Conjugate Reduction and Reductive Aldol Cyclization of $\alpha, \beta$-Unsaturated Thioesters Catalyzed by (BDP)CuH

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General Experimental

Preparative: All reactions were performed in oven-dried round-bottomed flasks under a positive pressure of dry argon. Reactions were monitored by thin layer chromatography (TLC) using E. Merck silica gel plates, Kieselgel 60 F254 with 0.2 mm thickness. Components were visualized by illumination with short-wavelength ultra-violet light and/or staining. Flash column chromatography was performed with E. Merck silica gel 60 (230-400 mesh ASTM). Solvents and chemicals were purified according to standard procedures. Dichloromethane (DCM), tetrahydrofuran (THF) and toluene were distilled from CaH2 under argon.

Analytical: All 1H and 13C NMR spectra were recorded in deuteriochloroform (CDCl3) unless otherwise specified, with tetramethylsilane (TMS) as an internal standard at ambient temperature on a Bruker DPX 300, 400, 500 or 600 MHz Fourier Transform Spectrometer operating at 300 MHz, 400 MHz, 500 MHz or 600 MHz for 1H and at 75 MHz, 100 MHz, 125 MHz or 150 MHz respectively for 13C. All the spectra were calibrated at δ 7.26 ppm for 1H and δ 77.03 ppm for 13C. Spectral features were designated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad. IR absorption spectra were recorded as a solution in CH2Cl2 or CCl4 on a BioRad Fourier Transform 165 Spectrophotometer from 4000 cm⁻¹ to 400 cm⁻¹. Mass Spectra were recorded on a Finnigan MAT 95 mass spectrometer or API QSTAR PULSAR LC/MS/TOF System for both low resolution and high resolution, with accurate mass reported for the molecular ion (M⁺) or next largest fragment thereof. Melting points were measured on Zeiss Asiolab Microscope using Linkam TC92 temperature controller.

Typical procedure A for the synthesis of unsaturated thioesters

![Chemical structure of 1a](image)

S-ethyl 2-(triphenylphosphoranylidene)ethanethioate (R1) was synthesized according to the literature procedure.¹

To a solution of 3-phenylpropanal (0.1459 g, 1.087 mmol) in HPLC grade CHCl3 (9 mL) was added R1 (8.1222 g, 2.3315 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was concentrated in vacuo and the residue was purified by flash chromatography (5% EtOAc in hexane) to afford 1a (0.2186 g, 98%) as a pale yellow oil. 1a: Rf
Typical procedure B for synthesis of unsaturated thioesters

EDCI (1.6318 g, 8.5122 mmol) and DMAP (69.5 mg, 0.568 mmol) were added to a solution of (E)-5-phenylpent-2-enoic acid (0.9997 g, 5.673 mmol) in DCM (60 mL) at 0 °C. Butanethiol (0.795 mL, 7.38 mmol) was added after 15 minutes. The resulting mixture was allowed to slowly warm to room temperature overnight. The mixture was washed with a saturated aqueous solution of NaHCO₃, then H₂O. The organics were dried over anhydrous MgSO₄, and concentrated under reduced pressure. The residue was purified by flash chromatography (5% EtOAc in hexane) to afford 1b (1.1332 g, 80%) as a pale yellow oil. 1b: Rf (5% EtOAc in hexane): 0.36; IR (CH₂Cl₂): 3065, 3028, 2960, 2932, 1668 (C=O), 1454 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.29-7.26 (m, 2H), 7.23-7.16 (m, 3H), 6.92 (dt, J = 15.5, 6.8 Hz, 1H), 6.13 (dt, J = 15.5, 1.5 Hz, 1H), 2.94 (t, J = 7.3 Hz, 2H), 2.81-2.75 (m, 2H), 2.55-2.48 (m, 2H), 1.63-1.53 (m, 2H), 1.46-1.36 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 190.2, 143.9, 140.7, 129.2, 128.5 (2C), 128.4 (2C), 126.2, 34.4, 33.9, 31.7, 28.4, 22.0, 13.6 ppm; LRMS (EI, 20 eV): m/z 248 (M⁺, 1), 159 (100), 91 (76), 77 (24); HRMS (EI, 20 eV): calcd for C₁₅H₂₀OS (M⁺), 248.1229 found 248.1230.

According to the typical procedure B, EDCI (0.83 g, 4.3 mmol) and DMAP (40 mg, 0.33 mmol) were treated with (E)-5-phenylpent-2-enoic acid (0.50 g, 2.8 mmol) in DCM (10.0 mL) and dodecanethiol (0.87 g, 4.3 mmol). After workup, the residue was purified by flash chromatography (5% EtOAc in hexane) to afford 1c (1.0 g, 97%) as a pale yellow oil. 1c: Rf (5% EtOAc in hexane): 0.69; IR (CH₂Cl₂): 2928, 2856, 1666 (C=O), 1632, 1455, 1035 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.34-7.28 (m, 2H), 7.22-7.18 (m, 3H), 6.94 (dt, J = 15.4, 6.9 Hz, 1H), 6.14 (td, J = 15.5, 1.5 Hz, 1H), 2.95 (t, J = 7.3 Hz, 2H), 2.80 (t, J = 7.4 Hz, 1H), 2.54-2.52 (m, 2H), 1.63-1.59 (m, 3H), 1.40-1.29 (m, 18H), 0.92-0.87 (t, J = 6.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 190.1, 143.8, 140.7, 129.2, 128.5, 128.4, 126.1, 34.2, 33.7, 22.9, 14.7 ppm.
128.3, 126.2, 34.3, 33.9, 31.9, 29.6, 29.5, 29.4, 29.1, 28.9, 28.7, 22.7, 14.1 ppm. LRMS (EI, 20 eV): m/z 360.2 (M⁺, 1.29), 90.1 (39), 159.1 (100); HRMS (EI, 20 eV): calcd for C₂₃H₃₆OS (M⁺) 360.2481, found 360.2478.

**Typical procedure C for synthesis of unsaturated thioesters**

![Diagram](image)

Oxalyl chloride (2.2 mL, 26 mmol) in 10 mL THF and six drops of DMF was added to a solution of (E)-5-phenylpent-2-enoic acid (2.9981 g, 17.014 mmol) in 120 mL THF. The resulting mixture was stirred for 1 hour and then concentrated under reduced pressure. The residue was dissolved in 150 mL PhMe. Then tBuSH (2.0 mL, 17 mmol) and zinc dust (1.13 mg, 17.0 mmol) were added. After stirring for 1 hour, the mixture was washed with saturated aqueous solution of NaHCO₃, and the aqueous layer was extracted by 50% EtOAc in hexane. The extracts were dried over anhydrous MgSO₄, and concentrated under reduced pressure. The residue was purified by flash chromatography (3% EtOAc in hexane) to afford 1d (2.9921 g, 71%) as a pale yellow oil. 1d: Rf (5% EtOAc in hexane): 0.44; ¹H NMR (400 MHz, CDCl₃): δ 7.31-7.26 (m, 2H), 7.23-7.17 (m, 3H), 6.86 (dt, J = 6.8, 15.5 Hz, 1H), 6.05 (dt, J = 15.5, 1.5 Hz, 1H), 2.79-2.75 (m, 2H), 2.52-2.46 (m, 2H), 1.51 (s, 9H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 190.7, 142.8, 140.8, 129.8, 128.5 (2C), 128.3 (2C), 126.2, 47.9, 33.8, 30.0 ppm; LRMS (EI, 20 eV): m/z 248 (M⁺, 1), 191 (9), 159 (100), 131 (11); HRMS (EI, 20 eV): calcd for C₁₅H₂₀OS (M⁺) 248.1235, found 248.1232 ppm. The characterization corresponded to that of 1d documented in the literature.

