
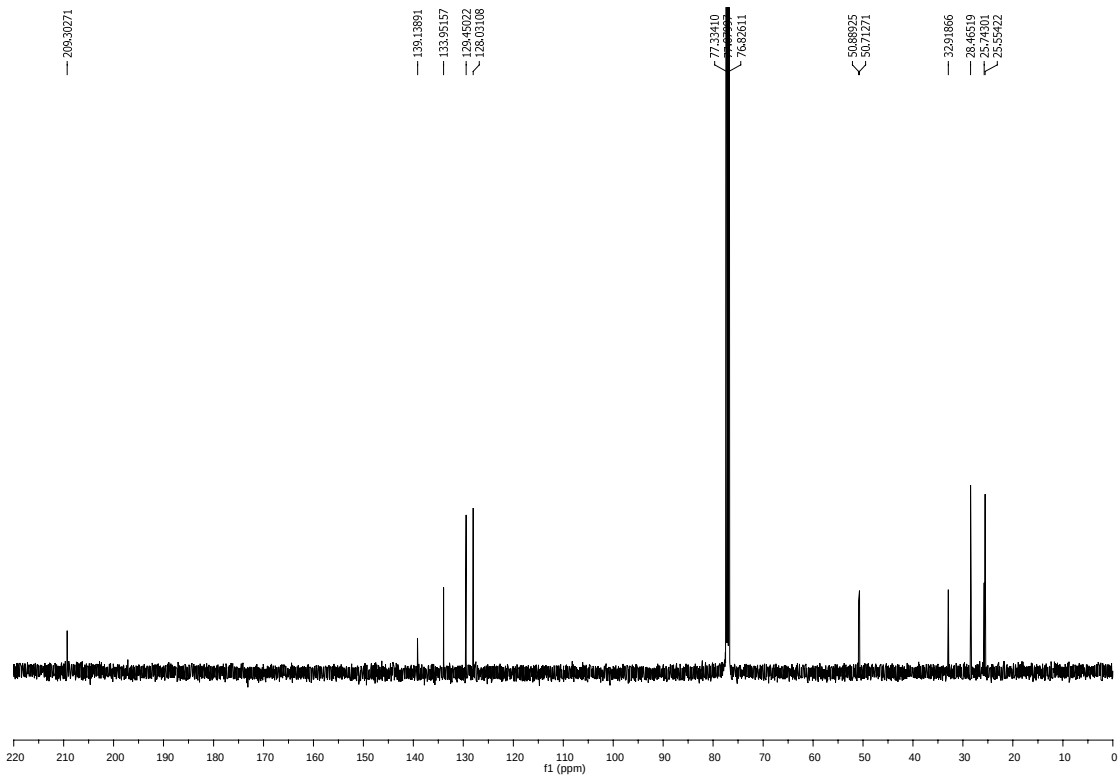
34.94664
17.21150
13.68081
f1 (ppm)

3-Benzenesulfonyl-1-cyclohexyl-propan-1-one

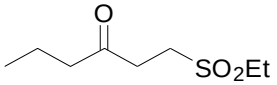


Purification by column chromatography (10-30% EtOAc/petrol) and recrystallisation (petrol) gave 3-benzenesulfonyl-1-cyclohexyl-propan-1-one as a white solid (171 mg, 0.61 mmol, 61%): m.p. 78-80 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (m, 2H), 7.66 (m, 1H), 7.58 (m, 2H), 3.37 (m 2H), 2.95 (m, 2H), 2.34 (m, 1H), 1.80-1.67 (m, 5H), 1.32-1.18 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.3 (s), 139.2 (s), 134.0 (d), 129.5 (d), 128.0 (d), 50.9 (d), 50.7 (t), 32.9 (t), 28.5 (t), 25.7 (t), 25.6 (t); IR (solid) 2929, 1709, 1308, 1151 cm^{-1}; LRMS (CI) 298 (100, $[M+NH_4]^+$), 156 (8%); HRMS (ES) calcd for $C_{15}H_{24}NO_3S$ $[M+NH_4]^+$ 298.1471; observed 298.1473.

