Distant Functionalization *via* Incorporation of Thiophene Moieties in Electrophilic Reactions Promoted by Samarium Diiodide

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Supporting Information

Experimental procedures, physical and spectral data for new compounds, as well as ORTEP drawings of compounds **5a**, **5c**, **6d** and **10** (20 pages).

Experimental

All reactions requiring anhydrous conditions were conducted in flame-dried apparatus under an atmosphere of nitrogen. Syringes and needles for the transfer of reagents were dried at 120 ^{o}C and allowed to cool in a desiccator over P_2O_5 before use. THF was distilled from sodium benzophenone ketyl. Reactions were monitored by TLC using pre-coated with a 0.25 mm layer of silica gel containing a fluorescent indicator (Merck Art. 5544). Column chromatography was carried out on Kieselgel 60 (40–63 μm). ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-200 and AM-300 WB spectrometers. Chemical shifts are reported relative to $CHCl_3$/$CDCl_3$ [δ_H 7.26/ δ_C 77.0 (central line of t)]. Coupling constants (*J*) are given in Hz.

Representative Procedure for the Reactions Promoted by Samarium Diiodide and HMPA. A dark blue solution of SmI_2 was prepared by treating Sm metal (660 mg, 4.4 mmol) with 1,2-diiodoethane (1.02 g, 3.6 mmol) and HMPA (2.8 mL, 16 mmol) in THF (40 mL) at room temperature under argon atmosphere. A mixture of methyl 2-thiophenecarboxylate (**1a**) (142 mg, 1.0 mmol) and 4-methylbenzaldehyde (146 mg, 1.2 mmol) in THF (10 mL) were added dropwise to the SmI_2 solution at 0 ^{o}C. The reaction mixture was warmed to room temperature and stirred for 1.5 h. The reaction mixture was quenched with saturated aqueous NH_4Cl solution, and then passed through a bed of silica gel by elution of EtOAc/hexane (1:1) to remove HMPA. The crude material was purified by column chromatography (silica gel) with elution of gradients of EtOAc and hexane to give the desired coupling product **2a** (223 mg, 85% yield as a mixture of four diastereomers).

Representative Procedure for Desulfurization of the Didydrothiophene Derivatives 2a–g. A solution of **2a** (100 mg, 0.38 mmol) was stirred with an excess of Raney Ni in refluxing MeOH (25 mL) for 1 h. The reaction mixture was filtered, concentrated and purified by column chromatography (silica gel) with elution of EtOAc/hexane (1:9) to yield **4a** as an oil (59 mg, 66%).

Hydrolysis of Esters 3b, 3e and 8b. A solution of **3b** (76 mg, 0.25 mmol) in THF (6 mL) was stirred with an aqueous LiOH solution (0.5 N, 3 mL) at room temperature for 5–8 h. The reaction mixture was washed with hexane. The aqueous phase was acidified with HCl (2 N), and extracted with $CHCl_3$ (10 mL × 2). The combined extracts were dried (Na_2SO_4), filtered, and concentrated to give 6-hydroxy-6-(6-methoxynaphth-2-yl)hexanoic acid (**4b**, 69 mg, 96%), mp 158–159 ^{o}C (lit.[6] 157–159 ^{o}C). By similar procedures, hydrolysis of **3e** (103 mg, 0.4 mmol) and **8b** (115 mg, 0.4 mmol) gave, respectively, 6-hydroxytetradecanoic acid (**4e**, 93 mg, 95%), mp 58–59 ^{o}C (lit.[7] 58–59 ^{o}C) and 8-hydroxyhexadecanoic acid (**9b**, 103 mg, 94%), mp 72–74 ^{o}C (lit.[8] 73.5–74.5 ^{o}C).

Formation of ε-Lactones. The ester **3a** (26 mg, 0.11 mmol) was hydrolyzed in aqueous LiOH, by a procedure similar to that for **3b**, to give the corresponding acid. The acid was dissolved in THF (2 mL) and treated with 1,1’-carbonyldiimidazole (23 mg, 0.14 mmol) at room temperature for 18 h. After addition of anhydrous benzene (5 mL) and DBU (0.05 mL), the mixture was stirred for 30 min, and chromatographed on a silica gel column by elution with EtOAc/hexane (1:4) to give 7-(4-methylphenyl)oxepan-2-one (19 mg, 86%).

