Chelation Controlled Intermolecular Alkene and Alkyne Hydroacylation: The Utility of β -Thioacetal Aldehydes

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Supporting Information

General information: IR spectra were recorded on a Perkin-Elmer 1600 FT IR spectrophotometer, using NaCl discs. ¹H NMR spectra were obtained on a Bruker Avance 300 spectrometer operating at 300 MHz, unless otherwise noted, with tetramethylsilane as an internal standard. *J* values are given in Hz. ¹³C NMR spectra were obtained on a Bruker Avance 300 spectrometer operating at 75 MHz, unless otherwise noted. All dry solvents were freshly distilled under nitrogen prior to use. Tetrahydrofuran was distilled over sodium wire. Dichloromethane was distilled over calcium hydride. DMF was distilled under reduced pressure over 4Å molecular sieves. MeOH was distilled over 4Å molecular sieves. DMF and MeOH were stored over 4Å molecular sieves. Acetone was distilled over drierite and stored over 4Å molecular sieves. Petroleum ether refers to that fraction 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.

Aldehydes used for hydroacylation reactions leading to product 1-3 and 9 were prepared by literature procedures.^{1,2}

General preparation of aldehyde compounds as exemplified by nona-2,7-diynedial

n-BuLi 2.5M (3.44 mL, 8mmol) was added dropwise to 1,6-heptadiyne (0.4 g, 4 mmol) in THF (50 L) at -78 °C. It was stirred at -78 °C for 1 hour and then LiBr (0.9 g, 10 mmol) was added followed by DMF (3.3 mL, 40 mmol) dropwise over 10 minutes. It was stirred at -78 °C for 30 minutes and then raised to 0 °C overnight. The reaction was quenched with NH₄Cl (30 ml) and extracted with Et₂O (3 × 30 ml). The combined organic extracts were washed with brine (30 ml) and water (30 ml) and dried (MgSO₄). Flash chromatography (1:4 EtOAc:Petrol) gave the title compound as a colourless oil (0.50 g, 80% yield); δ_H (300 MHz; CDCl₃) 9.12 (2H, t, *J* 0.7), 2.52 (4H, td, *J* 7.0 0.7), 1.85 (2H, tt, *J* 7.0, 7.0); δ_C (75 MHz; CDCl₃) 177.2 (2 CH), 96.7 (2 C), 82.7 (2 C), 25.9, 18.5(2 CH₂); ν_{max} (film) /cm⁻¹ 1731 (C=O); *m/z* (EI) 148 (1 %, M), 119 (70 % M-CHO), 91 (100 % M- CHOCHO).

General procedure for the preparation of dithiane compounds as exemplified by (2-{3-[2-(2-Oxo-ethyl)-[1,3]dithiane-2-yl]-propyl}-[1,3]dithiane-2-yl)-acetaldehyde

1,3-propanedithiol (0.2 mL, 1.8 mmol) and NaOMe (0.12 g, 2.2 mmol) were added to nona-2,7-diynedial (0.13 g, 0.8 mmol), in MeOH (16 mL) and DCM (4 mL) at -10 °C. The reaction was stirred at -10 °C for 1 hour and then slowly warmed to 0 °C overnight (16 hours). After this time the reaction was warmed to room temperature and quenched with NH₄Cl (aq) (30 mL). The solution was separated and washed with EtOAc (3 × 30 mL). The organic extracts were combined and washed with water (30 mL) and brine (30 mL), dried (MgSO₄) and purified under flash chromatography (1:1, EtOAc:Petrol) yielding the title compound as a yellow oil (0.23 g, 80%); δ_H (300 MHz; CDCl₃) 9.73 (2H, t, *J* 2.8), 2.84-2.78 (12H, m), 1.99-1.94 (8H, m), 1.78-1.69 (2H, m); δ_C (75 MHz; CDCl₃) 198.5 (2 CH), 59.4 (2 CH₂), 49.4 (2 C), 48.2 (2 CH₂), 39.2 (2 CH₂), 25.3 (4 CH₂), 18.4; ν_{max} (film) /cm⁻¹ 1741 (C=O); *m/z* (EI) 364 (50 %, M), 229 (100 % M- M-HCOSCH₂CH₂CH₂S), 175 (75 % M- HCOCH₂CSCH₂CH₂CH₂SCH₂CH₂); found [M+H]⁺ 365.0732, C₁₅H₂₅O₂S₄ requires 365.0740.