According to Typical procedure C, oxalyl chloride (360 μL, 4.26 mmol) in 2 mL THF and two drops of DMF was added to a solution of (E)-5-phenylpent-2-enoic acid (492.0 mg, 2.792 mmol) in 18 mL THF. The resulting mixture was stirred for 1 hour and then concentrated under reduced pressure. Then PhSH (290 μL, 2.84 mmol) and zinc (185.9 mg, 2.843 mmol) was added and stirred for 1 hour. After workup, the residue was purified by flash chromatography (3% EtOAc in hexane) to afford 1e (566.7 mg, 76%) as a pale yellow oil. 1e: Rf (5% EtOAc in hexane): 0.41; ¹H NMR (400 MHz, CDCl₃): δ 7.42-7.38 (m, 5H), 7.32-7.27 (m, 2H), 7.23-7.16 (m, 3H), 7.01 (dt, J = 15.5, 6.8 Hz, 1H), 6.19 (dt, J = 15.5, 1.4 Hz, 1H), 2.82-2.76 (m, 2H), 2.57-2.50 (m, 2H) ppm; ¹³C NMR (100 MHz,
CDCl$_3$: $\delta$ 187.9, 145.5, 140.6, 134.6 (2C), 129.36, 129.2 (2C), 128.6 (2C), 128.4 (2C), 128.3, 127.6, 126.3, 34.3, 34.0 ppm. The characterization corresponded to that of 1e documented in the literature.$^4$

DMSO (1.0 mL, 14 mmol) in 10 mL DCM was added to a solution of oxalyl chloride (600 $\mu$L, 7.09 mmol) in 10 mL DCM at – 78 °C. After stirring for 15 minutes, 4-penten-1-ol (498.0 mg, 5.782 mmol) was added over in 9 mL DCM. NEt$_3$ was added after 15 minutes. The resulting mixture was allowed to slowly warm to room temperature after 1 hour and stirred at room temperature for another 1 hour.

Wittig reagent R$_1$ (1.715 g, 4.706 mmol) was then added and the mixture was allowed to stir overnight. The mixture was quenched with water, and extracted with 50% EtOAc/ hexane. The extracts were dried over anhydrous MgSO$_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography (2% EtOAc in hexane) to afford 1f (0.6120 g, 77%). 1f: $R_f$ (3% EtOAc in hexane): 0.31; IR (CH$_2$Cl$_2$): 3051, 2974, 2931, 2874, 1668 (C=O), 1450 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.88 (dt, $J = 15.5, 6.5, 1H$), 6.11 (dt, $J = 15.5, 1.5$ Hz, 1H), 5.84-5.74 (m, 1H), 5.08-5.00 (m, 2H), 2.94 (q, $J = 7.4$ Hz, 2H), 2.32-2.15 (m, 4H), 1.27 (t, $J = 7.4$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 190.1, 144.2, 137.0, 129.1, 115.7, 32.0, 31.4, 23.1, 14.8 ppm; LRMS (ESI): m/z 171 ([M++H]$^+$, 23), 155 (21), 129 (100); HRMS (ESI): calcd for C$_9$H$_{14}$OS ([M++H]$^+$), 171.0843, found 171.0846.

According to the typical procedure B, EDCI (7.1931 g, 37.450 mmol) and DMAP (452.0 mg, 3.121 mmol) were treated with (E)-2-methylhex-2-enoic acid (3.9931 g, 31.155 mmol) in DCM (310 mL) and butanethiol (4.0 mL, 37 mmol). After workup, the residue was purified by flash chromatography (3% EtOAc in hexane) to afford 1g (4.8693 g, 78%) as a pale yellow oil. $R_f$ (5% EtOAc in hexane): 0.39; IR (CH$_2$Cl$_2$): 3035, 2963, 2933, 2874, 1650 (C=O), 1621, 1465, 1382, 1205 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.74-6.70 (m, 1H), 2.89 (t, $J = 7.4$ Hz, 2H), 2.19-2.14 (m, 2H), 1.86 (d, $J = 0.5$ Hz, 3H), 1.60-1.52 (m, 2H), 1.51-1.44 (m, 2H), 1.44-1.35 (m, 2H), 0.94 (t, $J = 7.4$ Hz, 3H), 0.91 (t, $J = 7.3$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 194.0, 140.6, 136.2, 31.7, 30.7, 28.6, 22.1, 21.8, 13.9, 13.6, 12.4 ppm; LRMS (EI, 20 eV): m/z 200 (M$^+$, 3), 136 (46), 111 (100); HRMS (EI, 20 eV): calcd for C$_{11}$H$_{20}$OS (M$^+$), 200.1229 found 200.1228.
According to the typical procedure B, EDCI (4.6155 g, 24.077 mmol) and DMAP (0.2110 mg, 1.727 mmol) were treated with cyclohex-1-enecarboxylic acid (1.9983 g, 15.839 mmol) in DCM (150 mL) and ethane thiol (1.4 mL, 19 mmol). After workup, the residue was purified by flash chromatography (5% EtOAc in hexane) to afford 1h (2.3117 g, 86%) as a pale yellow oil.  

1h: Rf (5% EtOAc in hexane): 0.78; IR (CH2Cl2): 3057, 2933, 2862, 1654 (C=O), 1641 (C=C), 1450, 1258 cm⁻¹; ¹H NMR (400 MHz, CDCl3): δ 6.98-6.95 (m, 1H), 2.91 (q,  J = 7.4 Hz, 2H), 2.32-2.28 (m, 2H), 2.24-2.19 (m, 2H), 1.68-1.60 (m, 4H), 1.26 (t,  J = 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl3): δ 193.2, 138.6, 138.0, 25.8, 24.1, 22.9, 22.0, 21.6, 14.9 ppm; LRMS (EI, 20 eV): m/z 170 (M⁺, 2), 109 (100), 81 (36), 89 (8); HRMS (EI, 20 eV): calcd for C₉H₁₄OS (M⁺) 170.0760, found 170.0758.

