Rhodium Catalysed Intermolecular Chelation Controlled Alkene and Alkyne Hydroacylation: Synthetic Scope of β -S-Substituted Aldehyde Substrates

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General

IR spectra were recorded using NaCl discs. ^1H NMR spectra were obtained at 300 MHz, unless otherwise noted, with tetramethylsilane as an internal standard. J values are given in Hz. ^{13}C NMR spectra were obtained at 75 MHz, unless otherwise noted. All dry solvents were freshly distilled under nitrogen prior to use. Acetone was distilled from Drierite and stored over 4Å molecular sieves. Petrol refers to the fraction of petroleum ether obtained between 40-60 °C. All glassware was dried in an oven and allowed to cool under nitrogen prior to use. All reactions were carried out under argon unless otherwise stated. All commercial reagents were used as obtained. Flash chromatography was conducted under medium pressure, using matrix 60 silica.

General procedure for aldehyde reactions as exemplified by 3-ethanesulfanylpropionaldehyde, Table 3 entry 1 substrate

Following the general procedure as described by Weber,¹ employing sodium hydride in place of sodium. In a representative example; to a neat solution of ethane thiol (13.0 g, 226 mmol) and acrolein (10.0 g, 178 mmol) was added NaH (36 mg, 0.89 mmol), cautiously over 30 minutes, (**care!** extremely exothermic reaction ensues). The resulting mixture was stirred at room temperature for 16 hours before removal of volatiles in *vacuo* and subsequent short path distillation under reduced pressure afforded the aldehyde as a colorless oil, which was used directly in subsequent hydroacylation reactions (14 g, 62 %); δ_{H} (300 MHz, CDCl_3) 9.72 (1 H, s), 2.78-2.72 (2 H, m), 2.70-2.62 (2 H, m), 2.50 (2 H, q, J 7.6), 1.20 (3 H, t, J 7.6).

General procedure for hydroacylation reactions as exemplified by methyl 6-ethanesulfanyl-4-oxo-hexanoate, Table 3 entry 1

Acetone (2.0 mL) was added under argon to pre-catalyst $[\text{Rh}(\text{nbd})(\text{dppe})]\text{ClO}_4$ (10 mg, 0.015 mmol). The catalyst was activated *in situ* by bubbling through the solution with H_2 for 2 minutes until a colour change from orange to yellow was observed.

¹ Weber, H. DE855704, 1952.

After this time the solution was purged with argon. To this solution 3-(ethanesulfanyl)propionaldehyde (17 μ L, 0.15 mmol) was added followed by methacrylate (65 μ L, 0.7 mmol). The resulting mixture was stirred and heated at 55 $^{\circ}$ C for 16 hours. After this time the solution was reduced *in vacu* and purified by flash chromatography (1:4 EtOAc:Petrol) to give title compound as a colourless oil (20 mg, 68 %); δ_{H} (300 MHz, CDCl_3) 3.61 (3H, s), 2.71-2.65 (4H, m), 2.59-2.51 (2H, m), 2.48 (2H, q, J 7.3), 1.19 (3H, t, J 7.3); δ_{C} (75 MHz, CDCl_3) 207.5, 173.6, 52.3, 43.2, 37.7, 28.0, 26.6, 25.7, 15.1; ν_{max} (film) / cm^{-1} 2927, 1737, 1719, 1438; m/z (EI+) 204 (15 %, M^+), 186, 143, 111; found 204.0814 $[\text{M}]^+$ $\text{C}_9\text{H}_{16}\text{O}_3\text{S}$ requires 204.0815.

3-phenylsulfanyl-propionaldehyde, Table 3 entry 2 substrate

The general procedure for the aldehyde preparation was followed employing benzenethiol (12.3 g, 111 mmol), acrolein (5.0 g, 89 mmol), and NaH (18 mg, 0.44 mmol) to yield the tile compound as a colourless oil (11.4 g, 66%); δ_{H} (300 MHz, CDCl_3) 9.69 (1 H, s), 7.32-7.05 (5 H, m), 3.11 (2H, t, J 7.2), 2.70 (2 H, t, J 7.2). Used directly in subsequent hydroacylation reactions.

Methyl 4-oxo-6-phenylsulfanyl-hexanoate, Table 3 entry 2

The general procedure for the hydroacylation reaction was followed employing pre-catalyst $[\text{Rh}(\text{nbd})\text{dppe}]\text{ClO}_4$ (10 mg, 0.014 mmol), 3-(phenylsulfanyl)-propionaldehyde (23 mg, 0.14 mmol) and methacrylate (65 μ L, 62 mg, 0.70 mmol). Heated at 55 $^{\circ}$ C for 16 hours to give the title compound as a colourless oil (33 mg, 92 %) Data in accordance with the literature;² δ_{H} (300 MHz, CDCl_3) 7.30-7.08 (5H, m), 3.59 (3H, s), 3.59 (2H, J 7.2), 2.71 (2H, t, J 7.2), 2.67-2.60 (2H, m) 2.55-2.48 (2H, m); δ_{C} (75 MHz, CDCl_3) 207.5, 173.6, 52.3, 43.2, 37.7, 28.0, 26.6, 25.7, 15.1; m/z (EI+) 252 (100 %, M^+), 221, 165, 137; found 252.0816 $[\text{M}]^+$ $\text{C}_{13}\text{H}_{16}\text{O}_3\text{S}$ requires 252.0816.

² Grimm, E. L.; Zschwiesche, R.; Reissig, H.-U. *J. Org. Chem.* **1985**, *50*, 5543-5545.

3-Ethanesulfanyl-2-methyl-propionaldehyde, Table 3 entry 3 substrate

The general procedure for the aldehyde preparation was followed employing ethane thiol (1.9 g, 30.32 mmol), methacrolein (1.7 g, 24.25 mmol), and NaH (10 mg, 0.24 mmol) to yield the title compound as a colourless oil (2.40 g, 67%); δ_{H} (300 MHz, CDCl_3) 9.62 (1 H, d, J 1.5), 2.85-2.75 (1 H, m), 2.60-2.42 (2 H, m), 2.49 (2 H, q, J 7.6), 1.20 (3 H, t, J 7.6), 1.15 (3 H, d, J 6.9). Used directly in subsequent hydroacylation reactions.