6-Chloro-hex-2-ynal

The general procedure for the preparation of aldehyde compounds was followed employing 5-chloro-1-pentyne (1 g, 9.7 mmol), THF (100 mL), n-BuLi 2.5M (3.90 mL, 9.7 mmol), LiBr (1.0 g, 11mmol) and DMF (3.8 mL, 49 mmol). Flash chromatography (1:4 EtOAc:Petrol) gave the title compound as a yellow oil (0.89 g, 71% yield); δ_{H} (300 MHz; CDCl_3) 9.17 (1H, t, J 0.8), 3.65 (2H, t, J 6.1), 2.63 (2H, td, J 6.9, 0.8), 2.05 (2H, tt, J 6.9 6.1); δ_{C} (75 MHz; CDCl_3) 177.1, 96.7, 82.2, 43.3, 30.4, 16.7; ν_{max} (film) $/\text{cm}^{-1}$ 1684 (C=O), 723 (C-Cl); m/z (EI) 130 (40 %, M), 89 (30 % M-CHOC), 54 (40 % M-ClCHOC); found $[\text{M}-\text{H}]^+$ 129.0102, $\text{C}_6\text{H}_6\text{ClO}$ requires 129.0100.

[2-(3-Chloro-propyl)-[1,3]dithiane-2-yl]-acetaldehyde

The general procedure for the preparation of dithiane compounds was followed employing 6-chloro-hex-2-ynal (1.07 g, 8.2 mmol), 1,3-propanedithiol (0.9 mL, 9.0 mmol), MeOH (64 mL), DCM (16 mL) and NaOMe (0.58 g, 10.7 mmol). Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (1.23 g, 63%); δ_{H} (300 MHz; CDCl_3) 9.69 (1H, t, J 2.8), 3.49 (2H, t, J 6.2), 2.81-2.75 (6H, m), 2.70 (2H, t, J 6.1), 2.09 (2H, tt, J 6.2 6.1), 2.02-1.97 and 1.82-1.77 (2H, m); δ_{C} (75 MHz; CDCl_3) 199.7, 50.8, 49.2, 45.1, 37.8, 27.9, 26.5 (2 CH_2), 24.8; ν_{max} (film) $/\text{cm}^{-1}$ 1739 (C=O); m/z (EI) 238 (40 % M), 195 (20 % M- CHOCH_2). The aldehyde was unstable and used directly in the hydroacylation procedures.

{2-[3-(Tetrahydro-pyran-2-yloxy)-propyl]-[1,3]dithian-2-yl}-acetaldehyde

The general procedure for the preparation of dithiane compounds was followed employing 6-(tetrahydro-pyran-2-yloxy)-hex-2-ynal (200 mg, 1.0 mmol), 1,3-

propanedithiol (0.11 mL, 12 mmol), MeOH (8 mL), DCM (2 mL) and NaOMe (0.1 g, 18 mmol). Flash chromatography (1:9 EtOAc: Petrol) gave the title compound (0.19 g, 63 %) as a yellow oil; δ_{H} (300 MHz; CDCl_3) 9.75 (1H, t, J 2.8), 4.54 (1H, t, J 4.1), 3.84-3.68 (2H, m), 3.50-3.35 (2H, m), 2.85-2.81 (6H, m) 2.12-2.06 (2H, m) 2.00-1.89 (2H, m) 1.83-1.74 (4H, m) 1.57-1.45 (4H, m); δ_{C} (75 MHz; CDCl_3) 198.9, 98.1, 66.2, 61.7, 49.6, 48.5, 36.3, 30.1, 25.5, 24.8 (2 CH_2), 24.04, 23.96, 18.95; ν_{max} (film) $/\text{cm}^{-1}$ 1715 (C=O), 1260 (C-O); m/z (EI) 304 (90 %, M), 220 (60 % M- $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{C}$), 85 (60 % M- $\text{CHOCH}_2\text{CS}_2\text{C}_3\text{H}_6\text{C}_3\text{H}_6\text{O}$); found $[\text{M}+\text{NH}_4]^+$ 322.1505, $\text{C}_{14}\text{H}_{28}\text{NO}_3\text{S}_2$ requires 322.1503.