According to the typical procedure B, EDCI (5.5698 g, 23.779 mmol) and DMAP (0.1986 mg, 1.585 mmol) were treated with cyclohex-1-enecarboxylic acid (1.9996 g, 15.850 mmol) in DCM (160 mL) and butanethiol (2.0 mL, 19 mmol). After workup, the residue was purified by flash chromatography (2% EtOAc in hexane) to afford 1i (2.6289 g, 84%) as a pale yellow oil.  

1i: Rf (5% EtOAc in hexane): 0.78; IR (CH₂Cl₂): 3064, 2984, 2933, 1733 (C=O), 1447, 1374, 1247 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 6.99-6.96 (m, 1H), 2.90 (t,  J = 7.4 Hz, 2H), 2.32-2.29 (m, 2H), 2.23-2.19 (m, 2H), 1.66-1.55 (m, 6H), 1.43-1.37 (m, 2 H), 0.92 (t,  J = 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 193.2, 138.6, 138.0, 31.8, 28.2, 25.8, 24.1, 22.1, 22.0, 21.6, 13.7 ppm; LRMS (EI, 20 eV): m/z 198 (M⁺, 5), 109 (100), 89 (40), 81 (36); HRMS (EI, 20 eV): calcd for C₁₁H₁₈OS (M⁺), 198.1073 found 198.1079.

According to the typical procedure B, EDCI (5.4882 g, 28.629 mmol) and DMAP (0.3120 mg, 2.554 mmol) were treated with (E)-3,7-dimethylocta-2,6-dienoic acid (4.001 g, 23.78 mmol) in DCM (230 mL) and ethanethiol (2.1 mL, 29 mmol). After workup, the residue was purified by flash chromatography (3% EtOAc in hexane) to afford 1j (4.025 g, 80%) as a pale yellow oil.  

1j: Rf (5% EtOAc in hexane): 0.41; IR (CH₂Cl₂): 3025, 2992, 2922, 2851, 1668 (C=O), 1623 (C=C), 1447, 1378, 1258 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 5.94 (s, 1H), 5.15-5.11 (m, 1H), 2.89 (q,  J = 7.4 Hz, 2H), 2.62-2.58 (m, 2H), 2.18-2.12 (m, 2H), 1.86 (s, 3H), 1.67 (s, 3H), 1.61 (s, 3H), 1.26 (t,  J = 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 188.9, 157.2, 132.3, 123.6, 123.5, 34.4, 26.8, 25.7, 25.2, 23.2, 17.7, 15.0 ppm; LRMS (EI, 20 eV): m/z 212 (M⁺, 9), 151 (100), 123(90), 109 (94);
According to the typical procedure B, EDCI (1.0579 g, 5.518 mmol) and DMAP (70 mg, 0.57 mmol) were treated with cinnamic acid (0.7482 g, 5.050 mmol) in DCM (25 mL) and ethanethiol (450 μL, 6.08 mmol). After workup, the residue was purified by flash chromatography (5% EtOAc in hexane) to afford 1k (0.8532 g, 88%) as a pale yellow oil. 1k: R_f (5% EtOAc in hexane): 0.38; 1H NMR (400 MHz, CDCl_3): δ 7.60 (d, J = 15.8 Hz, 1H), 7.55-7.51 (m, 2H), 7.40-7.37 (m, 3H), 6.71 (d, J = 15.8 Hz, 1H), 3.02 (q, J = 7.4 Hz, 2H), 1.32 (t, J = 7.4 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl_3): δ 189.8, 140.1, 134.1, 130.4, 128.8 (2C), 128.3 (2C), 125.1, 23.3, 14.8 ppm. The characterization corresponded to that of 1k documented in the literature.3

According to the typical procedure B, EDCI (5.4862 g, 28.476 mmol) and DMAP (285.6 mg, 2.190 mmol) were treated with (E)-3-(2-chlorophenyl)acrylic acid (4.0001 g, 21.905 mmol) in DCM (210 mL) and ethanethiol (2.0 mL, 26 mmol). After workup, the residue was purified by flash chromatography (3% EtOAc in hexane) to afford 1l (4.1467 g, 84%) as a pale yellow oil. 1l: R_f (10% EtOAc in hexane): 0.39; IR (CH_2Cl_2): 3055, 2992, 2911, 1733 (C=O), 1664 (C=C), 1616, 1464, 1371, 1247 cm^{-1}; 1H NMR (400 MHz, CDCl_3): δ 8.02 (d, J = 15.8 Hz, 1H), 7.64-7.61 (m, 1H), 7.43-7.41 (m, 1H), 7.34-7.27 (m, 2H), 6.69 (d, J = 15.8 Hz, 1H), 3.03 (q, J = 7.4 Hz, 2H), 1.33 (t, J = 7.4 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl_3): δ 189.8, 136.2, 135.5, 132.6, 131.2, 130.3, 127.7, 127.6, 127.1, 23.5, 14.8; LRMS (EI, 20 eV): m/z 226 (M^+, 18), 191 (14), 165 (100), 76 (15); HRMS (EI, 20 eV): calcd for C_{11}H_{11}OClS (M^+) 226.0214, found 226.0206.

According to the typical procedure B, EDCI (5.2507 g, 27.390 mmol) and DMAP (296.5 mg, 2.427 mmol) were treated with (E)-3-(3-nitrophenyl)acrylic acid (4.0003 g, 20.709 mmol) in DCM (200 mL) and ethanethiol (2 mL, 25 mmol). After workup, the residue was purified by flash chromatography (EtOAc: DCM: hexane= 5: 1: 94) to afford 1m (3.7841 g, 77%) as a pale yellow solid. 1m: R_f (10% EtOAc in hexane): 0.39; mp: 77-79 °C; IR (CH_2Cl_2): 3046, 2986, 2938, 2878, 1661 (unsaturated C=O), 1621, 1523, 1348 cm^{-1}; 1H NMR (400 MHz, CDCl_3): δ 8.38-8.37 (m, 1H), 8.24-8.21 (m, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.60 (d, J = 15.8 Hz, 1H), 7.60-7.56 (m, 1H), 6.79 (d, J = 15.8 Hz, 1H), 3.03 (q, J = 7.4 Hz, 2H), 1.32 (t, J = 7.4 Hz, 3H) ppm; 13C NMR
According to the typical procedure B, EDCI (5.1917 g, 26.921 mmol) and DMAP (286.5 mg, 2.071 mmol) were treated with (E)-3-(4-nitrophenyl)acrylic acid (3.9993 g, 20.704 mmol) in DCM (200 mL) and ethanethiol (2 mL, 25 mmol). After workup, the residue was purified by flash chromatography (6% EtOAc in hexane) to afford 1n (4.182 g, 85%) as a pale yellow solid. 1n: R\textsubscript{f} (10% EtOAc in hexane): 0.38; mp: 106-108; IR (CH\textsubscript{2}Cl\textsubscript{2}): 3080, 2974, 2993, 2934, 1662 (unsaturated C=O), 1622, 1523, 1457, 1347 cm\textsuperscript{-1}; ¹H NMR (400 MHz, CDCl\textsubscript{3}): δ 8.26-8.23 (m, 2H), 7.70-7.67 (m, 2H), 7.61 (d, J = 15.8 Hz, 1H), 6.79 (d, J = 15.8 Hz, 1H), 3.05 (q, J = 7.4 Hz, 2H), 1.34 (t, J = 7.4 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl\textsubscript{3}): δ 189.4, 148.6, 140.5, 137.0, 128.9 (2C), 128.8 (2C), 124.2, 23.7, 14.7 ppm; LRMS (EI, 20 eV): m/z 237 (M\textsuperscript{+}, 2), 176 (86), 130 (39), 77 (100); HRMS (EI, 20 eV): calcd for C\textsubscript{11}H\textsubscript{11}O\textsubscript{3}NS (M\textsuperscript{+}) 237.0454, found 237.0453.