6-Ethanesulfanyl-5-methyl-4-oxo-hexanoic acid methyl ester, Table 3 entry 3

The general procedure for the hydroacylation reaction was followed employing pre-catalyst $[\text{Rh}(\text{nbd})(\text{dppe})]\text{ClO}_4$ (7 mg, 0.01 mmol), acetone (2.0 mL), 3-ethanesulfanyl-2-methyl-propionaldehyde (26 μL , 0.2 mmol) and methyl acrylate (70 μL , 0.6 mmol). Heated at 55 $^{\circ}\text{C}$ for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (36 mg, 83 %); ν_{max} (film) $/\text{cm}^{-1}$ 3045, 2977, 1742, 1427, 1264, 753; δ_{H} (300 MHz; CDCl_3) 3.61 (3H, s), 2.86-2.64 (4H, m), 2.57-2.43 (5H, m), 1.20-1.10 (6H, m); δ_{C} (75 MHz; CDCl_3) 210.7, 172.9, 51.5, 46.1, 36.0, 33.9, 27.3, 26.4; m/z (EI) 218 (5 %, M), 157 (90%, M- $\text{H}_2\text{CO}_2\text{Me}$), 125 (100%, EtSHOMe); found $[\text{M}]^+$ 218.0971, $\text{C}_{10}\text{H}_{18}\text{O}_3\text{S}$ requires 218.0972.

3-Ethanesulfanyl-butyraldehyde, Table 3 entry 4 substrate

The general procedure for the aldehyde preparation was followed employing ethane thiol (5.5 g, 88.75 mmol), crotonaldehyde (5.0 g, 71.00 mmol), and NaH 15 mg, 0.41 mmol) to yield the title compound as a colourless oil (7.3 g, 70%); δ_{H} (300 MHz, CDCl_3) 9.71 (1 H, t, J 1.9), 3.23 (1 H, dq, J 7.6, 6.7), 2.67-2.50 (3 H, m), 2.52 (2 H, q,

J 7.6), 1.29 (3 H, d, *J* 6.7), 1.20 (3 H, d, *J* 7.6). Used directly in subsequent hydroacylation reactions.

6-Ethanesulfanyl-4-oxo-heptanoic acid methyl ester, Table 3 entry 4

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (9 mg, 0.013 mmol), acetone (2.0 mL), 3-ethanesulfanyl-butyraldehyde (33 mg, 0.25 mmol) and methyl acrylate (112 μ L, 0.75 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (42 mg, 77 %); ν_{max} (film) /cm⁻¹ 2950, 1736, 1652, 1556, 899, 731; δ_{H} (300 MHz; CDCl₃) 3.67 (3H, s), 3.34-3.22 (1H, m), 2.79-2.71 (4H, m), 2.62-2.52 (4H, m), 1.28 (3H, d, *J* 6.8), 1.24 (3H, t, *J* 7.4); δ_{C} (75 MHz; CDCl₃) 206.7, 173.0, 51.7, 50.0, 37.8, 34.6, 27.5, 24.5, 21.5, 14.6; *m/z* (EI) 218 (10 %, M), 115 (90%, M-EtSMeCHCH₂) 89 (100% M-CH₂COCH₂CH₂CO₂Me); found [M]⁺ 218.0968, C₁₀H₁₈O₃S requires 218.0971.

3-Ethanesulfanyl-3-phenyl-proionaldehyde, Table 3 entry 5 substrate

The general procedure for the aldehyde preparation was followed employing ethane thiol (2.2 g, 34.0 mmol), cinnamaldehyde (3.0 g, 22.0 mmol), and NaH (8 mg, 0.22 mmol) to yield the tile compound as a colourless oil (2.8 g, 66%); δ_{H} (300 MHz, CDCl₃) 9.63 (1 H, t, *J* 1.8), 7.40-71.5 (5 H, m), 4.29 (1 H, t, *J* 7.6), 2.88 (2 H, m), 2.36-2.18 (2 H, m), 1.09 (3 H, t, *J* 7.6). Used directly in subsequent hydroacylation reactions.

6-Ethanesulfanyl-4-oxo-6-phenyl-hexanoic acid methyl ester, Table 3 entry 5

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (5 mg, 0.0075 mmol), acetone (2.0 mL), 3-ethanesulfanyl-3-phenyl-propionaldehyde (29 mg, 0.15 mmol) and methyl acrylate

(67 μ L, 0.45 mmol). Heated at 55 $^{\circ}$ C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (37 mg 87 %); ν_{max} (film) / cm^{-1} 3060, 1709, 1658, 1411, 1252, 903, 718; δ_{H} (300 MHz; CDCl_3) 7.29-7.12 (5H, m), 4.29 (1H, t, J 7.3), 3.56 (3H, s), 2.93 (2H, d, J 7.3), 2.71-2.43 (4H, m), 2.30-2.18 (2H, m), 1.08 (3H, t, J 7.4); δ_{C} (75 MHz; CDCl_3) 205.2, 172.5, 141.4, 128.1 (2 CH), 127.2 (2 CH), 126.8, 51.3, 48.8, 43.3, 37.5, 27.1, 24.9, 13.9; m/z (EI) 280 (10 %, M), 115 (100%, M-EtSPhCHCH₂); found $[M]^+$ 280.1126, $\text{C}_{15}\text{H}_{20}\text{O}_3\text{S}$ requires 280.1128.