The carboxylic acid obtained by hydrolysis of **3d** (100mg, 0.46 mmol) was dissolved in toluene (30 mL) and treated with *p*-TsOH (small amount). The mixture was heated under reflux for 2 h, and Dean-Stark apparatus was used to remove water. The lactone product, 7-pentyloxepan-2-one (77 mg, 91% yield from **3d**), was obtained by chromatography (silica gel, EtOAc/hexane (1:9)).

Methyl 5-(α-hydroxy-4-methylbenzyl)-2,5-dihydrothiophene-2-carboxylate (2a) and Methyl 6-hydroxy-6-(4-methylphenyl)hexanoate (3a). 2a: ^{1}H NMR ($CDCl_3$, 200 MHz) (A mixture of two isomers **2a**-1 and **2a**-2): δ 7.27–7.10 (4 H, m), 5.90–5.74 (2 H, m), 4.78–4.48 (3 H, m), 3.87/3.86 (3 H, s), 2.31/2.29 (3 H, s). (A mixture of two isomers **2a**-3 and **2a**-4): δ 7.23–6.91 (4 H, m), 5.94–5.68 (2 H, m), 4.75–4.53 (3 H, m), 3.67/3.66 (3 H, s), 2.31/2.26 (3 H, s). **3a**: oil; TLC (EtOAc/hexane, 3:7) R_f = 0.26; IR (neat) 3448, 1736 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.18 (2 H, d, *J* = 8.2 Hz), 7.10 (2 H, d, *J* = 8.2 Hz), 4.57 (1 H, t, *J* = 6.6 Hz), 3.61 (3 H, s), 2.31 (3 H, s), 2.26 (1 H, br s), 2.25 (2 H, t, *J* = 7.3 Hz), 1.79–1.53 (4 H, m), 1.43–1.24 (2 H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 174.1 (C), 141.7 (C), 137.0 (C), 129.0 (2 CH), 125.7 (2 CH), 74.0 (CH), 51.4 (CH_3), 38.4 (CH_2), 33.8 (CH_2), 25.3 (CH_2), 24.6 (CH_2), 21.0 (CH_3); FAB-MS *m/z* 236 (M^+), 219 ($M^+ + 1 - H_2O$); HRMS calcd for $C_{14}H_{20}O_3$: 236.1412; found: 236.1406.

Methyl 5-(α-hydroxy-6-methoxylnaphth-2-yl)methyl-2,5-dihydrothiophene-2-carboxylate (2b) and Methyl 6-hydroxy-6-(6-methoxynaphth-2-yl)hexanoate (3b). The reaction of **1a** (142 mg, 1.0 mmol) with 6-methoxy-2-napthaldehyde (223 mg, 1.2 mmol), by a procedure similar to that for **2a**, gave the title compound **2b** (243 mg, 74% yield as a mixture of four diastereomers). Treatment of **2b** (132 mg, 0.40 mmol) with an excess of Raney Ni in MeOH at 25 °C for 5 min gave the title compound **3b** (110 mg, 91% yield).

