One-Step Conversion of Alcohols to Thioesters

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General experimental information

All reagents, unless otherwise stated, were used as received from commercial suppliers. Thin layer chromatography (TLC) was performed on UV-active aluminum-backed plates of silica gel (TLC Silica gel 60 F₂₅₄). Flash chromatography was performed using silica gel (60 Å, 230-400 mesh) with reagent grade solvents. NMR spectra were recorded at 400 MHz (¹H NMR) and 100 MHz (¹³C NMR) referenced to an internal standard (TMS) or residual solvent protons and signals are reported in ppm (δ). Melting points were obtained on a Fisher-Johns melting point apparatus and are
uncorrected. FT-IR spectra were obtained on a Perkin-Elmer Spectrum 1000 with samples loaded as KBr discs.

**General procedure for the preparation of benzothioamides**

In a round bottom flask, a mixture of benzonitrile derivative (50 mmol), (NH₄)₂S (20%, 40 ml) ammonia solution (32%, 20 ml) was dissolved (or suspended) in EtOH (50 ml) and stirred at room temperature for 16 h. Then, water (75 ml) was added to the reaction mixture and the precipitated compound was filtered. Then the resulting crude benzothioamide derivative was recrystallized from a suitable solvent to obtain pure compounds as light yellow prisms.

**A typical procedure for the synthesis of thioesters in DMF.** In a round bottom flask, 4-nitrobenzyl alcohol 1a (1.5 mmol), benzothioamide 2a (1 mmol), and p-TsOH (1 mmol) were dissolved in DMF (1 ml) with stirring and heated to 100 °C for 60 minutes. Then to the reaction mixture, water (10 ml) was added to precipitate the resulting crude thioester as a semi-solid material. After that, the residue was subjected to flash column chromatography (silica gel, 1:8 EtOAc-Hexane) to afford S-4-nitrobenzyl benzothioate 3a as pale yellow solid in moderate yield (66%).

**A typical procedure for the synthesis of thioesters in acetic acid.** In a round bottom flask, 4-nitrobenzyl alcohol 1a (1.5 mmol), benzothioamide 2a (1 mmol), and p-TsOH (1 mmol) were dissolved in acetic acid (1 ml) with stirring and heated to 100 °C for 60 minutes. Then the reaction mixture was cooled, poured in water (102 ml), and extracted with EtOAc (2×10 ml). The solvent was removed under reduced pressure and the residue was chromatographed (silica gel, 1:8 EtOAc-Hexane) to afford S-4-nitrobenzyl benzothioate 3a in moderate yield (57%).

**General procedure for the preparative synthesis of thioesters in solvent-free conditions.** In a round bottom flask, a mixture of alcohol (45 mmol), thioamide (30 mmol), and p-TsOH (30 mmol) were heated to make a homogenous solution and heating was continued at 100 °C for 60 minutes. Then the hot reaction mixture was poured in water (100 ml) with vigorous stirring. Thereafter an oily residue was left which soon solidified to a semi-crystalline mass. After that, the solid was filtered and washed with warm water (45 °C, 2×50 ml). Finally, the solid compound was...
recrystallized from EtOH (95%) to afford pure thioesters as white or pale yellow needles.

**Spectroscopic data for compounds**

Thioesters 3a-3k are known compounds.1

(3l): mp (EtOH): 48 °C; ¹H NMR (400 MHZ, CDCl₃): δ 8.50 (s, 1H), 7.94 -7.96 (m, 2H), 7.87 (d, J= 8.4 Hz, 2H), 7.27 (m, 2H), 1.64 (s, 9H); ¹³C NMR (100 M Hz, CDCl₃): δ 192.1, 162.5, 135.5, 132.4, 129.5, 128.3, 128.2, 127.7, 126.8, 123.48, 30.0; Anal. Calcd. for C₁₅H₁₆OS: C, 73.73; H, 6.60; S, 13.12 Found: C, 73.96; H, 6.41; S, 12.98.

(3m): mp (EtOH): 85-89 °C; ¹H NMR (400 MHZ, CDCl₃): δ 7.7.27-7.42 (m, 14H), 5.40 (s, 1H), 2.40 (s, 3H); ¹³C NMR (100 M Hz, CDCl₃): δ 189.8, 144.5, 142.3, 13134.2, 129.4, 128.7, 128.6, 128.5, 127.6, 127.4, 51.9, 21.8; Anal. Calcd. for C₂₁H₁₈OS: C, 79.21; H, 5.70; S, 10.07 Found: C, 79.46; H, 5.48; S, 10.31.

(3n): mp (EtOH): 96-100 °C; ¹H NMR (400 MHZ, CDCl₃): δ 7.7-7.38 (m, 13H), 5.41 (s, 1H), 3.95 (s, 3H), 3.92 (s, 3H); ¹³C NMR (100 M Hz, CDCl₃): δ 188.8, 153.6, 149.0, 142.3, 128.7, 128.6, 128.5, 127.4, 121.9, 110.3, 109.6, 56.1, 56.0, 56.0, 56.0; Anal. Calcd. for C₂₂H₂₀O₃S: C, 72.50; H, 5.53; S, 8.80 Found: C, 72.66; H, 5.29; S, 8.98.

(3o): mp (EtOH): 46 °C; ¹H NMR (400 MHZ, CDCl₃): δ 7.57 (d, J= 8.4 Hz, 1H), 7.40 (s, 1H), 6.80 (d, J= 8.4 Hz, 1H), 5.83 (m, 1H), 5.25 (d, J= 16.8 Hz, 1H), 5.07 (d, J= 9.6 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.65 (d, J= 6.8 Hz, 2H); ¹³C NMR (100 M Hz, CDCl₃): δ 189.6, 153.4, 148.8, 133.3, 130.8, 130.8, 121.6, 117.8, 110.2, 109.3, 55.36, 31.8; Anal. Calcd. for C₁₂H₁₄O₂S: C, 60.48; H, 5.92; S, 13.46 Found: C, 60.60; H27 5.79; S, 13.62.