3-Ethanesulfanyl-2-methyl-butyraldehyde, Table 3 entry 6 substrate

The general procedure for the aldehyde preparation was followed employing ethane thiol (4.6 g, 74.3 mmol), 2-methylcrotonaldehyde (5.0 g, 59.43 mmol), and NaH (12 mg, 0.30 mmol) to yield the tile compound as a colourless oil as a 1:1 mixture of diastereomers (4.5 g, 47 %); δ_{H} (300 MHz, CDCl_3) ; 9.67 (0.5 H, d, J 1.8), 9.61 (0.5 H, d, J 1.8), 3.19-3.05 (1 H, m), 2.67-2.40 (3 H, m), 1.29 (3 H, d J 7.3) 1.19 (3 H, t, J 7.6), 1.10 (1.5 H, d, J 7.2), 1.10 (1.5 H, d, J 7.1). Used directly in subsequent hydroacylation reactions.

Methyl 6-ethanesulfanyl-5-methyl-4-oxo-heptanoate, Table 3 entry 6

The general procedure for the hydroacylation reaction was followed employing pre-catalyst $[\text{Rh}(\text{nbd})\text{dppe}]\text{ClO}_4$ (10 mg, 0.014 mmol), 3-(ethanesulfanyl)-2-methylbutryaldehyde (20 mg, 0.14 mmol) and methacrylate (65 μ L, 62 mg, 0.70 mmol). Heated at 55 $^{\circ}$ C for 20 hours to give the title compound as a colourless oil as a 1:1 mixture of diastereomers (25 mg, 77 %); δ_{H} (300 MHz, CDCl_3) (Major Diastereomer) 3.61 (3H, s), 3.07-2.92 (1H, m), 2.80-2.72 (2H, m), 2.61-2.42 (5H, m), 1.24-1.14 (6H, m), 1.07 (3H, d, J 6.7); δ_{H} (300 MHz, CDCl_3) (Minor Diastereomer) 3.61 (3H, s), 3.07-2.92 (1H, m), 2.80-2.72 (2H, m), 2.61-2.42 (5H, m), 1.24-1.105 (9H, m); δ_{C} (75 MHz, CDCl_3) 211.1, 210.8, 173.3, 173.3, 51.8, 51.7, 51.1, 42.3, 40.9, 37.1, 36.8, 31.9, 28.3, 27.62, 27.59, 25.3, 24.8, 20.3, 18.1, 14.8, 14.73, 14.68, 13.0;

$\nu_{\max}$ (film) / cm^{-1} 2970, 2903, 1741, 1714, 1438; m/z (EI+) 232 (5 %, M+), 171, 138, 115; found 232.1129 $[\text{M}]^+$ $\text{C}_{11}\text{H}_{20}\text{O}_3\text{S}$ requires 232.1128.

(E)-6-Methanesulfanyl-4-oxo-hex-2-enoic acid ethyl ester, 4

The general procedure for the hydroacylation reaction was followed employing pre-catalyst $[\text{Rh}(\text{nbd})(\text{dppe})]\text{ClO}_4$ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μL , 0.3 mmol) and ethyl propiolate (152 μL , 1.5 mmol). Heated at 55 $^\circ\text{C}$ for 1 hour. Flash chromatography (CH_2Cl_2) yielded the title compound as a yellow oil (44 mg, 73 %); $\nu_{\max}$ (film) / cm^{-1} 2930, 1697 1629, 1245, 1030; δ_{H} (300 MHz; CDCl_3) 7.00 (1H, d, J 16.0), 6.63 (1H, d, J 16.0), 4.20 (2H, q, J 7.1), 2.89 (2H, t, J 7.5), 2.73 (2H, t, J 7.5), 2.06 (3H, s), 1.26 (3H, t, J 7.1); δ_{C} (75 MHz; CDCl_3) 198.2, 165.8, 139.3, 131.7, 61.9, 41.7, 28.2, 16.3, 14.5; m/z (EI) 202 (15 %, M), 157 (40%, M- OCH_2CH_3), 61 (100%, M- $\text{MeSCH}_2\text{CH}_2\text{COCHCHC}$); found $[\text{M}]^+$ 202.0658, $\text{C}_9\text{H}_{14}\text{O}_3\text{S}$ required 202.0655.

(E)-1-Methanesulfanyl-non-4-en-3-one, Table 5 entry 1

The general procedure for the hydroacylation reaction was followed employing pre-catalyst $[\text{Rh}(\text{nbd})(\text{dppe})]\text{ClO}_4$ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μL , 0.3 mmol) and 1-hexyne (160 μL , 1.5 mmol). The resulting mixture was stirred and heated at 55 $^\circ\text{C}$ for 1 hour. Flash chromatography (1:4 EtOAc:Petrol) yielded the title compound as a yellow oil (54 mg, 98%); $\nu_{\max}$ (film) / cm^{-1} 3049, 1704, 1658, 1421, 1267, 733; δ_{H} (300 MHz; CDCl_3) 6.86 (1H, dt, J 15.9, 6.9), 6.10 (1H, dt, J 15.9, 1.4), 2.87-2.73 (4H, m), 2.26-2.18 (2H, m), 2.12 (3H, s), 1.48-1.30 (4H, m), 0.91 (3H, t, J 7.2); δ_{C} (75 MHz; CDCl_3) 198.4, 148.1, 129.9, 39.6, 32.1, 30.0, 28.2, 22.1, 15.7, 13.7; m/z (EI) 186 (20 %, M), 129 (40%, M- $\text{C}_3\text{H}_6\text{CH}_3$) 55 (100%, M- $\text{MeSCH}_2\text{CH}_2\text{COCHCH}_3$); found $[\text{M}]^+$ 186.1073, $\text{C}_{10}\text{H}_{18}\text{O}$ requires 186.1073.