General procedure for hydroacylation reactions as exemplified by table 1, entry 1; 5-[1,3]Dithian-2-yl-4-oxo-pentanoic acid methyl ester

Acetone (2.5 ml) was added under argon to pre-catalyst $[\text{Rh}(\text{nbd})(\text{dppe})]\text{ClO}_4$ (13 mg, 0.02 mmol). The catalyst was activated *in situ* by bubbling through the solution with H_2 for 2 minutes until a colour change was observed. After this time the solution was purged with argon. To this solution methyl acrylate (100 μL , 0.9 mmol) was added followed by [1,3]dithiane-2-yl-acetaldehyde (30 mg, 0.2 mmol). The resulting mixture was stirred and heated at 55 $^\circ\text{C}$ for 2 hours. After this time the solution was reduced *in vacuo* and purified by flash chromatography (1:4 EtOAc:Petrol) giving the title compound as a yellow oil (32 mg, 74%); δ_{H} (300 MHz; CDCl_3) 4.50 (1H, t, J 7.0), 3.67 (3H, s), 2.94-2.75 (8H, m), 2.62 (2H, t, J 6.5), 2.17-2.06 and 1.93-1.79 (2H, m); δ_{C} (75 MHz; CDCl_3) 203.3, 172.0, 50.9, 46.8, 40.1, 37.0, 29.2 (2 CH_2), 26.6, 24.2; ν_{max} (film) $/\text{cm}^{-1}$ 1735, 1670 (C=O), 1265 (C-O); m/z (EI) 248 (40 %, M), 161 (40%, M- $\text{C}_2\text{H}_4\text{CO}_2\text{Me}$); found $[\text{M}]^+$ 248.0535, $\text{C}_{10}\text{H}_{16}\text{O}_3\text{S}_2$ required 248.0535.

Table 1 entry 2; 5-[1,3]dithiolan-2-yl-4-oxo-pentanoic acid methyl ester

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (9 mg, 0.027 mmol), acetone (2 mL), [1,3]dithiolan-2-yl-acetaldehyde (40 mg, 0.27 mmol) and methyl acrylate (121 μ L, 1.35 mmol). Heated at 55 °C for 4 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (44 mg, 71 %); δ_{H} (300 MHz; CDCl₃) 4.83 (1H, br. s), 3.67 (3H, s), 3.22 (4H, br. s), 3.04 (2H, d, *J* 7.0), 2.72 (2H, d, *J* 6.4), 2.61 (2H, d, *J* 6.4); δ_{C} (75 MHz; CDCl₃) 206.4, 173.4, 53.0, 52.3, 47.1, 38.9 (2 CH₂), 37.8, 27.9; ν_{max} (film) /cm⁻¹ 1720 1665 (C=O), 1265 (C-O); *m/z* (ES) 235 (20 % M) 105 (10 %, M-CH₂COCH₂CH₂CO₂Me); found [M+NH₄]⁺ 252.0723, C₉H₁₈NO₃S₂ requires 252.0728.

Table 1 entry 3; 5-(2-butyl-[1,3]dithian-2-yl)-4-oxo-pentanoic acid methyl ester

The general procedure for hydroacylation reactions was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2 mL), (2-pentyl-[1,3]dithian-2-yl)-acetaldehyde (30 mg, 0.15 mmol) and methyl acrylate (67 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 (36 mg, 77 %); δ_{H} (300 MHz; CDCl₃) 3.68 (3H, s), 3.12 (2H, s), 2.99-2.76 (6H, m), 2.59 (2H, t, *J* 6.3), 2.12-1.86 (4H, m), 1.55-1.43 (2H, m), 1.41-1.28 (2H, m), 0.93 (3H, t, *J* 7.2); δ_{C} (75 MHz; CDCl₃) 205.1, 173.5, 52.1, 50.6, 49.6, 39.9, 39.0, 28.1, 26.8 (2 CH₂), 26.6, 25.4, 23.1, 14.3; ν_{max} (film) /cm⁻¹ 1790, 1740 (C=O), 1251 (C-O); *m/z* (ES) 322 (100 %, M+NH₄), 175 (90%, M-COCH₂CH₂CO₂Me); found [M+NH₄]⁺ 322.1505, C₁₄H₂₈NO₃S₂ requires 322.1505.