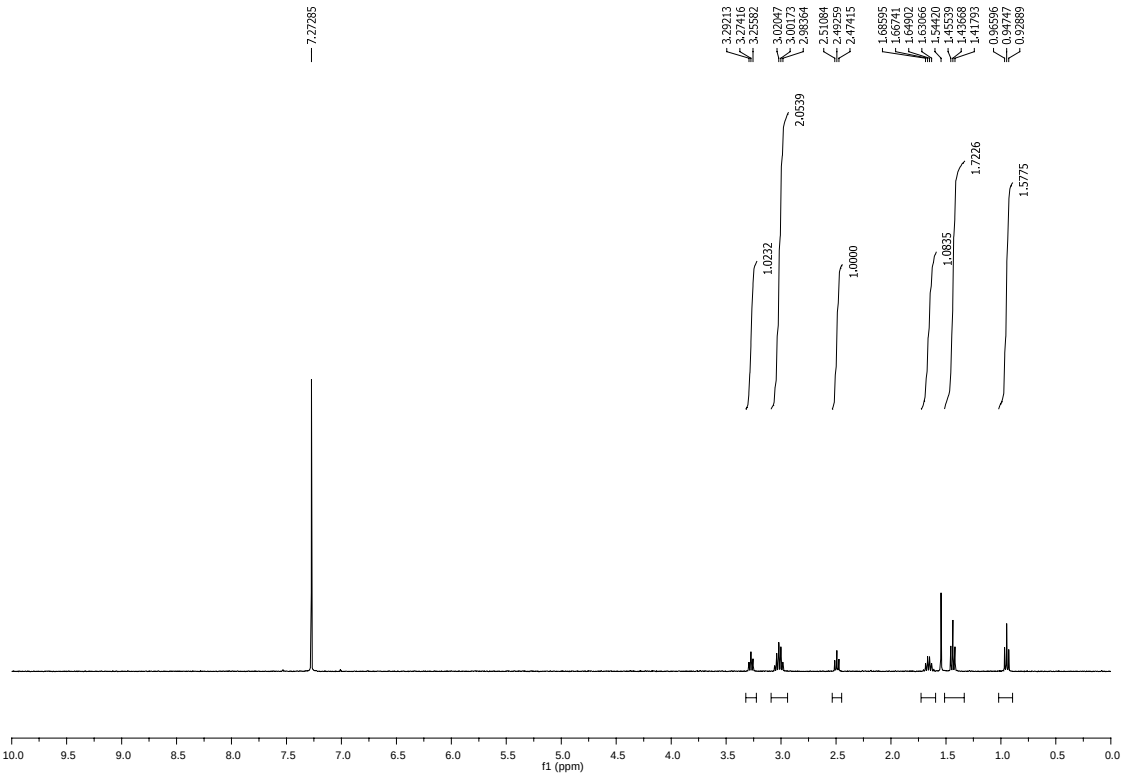




1-Ethanesulfonyl-hexan-3-one



Purification by column chromatography (50% EtOAc/petrol) and recrystallisation (CH_2Cl_2/petrol) gave 1-ethanesulfonyl-hexan-3-one as a white solid (123 mg, 0.64 mmol, 64%): m.p. 70-73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.29-3.26 (m, 2H), 3.06-2.98 (m, 4H), 2.51-2.47 (m, 2H), 1.58 (sextet, J = 7.5, 2H), 1.44 (t, J = 7.5, 3H), 0.95 (t, J = 7.5, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.8 (s), 48.2 (t), 46.0 (t), 44.7 (t), 34.1 (t), 17.2 (t), 13.7 (q), 6.72 (q); IR (solid) 2961, 2874, 1712, 1293, 1127 