(E)-8-Chloro-2-methanesulfanyl-oct-4-en-3-one, Table 5 entry 3

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μL, 0.3 mmol) and 5-chloro-1-pentyne (158 μL, 1.5 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (53 mg, 85 %); ν_{max} (film) /cm⁻¹ 3049, 1632, 1416, 1252, 733; δ_{H} (300 MHz; CDCl₃) 6.83 (1H, dt, *J* 15.9, 6.9), 6.17 (1H, dt, *J* 15.9, 1.5), 3.56 (2H, t, *J* 6.4), 2.88-2.74 (4H, m), 2.45-2.37 (2H, m), 2.12 (3H, s), 1.99-1.91 (2H, m); δ_{C} (75 MHz; CDCl₃) 197.7, 145.1, 130.3, 43.5, 39.6, 30.2, 29.0, 27.8, 15.4; ν_{max} (film) /cm⁻¹ 1669 (C=O), 735 (C-Cl); *m/z* (EI) 206 (20%, M), 159 (60% M-OCO) 131 (100%, M-CH₄CO₂Me); found [M]⁺ 206.0527, C₉H₁₅ClOS requires 206.0527.

(E)-8-Hydroxy-1-methanesulfanyl-oct-4-en-3-one, Table 5 entry 5

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μL, 0.3 mmol) and 4-pentyn-1-ol (56 μL, 0.6 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:1, EtOAc:Petrol) yielded the title compound as a colourless oil (54 mg, 95 %); ν_{max} (film) /cm⁻¹ 3415, 2921, 1669, 1618, 1399, 1051; δ_{H} (300 MHz; CDCl₃) 6.86 (1H, dt, *J* 15.9, 6.9), 6.12 (1H, dt, *J* 15.9, 1.5), 3.65 (2H, t, *J* 6.3), 2.86-2.81 (2H, m), 2.76-2.71 (2H, m), 2.35-2.28 (2H, m), 2.10 (3H, s), 1.86 (1H, br. s), 1.76-1.67 (2H, m); δ_{C} (75 MHz; CDCl₃) 197.9, 146.7, 129.6, 61.2, 39.1, 30.2, 28.2, 27.6, 15.1; *m/z* (EI) 188 (3%, M), 140 (80%, M-MeSH) 71 (100% M-MeSCH₂CH₂CO); found [M]⁺ 218.0968, C₁₀H₁₈O₃S requires 218.0971.

(E)-8-(tert-Butyl-dimethyl-silyloxy-1-methanesulfanyl-oct-4-en-3-one, Table 5 entry 6

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and *t*-butyl-dimethyl-pent-4-ynyloxy-silane (136 mg, 0.6 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:3, EtOAc:Petrol) yielded the title compound as a pale yellow oil (81 mg, 89 %); ν_{max} (film) /cm⁻¹ 2921, 1653, 1345, 667; δ_{H} (300 MHz; CDCl₃) 6.86 (1H, dt, *J* 15.9, 6.9), 6.09 (1H, dt, *J* 15.9, 1.5), 3.60 (2H, t, *J* 6.1), 2.85-2.71 (4H, m), 2.32-2.24 (2H, m), 2.09 (3H, s), 1.70-1.61 (2H, m), 0.86 (9H, s), 0.02 (6H, s); δ_{C} (75 MHz; CDCl₃) 197.8, 147.1, 129.5, 61.5, 39.1, 30.4, 28.4, 27.6, 25.2 (3 CH₃), 17.6, 15.2, -5.9 (2 CH₃); *m/z* (CI +) 303 (100 %, M+H), 255 (40%, M-MeS); found [M]⁺ 303.1809, C₁₅H₃₀O₂SSi requires 303.1809.

(E)-1-Methanesulfanyl-8-(tetrahydro-pyran-2-yloxy)-oct-4-en-3-one, Table 5 entry 7

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and 2-pent-4-ynyloxy-tetrahydro-pyran (118 mg, 0.6 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:3, EtOAc:Petrol) yielded the title compound as a pale yellow oil (76 mg, 93 %); ν_{max} (film) /cm⁻¹ 2961, 2865, 1686, 1276, 911; δ_{H} (300 MHz; CDCl₃) 6.88 (1H, dt, *J* 15.9, 6.9), 6.11 (1H, dt, *J* 15.9, 1.5), 4.55 (1H, t, *J* 3.0), 3.87-3.71 (2H, m), 3.52-3.36 (2H, m), 2.87-2.71 (4H, m), 2.36-2.29 (2H, m), 2.10 (3H, s), 1.83-1.69 (4H, m), 1.58-1.47 (4H, m); δ_{C} (75 MHz; CDCl₃) 198.3, 147.3, 130.0, 98.7, 66.3, 62.2, 39.5, 30.4, 29.2, 28.1, 27.9, 25.2, 19.4, 15.6; *m/z* (EI) 272 (5%, M), 225 (40%, M-MeS), 172 (80%, M-OTHP), 169 (100% M-MeSCH₂CH₂CO); found [M]⁺ 272.1442, C₁₄H₂₄O₃S requires 272.1446.

(E)-10-Methanesulfanyl-dec-6-ene-2,8-dione Table 5 entry 8

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and hept-6-yn-2-one (66 mg, 0.6 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (44 mg, 69%); ν_{max} (film) /cm⁻¹ 3049, 2978, 2295, 1704, 1673, 1617, 1411, 1252, 903, 744; δ_{H} (300 MHz; CDCl₃) 6.82 (1H, dt, *J* 15.9, 6.6), 6.11 (1H, dt, *J* 15.9, 1.5), 2.88-2.74 (4H, m), 2.47 (2H, t, *J* 7.2), 2.28-2.20 (2H, m), 2.14 (3H, s), 2.12 (3H, s), 1.81-1.71 (2H, m); δ_{C} (75 MHz; CDCl₃) 207.8, 198.1, 146.6, 130.3, 42.3, 39.6, 31.4, 29.8, 28.0, 21.6, 15.6; *m/z* (EI+) 214 (5%, M⁺), 73 (90%, M-COCHCH(CH₂)₃COCH₃), 59 (100%, M-CH₂COCHCH(CH₂)₃COCH₃); found 214.1022 [M]⁺ C₁₁H₁₈O₂S requires 214.1022.