Table 1 entry 4; 5-[2-(3-chloro-propyl)-[1,3]dithiane-2-yl]-4-oxo-pentanoic methyl ester

The general procedure for the preparation of ketone compounds was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.015 mmol), acetone (2.5 mL), 6-chloro-hex-2-ynal (36 mg, 0.15 mmol) and methyl acrylate (70 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 (34 mg, 72%); δ_{H} (300 MHz; CDCl₃) 3.61 (3H, s), 3.57 (2H, t, *J* 6.4), 3.06 (2H, s), 2.90-2.84 (6H, m), 2.59 (2H, t, *J* 6.6), 2.26-2.20 (2H, m), 2.06-1.96 (4H, m); δ_{C} (75 MHz; CDCl₃) 205.2, 173.5, 52.3, 50.1, 50.0, 45.3, 40.1, 36.2, 28.2 (2 CH₂), 28.1, 26.8, 25.2; ν_{max} (film) /cm⁻¹ 1740, 1647 (C=O), 1231 (C-O); *m/z* (ES) 342 (100%, M+NH₄), 289 (100%, M-Cl); found [M+NH₄]⁺ 342.0959, C₁₃H₂₅ClNO₃S₂ requires 342.0961.

Table 1 entry 5; 4-oxo-5-{2-[3-(tetrahydro-pyran-2-yloxy)-propyl]-[1,3]dithiane-2-yl}-pentanoic acid methyl ester

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (5 mg, 0.013 mmol), acetone (2 mL), {2-[3-(tetrahydro-pyran-2-yloxy)-propyl]-[1,3]dithian-2-yl}-acetaldehyde (40 mg, 0.13 mmol) and methyl acrylate (60 μ L, 0.68 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (37 mg, 70 %); δ_{H} (300 MHz; CDCl₃) 4.53 (1H, t, *J* 3.4), 3.83-3.65 (2H, m), 3.61 (3H, s), 3.47-3.32 (2H, m), 3.04-3.02 (2H, m), 2.81 (2H, t, *J* 7.7), 2.80 (2H, t, *J* 6.6), 2.52 (2H, t, *J* 6.6), 2.13-2.07 (2H, m), 2.01-1.86 (2H, m), 1.80-1.60 (4H, m), 1.52-1.45 (6H, m); δ_{C} (75 MHz; CDCl₃) 205.1, 173.5, 99.0, 62.6, 52.2, 50.5, 46.9, 43.9, 40.0, 35.8, 31.1, 28.1, 28.0, 26.8 (2 CH₂), 25.3, 25.1, 20.0; ν_{max} (film) /cm⁻¹ 1710 (C=O), 1664 (C=O), 1385 (C-O); *m/z* (EI) 390 (40 %, M), 289 (100 % M-OCH₂CH₂CH₂CH₂COH), 275 (90 % M-MeOCOCH₂CH₂CO); found [M+NH₄]⁺ 408.1873, C₁₈H₃₄NO₅S₂ requires 408.1877.

Table 1 entry 7; 5-(2-{3-[2-(4-methoxycarbonyl-2-oxo-butyl)-[1,3]dithiane-2-yl]-propyl}-[1,3]dithiane-2-yl)-4-oxo-pentanoic acid methyl ester