According to the typical procedure B, EDCI (2.5933 g, 13.470 mmol) and DMAP (162.3 mg, 1.122 mmol) were treated with (E)-3-(3-methoxyphenyl)acrylic acid (1.9996 g, 11.222 mmol) in DCM (25 mL) and ethanethiol (970 μL, 13.4 mmol). After workup, the residue was purified by flash chromatography (3% EtOAc in hexane) to afford 1o (1.8644 g, 75%) as a pale yellow oil. 1o: R\textsubscript{f} (5% EtOAc in hexane): 0.41; IR (CH\textsubscript{2}Cl\textsubscript{2}): 3056, 2970, 2934, 2839, 1664 (C=O), 1612, 1581, 1486, 1455, 1292, 1244 cm\textsuperscript{-1}; ¹H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.57 (d, J = 15.8 Hz, 1H), 7.30 (t, J = 7.9 Hz, 1H), 7.13 (d, J = 7.6 Hz, 1H), 7.05 (t, J = 2.2 Hz, 1H), 6.94 (dd, J = 8.1, 2.4 Hz, 1H), 6.69 (d, J = 15.8 Hz, 1H), 3.83 (s, 3H), 3.04 (d, J = 7.4 Hz, 1H), 3.00 (d, J = 7.4 Hz, 1H), 1.25 (t, J = 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl\textsubscript{3}): δ 198.7, 159.8, 141.8, 129.5, 120.7, 114.1, 111.7, 55.2, 45.5, 31.5, 23.4, 14.8 ppm; LRMS (EI, 20 eV): m/z 222 (M\textsuperscript{+}, 15), 161 (100), 133 (43), 77 (13); HRMS (EI, 20 eV): calcd for C\textsubscript{12}H\textsubscript{14}O\textsubscript{2}S (M\textsuperscript{+}) 222.0709, found 222.0712.
Thioester 1p was prepared according to typical procedure for the preparation of 1a, using aldehyde S15 (2.7243 g, 12.040 mmol), R1 (6.582 g, 18.06 mmol) in HPLC grade CHCl3 (20 mL) to afford 1p (3.1051 g, 83%) as a pale yellow oil. 1p: Rf (20% EtOAc in hexane): 0.53; IR (CH2Cl2): 3054, 2945, 2870, 1711 (saturated C=O), 1668 (unsaturated C=O), 1631 (C=C), 1452, 1311, 1253, 1191 cm⁻¹; 1H NMR (400 MHz, CDCl3): δ 6.57 (dt, J = 15.5, 6.5 Hz, 1H), 5.83 (dt, J = 15.5, 1.5 Hz, 1H), 3.96-3.91 (m, 2H), 2.65 (q, J = 7.4 Hz, 2H), 2.26-2.16 (m, 3H), 1.96-1.94 (m, 1H), 1.84-1.69 (m, 3H), 1.49-1.34 (m, 4H), 1.00-0.97 (m, 6H); 13C NMR (100 MHz, CDCl3): δ 207.4, 189.8, 171.5, 143.9, 128.8, 61.3, 60.2, 40.9, 36.3, 32.8, 27.4, 27.0, 22.9, 22.5, 14.7, 14.0 ppm; LRMS (EI, 20 eV): m/z 312 (M⁺, 3), 251 (77), 205 (100), 170 (79); HRMS (EI, 20 eV): calcd for C16H24O4S (M⁺) 312.1395, found 312.1399.

To a solution of ethyl 1-allyl-2-oxocyclohexanecarboxylate⁶ (3.16 g, 15 mmol) in THF (22 mL) and H₂O (4.5 mL) was added OsO₄ (0.038 g, 0.15 mmol) in t-BuOH (0.5 mL). When the solution turned black, NMO (4.02 g, 30.1 mmol) was added in portions to the reaction mixture. The black color faded and stirring was continued overnight at RT. The crude mixture was filtered through celite. The filtrate was extracted with Et₂O (3 x 30 mL). The combined organic extracts were dried over anhydrous MgSO₄ and concentrated in vacuo.

The residue was dissolved in DCM (15 mL). To this was added H₂O (6 mL) and NaIO₄ (7.07 g, 33.1 mmol). The reaction mixture was stirred overnight at room temperature. The mixture was filtered through celite. The filtrate was extracted with DCM (3 x 3 mL). The combined organic extracts were dried over anhydrous MgSO₄ and concentrated in vacuo. The residue was purified by flash chromatography (20% EtOAc in hexane) to afford S2 (2.6 g, 82%) as a pale yellow oil. S2: Rf (20% EtOAc in hexane): 0.29; IR (CCl₄): 2942, 2869, 1805, 1736, 1718, 1447, 1370, 1315, 1205, 1161, 1131, 1094, 1031, 956 cm⁻¹; 1H NMR (300 MHz, CDCl₃): δ 9.66 (t, J = 1.6 Hz, 1H), 4.21-4.12 (m, 2H), 2.78-2.59 (m, 3H), 2.45-2.36 (m, 2H), 2.14-1.96 (m, 1H), 1.78-1.51 (m, 4H), 1.22 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (75 MHz, CDCl₃): δ 207.0, 199.1, 171.3, 61.9, 59.1, 47.8, 40.5, 36.8, 27.0, 22.0, 14.0 ppm; HRMS (EI, 20 eV): calcd for C₁₁H₁₄O₄ (M⁺) 212.1049, found: 212.1049.
Supporting Information

Typical procedure for 1,4-reduction of unsaturated thioesters using (BDP)CuH

A solution of 3 (39.4 mg, 0.200 mmol) and BDP (89.1 mg, 0.199 mmol) in 1.0 mL PhMe was stirred at room temperature for 5 minutes. PMHS (360 μL, 6.01 mmol) was added and the reaction mixture became greenish-yellow. Thioester 1a (440.5 mg, 1.999 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added sequentially. The reaction was monitored by TLC and quenched by the addition of saturated aqueous NH₄Cl solution. The reaction mixture was filtered through a pad of silica gel. The filtrate was extracted with EtOAc (3 x 10 mL), dried over anhydrous MgSO₄ and concentrated. The residue was purified by flash chromatography using 1.5% EtOAc in hexane to afford 2a (403.8 mg, 91%) as a pale yellow oil. 2a: Rf (5% EtOAc in hexane): 0.56; IR (CH₂Cl₂): 3035, 2938, 2857, 1684 (C=O), 1449, 1264 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.25-7.29 (m, 2H), 7.16-7.20 (m, 3H), 2.87 (q, J = 7.4 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 2.56 (m, 2H), 1.63-1.73 (m, 4H), 1.24 (t, J = 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 199.6, 142.1, 128.42, 128.37, 128.35, 125.8, 43.9, 35.6, 30.7, 25.3, 23.3, 14.8 ppm; LRMS (ESI): m/z 245 ([M+Na⁺], 32), 161 (100), 162 (13); HRMS (ESI): calcd for C₁₃H₁₈OS ([M+Na⁺], 245.0976, found 245.0983.