(E)-1-Methanesulfanyl-dec-4-en-9-yn-3-one, Table 5 entry 9

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and 1,6-heptadiyne (104 μ L, 0.9 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a pale yellow oil (44 mg, 74 %); ν_{max} (film) /cm⁻¹ 2976, 1652, 916, 731; δ_{H} (300 MHz; CDCl₃) 6.85 (1H, dt, *J* 15.9, 6.9), 6.15 (1H, dt, *J* 15.9, 1.5), 2.88-2.74 (4H, m), 2.40-2.32 (2H, m), 2.24 (2H, td, *J* 7.0, 2.6), 2.12 (3H, s), 1.98 (1H, t, *J* 2.6), 1.76-1.66 (2H, m); δ_{C} (75 MHz; CDCl₃) 198.3, 146.5, 83.4, 69.1, 39.9, 31.2, 28.3, 26.7, 17.9, 15.8; *m/z* (ES+) 196 (5%, M), 181 (40%, M-CH₃), 81 (100%, M-CHC(CH₂)₄), 61 (90%, M-CHC(CH₂)₃CHCHCOCH₂); found [M+H]⁺ 197.0993, C₁₁H₁₇OS requires 197.0995.

(4E, 9E)-1,13-bis(methanesulfonyl)trideca-4,9-diene-3,11-dione, Table 5 entry 10

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfonyl propanal (30 μ L, 0.3 mmol) and 1,6-heptadiyne (17 μ L, 0.15 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a pale yellow oil (27 mg, 60 %); ν_{max} (film) /cm⁻¹ 2980, 1700, 1650, 900; δ_{H} (300 MHz; CDCl₃) 6.8 (H, dt, *J* 15.8, 6.98), 6.06 (2H, dt, *J* 15.8, 1.5), 2.81-2.76 (4H, m), 2.76-2.73 (4H, m), 2.24-2.16 (4H, m), 2.06 (6H, s), 1.65-1.58 (2H, m); δ_{C} (75 MHz; CDCl₃) 198.7 (2C), 146.9 (2 CH), 131.0 (2 CH), 40.4 (2 CH₂), 32.2 (2 CH₂), 28.7 (2 CH₂), 26.8 (2 CH₂), 16.3; *m/z* (CI⁺, NH₃) 318 (7%, M⁺ NH₄), 272 (100%, M-SCH₃), 224 (30%, M- CH₃SCH₂CH₃); found [M+H]⁺ 318.1557, C₁₅H₂₈O₂N₁S₂ requires 318.1556.

(E)-5-Methanesulfonyl-1-trimethylsilyl-pent-1-en-3-one, Table 5 entry 11

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfonyl propanal (30 μ L, 0.3 mmol) and (trimethylsilyl)acetylene (85 μ L, 0.6 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a pale yellow oil (53 mg, 89%); ν_{max} (film) /cm⁻¹ 2957, 1678, 1432, 1250, 995, 836; δ_{H} (300 MHz, CDCl₃) 7.06 (1H, d, *J* 19.2), 6.45 (1H, d, *J* 19.2), 2.92-2.87 (2H, m), 2.77-2.72 (2H, m), 2.10 (3H, s), 0.12 (9H, s); δ_{C} (75 MHz, CDCl₃) 198.4, 147.4, 141.8, 39.1, 28.1, 15.8, -1.9 (3C); *m/z* (ES⁺) 202 (10%, M⁺), 139 (40%, M-MeSCH₂CH₂), 73 (80%, M- MeSCH₂CH₂COCHCH); found 203.0918 [M+H]⁺ C₉H₁₉OSSi requires 203.0920.

(E)-1-Methanesulfanyl-4-methyl-hex-4-en-3-one, Table 5 entry 12

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and 2-butyne (71 μ L, 0.9 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a pale yellow oil (36 mg, 76 %); ν_{max} (film) /cm⁻¹ 2916, 1663, 1421, 1242, 908, 723; δ_{H} (300 MHz; CDCl₃) 6.70 (1H, qd, *J* 6.9, 1.1), 2.89 (2H, t, *J* 7.4), 2.70 (2H, t, *J* 7.4), 2.06 (3H, s), 1.81 (3H, d, *J* 6.9), 1.72 (3H, d, *J* 1.1); δ_{C} (75 MHz; CDCl₃) 200.1, 138.6, 138.2, 37.5, 29.5, 16.3, 15.3, 11.4; *m/z* (EI) 158 (10%, M), 110 (100%, M-CH₃SH), 83 (80%, M-MeSCH₂CH₂), 61 (40%, M-CH₃CHC(CH₃)COCH₂); found [M] 158.0760, C₈H₁₄OS requires 158.0760.

(E)-1-Methanesulfanyl-4-phenyl-hex-4-en-3-one, Table 5 entry 13

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (5 mg, 0.0075 mmol), acetone (1.5 mL), 3-methanesulfanyl propanal (15 μ L, 0.15 mmol) and 1-phenyl-1-propyne (56 μ L, 0.45 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a pale yellow oil (22 mg, 67%); ν_{max} (film) /cm⁻¹ 2916, 2346, 1668, 1647, 1432, 1267, 1047, 728; δ_{H} (300 MHz; CDCl₃) 7.54 (1H, d, *J* 1.4), 7.43-7.35 (5H, m), 3.14 (2H, t, *J* 7.6), 2.85 (2H, t, *J* 7.6), 2.17 (3H, s), 2.07 (3H, d, *J* 1.4); δ_{C} (75 MHz; CDCl₃) 200.2, 138.8, 137.0, 135.5, 129.5 (2CH), 128.4, 128.3 (2CH), 37.4, 28.9, 15.7, 12.9; *m/z* (ES⁺) 220 (20%, M⁺) 172 (10%, M-MeSH); found 221.0996 [M+H]⁺ C₉H₁₆O₃S requires 221.0995.