The general procedure for hydroacylation reactions was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (20 mg, 0.03 mmol), acetone (2.5 mL), (2-{3-[2-(2-oxo-ethyl)-[1,3]dithiane-2-yl]-propyl}-[1,3]dithiane-2-yl)-acetaldehyde (55 mg, 0.15 mmol) and methyl acrylate (67 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 (67 mg, 84%); δ_{H} (300 MHz; CDCl₃) 3.60 (6H, s), 3.02 (4H, s), 2.82-2.78 (12H, m), 2.52 (4H, t, *J* 6.5), 2.08-1.88 (8H, m), 1.73-1.61 (2H, m); δ_{C} (75 MHz; CDCl₃) 205.1 (2 CH₂), 173.6 (2 CH₂), 52.2 (2 CH₂), 50.7 (2 CH₂), 50.0 (2 CH₂), 47.3 (2 CH₂), 40.0 (2 CH₂), 38.9 (4 CH₂), 28.2 (2 CH₂), 26.8 (2 CH₂), 25.3; ν_{max} (film) /cm⁻¹ 1735 (C=O), 1570 (C=O), 1265 (C-O); *m/z* (EI) 536 (30 %, M), 429 (40 % M-SCH₂CH₂CH₂SH), 315 (100 % M-SCH₂CH₂CH₂SCoCH₂CH₂CO₂Me), 115 (90 % M-C₁₈H₂₉O₃S₄); found [M+NH₄]⁺ 554.1733, C₂₃H₄₀NO₆S₄ requires 554.1728.

Table 2 entry 2; 5-(2-Butyl-[1,3]dithiane-2-yl)-4-oxo-pentanoic acid *tert*-butyl ester

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.013 mmol), acetone (2 mL), [1,3]dithiolan-2-yl-acetaldehyde (30 mg, 0.13 mmol) and *t*-butyl acrylate (95 μ L, 0.65 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (33 mg, 70%); δ_{H} (300 MHz; CDCl₃) 3.05 (2H, s), 2.90-2.70 (6H, m), 2.43 (2H, t, *J* 6.6), 2.01-1.82 (4H, m), 1.51-1.43 (2H, m), 1.37 (9H, s), 1.30-1.23 (2H, m), 0.85 (3H, t, *J* 7.2); δ_{C} (75 MHz; CDCl₃) 205.4, 172.4, 81.0, 50.6, 49.7, 40.0, 39.1, 29.7, 28.5, 26.9 (2 CH₂), 26.7, 25.5, 23.2, 14.4; ν_{max} (film) /cm⁻¹ 1740, 1647 (C=O), 1334 (C-O); *m/z* (ES) 346 (10 %, M), 233 (20 % M-CH₂CO₂^tBu),

189 (40 % M-COCH₂CH₂CO₂^tBu), 175 (100%, M CH₂COCH₂CH₂CO₂^tBu); found [M+H]⁺ 247.1709, C₁₇H₁₁O₃S₂ requires 347.1708.

Table 2 entry 3; 5-(2-Butyl-[1,3]dithiane-2-yl)-4-oxo-pentanoic acid dimethylamide

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.013 mmol), acetone (2 mL), [1,3]dithiolan-2-yl-acetaldehyde (30 mg, 0.13 mmol) and dimethyl acrylamide (67 μL, 0.65 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (29 mg, 68 %); δ_H (300 MHz; CDCl₃) 3.13 (2H, s), 2.96 (3H, s), 2.94-2.96 (9H, m), 2.54 (2H, t, *J* 6.4), 2.02-1.82 (4H, m), 1.49-1.38 (2H, m), 1.33-1.21 (2H, m), 0.85 (3H, t, *J* 7.3); δ_C (75 MHz; CDCl₃) 206.7, 171.9, 50.7, 49.7, 40.2, 39.3, 37.5, 35.9, 27.8, 26.9 (2 CH₂), 26.5, 25.5, 23.2, 14.4; ν_{max} (film) /cm⁻¹ 1710 (C=O), 1683 (CON); *m/z* (EI) 317 (20 %, M), 217 (40 % M-CH₂CH₂CONMe₂), 175 (100 % M-CH₂COCH₂CH₂CONMe₂); found [M+H]⁺ 318.1556, C₁₅H₂₈NO₂S₂ requires 318.1555.