cm^{-1}; LRMS (CI) 193 (5, $[M+H]^+$), 109 (68), 99 (100); HRMS (ES) calcd for $C_8H_{17}O_3S$ $[M+H]^+$ 193.08984; observed 193.09007.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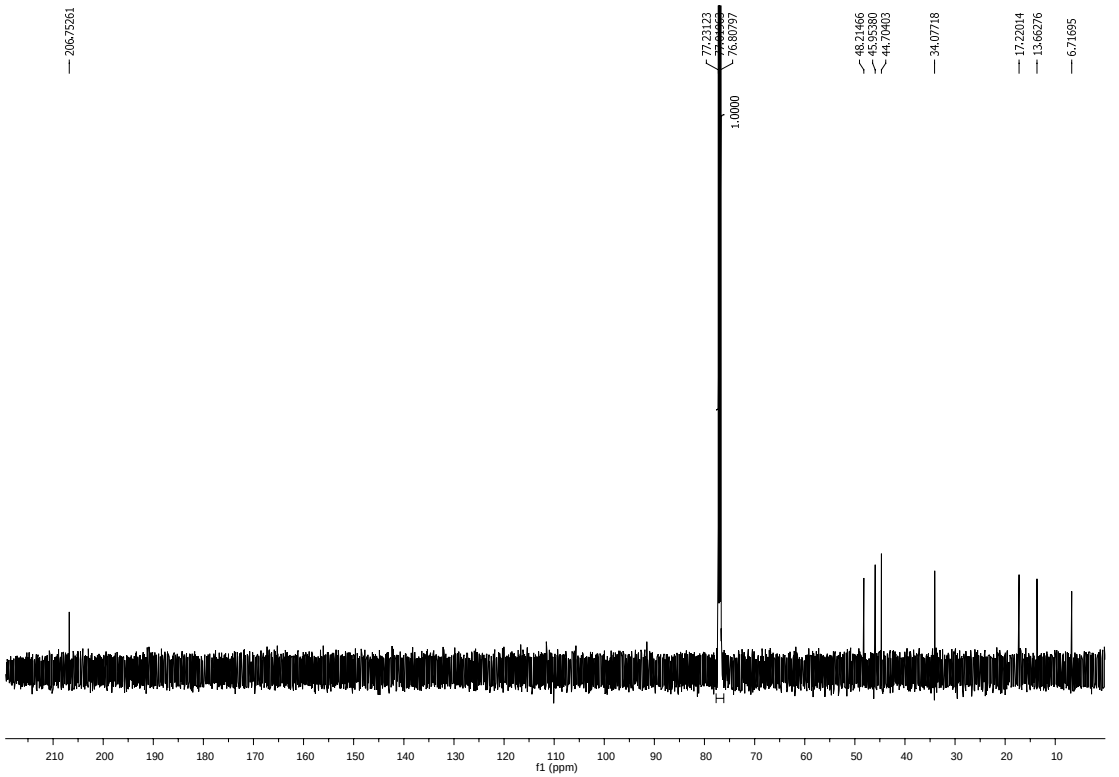
3.02047
3.00173
2.98364
2.51084
2.49259
2.47415
1.68595
1.66741
1.64902
1.63066
1.54420
1.45539
1.43668
1.41793
0.96596
0.94747
0.92889
2.0539
1.7226
1.5775
1.0232
1.0000
1.0835
f1 (ppm)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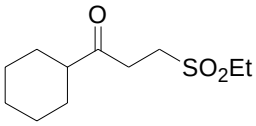
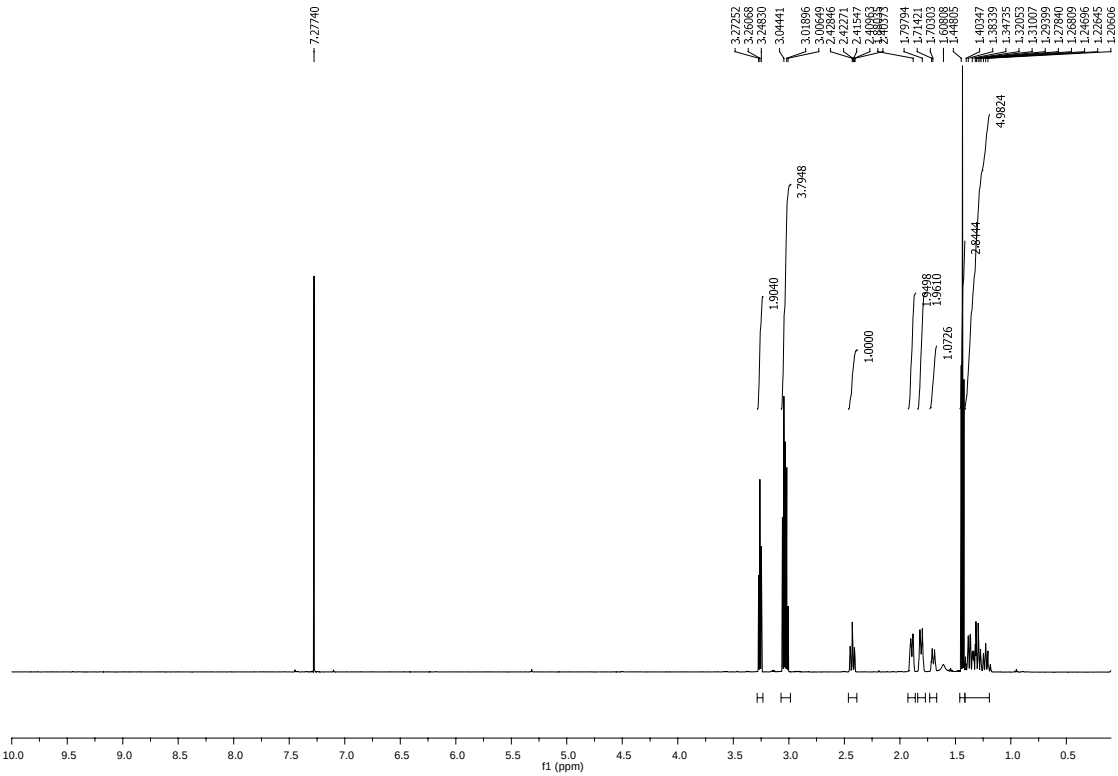
45.95380
44.70403
34.07718
17.22014
13.66276
6.71695
1.0000
f1 (ppm)