(Z)-2-Benzylidene-5-methanesulfanyl-1-phenyl-pentane-1,3-dione, Table 5 entry 14

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (5 mg, 0.00075 mmol), acetone (1.5 mL), 3-methanesulfanyl propanal (15 μ L, 0.15 mmol) and diphenylpropynone (93 μ L, 0.45 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a pale yellow oil (31 mg, 66 %); ν_{max} (film) /cm⁻¹ 2911, 1673, 1647, 1581, 1221, 913; δ_{H} (300 MHz; CDCl₃) 7.88-7.84 (2H, m), 7.77 (1H, s), 7.50-7.10 (8H, m), 2.92 (2H, t, *J* 7.0), 2.73 (2H, t, *J* 7.0), 2.01 (3H, s); δ_{C} (75 MHz; CDCl₃) 198.3, 196.5, 141.9, 139.3, 136.3, 134.6, 133.2, 131.0, 130.8 (2CH), 129.7 (2CH), 129.4 (2CH), 129.2 (2CH), 40.0, 28.7, 16.3; *m/z* (ES⁺) 310 (100 %, M⁺), 263 (60%, M-MeS); found 311.1098 [M+H]⁺ C₁₉H₁₉O₂S requires 311.1100.

(E)-6-Hydroxy-4-(hydroxymethyl)-1-methanesulfanyl-hex-4-en-3-one, Table 5 entry 15

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and 2-butyne-1,4-diol (180 mg, 0.9 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (48 mg, 85 %); ν_{max} (film) /cm⁻¹ 2921, 2860, 1653, 1354, 1043; δ_{H} (300 MHz; CDCl₃) 6.66 (1H, tt, *J* 3.7, 1.3), 4.50 (2H, dt, *J* 3.7, 2.0), 4.38 (2H, td, *J* 2.0, 1.3), 2.87 (2H, t, *J* 7.1), 2.69 (2H, t, *J* 7.1), 2.05 (3H, s); δ_{C} (75 MHz; CDCl₃) 198.2, 142.0, 141.4, 61.1, 59.9, 37.9, 29.0, 24.0, 16.3; *m/z* (ES⁺) 190 (10 %, M⁺), 143 (60%, M-MeS), 115 (100%, M-MeSCH₂CH₂), 87 (40%, M-MeSCH₂CH₂CO); found 191.5876 [M+H]⁺ C₈H₁₅O₃S requires 191.5874.

2-(-3-Methanesulfanyl-propionyl)-but-2-enedioic acid dimethyl ester Table 5 entry 17

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and dimethyl acetylenedicarboxylate (158 μ L, 1.5 mmol). Heated at 55 $^{\circ}$ C for 16 hours. Flash chromatography (DCM) yielded the title compound as a yellow oil (55 mg, 75 % 2:1 *Z:E*); ν_{max} (film) /cm⁻¹ 3427, 3011, 2966, 2489, 1731, 1728, 1455, 1248, 1051; δ_{H} (300 MHz; CDCl₃) (major *Z*) 6.80 (1H, s), 3.83 (3H, s), 3.78 (3H, s), 3.03-2.96 (2H, m), 2.90-2.84 (2H, m), 2.14 (3H, s); (minor *E*) 6.72 (1H, s), 3.91 (3H, s), 3.81 (3H, s), 3.03-2.96 (2H, m), 2.77 (2H, t, *J* 7.3), 2.12 (3H, s); δ_{C} (75 MHz; CDCl₃) (*E* and *Z*) 199.6, 193.1, 164.7, 163.5, 163.4, 162.0, 145.7, 143.0, 127.7, 127.2, 52.2, 52.0, 51.8, 51.7, 41.8, 38.6, 26.6, 26.3, 14.9, 14.7; *m/z* (EI) 246 (10%, M), 167 (100%, M-MeSO₂); found [M]⁺ 246.0556, C₁₀H₁₄O₅S required 246.0555.

5-(3-Methanesulfanyl-propionyl)-hex-5-enenitrile, 6

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and 5-hexynenitrile (157 μ L, 1.5 mmol). Heated at 55 $^{\circ}$ C for 1 hour. Flash chromatography (1:1, EtOAc:Petrol) yielded the title compound as a yellow oil (41 mg, 68 %); ν_{max} (film) /cm⁻¹ 2967, 2337, 1646, 1551, 1123, 750; δ_{H} (300 MHz; CDCl₃) 6.04 (1H, s), 5.83 (1H, t, *J* 1.0), 2.94 (2H, t, *J* 7.0), 2.71 (2H, t, *J* 7.0), 2.37 (2H, td, *J* 7.3, 1.0), 2.27 (2H, t, *J* 7.1), 2.06 (3H, s), 1.79-1.69 (2H, m); δ_{C} (75 MHz; CDCl₃) 199.9, 146.9, 126.5, 119.8, 37.9, 30.6, 29.1, 24.7, 17.1, 16.3; *m/z* (ES⁺) 197 (10 %, M), 149 (40%, M-MeSH) 75 (100% M-COCCH₂(CH₂)₃CN; found [M+H]⁺ 198.0945, C₁₀H₁₆NOS requires 198.0945.

(E)-9-Methanesulfanyl-7-oxo-non-5-enenitrile, 7

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol), MeCN (12 μ L, 6.0 mmol) and 5-hexynenitrile (62 μ L, 0.6 mmol). Heated at 55 °C for 4 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (48 mg, 81 %); ν_{max} (film) /cm⁻¹ 2908, 2357, 1665, 1662, 1428; δ_{H} (300 MHz; CDCl₃) 6.73 (1H, dt, *J* 15.9, 6.9), 6.13 (1H, d, *J* 15.9), 2.82-2.68 (4H, m), 2.38-2.31 (4H, m), 2.06 (3H, s), 1.84-1.75 (2H, m); δ_{C} (75 MHz; CDCl₃) 196.8, 143.1, 130.1, 117.8, 39.0, 29.8, 27.0, 22.6, 15.5, 14.7; *m/z* (ES⁺) 197 (5 %, M), 150 (40%, M-MeS), 121 (100%, M-(CH₂)₃CN), 75 (80% M-COCCH₂(CH₂)₃CN; found [M+NH₄]⁺ 215.1213, C₁₀H₁₉N₂OS requires 215.1213.