According to the typical procedure for 1,4-reduction using (BDP)CuH, 3 (20.0 mg, 0.10 mmol), BDP (45.0 mg, 0.10 mmol), Ph₂SiD₂ (0.28 g, 1.50 mmol) were stirred at in 0.5 mL PhMe. Then 1a (0.22 g, 1.0 mmol) and tBuOH (0.44 g, 2.0 mmol) in 0.5 mL toluene were added. After workup, the residue was purified by flash chromatography using 2% EtOAc in hexane to afford 2a-d₁ (129 mg, 58% yield) as pale yellow oil. Rf (5% EtOAc in hexane): 0.56; IR (CH₂Cl₂): 3035, 2938, 2860, 1683 (C=O), 1454 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.25-7.29 (m, 2H), 7.16-7.20 (m, 3H), 2.87 (q, J = 7.4 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 2.56 (m, 2H), 1.63-1.73 (m, 3H), 1.24 (t, J = 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 199.5, 142.0, 128.4, 128.4, 125.8, 43.8, 35.6, 30.6, 24.9 (t, J = 19.5 Hz), 23.2, 14.8 ppm; LRMS (ESI): m/z 246 ([M+Na⁺], 246(45), 162 (89), 118 (100); HRMS (ESI): calcd for C₁₃H₁₇ODS ([M+Na⁺⁺], 246.1033, found 246.1039.

According to the typical procedure for 1,4-reduction using (BDP)CuH, 3 (39.4 mg, 0.200 mmol) and BDP (89.1 mg, 0.199 mmol) were stirred in 1.0
mL PhMe. PMHS (360 μL, 6.01 mmol), thioester 1b (496.4 mg, 1.999 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 2% EtOAc in hexane to afford 2b (449.8 mg, 90%) as a pale yellow oil. 2b: Rf (5% EtOAc in hexane): 0.44; IR (CH₂Cl₂): 3084, 3026, 2926, 2862, 1670 (C=O), 1602, 1494, 1454 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.29-7.25 (m, 2H), 7.19-7.15 (m, 3H), 2.87 (t, J = 7.3 Hz, 2H), 2.64-2.60 (m, 2H), 1.73-1.63 (m, 4H), 1.41-1.35 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 199.7, 142.2, 128.5 (2C), 128.4 (2C), 125.9, 44.0, 35.7, 31.8, 30.8, 28.7, 25.4, 22.1, 13.7 ppm; LRMS (EI, 20 eV): m/z 161 (M⁺-C₄H₉S, 96), 117 (84), 91 (100); HRMS (EI, 20 eV): calcd for C₁₁H₁₃O (M⁺-C₄H₉S) 161.0961, found 161.0954.

According to the typical procedure for 1, 4-reduction using (BDP)CuH, 3 (39.4 mg, 0.200 mmol) and BDP (89.1 mg, 0.199 mmol) were dissolved in 1.0 mL PhMe. PMHS (360 μL, 6.01 mmol), thioester 1b (721.2 mg, 1.999 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 3% EtOAc in hexane to afford 2c (435.1 mg, 60%) as a pale yellow oil, along with recovered 1c (129.8 mg, 18%) 2c: Rf (5% EtOAc in hexane): 0.49; IR (CH₂Cl₂): 3063, 3042, 2927, 2854, 1686 (C=O), 1455, 1267 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.31-7.27 (m, 2H), 7.21-7.16 (m, 3H), 2.87 (t, 2H, J = 7.27), 2.66-2.55 (m, 3H), 1.72-1.68 (m, 3H), 1.66-1.54 (m, 3H), 1.25-1.27 (m, 19H), 0.92-0.87 (t, 3H, J = 6.4 Hz) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 199.5, 142.0, 128.4, 126.1, 43.9, 41.7, 35.6, 31.9, 30.7, 29.6, 29.6, 29.5, 29.4, 29.2, 29.1, 28.9, 28.8, 25.3, 22.7, 14.1 ppm; LRMS (EI, 20 eV): m/z 161 (M⁺-C₁₂H₂₅, 100), 160.1 (90); HRMS (EI, 20 eV): calcd for C₂₃H₃₈OS, 362.2638, found 362.2538.

According to the typical procedure for 1, 4-reduction using (BDP)CuH, 3 (39.2 mg, 0.199 mmol) and BDP (89.5 mg, 0.200 mmol) were stirred in 1.0 mL PhMe. PMHS (600 μL, 10.0 mmol), thioester 1b (496.3 mg, 1.998 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 3% EtOAc in hexane to afford 2d (260.0 mg, 51%) as a pale yellow oil, along with recovered 1d (170.0 mg, 34%). 2d: Rf (5% EtOAc in hexane): 0.49; IR (CH₂Cl₂): 3066, 3029, 2966, 2829, 2863, 1679 (C=O), 1455, 1365 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.29-7.24 (m, 2H), 7.19-7.15 (m, 3H), 2.64-2.59 (m, 2H), 2.49-2.40 (m, 2H), 1.72-1.58 (m, 4H), 1.45 (s, 9H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 200.3, 142.1, 128.4 (2C), 128.3 (2C), 125.8,
According to the typical procedure for 1,4-reduction using (BDP)CuH, 3 (78.6 mg, 0.400 mmol) and BDP (89.2 mg, 0.200 mmol) were dissolved in 1.0 mL PhMe. PMHS (600 μL, 10.0 mmol), thioester 1e (536.1 mg, 1.998 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 3% EtOAc in hexane to afford 2e (44.4 mg, 8%) as a pale yellow oil, along with recovered 1e (440.7 mg, 82%).  **2e:** Rf (5% EtOAc in hexane): 0.46; IR (CH2Cl2): 3065, 3028, 2937, 2860, 1703 (C=O), 1477, 1440 cm−1; 1H NMR (400 MHz, CDCl3): δ 7.45 (s, 5H), 7.35-7.32 (m, 2H), 7.26-7.22 (m, 3H), 2.74-2.67 (m, 4H), 1.85-1.75 (m, 4H) ppm; 13C NMR (100 MHz, CDCl3): δ 197.3, 141.9, 134.4 (2C), 129.3, 129.1 (2C), 128.4 (2C), 128.3 (2C), 127.9, 125.8, 43.5, 35.5, 30.7, 25.2 ppm; LRMS (ESI): m/z 191 (M+-C6H5S, 84), 117 (46), 91 (100); HRMS (ESI): calcd for C11H13O (M+-C6H5S) 161.0961, found 161.0964.