1-Cyclohexyl-3-ethanesulfonyl-propan-1-one



Purification by column chromatography (10-30% EtOAc/petrol) and recrystallisation (CH_2Cl_2/petrol) gave 1-cyclohexyl-3-ethanesulfonyl-propan-1-one as a white solid (132 mg, 0.57 mmol, 57%): m.p. 82-84 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.26 (m, 2H), 3.04 (m, 4H), 2.43 (tt, *J* = 11.0, 3.5, 1H), 1.92-1.87 (m, 2H), 1.83-1.78 (m, 2H), 1.70 (m, 1H), 1.44 (t, *J* = 7.5, 3H). 1.42-1.17 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.9 (s), 50.8 (d), 48.2 (t), 46.1 (t), 32.1 (t), 28.5 (t), 25.7 (t), 25.5 (t), 6.7 (q); IR (solid) 2929, 2854, 1702, 1300, 1130 cm^{-1}; LRMS (EI) 232 (12, $[M]^{+\cdot}$), 204 (55), 139 (100); HRMS (EI) calcd for $C_{11}H_{20}O_3S$ $[M]^{+\cdot}$ 232.11277; observed 232.11174.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2.38093
1.79794
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1.69888
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1.40347
1.38339
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1.32053
1.31007
1.29399
1.27840
1.26809
1.24696
1.22645
1.20606
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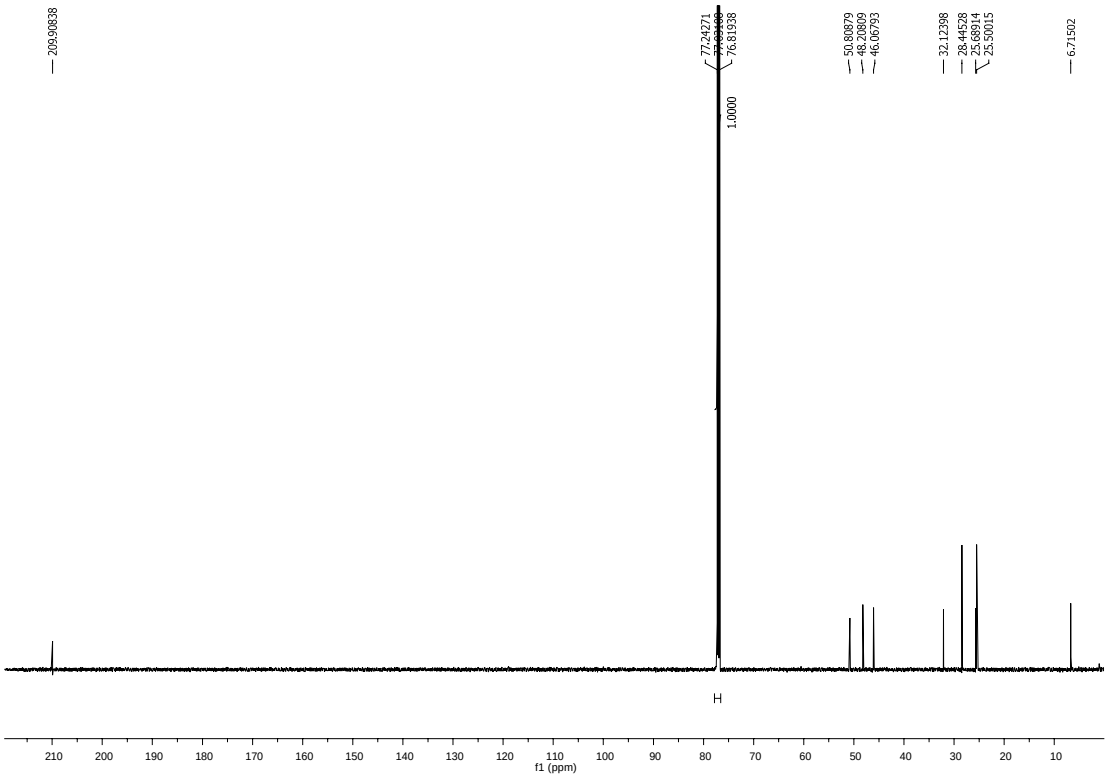
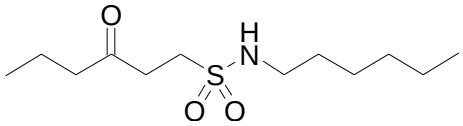
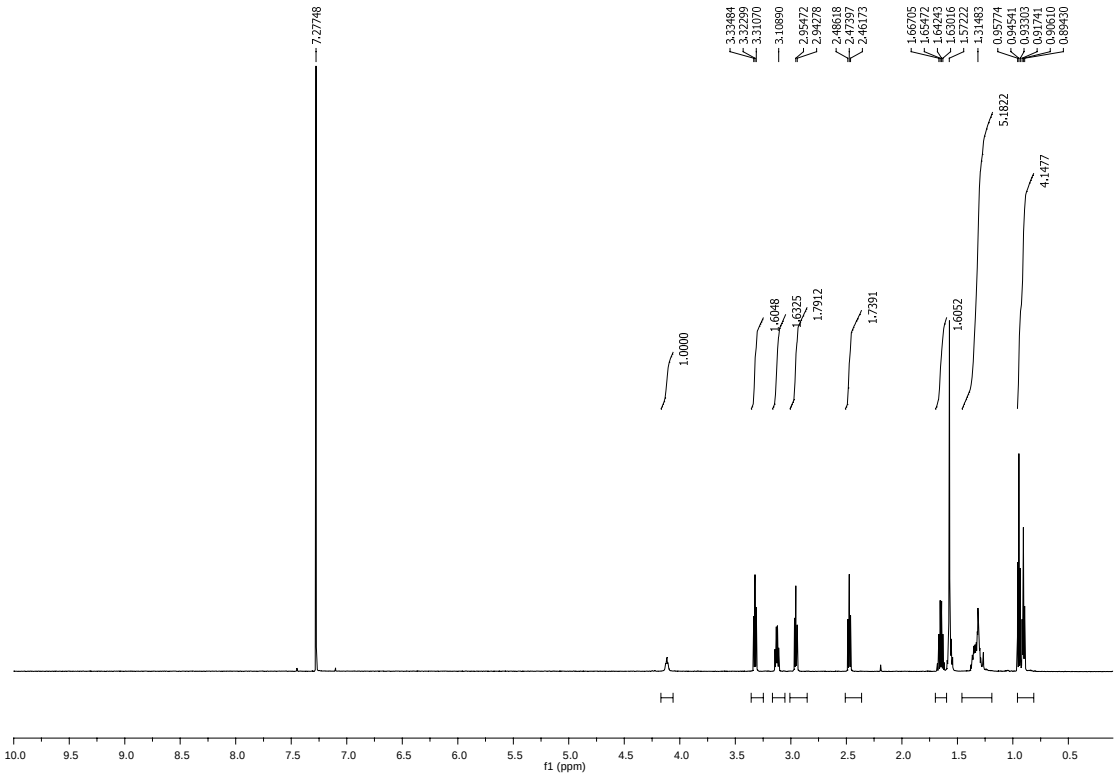
1.9040
1.9498
1.9610
1.0000
1.0726
f1 (ppm)