Table 2 entry 5; 5-(2-Butyl-[1,3]dithiane-2-yl)-4-oxo-pent-2-enoic acid ethyl ester

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.013 mmol), acetone (2 mL), [1,3]dithiolan-2-yl-acetaldehyde (30 mg, 0.13 mmol) and ethyl propiolate (66 μL, 0.65 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (32 mg, 75% 4:1 *E:Z*); δ_H (300 MHz; CDCl₃) (major *E*) 7.18 (1H, d, *J* 15.8), 6.82 (1H, d, *J* 15.8), 4.26 (2H, q, *J* 7.1), 3.26 (2H, s), 2.97-2.77 (4H, m), 2.11-1.91 (4H, m), 1.43-1.23 (4H, m), 0.93 (3H, t, *J* 7.3); (minor *Z*) 6.65 (1H, d, *J* 12.1), 5.97 (1H, d, *J* 12.1), 4.44 (2H, q, *J* 7.1) 3.41 (2H, s), 2.97-2.77 (4H, m), 2.11-1.91 (4H, m), 1.43-1.23 (4H, m), 0.93 (3H, t, *J* 7.3); δ_C (75 MHz; CDCl₃)

195.9, 165.9, 140.3, 130.9, 61.8, 50.9, 48.9, 39.3, 30.1, 26.9 (2 CH₂), 25.3, 23.2, 14.5; ν_{max} (film) /cm⁻¹ 1718, 1653 (C=O); m/z (ES⁺) 316 (20%, M), 189 (80% M-COCHCHCOOEt), 99 (100% M-CH₃(CH₂)₃CS(CH₂)₃SCH₂CO); found [M+H]⁺ 317.1240, C₁₅H₂₅O₃S₂ requires 317.1240.

Table 2 entry 6; 1-(2-Butyl-[1,3]dithiane-2-yl)-oct-3-en-2-one

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.013 mmol), acetone (2 mL), [1,3]dithiolan-2-yl-acetaldehyde (30 mg, 0.13 mmol) and *t*-butyl acrylate (75 μ L, 0.65 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (31 mg, 75%); δ_{H} (300 MHz; CDCl₃) 6.80 (1H, dt, *J* 15.6, 6.9), 6.12 (1H, dt, *J* 15.6, 1.5), 3.06 (2H, s), 2.82-2.77 (4H, m), 2.15 (2H, tdd, *J* 7.0, 6.9, 1.4), 2.05-1.85 (4H, m), 1.47-1.19 (8H m), 0.86 (3H, t, *J* 7.2), 0.84 (3H, t, *J* 7.1); δ_{C} (75 MHz; CDCl₃) 196.4, 148.3, 131.4, 51.6, 47.8, 38.9, 32.6, 30.6, 26.9 (2 CH₂), 26.8, 25.5, 23.3, 22.7, 14.4, 14.2; ν_{max} (film) /cm⁻¹ 1710 (C=O); m/z (EI) 300 (100 %, M), 243 (80 % M-CH₃CH₂CH₂CH₂), 225 (60 % M-SCH₂CH₂CH₃); found [M+H]⁺ 301.1654, C₁₆H₂₉OS₂ requires 301.1651

Table 2 entry 7; 1-(2-Butyl-[1,3]dithiane-2-yl)-7-chloro-hept-3-en-2-one

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.013 mmol), acetone (2 mL), [1,3]dithiolan-2-yl-acetaldehyde (30 mg, 0.13 mmol) and 5-chloro-1-pentyne (69 μ L, 0.65 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4 EtOAc:Petrol) yielded the title compound as a yellow oil (44 mg, 73%); δ_{H} (300 MHz; CDCl₃) 6.82 (1H, dt *J* 15.6, 7.0), 6.26 (1H, dt *J* 15.6, 1.4), 3.55 (2H, t, *J* 6.4), 3.13 (2H, s), 2.89-2.84 (4H, m), 2.40 (2H, tdd, *J* 7.1, 7.0, 1.4), 2.10-1.91 (4H, m), 1.55-1.26 (4H, m), 0.93 (3H, t, *J* 7.3); δ_{C} (75 MHz; CDCl₃) 195.3, 144.9, 131.5, 50.6,

47.5, 43.7, 38.2, 30.4, 29.1, 26.2 (2 CH₂), 24.7, 22.5, 13.7; $\nu_{\max}$ (film) /cm⁻¹ 1703 (C=O), 719 (C-Cl); m/z (EI) 320 (60 %, M), 263 (100 % M-CH₃CH₂CH₂CH₂), 245 (70 % M-ClCH₂CH₂C), 213 (60 % M-SCH₂CH₂CH₂S); found [M+H]⁺ 321.1108, C₁₅H₂₆ClOS₂ requires 321.1113