(E)-8-Methanesulfanyl-6-oxo-oct-4-enenitrile (a) and 4-(3-methanesulfanyl-propionyl)-pent-4-enenitrile (b), Table 6 entry 1

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and 4-cyano-1-butyne (50 mg, 0.6 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:4, EtOAc:Petrol) yielded 8-methanesulfanyl-6-oxo-oct-4-enenitrile (**a**) as a pale yellow oil (25 mg, 46%); ν_{max} (film) /cm⁻¹ 3049, 2295, 1668, 1411, 1252, 893, 728; δ_{H} (300 MHz; CDCl₃) 6.74 (1H, dt, *J* 15.9, 6.4), 6.17 (1H, d, *J* 15.9), 2.82 (2H, t, *J* 6.5), 2.71 (2H, t, *J* 6.5), 2.57-2.46 (4H, m), 2.06 (3H, s); δ_{C} (75 MHz; CDCl₃) 196.6, 140.4, 130.6, 117.3, 39.3, 26.9, 26.8, 15.1, 14.7; *m/z* (EI) 183 (7%, M), 135 (50%, M-MeSH), 108 (90%, M-MeSCH₂CH₂); found [M]⁺ 183.0713, C₉H₁₃NOS requires 183.0712; and 4-(3-methylsulfanyl-propionyl)-pent-4-enenitrile (**b**) as a pale yellow oil (17 mg, 31%); ν_{max} (film) /cm⁻¹ 3049, 2295, 1668, 1411, 1252, 893, 728; δ_{H} (300 MHz; CDCl₃) 6.22 (1H, s), 6.04 (1H, s), 3.06 (2H, t, *J* 7.3), 2.77 (2H, t, *J* 7.3), 2.63-2.52 (4H, m), 2.13

(3H, s); δ_C (75 MHz; $CDCl_3$) 198.5, 143.7, 127.2, 118.3, 36.7, 27.8, 26.9, 16.2, 15.2; m/z (EI) 183 (7%, M), 135 (50%, M-MeSH), 108 (90%, M-MeSCH₂CH₂); found $[M]^+$ 183.0714, C₉H₁₃NOS requires 183.0712

(E)-10-Methanesulfanyl-8-oxo-dec-6-enenitrile (a) and 6-(3-methanesulfanylpropionyl)-hept-6-enenitrile (b), Table 6 entry 2

The general procedure for the hydroacylation reaction was followed employing pre-catalyst $[Rh(nbd)(dppe)]ClO_4$ (10 mg, 0.015 mmol), acetone (2.0 mL), 3-methanesulfanyl propanal (30 μ L, 0.3 mmol) and hept-6-ynenitrile³ (64 mg, 0.6 mmol). Heated at 55 °C for 1 hour. Flash chromatography (1:4, EtOAc:Petrol) yielded 10-methanesulfanyl-8-oxo-dec-6-enenitrile (**a**) as a pale yellow oil (31 mg, 49%); ν_{max} (film) /cm⁻¹ 3049, 2978, 1673, 1416, 1252, 887, 744; δ_H (300 MHz; $CDCl_3$) 6.76 (1H, dt, J 15.9, 6.9), 6.08 (1H, dt, J 15.9, 1.5), 2.82-2.68 (4H, m), 2.32 (2H, t, J 6.7), 2.26-2.19 (2H, m), 2.06 (3H, s), 1.69-1.56 (4H, m); δ_C (75 MHz; $CDCl_3$) 197.6, 145.4, 130.0, 118.7, 39.3, 30.8, 27.6, 26.3, 24.2, 16.4, 15.2; m/z (ES+) 211 (5%, M+), 164 (30%, M-MeS), 74 (80%, M- CN(CH₂)₄CHCHCOH), 55 (100%, M-CH₃CH₂CN); found 212.1099 $[M+H]^+$ C₁₁H₁₇NOS requires 212.1104; and 6-(3-methanesulfanylpropionyl)-hept-6-enenitrile (**b**) as a colourless oil (20 mg, 32%); ν_{max} (film) /cm⁻¹ 3048, 2978, 1650, 1420, 1235, 900; δ_H (300 MHz; $CDCl_3$) 6.06 (1H, s), 5.82 (1H, s), 3.00 (2H, t, J 6.9), 2.77 (2H, t, J 6.9), 2.42-2.26 (4H, m), 2.13 (3H, s), 1.70-1.54 (4H, m); δ_C (75 MHz; $CDCl_3$) 200.2, 148.1, 125.5, 120.0, 38.0, 30.4, 29.1, 28.0, 25.5, 17.4, 16.3; m/z (ES+) 211 (5%, M+), 164 (30%, M-MeS), 74 (80%, M- CN(CH₂)₄CHCHCOH), 55 (100%, M-CH₃CH₂CN); found 212.1099 $[M+H]^+$ C₁₁H₁₇NOS requires 212.1104.

³ Davison, E. C.; Fox, M. E.; Holmes, A. B.; Roughley, S. D.; Smith, C. J.; Williams, G. M.; Davies, J. E.; Raithby, P. R.; Adams, J. P.; Forbes, I. T.; Press, N. J.; Thompson, M. J. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1494-1514.