209.90838
77.24271
77.03368
76.81938
50.80879
48.20809
46.06793
32.12398
28.44528
25.68914
25.50015
6.71502
1.0000
f1 (ppm)

3-Oxo-hexane-1-sulfonic acid hexylamide



To a stirring solution of 3-oxo-hexane-1-sulfonic acid pentafluorophenyl ester **X** (0.29 mmol) in NMP (2.5 mL) was added a solution of *n*-hexylamine (0.64 mmol) in NMP (1 mL) at 0 °C dropwise. After addition was complete, the reaction mixture was left to warm to room temperature and stirred at room temperature for a further 4 h. To work-up, the reaction mixture was diluted with Et_2O (20 mL), washed with sat. LiCl (3 × 20 mL), sat. $NaHCO_3$ (3 × 20 mL), 2M HCl (3 × 20 mL), dried ($MgSO_4$) and the solvent removed *in vacuo* to afford 3-oxo-hexane-1-sulfonic acid hexylamide as a white solid (64 mg, 0.25 mmol, 82%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.12 (br t, *J* = 6.0 Hz, 1H, NH), 3.34-3.31 (m, 2H), 3.12 (q, *J* = 7.0 Hz, 2H), 2.97-2.94 (m, 2H), 2.47 (t, *J* = 7.5 Hz, 2H), 1.63 (sextet, *J* = 7.5 Hz, 2H), 1.57 (quintet, *J* = 7.5 Hz, 2H), 1.38-1.24 (m, 6H), 0.94 (t, *J* = 7.5 Hz, 3H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.1 (s), 46.6 (t), 44.8 (t), 43.4 (t), 36.5 (t), 33.3 (t), 30.2 (t), 26.3 (t), 22.5 (t), 17.2 (t), 14.0 (q), 13.7 (q); IR (solid) 3288, 2957, 2930, 2859, 1703, 1312, 1136 cm^{-1}; LRMS (CI) 264 (45, $[M+H]^+$), 102 (100); HRMS (CI) calcd for $C_{12}H_{26}NO_3S$ $[M+H]^+$ 264.1633; observed 264.1624.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2.47397
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1.65472
1.64243
1.63016
1.57222
1.31483
0.95774
0.94541
0.93303
0.91741
0.90610
0.89430
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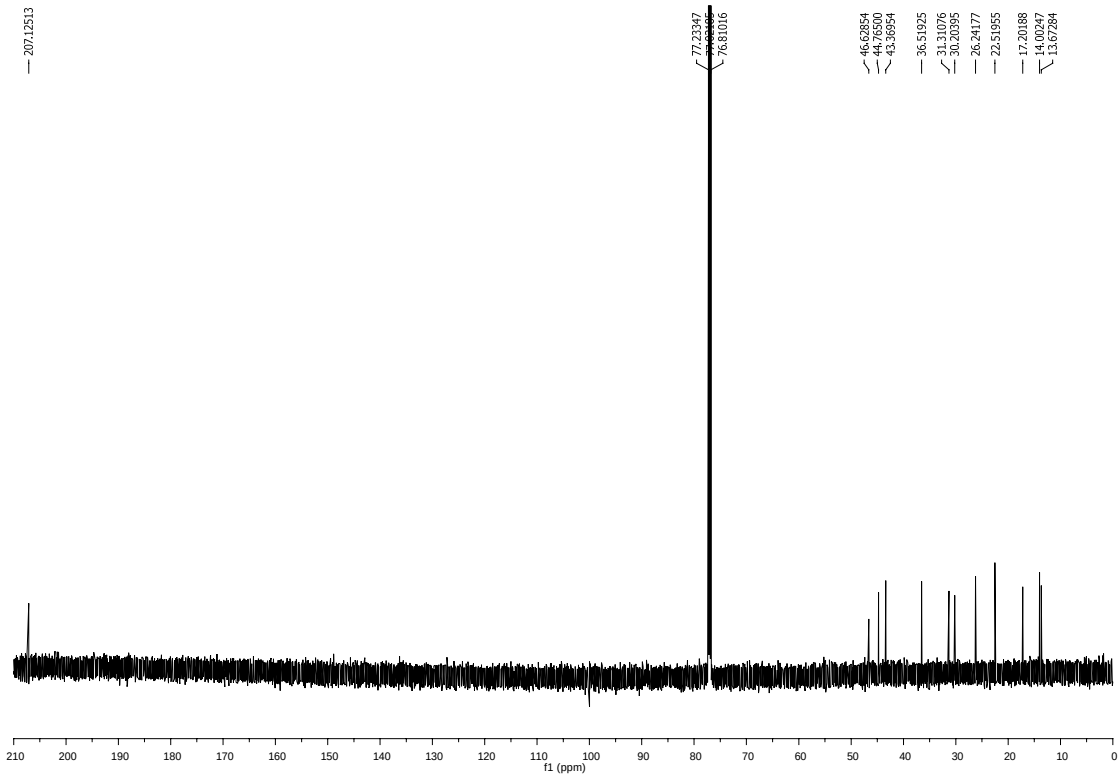
4.1477
1.0000
1.6048
1.6325
1.7912
1.7391
1.6052
f1 (ppm)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43.36954
36.51925
31.31076
30.20395
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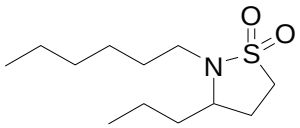
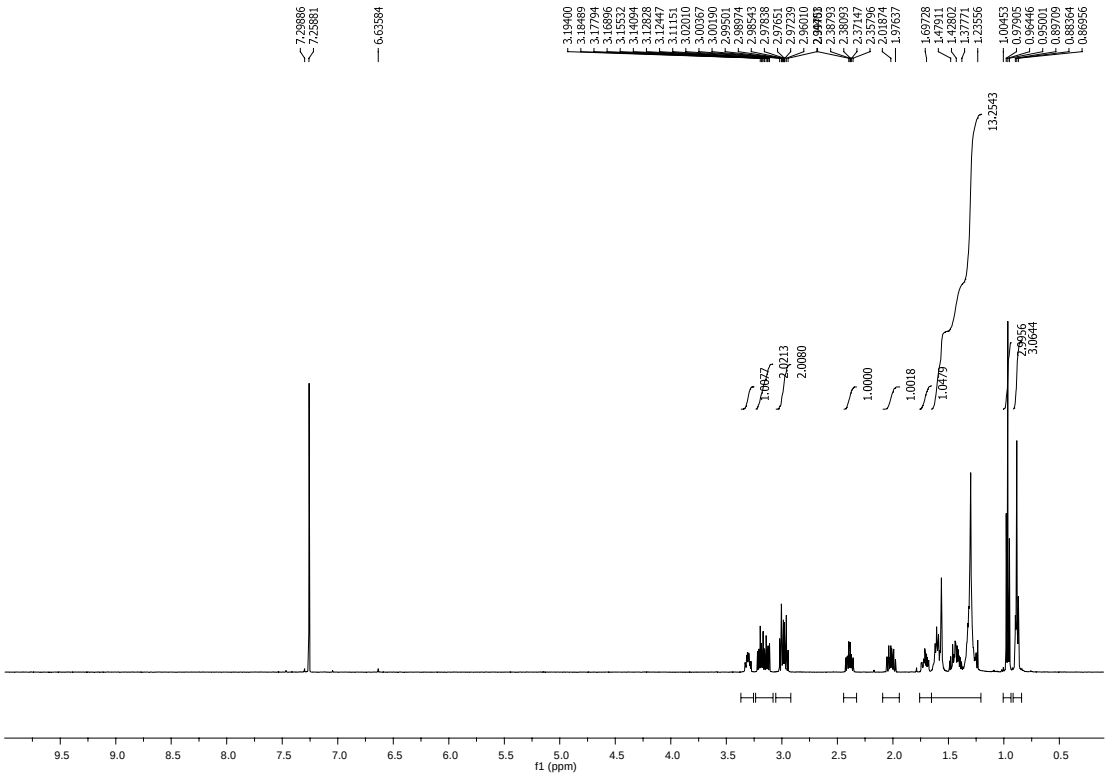
17.20188
14.00247
13.67284
f1 (ppm)