(3p): mp (EtOH): 52 °C; ¹H NMR (400 MHZ, CDCl₃): δ 8.55 (s, 1H), 7.99 (m, 3H), 7.89 (t, J= 7 Hz, 2H), 7.59 (m, 2H), 5.96 (m, 1H), 5.38 (d, d, J= 16 Hz, J= 1 Hz, 3H), 5.19 (d, J=10 Hz, 1H), 3.81 (d, J= 7.2 Hz, 2H); ¹³C NMR (100 M Hz, CDCl₃):
191.2, 135.8, 134.2, 132.4, 131.2, 129.6, 128.7, 128.5, 127.8, 126.9, 125.3, 123.2, 118.2, 32.0; Anal. Calcd. for C_{14}H_{12}O_{3}: C, 73.65; H, 5.30; S, 14.04 Found: C, 73.89; H, 5.19; S, 14.21.

(3q): mp (EtOH): 89-91 °C; ^1H NMR (400 MHz, CDCl$_3$): $\delta$ 7.92 (d, $J = 7.6$ Hz, 2H), 7.54 (t, $J = 7.4$ Hz, 1H), 7.43 (t, $J = 7.4$ Hz, 2H), 2.29 (s, 6H), 2.12 (s, 3H), 1.84 (d, $J = 12.4$ Hz, 3H), 1.77 (d, $J = 12.8$ Hz, 3H); ^13C NMR (100 MHz, CDCl$_3$): $\delta$ 192.5, 138.4, 132.8, 128.4, 126.9, 51.1, 45.9, 42.0, 36.4, 29.9; Anal. Calcd. for C_{17}H_{20}O_{3}: C, 74.96; H, 7.40; O, 5.87; S, 11.77 Found: C, 75.22; H, 7.21; S, 11.91.

(3r): mp (EtOH): 110-111 °C; ^1H NMR (400 MHz, CDCl$_3$): $\delta$ 7.81 (d, $J = 8$ Hz, 2H), 7.21 (d, $J = 8$ Hz, 2H), 2.40 (s, 3H), 2.27 (d, $J = 2$ Hz, 6H), 2.10 (s, 3H), 1.83 (d, $J = 12$ Hz, 3H), 1.75 (d, 12.4 Hz, 3H); ^13C NMR (100 MHz, CDCl$_3$): $\delta$ 192.2, 143.6, 135.9, 129.1, 127.0, 50.9, 42.0, 36.4, 36.1, 29.9, 21.6; Anal. Calcd. for C_{18}H_{22}O_{3}: C, 75.48; H, 7.74; O, 5.87; S, 11.19 Found: C, 75.55; H, 7.61; S, 11.21.

(3s): mp (EtOH): 127-129 °C; ^1H NMR (400 MHz, CDCl$_3$): $\delta$ 7.86 (d, $J = 7.6$ Hz, 2H), 7.40 (d, $J = 7.6$ Hz, 2H), 2.27 (s, 6H), 2.11 (s, 3H), 1.83 (d, $J = 12$ Hz, 3H); ^13C NMR (100 MHz, CDCl$_3$): $\delta$ 191.3, 139.2, 136.7, 128.7, 128.3, 51.5, 41.9, 36.39 29.9; Anal. Calcd. for C_{18}H_{19}ClO_{3}: C, 66.54; H, 6.24; S, 10.45 Found: C, 66.75; H, 6.09; S, 10.59.

(3t): mp (EtOH): 123-125 °C; ^1H NMR (400 MHz, CDCl$_3$): $\delta$ 7.86 (d, $J = 6.8$ Hz, 2H), 7.28 (d, $J = 7.2$ Hz, 2H), 2.96 (m, 1H), 2.28 (s, 6H), 3.21 (s, 3H), 1.84 (d, $J = 12$ Hz, 3H), 1.76 (d, 12.4 Hz, 3H), 1.27 (d, $J = 6.4$ Hz, 6H); ^13C NMR (100 MHz, CDCl$_3$): $\delta$ 192.2, 154.3, 136.2, 127.1, 126.5, 50.9, 42.0, 36.4, 36.1, 34.2, 29.9, 23.7; Anal. Calcd. for C_{20}H_{26}O_{3}: C, 76.38; H, 8.33; S, 10.20 Found: C, 76.56; H, 8.24; S, 10.34.

(3u): mp (EtOH): 123-125 °C; ^1H NMR (400 MHz, CDCl$_3$): $\delta$ 7.61 (d, $J = 8.4$ Hz, 2 Hz), 7.43 (d, $J = 2$ Hz, 1H), 6.86 (d, $J = 8.4$ Hz, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 2.27 (d, $J = 1.6$ Hz, 6H), 2.10 (s, 3H), 1.82 (d, $J = 12$ Hz, 3H), 1.75 (d, $J = 12.4$ Hz, 3H); ^13C NMR (100 MHz, CDCl$_3$): $\delta$ 191.4, 153.0, 148.7, 131.3, 121.3, 110.0, 109.82
56.0, 55.9, 51.0, 42.1, 36.4, 29.9; Anal. Calcd. for C_{19}H_{24}O_3S: C, 68.64; H, 7.28; O, 14.44; S, 9.64 Found: C, 68.76; H, 8.21; S, 9.55.

Reference