Table 2 entry 8; 5-[2-(2-Butyl-[1,3]dithiane-2-yl)-acetyl]-hex-5-enitrile

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.013 mmol), acetone (2 mL), [1,3]dithiolan-2-yl-acetaldehyde (30 mg, 0.13 mmol) and 5-hexynenitrile (69 μ L, 0.65 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4 EtOAc:Petrol) yielded the title compound as a yellow oil (28 mg, 68%); δ_{H} (300 MHz; CDCl₃) 6.10 (1H, s), 5.87 (1H, s), 3.28 (2H, s), 2.85-2.82 (4H, m), 2.50 (2H, t, J 7.2), 2.34 (2H, t, J 7.2), 2.11-2.06 (2H, m), 2.02-1.96 (2H, m), 1.61-1.50 (2H, m), 1.43-1.42 (2H, m), 0.94 (3H, t, J 7.2); δ_{C} (75 MHz; CDCl₃) 197.6, 148.4, 125.7, 119.6, 51.1, 43.4, 38.4, 30.6, 26.6 (2 CH₂), 26.5, 25.0, 24.3, 22.9, 16.8, 14.2; $\nu_{\max}$ (film) /cm⁻¹ 2361 (C $\equiv$ N), 1653 (C=O); m/z (EI) 312 (60 %, M), 255 (90 % M-CH₃CH₂CH₂CH₂), 218 (80 % M-CNCH₂CH₂CH₂CCH₂); found [M+H]⁺ 312.1447, C₁₆H₂₆NOS₂ requires 312.1450.

Table 2 entry 9; 2-[2-(2-Butyl-[1,3]dithiane-2-yl)-acetyl]-but-2-enedioic acid dimethyl ester

The general procedure for the hydroacylation reaction was followed employing pre-catalyst [Rh(nbd)(dppe)]ClO₄ (10 mg, 0.013 mmol), acetone (2 mL), [1,3]dithiolan-2-yl-acetaldehyde (30 mg, 0.13 mmol) and dimethyl acetylenedicarboxylate (80 μ L, 0.65 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a yellow oil (35 mg, 71 % 3:1 *Z:E*); δ_{H} (300 MHz; CDCl₃) (major *Z*) 6.76 (1H, s), 3.81 (3H, s), 3.79 (3H, s), 3.50 (2H, s), 2.95-2.72 (4H,

m), 2.19-2.13 (2H, m), 2.11-1.82 (2H, m), 1.58-1.22 (4H, m), 0.92 (3H, t, J 7.2); (minor *E*) 6.70 (1H, s), 3.89 (3H, s), 3.79 (3H, s), 3.30 (2H, s), 2.95-2.72 (2H, m), 2.19-2.13 (2H, m), 2.11-1.82 (2H, m), 1.58-1.22 (4H, m), 0.92 (3H, t, J 7.2); δ_{C} (75 MHz; CDCl_3) (*E* and *Z*) 197.1, 196.7, 165.3, 164.3, 164.2, 163.0, 146.1, 144.9, 128.1, 127.8, 52.8, 52.7, 52.4, 52.3, 50.2, 49.6, 49.3, 45.2, 38.2, 37.9, 26.2 (2 CH_2), 26.1 (2 CH_2), 26.0, 25.6, 24.8, 24.6, 22.6, 22.5, 13.7, 13.6 ; ν_{max} (film) $/\text{cm}^{-1}$ 1791, 1740, 1714 ($\text{C}=\text{O}$); m/z (EI) 360 (30 %, M), 254 (60 % M- $\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 217 (100 % M- $\text{CO}_2\text{MeCCHCO}_2\text{Me}$); found $[\text{M}+\text{H}]^+$ 360.1065, $\text{C}_{16}\text{H}_{25}\text{O}_5\text{S}_2$ requires 360.1065.