According to the typical procedure for 1,4-reduction using (BDP)CuH, 3 (39.5 mg, 0.201 mmol) and BDP (89.3 mg, 0.200 mmol) were dissolved in 1.0 mL PhMe. PMHS (360 μL, 6.01 mmol), thioester 1f (340.0 mg, 1.997 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 3% EtOAc in hexane to afford 4.3a (300.5 mg, 87%) as a pale yellow oil.  **2f:** Rf (5% EtOAc in hexane): 0.55; IR (CH2Cl2): 3078, 2974, 2934, 2862, 1686 (C=O), 1455 cm−1; 1H NMR (400 MHz, CDCl3): δ 5.82-5.75 (m, 1H), 5.08-4.94 (m, 2H), 2.87 (q, J = 7.4 Hz, 2H), 2.56-2.52 (m, 2H), 2.09-2.03 (m, 2H), 1.71-1.64 (m, 2H), 1.46-1.34 (m, 2H), 1.24 (t, J = 7.4 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3): δ 199.6, 138.3, 114.8, 44.0, 33.4, 28.2, 25.1, 23.2, 14.8 ppm; LRMS (EI, 20 eV): m/z 111 (M+-C2H5, 100), 83 (78), 69 (31); HRMS (EI, 20 eV): calcd for C7H11O (M+-C2H5), 111.0804, found 111.0789.

According to the typical procedure for 1,4-reduction using (BDP)CuH, 3 (78.7 mg, 0.400 mmol) and BDP (89.6 mg, 0.201 mmol) were dissolved in 1.0 mL PhMe. PMHS (600 μL, 10.0 mmol), thioester 1g (400.1 mg, 1.999 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 2% EtOAc in hexane to afford 2g (391.8 mg, 97%) as a pale yellow oil.  **2g:** Rf (5% EtOAc in hexane): 0.64; IR (CH2Cl2): 3101, 2974, 2858, 2733, 1668 (C=O), 1458, 1408, 1383 cm−1; 1H NMR (400 MHz, CDCl3): δ 7.45 (s, 5H), 7.40-7.37 (m, 2H), 7.29-7.25 (m, 3H), 2.74-2.67 (m, 4H), 1.84-1.73 (m, 4H) ppm; 13C NMR (100 MHz, CDCl3): δ 197.3, 141.9, 134.4 (2C), 129.3, 129.1 (2C), 128.4 (2C), 128.3 (2C), 127.9, 125.8, 43.5, 35.5, 30.7, 25.2 ppm; LRMS (ESI): m/z 273 ([M++Na+]+, 38), 161 (100), 117 (27); HRMS (ESI): calcd for C13H22ONaS ([M++Na+]+) 273.1289, found 273.1294.
According to the typical procedure for 1,4-reduction using (BDP)CuH, \textbf{3} (39.4 mg, 0.200 mmol) and BDP (89.2 mg, 0.200 mmol) were dissolved in 1.0 mL PhMe. PMHS (600 μL, 10.0 mmol), thioester \textbf{1h} (340.5 mg, 1.998 mmol) in 1.0 mL PhMe and \textsuperscript{1}BuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 3% EtOAc in hexane to afford \textbf{2h} (87.5 mg, 25%) as a pale yellow oil along with recovered \textbf{1h} (233.6 mg, 69%). \textbf{2h}: \textit{Rf} (5% EtOAc in hexane): 0.50; IR (CH\textsubscript{2}Cl\textsubscript{2}): 2924, 2856, 1674 (C=O), 1450 cm\textsuperscript{-1}; \textit{H NMR} (400 MHz, C\textsubscript{6}D\textsubscript{6}): \textit{δ} 2.82 (q, \textit{J} = 7.4 Hz, 2H), 2.76-2.42 (m, 1H), 1.96-1.93 (m, 2H), 1.63-1.58 (m, 4H), 1.14 (t, \textit{J} = 7.4 Hz, 3H), 1.12-1.04 (m, 3H) ppm; \textit{13}C NMR (125 MHz, C\textsubscript{6}D\textsubscript{6}): \textit{δ} 202.0, 53.2, 30.2 (2C), 26.2, 26.0 (2C), 23.4, 15.4 ppm; LRMS (EI, 20 eV): m/z 171 (M\textsuperscript{+}-H, 4), 111 (56), 83 (100); HRMS (EI, 20 eV): calcd for C\textsubscript{9}H\textsubscript{15}OS (M\textsuperscript{+}-H) 171.0838, found 171.0839.

The characterization corresponded to that of \textbf{2i} documented in the literature.\textsuperscript{7}

According to the typical procedure for 1,4-reduction using (BDP)CuH, \textbf{3} (78.5 mg, 0.400 mmol) and BDP (89.4 mg, 0.200 mmol) were dissolved in 1.0 mL PhMe. PMHS (600 μL, 10.0 mmol), thioester \textbf{1j} (424.5 mg, 1.999 mmol) in 1.0 mL PhMe and \textsuperscript{1}BuOH (380 μL, 3.97 mmol) were added. After workup, the
residue was purified by flash chromatography using 3% EtOAc in hexane to afford **2j** (375.4 mg, 88%) as a pale yellow oil, along with recovered **2j** (14.9 mg, 4%). **2j**: Rf (5% EtOAc in hexane): 0.55; IR (CH2Cl2): 3057, 2966, 2930, 2854, 1682 (C=O), 1456 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 5.10-5.06 (m, 1H), 2.87 (q, J = 7.4 Hz, 2H), 2.54 (dd, J = 14.4, 5.9 Hz, 1H), 2.34 (dd, J = 14.4, 8.2 Hz, 1H), 2.06-1.94 (m, 3H), 1.68 (d, J = 1.0 Hz, 3H), 1.60 (s, 3H), 1.39-1.31 (m, 1H), 1.26-1.20 (m, 1H), 1.24 (t, J = 7.4 Hz, 3H), 0.94 (d, J = 6.6 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 199.3, 131.6, 124.2, 51.4, 36.7, 30.8, 25.7, 25.4, 23.3, 19.5, 17.7, 14.8 ppm; LRMS (EI, 20 eV): m/z 213 (M⁺-H, 10), 153 (23), 111 (48), 109 (100); HRMS (EI, 20 eV): calcd for C₁₂H₂₂OS (M⁺-H) 213.1308, found 213.1306.