2-Hexyl-3-propyl-isothiazolidine 1,1-dioxide



A solution of 3-oxo-hexane-1-sulfonic acid hexylamide (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 further 20 min. The solvents were removed *in vacuo*, the crude residue diluted with EtOAc (50 mL), washed with sat. $NaHCO_3$ (3 × 100 mL) and 2M HCl (3 × 100 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude residue was purified by column chromatography (50% Et_2O/petrol) to afford 2-hexyl-3-propyl-isothiazolidine 1,1-dioxide as a colourless oil (41 mg, 0.17 mmol, 87%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.34-3.30 (m, 1H), 3.22 (ddd, *J* = 12.5, 8.0, 4.5 Hz, 1H), 3.16 (ddd, *J* = 14.5, 8.0, 7.0 Hz, 1H), 3.00 (app dddd, *J* = 21.0, 12.5, 9.0, 8.5 Hz, 2H), 2.41 (dddd, *J* = 18.0, 11.5, 6.5, 4.5 Hz, 1H), 2.03 (ddt, *J* = 21.0, 13.0, 8.0 Hz, 1H), 1.73 (dddd, *J* = 19.0, 11.0, 5.0, 4.0 Hz, 1H), 1.65-1.24 (m, 11H), 0.98 (t, *J* = 7.5 Hz, 3H). 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 58.1 (d), 46.5 (t), 43.8 (t), 36.0 (t), 31.5 (t), 28.6 (t), 26.7 (t), 25.0 (t), 22.6 (t), 17.8 (t), 14.1 (q), 14.1 (q); IR (thin film) 2957, 2930, 2872, 1305, 1134 cm^{-1}; LRMS (CI) 248 (60, $[M+H]^+$), 204 (100); HRMS (CI) calcd for $C_{12}H_{26}NO_2S$ $[M+H]^+$ 248.1684; observed 248.1686.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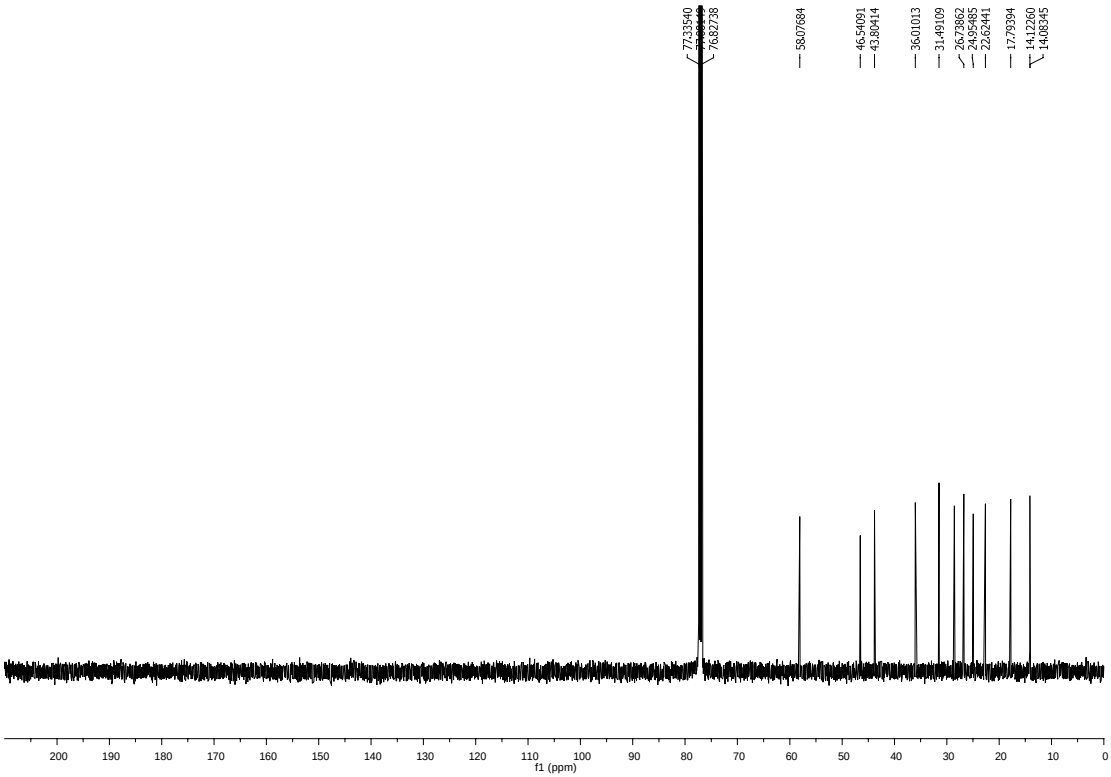
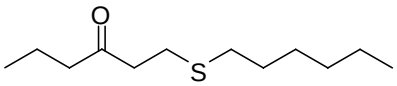
3.12447
3.11151
3.02010
3.00167
2.99501
2.98074
2.98543
2.97838
2.97651
2.97239
2.96010
2.38793
2.38093
2.37147
2.35796
2.01874
1.97637
1.69728
1.47911
1.42802
1.37271
1.23556
1.00453
0.97905
0.96446
0.95001
0.89709
0.88364
0.86956
13.2543
1.0827
2.4213
2.0080
1.0000
1.0018
1.0479
2.9956
3.0644
f1 (ppm)


77.33540
77.01240
76.82738
58.07684
46.54091
43.80414
36.01013
31.49109
26.73862
24.95485
22.62441
17.79394
14.12260
14.08345
f1 (ppm)

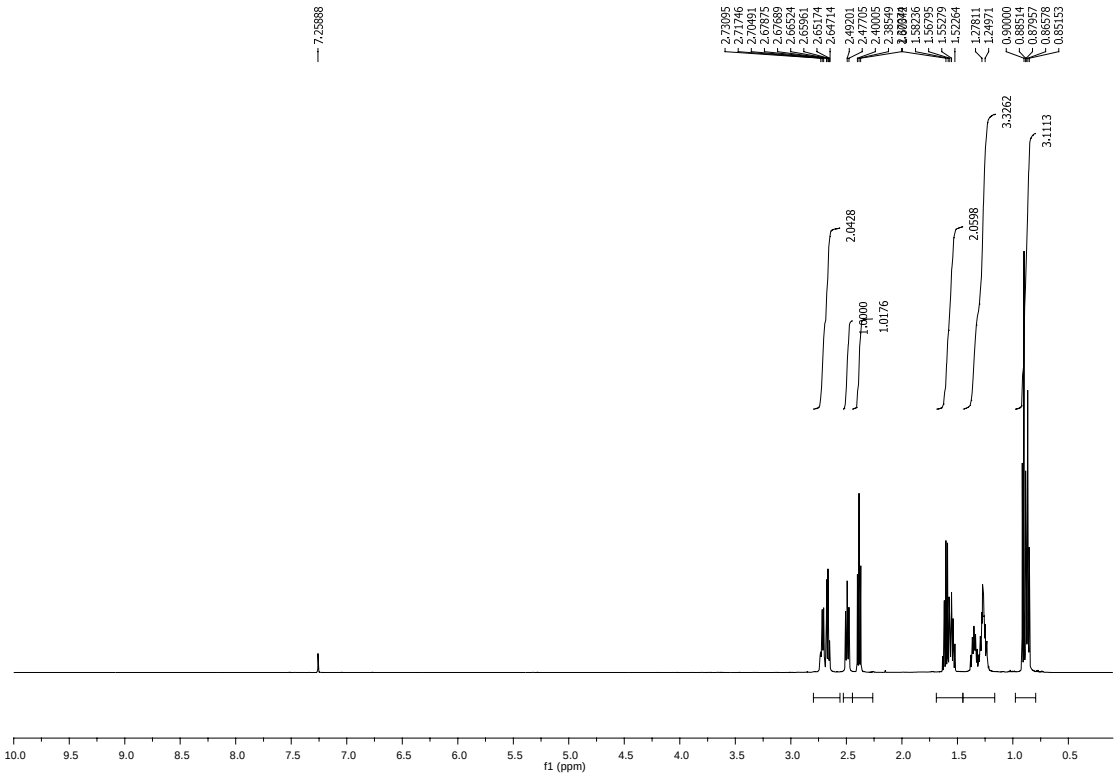
Typical procedure for the synthesis of *β*-keto-sulfides

To a stirring solution of *β*-keto-sulfone/sulfonate (1 mmol) in CH_2Cl_2 (3 mL) was added thiol (1.3 mmol) and then DBU (2 mmol) and the reaction mixture left to stir for 1 h. The solvent was removed *in vacuo* and the crude residue purified as described below to afford the desired *β*-keto-sulfide.