Table 2 entry 10; 1-(2-butyl-[1,3]dithiane-2-yl-5-hydroxymethyl-pent-3-en-2-one

The general procedure for the hydroacylation reaction was followed employing pre-catalyst $[\text{Rh}(\text{nbd})(\text{dppe})]\text{ClO}_4$ (10 mg, 0.013 mmol), acetone (2 mL), [1,3]dithiolan-2-yl-acetaldehyde (30 mg, 0.13 mmol) and 2-Butyne-1,4-diol (60 mg, 0.65 mmol). Heated at 55 °C for 16 hours. Flash chromatography (1:4, EtOAc:Petrol) yielded the title compound as a colourless oil (35 mg, 83 % 4:1 *E:Z*); δ_{H} (300 MHz; CDCl_3) 6.65 (1H, tt, J 3.7, 1.4), 4.50 (2H, td, J 1.9, 1.4), 4.37 (2H, dt, J 3.7, 1.9), 3.16 (2H, s), 2.84-2.69 (4H, m), 2.08-2.02 (2H, m), 1.94-1.87 (2H, m), 1.41-1.24 (4H, m) 0.86 (3H, t, J 7.1); δ_{C} (75 MHz; CDCl_3) 195.7, 143.2, 140.3, 60.6, 59.7, 50.9, 43.8, 38.0, 26.4 (2 CH_2), 24.9, 23.6, 22.8, 14.0; ν_{max} (film) $/\text{cm}^{-1}$ 2921, 2860 (OH), 1653 ($\text{C}=\text{O}$); m/z (EI) 304 (30 %, M), 273 (100 % M- CH_2OH), 217 (70 % M- $\text{CH}_2\text{OHCCHCH}_2\text{OH}$); found $[\text{M}+\text{H}]^+$ 304.4705, $\text{C}_{14}\text{H}_{25}\text{O}_3\text{S}_2$ requires 304.4706.

4,6-dioxo-decanoic acid methyl ester (2)

Table 1 entry 3 (50 mg, 0.18 mmol) in MeCN (2 mL) was added to a solution of NBS (190 mg, 1.07 mmol), AgNO_3 (112 mg, 0.67 mmol) and 2,6-lutidine (39 μL , 0.33 mmol) in MeCN (5 mL) and water (1.2 mL) at 0 °C. The resulting solution was stirred for 30 minutes then warmed to room temperature. The reaction was diluted with ethyl acetate (20 mL), washed with ammonium chloride (20 mL), sodium sulfate (20 mL),

brine (20 mL), water (20 mL) and dried (MgSO₄). It was then purified by flash chromatography (1:4 EtOAc: Petrol) to yield the title compound as a pale yellow oil (35 mg, 76%); δ_{H} (300 MHz; CDCl₃) (major enol) 15.18 (1H, br.s), 5.51 (1H, s), 3.69 (3H, s), 2.66-2.59 (4H, m), 2.26 (2H, t, *J* 7.4), 1.63-1.51 (2H, m), 1.42-1.25 (2H, m), 0.92 (3H, t, *J* 7.3); δ_{C} (75 MHz; CDCl₃) (minor ketone) 3.68 (3H, s), 3.61 (2H, s), 2.66-2.59 (2H, m), 2.83 (2H, t, *J* 6.7), 2.52 (2H, t, *J* 6.7), 1.63-1.51 (2H, m) 1.42-1.25 (2H, m), 0.90 (3H, t, *J* 7.3); δ_{C} (75 MHz; CDCl₃) (keto/enol) 204.5, 202.8, 195.6, 191.1, 173.4, 173.3, 99.5, 57.6, 52.2, 43.9, 38.5, 37.5, 34.2, 30.1, 29.2, 28.4, 28.0, 25.9, 22.7, 22.6, 14.2, 14.1; ν_{max} (film) /cm⁻¹ 1736, 1719, 1709 (C=O). *m/z* (EI) found [M+H]⁺ 215.1280, C₁₁H₁₉O₄ requires 215.1278.

Dodecane-3,6-dione (6)

Raney-nickel (0.5 g) was added to a solution of (table 1 entry 3) (30 mg, 0.1 mmol) in EtOH (5 ml). The resulting mixture was heated to reflux for 4 hours and then cooled to room temperature. The reaction was filtered through celite and purified by flash chromatography (1:4 EtOAc: Petrol). Data consistent to that reported in literature.³

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