(E)-4-Methyl-1-methanesulfanyl-dec-4-en-3-one (a) and (E)-4-Ethylidene-1-methanesulfonyl-nonan-3-one (b), Table 6 entry 3

The general procedure for the hydroacylation reaction was followed employing pre-catalyst $[\text{Rh}(\text{nbd})(\text{dppe})]\text{ClO}_4$ (10 mg, 0.015 mmol), acetone (2 mL), 3-methanesulfanyl propanal (30 μL , 0.3 mmol) and 2-octyne (87 μL , 0.6 mmol). Heated at 55 $^{\circ}\text{C}$ for 48 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compounds as a colourless oil as a 3:1 mixture of **a** and **b** (37 mg, 58%); ν_{max} (film) $/\text{cm}^{-1}$ 2921, 2854, 2253, 1663, 1468, 1375, 903, 723; δ_{H} (300 MHz; CDCl_3) (major **a**) 6.58 (1H, td, J 7.2, 1.2), 2.93-2.88 (2H, m), 2.73-2.67 (2H, m), 2.24-2.14 (2H, m), 2.06 (3H, s), 1.71 (3H, br. s), 1.45-1.36 (2H, m), 1.28-1.20 (4H, m), 0.86-0.78 (3H, m); (minor **b**) δ_{H} (300 MHz; CDCl_3) 6.66 (1H, q, J 7.0), 2.93-2.88 (2H, m), 2.73-2.67 (2H, m), 2.24-2.14 (2H, m), 2.05 (3H s), 1.76 (3H, d, J 7.0), 1.45-1.36 (6H, m); δ_{C} (75 MHz; CDCl_3) (mixture) 199.6, 199.3, 143.2, 142.9, 137.4, 136.8, 37.0, 36.9, 31.7, 31.4, 28.9, 28.8, 28.4, 28.1, 25.1, 22.3, 22.2, 15.7, 14.5, 13.83, 13.78, 11.1; m/z (EI $^{+}$) 214 (20 %, M^{+}), 166 (95%, MeSH), 109 (100%, $\text{MeS}(\text{CH}_2)_2\text{COH}$); found 214.1385 $[\text{M}]^{+}$ $\text{C}_{12}\text{H}_{22}\text{OS}$ requires 214.1386.

Hept-5-yne nitrile, Table 6 entry 4 substrate

6-Chlorohex-2-yne (1.16g, 0.01 mol) was added to a solution of NaCN (0.5g, 0.011 mol) in EtOH (10.5 mL) and water (3 mL). The resulting solution was heated at reflux for 16 hours. It was then cooled to room temperature diluted with DCM (50 mL). The solution was extracted with water (3×50 mL) and dried (MgSO_4). After this time the solution was reduced *in vacuo* and purified by flash chromatography (1:9 EtOAc:Petrol) giving the title compound as a colourless oil (0.95 g, 89%); ν_{max} (film) $/\text{cm}^{-1}$ 2921, 2243, 1422, 1267, 749; δ_{H} (300 MHz; CDCl_3) 2.42 (2H, t, J 7.2), 2.28-2.21 (2H, m), 1.81-1.74 (2H, m), 1.72 (3H, t, J 2.5); δ_{C} (75 MHz; CDCl_3) 119.3, 77.6, 76.2, 24.8, 17.8, 16.0, 3.4; m/z (EI) 107 (10%, M), 106 (100%, M-H), 79 (40%, M-

H₂CN), 53 (50%, M-CH₃CCCH₂), 41 (70%, M-CNCH₂CH₂C); found [M-H]⁺ 106.0651, C₇H₉N requires 106.0651.

(E)-5-(3-Methanesulfanyl-propionyl)-hept-5-enenitrile (a) and (E)-6-methyl-9-methanesulfanyl-7-oxo-non-5-enenitrile (b), Table 6 entry 4

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2 mL), 3-methanesulfanyl propanal (30 μL, 0.3 mmol) and hept-5-ynenitrile (64 mg, 0.6 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded 5-(3-Methanesulfanyl-propionyl)-hept-5-enenitrile **(a)** (33 mg, 53 %); $\nu_{\max}$ (film) /cm⁻¹ 2926, 1673, 1432, 1252, 733; δ_{H} (300 MHz; CDCl₃) 6.85 (1H, q, *J* 7.0), 2.95 (2H, t, *J* 6.8), 2.76 (2H, t, *J* 6.8), 2.45 (2H, t, *J* 7.6), 2.32 (2H, t, *J* 7.1), 2.32 (2H, t, *J* 7.1), 2.12 (3H, s), 1.94 (3H, d, *J* 7.0), 1.76-1.66 (2H, m); δ_{C} (75 MHz; CDCl₃) 199.0, 140.6, 139.6, 119.5, 36.7, 28.8, 24.3, 24.0, 16.8, 15.7, 14.7; *m/z* (EI) 211 (10%, M), 162 (100%, M-CH₃SH₂), 108 (80%, M-CH₃CHC(CH₂)₃CN), 75 (50%, M-COCH₃CHC(CH₂)₃CN); found [M] 211.1024, C₁₁H₁₇NOS requires 211.1025; and 6-methyl-9-methanesulfanyl-7-oxo-non-5-enenitrile **(b)** (17 mg, 27%); $\nu_{\max}$ (film) /cm⁻¹ 2920, 1650, 1454, 1234, 722; δ_{H} (300 MHz; CDCl₃) 6.56 (1H, td, *J* 7.2, 1.3), 2.96 (2H, t, *J* 7.1), 2.77 (2H, t, *J* 7.1), 2.47-2.38 (4H, m), 2.13 (3H, s), 1.91-1.81 (5H, m); δ_{C} (75 MHz; CDCl₃) 199.3, 138.8, 138.6, 118.8, 37.1, 28.7, 27.5, 24.2, 16.6, 15.7, 11.4; *m/z* (EI) 211 (5%, M), 162 (100%, M-CH₃SH₂), 108 (80%, M-CH₃CHC(CH₂)₃CN), 75 (40%, M-COCH₃CHC(CH₂)₃CN); found [M] 211.1023, C₁₁H₁₇NOS requires 211.1025.

Methyl 6-ethylsulfanyl-4-oxo-hexanoate, **Table 3 entry 1**

Methyl 4-oxo-6-phenylsulfanyl-hexanoate, **Table 3 entry 2**

Methyl 6-ethylsulfanyl-5-methyl-4-oxo-heptanoate, **Table 3 entry 6**

(E)-5-(methylthio)-1-trimethylsilyl)pent-1-en-3-one,
 Table 5 entry 11

4-Methylene-7-(methylthio)-5-oxoheptanenitrile,
Table 6 entry 1