1-Hexylsulfanyl-hexan-3-one



Purification by column chromatography (60% CH_2Cl_2/petrol to neat CH_2Cl_2) afforded 1-hexylsulfanyl-hexan-3-one as a colourless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.71 (m, 2H), 2.67 (m, 2H), 2.49 (t, J = 7.5, 2H), 2.39 (t, J = 7.5 Hz, 2H), 1.62-1.55 (m, 4H), 1.38-1.23 (m, 6H), 0.90 (t, J = 7.5 Hz, 3H), 0.88 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.8 (s), 45.1 (d), 42.9 (t), 32.6 (t), 31.5 (t), 29.6 (t), 28.6 (t), 25.9 (t), 22.6 (t), 17.3 (t), 14.1 (q), 13.8 (q); IR (thin film) 2959, 2927, 1714 cm^{-1}; LRMS (CI) 217 (100, $[M+H]^+$), 131 (50); HRMS (CI) calcd for $C_{12}H_{25}OS$ $[M+H]^+$ 217.16260; observed 217.16211.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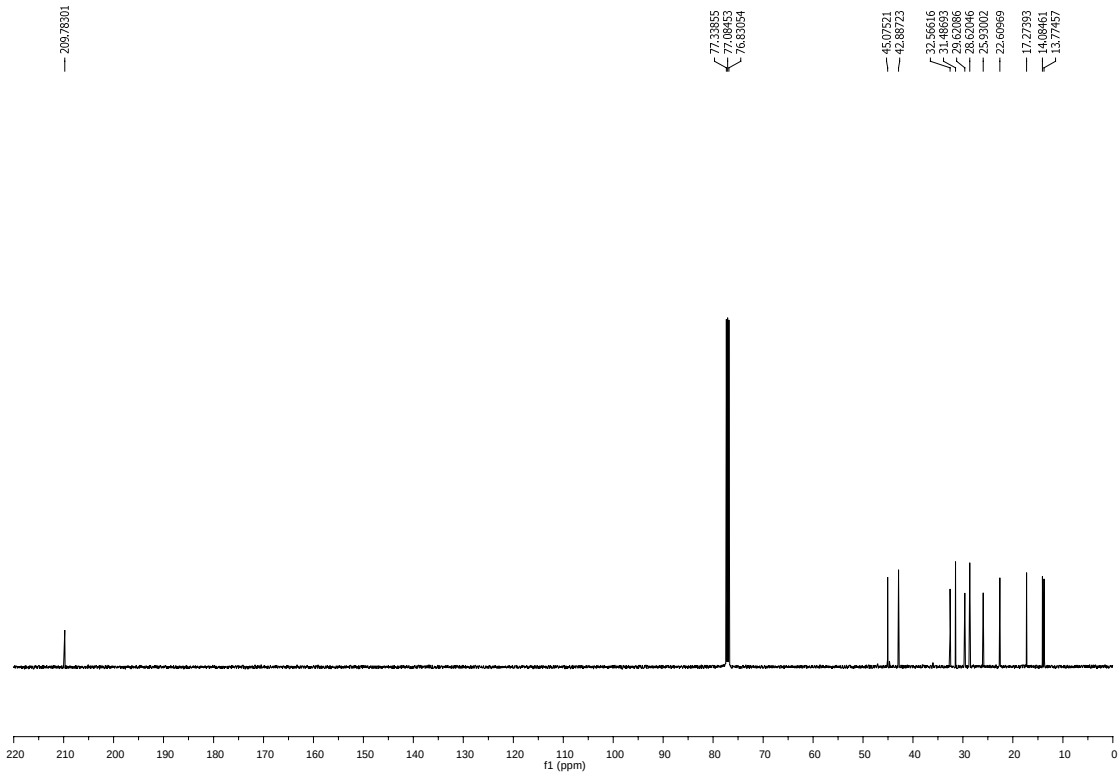
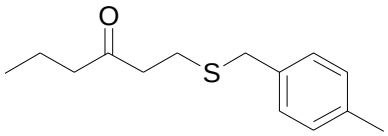
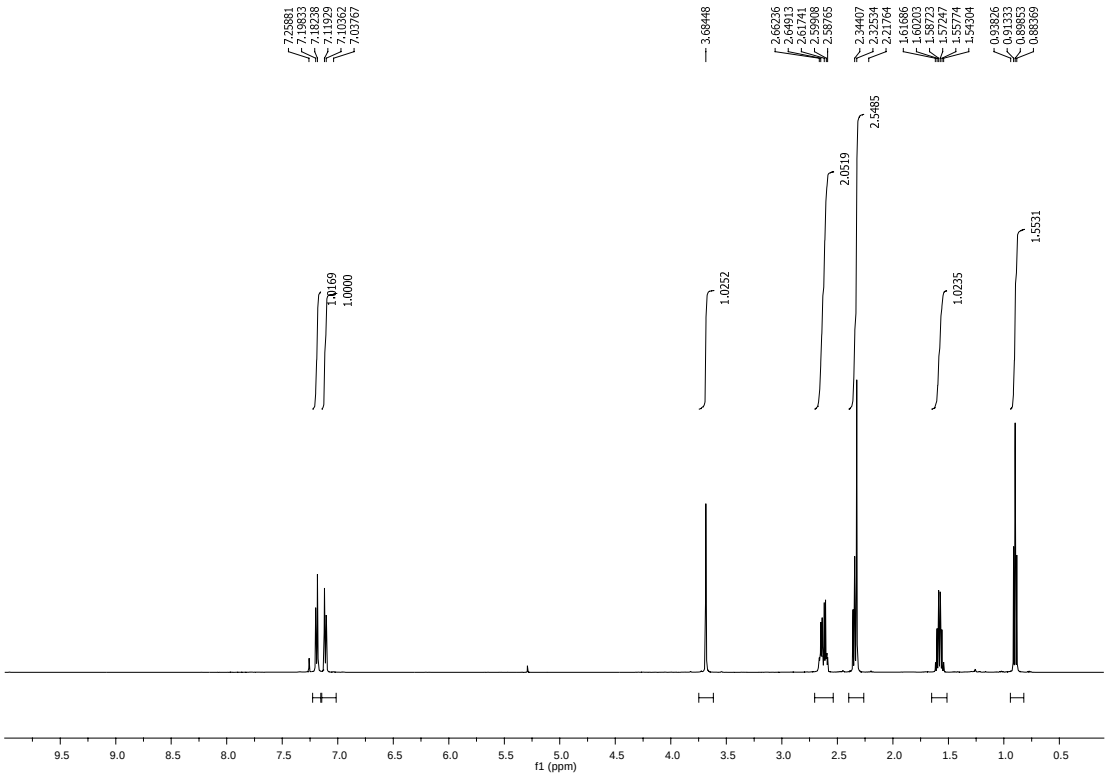
2.73095
2.71746
2.70491
2.67875
2.67599
2.66524
2.65961
2.65174
2.64714
2.49201
2.47705
2.40455
2.38549
1.58236
1.56795
1.55279
1.52264
1.27811
1.24971
0.90000
0.88514
0.87957
0.86578
0.85153
3.3262
3.1113
2.0428
2.0598
1.9000
1.0176
f1 (ppm)