According to the typical procedure for 1,4-reduction using (BDP)CuH, **3** (78.5 mg, 0.400 mmol) and BDP (89.1 mg, 0.199 mmol) were dissolved in 1.0 mL PhMe. PMHS (600 μL, 10.0 mmol), thioester **1k** (384.0 mg, 1.997 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 3% EtOAc in hexane to afford **2k** (348.8 mg, 90%) as a pale yellow oil. **2k**: Rf (5% EtOAc in hexane): 0.45; IR (CH₂Cl₂): 3067, 3031, 2972, 2933, 2876, 1685 (C=O), 1497, 1454 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.35-7.34 (m, 2H), 7.31-7.23 (m, 3H), 3.07-3.00 (m, 2H), 2.95-2.88 (m, 4H), 1.30 (t, J = 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 198.7, 140.2, 128.5 (2C), 128.3 (2C), 126.3, 45.5, 31.5, 23.3, 14.8 ppm; LRMS (EI, 20 eV): m/z 194 (M⁺, 30), 133 (39), 105 (100), 77 (67); HRMS (EI, 20 eV): calcd for C₁₁H₁₄OS (M⁺) 194.0706, found 194.0759.

According to the typical procedure for 1,4-reduction using (BDP)CuH, **3** (78.6 mg, 0.400 mmol) and BDP (89.4 mg, 0.200 mmol) were dissolved in 1.0 mL PhMe. PMHS (600 μL, 10.0 mmol), thioester **2l** (453.1 mg, 1.998 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 3% EtOAc in hexane to afford **2l** (394.5 mg, 86%) as a pale yellow oil and recovered **1l** (15.4 mg, 3%). **2l**: Rf (5% EtOAc in hexane): 0.48; IR (CH₂Cl₂): 3070, 2974, 2934, 2876, 1690 (C=O), 1475, 1446 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.35-7.32 (m, 1H), 7.24-7.13 (m, 3H), 3.11-3.07 (m, 2H), 2.91-2.85 (m, 4H), 1.24 (t, J = 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 198.5, 137.7, 134.0, 130.6, 129.6, 127.9, 126.9, 43.5, 29.5, 23.4, 14.8 ppm; LRMS (EI, 20 eV): m/z 193 (M⁺-Cl, 45), 139 (100), 125 (58), 77 (25); HRMS (EI, 20 eV): calcd for C₁₁H₁₃OS (M⁺-Cl) 193.0682, found 193.0690.
According to the typical procedure for 1,4-reduction using (BDP)CuH, 3 (19.6 mg, 0.100 mmol) and BDP (44.7 mg, 0.100 mmol) were dissolved in 1.0 mL PhMe. PMHS (180 μL, 3.00 mmol), thioester 1m (237.1 mg, 0.9993 mmol) in 2.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 6% EtOAc in hexane to afford 2m (194.6 mg, 81%) as a pale yellow oil and recovered 1m (8.3 mg, 4%). 2m: \( R_f \) (10% EtOAc in hexane): 0.42; IR (CH\(_2\)Cl\(_2\)): 3063, 3045, 2972, 2931, 2874, 1682 (C=O), 1529, 1352 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.04 (t, \( J = 2.2 \), 2H), 7.51 (d, \( J = 7.6 \), 1H), 7.47-7.43 (m, 1H), 3.07 (q, \( J = 7.3 \) Hz, 2H), 2.91-2.82 (m, 4H), 1.23 (t, \( J = 7.4 \) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 198.0, 148.4, 142.1, 134.8, 129.4, 123.3, 121.6, 44.6, 30.9, 23.5, 14.7 ppm; LRMS (EI, 20 eV): m/z 239 (M\(^+\), 2), 150 (100), 136 (44), 77 (19); HRMS (EI, 20 eV): calcd for C\(_{11}\)H\(_{13}\)O\(_3\)NS (M\(^+\)) 239.0611, found 239.0610.

According to the typical procedure for 1,4-reduction using (BDP)CuH, 3 (39.1 mg, 0.199 mmol) and BDP (89.4 mg, 0.200 mmol) were dissolved in 2.0 mL PhMe. PMHS (600 μL, 10.0 mmol), thioester 1n (474.0 mg, 1.998 mmol) in 2.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 6% EtOAc in hexane to afford 2n (430.1 mg, 90%) as a pale yellow oil. 2n: \( R_f \) (10% EtOAc in hexane): 0.44; IR (CH\(_2\)Cl\(_2\)): 3078, 3047, 2972, 2934, 1682 (C=O), 1522, 1348 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.16-8.12 (m, 2H), 7.36-7.26 (m, 2H), 3.11-3.06 (m, 2H), 2.92-2.84 (m, 4H), 1.23 (t, \( J = 7.4 \) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 197.9, 147.9, 146.8, 129.3 (2C), 123.8 (2C), 44.4, 31.1, 23.5, 14.7 ppm; LRMS (EI, 20 eV): m/z 239 (M\(^+\)), 150 (100), 136 (44), 77 (92); HRMS (EI, 20 eV): calcd for C\(_{11}\)H\(_{13}\)O\(_3\)NS (M\(^+\)) 239.0611, found 239.0615.

According to the typical procedure for 1,4-reduction using (BDP)CuH, 3 (39.1 mg, 0.199 mmol) and BDP (89.4 mg, 0.200 mmol) were dissolved in 1.0 mL PhMe. PMHS (600 μL, 10.0 mmol), thioester 1o (444.0 mg, 1.999 mmol) in 1.0 mL PhMe and tBuOH (380 μL, 3.97 mmol) were added. After workup, the residue was purified by flash chromatography using 2% EtOAc in hexane to afford 2o (385.9 mg, 86%) as a pale yellow oil and recovered 1o (15.3 mg, 3%). \( R_f \) (5% EtOAc in hexane): 0.42; IR (CH\(_2\)Cl\(_2\)): 3071, 2974, 2934, 2876, 1685 (C=O), 1531, 1353 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.04 (t, \( J = 2.2 \), 2H), 7.51 (d, \( J = 7.6 \), 1H), 7.47-7.43 (m, 1H), 3.07 (q, \( J = 7.3 \) Hz, 2H), 2.91-2.82 (m, 4H), 1.23 (t, \( J = 7.4 \) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 198.0, 148.4, 142.1, 134.8, 129.4, 123.3, 121.6, 44.6, 30.9, 23.5, 14.7 ppm; LRMS (EI, 20 eV): m/z 239 (M\(^+\)), 150 (100), 136 (44), 77 (92); HRMS (EI, 20 eV): calcd for C\(_{11}\)H\(_{13}\)O\(_3\)NS (M\(^+\)) 239.0611, found 239.0615.
Supporting Information

7.22-7.17 (m, 1H), 6.79-6.74 (m, 3H), 3.79 (s, 3H), 2.96-2.83 (m, 6H), 1.25 (t, \(J = 7.4\) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 198.7, 159.8, 141.8, 129.5, 120.7, 114.1, 111.7, 55.2, 45.5, 31.5, 23.4, 14.8 ppm; LRMS (EI, 20 eV): m/z 224 (M\(^+\), 92), 163 (87), 121 (100), 91 (52); HRMS (EI, 20 eV): calcd for C\(_{12}\)H\(_{16}\)O\(_2\)S (M\(^+\)) 224.0871, found 224.0867.

According to the typical procedure for 1,4-reduction using (BDP)CuH, 3 (11.5 mg, 0.0585 mmol) and BDP (13.6 mg, 0.0305 mmol) were dissolved in 2.0 mL PhMe. PMHS (90 µL, 1.5 mmol), thioester 2.6c (93.4 mg, 0.299 mmol) in 1.0 mL PhMe and 1BuOH (60 µL, 0.63 mmol) were added.

After workup, the residue was purified by flash chromatography using 3% EtOAc in hexane to afford 2p (81.2 mg, 86%) as a pale yellow oil. 2p: \(R_f\) (10% EA in hexane): 0.51; IR (CH\(_2\)Cl\(_2\)): 2939, 2868, 1786 (ketone C=O), 1709 (thioester C=O), 1683 (ester C=O), 1452, 1273 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 4.20 (d, \(J = 7.6\) Hz, 1H), 4.17 (d, \(J = 7.6\) Hz, 1H), 2.85 (q, \(J = 7.4\) Hz, 2H), 2.54-2.40 (m, 5H), 2.01-1.97 (m, 1H), 1.88-1.82 (m, 1H), 1.76-1.51 (m, 8H), 1.45-1.39 (m, 1H), 1.25 (t, \(J = 7.1\) Hz, 3H), 1.23 (t, \(J = 7.4\) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 207.9, 199.4, 172.0, 61.2, 60.8, 43.8, 41.1, 36.1, 34.3, 27.6, 25.9, 23.7, 23.2, 22.6, 14.8, 14.2 ppm; LRMS (EI, 20 eV): m/z 314 (M\(^+\), 1), 253 (4), 179 (40), 133 (100); HRMS (EI, 20 eV): calcd for C\(_{16}\)H\(_{26}\)O\(_4\)S (M\(^+\)) 314.1552, found 314.1557.

**Typical procedure for reductive aldol reactions**

A solution of 3 (23.4 mg, 0.119 mmol) and BDP (26.6 mg, 0.0596 mmol) in 2.0 mL PhMe was stirred for 5 minutes. PMHS (90 µL, 1.5 mmol) was added and the reaction mixture turned greenish yellow. Thioester 1p (93.1 mg, 0.298 mmol) in 1.0 mL PhMe was added. The reaction was monitored by TLC and quenched by the addition of saturated aqueous NH\(_4\)Cl solution. The reaction mixture was filtered through a pad of silica gel. The filtrate was extracted with EtOAc (3 x 10 mL), dried over anhydrous MgSO\(_4\) and concentrated. The residue was purified by flash chromatography using 10% EtOAc in hexane to afford 4a (53.9 mg, 57 %) as a pale yellow oil and 2p (21.5 mg, 23%). 4a: \(R_f\) (10% EtOAc in hexane): 0.53; IR (CH\(_2\)Cl\(_2\)): 3468, 2937, 2870, 1695 (thioester C=O), 1655 (ester C=O), 1456, 1236 cm\(^{-1}\); \(^1\)H NMR (500 MHz, toluene-d\(_8\), 80 °C): \(\delta\) 4.33
According to typical procedure for reductive aldol reaction of 1p, 3 (11.9 mg, 0.0605 mmol) and BDP (13.5 mg, 0.0302 mmol) were dissolved in 2.0 mL PhMe. PMHS (90 μL, 1.5 mmol), thioester 1q (89.1 mg, 0.298 mmol) in 1.0 mL PhMe were added. The reaction was monitored by TLC. After the reaction was complete and worked up, the residue was purified by flash chromatography using 10% EtOAc in hexane to afford 4b (53.1 mg, 60%) as a pale yellow oil and 4c (10.3 mg, 14%) as a pale yellow oil. 4b: R_f (10% EA in hexane): 0.55; IR (CH2Cl2): 3452, 2982, 2941, 2866, 1647 (thioester C=O), 1636 (ester C=O), 1452 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 4.17 (q, J = 7.1 Hz, 2H), 3.93 (d, J = 1.1 Hz, 1H), 3.35-3.31 (m, 1H), 2.92 (q, J = 7.4 Hz, 2H), 2.46-2.36 (m, 2H), 2.26-2.23 (m, 1H), 2.02-1.85 (m, 3H), 1.80-1.76 (m, 1H), 1.67-1.62 (m, 1H), 1.48-1.29 (m, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.4 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 199.4, 175.9, 1647 (thioester C=O), 1636 (ester C=O), 1452 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 4.17 (q, J = 7.1 Hz, 2H), 3.93 (d, J = 1.1 Hz, 1H), 3.35-3.31 (m, 1H), 2.92 (q, J = 7.4 Hz, 2H), 2.46-2.36 (m, 2H), 2.26-2.23 (m, 1H), 2.02-1.85 (m, 3H), 1.80-1.76 (m, 1H), 1.67-1.62 (m, 1H), 1.48-1.29 (m, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.4 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 199.4, 175.9, 82.5, 60.7, 57.0, 56.0, 33.8, 33.3, 32.8, 23.6, 23.3 (2C), 22.4, 14.5, 14.1 ppm; LRMS (EI, 20 eV): m/z 300 (M⁺, 2), 239 (69), 193 (100), 165 (96); HRMS (EI, 20 eV): calcd for C₁₅H₂₄O₄S (M⁺) 300.1390, found 300.1388. 4c: R_f (10% EtOAc in hexane): 0.59; ¹H NMR (400 MHz, CDCl₃): δ 4.22-4.16 (m, 2H), 3.46 (m, 1H), 2.54-2.38 (m, 2H), 2.07-1.87 (m, 6H), 1.58-1.52 (m, 2H), 1.38-1.30 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H), 1.25-1.20 (m, 1H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ 172.7, 170.9, 88.0, 60.9, 58.6, 53.0, 33.3, 32.8, 29.5, 24.0, 22.6, 21.1, 14.2 ppm. The characterization corresponded to that of 4c documented in the literature.²
the reaction was complete and worked up, the residue was purified by flash chromatography using 10% EtOAc in hexane to afford 4b (72.2 mg, 81%) as a pale yellow oil.

References

$^1$H and $^{13}$C NMR Spectra of New Compounds
$1g$
Supporting Information

Electronic Supplementary Material (ESI) for Organic and Biomolecular Chemistry

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Supporting Information

1p

Chemical shifts and other spectral data are provided in the Electronic Supplementary Material (ESI) for this article.
2j
1k
H-H COSY of 4a

NOESY of 4a
H-H COSY of 4b

NOESY of 4b