209.78301
77.33855
77.08453
76.83054
45.07521
42.88723
32.56616
31.48693
29.62086
28.62046
25.93002
22.60969
17.27393
14.08461
13.77457
f1 (ppm)

1-(4-Methyl-benzylsulfanyl)-hexan-3-one



Purification by column chromatography (60% CH_2Cl_2/petrol to neat CH_2Cl_2) afforded 1-(4-methyl-benzylsulfanyl)-hexan-3-one as a colourless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 3.68 (s, 2H), 2.66-2.58 (m, 4H), 2.34 (t, *J* = 7.5 Hz, 2H), 2.32 (s, 3H), 1.59 (sextet, *J* = 7.5 Hz, 2H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.6 (s), 136.8 (s), 135.2 (s), 129.3 (d), 128.8 (d), 45.0 (t), 42.5 (t), 36.5 (t), 25.3 (t), 21.1 (q), 17.3 (t), 13.8 (q); IR (thin film) 2962, 2928, 2871, 1712, 1535, 1516 cm^{-1}; LRMS (CI) 237 (35, $[M+H]^+$), 236 (50, $[M]^+$), 107 (100); HRMS (CI) calcd for $C_{14}H_{21}OS$ $[M+H]^+$ 237.13131; observed 237.13180.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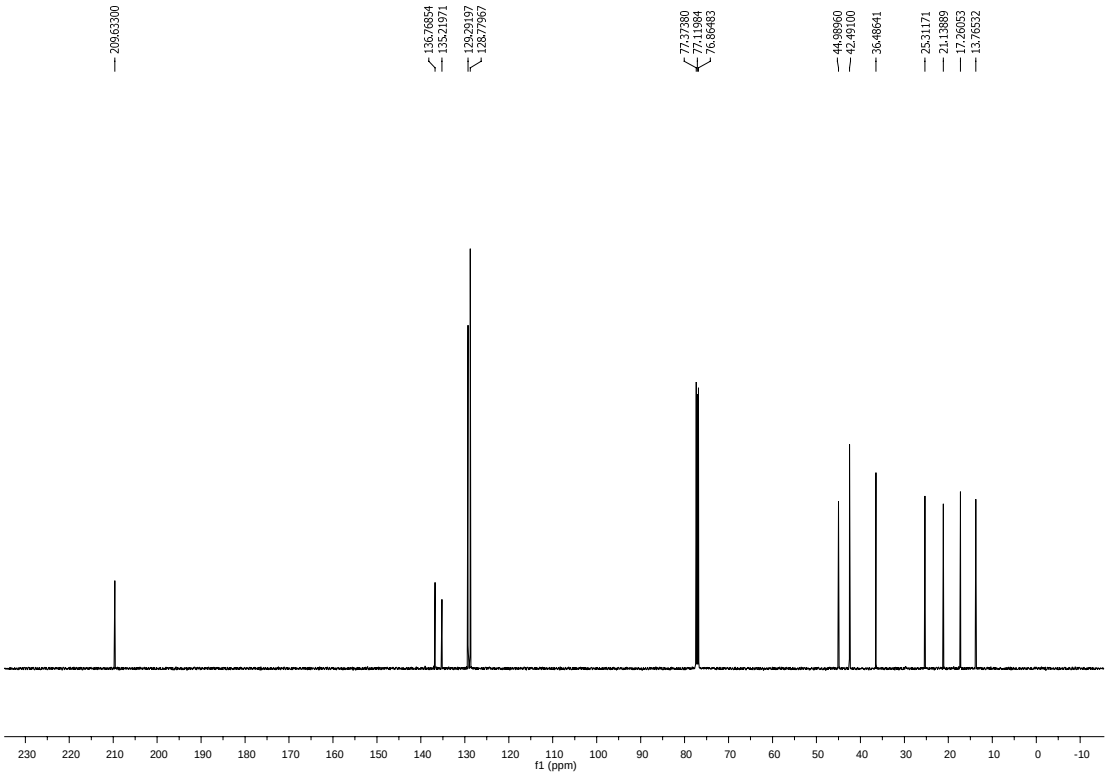
7.19833
7.18238
7.11929
7.10362
7.03767
3.68448
2.66236
2.64913
2.61741
2.59908
2.58765
2.34407
2.32534
2.21764
1.61686
1.60203
1.58723
1.57247
1.55774
1.54304
0.93826
0.91333
0.89853
0.88389
2.5485
2.0519
1.5531
1.0252
1.0235
1.0169
1.0000
f1 (ppm)


209.63300
136.76854
135.21971
129.29197
128.77967
77.37280
77.11984
76.86483
44.98960
42.49100
36.48641
25.31171
21.13889
17.26053
13.76532
f1 (ppm)

Reference

1. R. J. Fitzmaurice, J. M. Ahern and S. Caddick, *Org. Biomol. Chem.*, 2009, **7**, 235.