2b: ^{1}H NMR ($CDCl_3$, 300 MHz) (Isomer **2b**-1): δ 7.81 (1 H, s), 7.71 (2 H, d, *J* = 8.4 Hz), 7.42 (1 H, d, *J* = 8.6 Hz), 7.15–7.11 (1 H, m), 7.11 (1 H, s), 5.90–5.83 (1 H, m), 5.75–5.72 (1 H, m), 4.98 (1 H, d, *J* = 3.12 Hz), 4.79–4.71 (2 H, m), 3.90 (3 H, s), 3.79 (3 H, s). (A mixture of isomers **2b**-2 and **2b**-3): 7.75–7.69 (2 H, m), 7.50–7.35 (1 H, m), 7.15–7.08 (3 H, m), 5.92–5.85 (2 H, m), 4.98–4.67 (2 H, m), 3.89/3.87 (3 H, s), 3.78/3.75 (3 H, s). (Isomer **2b**-4): 7.73 (1 H, s), 7.69 (2 H, d, *J* = 8.4 Hz), 7.42-7.37 (1 H, m), 7.15–7.09 (2 H, m), 5.92–5.72 (2 H, m), 4.84–4.81 (3 H, m), 3.89 (3 H, s), 3.69 (3 H, s). **3b**: oil; TLC (EtOAc/hexane, 3:7) R_f = 0.20; IR (neat) 3448, 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70–7.65 (3 H, m), 7.40 (1 H, d, *J* = 8.2 Hz), 7.12 (1 H, dd, *J* = 8.2, 2.4 Hz), 7.10 (1 H, s), 4.75 (1 H, t, *J* = 6.6 Hz), 3.89 (3 H, s), 3.60 (3 H, s), 2.26 (2 H, t, *J* = 7.3 Hz), 2.05 (1 H, br s), 1.87–1.74 (2 H, m), 1.63 (2 H, quin, *J* = 7.6 Hz), 1.46–1.29 (2 H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.1 (C), 157.6 (C), 139.8 (C), 134.1 (C), 129.3 (CH), 128.7 (C), 127.1 (CH), 124.54 (CH), 124.48 (CH), 118.9 (CH), 105.7 (CH), 74.4 (CH), 55.3 (CH_3), 51.4 (CH_3), 38.4 (CH_2), 33.9 (CH_2), 25.3 (CH_2), 24.7 (CH_2); MS *m/z* (rel intensity) 302 (M^+, 15), 284 (34), 187 (100), 159 (33); HRMS calcd for $C_{18}H_{22}O_4$: 302.1518; found: 302.1517.

Methyl 5-(α-hydroxy-4-chlorophenyl)ethyl-2,5-dihydrothiophene-2-carboxylate (2c) and Methyl 6-hydroxy-6-(4-chlorophenyl)heptanoate (3c). The reaction of **1a** (142 mg, 1.0 mmol) with 4-chloroacetophenone (170 mg, 1.2 mmol), by a procedure similar to that for **2a**, gave the title compound **2c** (222 mg, 74% yield as a mixture of four diastereomers). Treatment of **2c** (215 mg, 0.72 mmol) with an excess of Raney Ni in refluxing MeOH for 8 h gave the title compound **3c** (125 mg, 64% yield).

2c (a mixture of four isomers): ^1H NMR ($CDCl_3$, 200 MHz) δ 7.43–7.07 (4 H, m), 6.12–6.03 (0.2 H, m), 5.92–5.84 (0.2 H, m), 5.79–5.65 (0.8 H, m), 5.48–5.38 (0.8 H, m), 4.84–4.79 (0.5 H, m), 4.69–4.67 (0.25 H, m), 4.60–4.58 (0.25 H, m), 4.10–4.05 (0.5 H, m), 3.73/3.72/3.70/3.65 (3 H, s), 1.59/1.54/1.51/1.48 (3H, s). **3c**: oil; TLC (EtOAc/hexane, 1:4) R_f = 0.15; IR (neat) 3484, 1736 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 7.31 (2 H, dd, *J* = 8.5, 2.0 Hz), 7.24 (2 H, dd, *J* = 8.5, 2.0 Hz), 3.58 (3 H, s), 2.20 (2 H, t, *J* = 7.4 Hz), 2.14 (1 H, br s), 1.73 (2 H, t, *J* = 8.0 Hz), 1.59−1.44 (2 H, m), 1.48 (3 H, s), 1.30−1.11 (2 H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 174.1 (C), 146.3 (C), 132.1 (C), 128.1 (2 CH), 126.3 (2 CH), 74.1 (C), 51.4 (CH_3), 43.6 (CH_2), 33.8 (CH_2), 30.1 (CH_3), 25.0 (CH_2), 23.4 (CH_2); MS *m/z* (rel intensity) 270 (M^+, 5), 239 (4), 155 (100), 121 (7); HRMS calcd for $C_{14}H_{19}O_3Cl$: 270.1022; found: 270.1019.

Methyl 5-(1-hydroxyhexyl)-2,5-dihydrothiophene-2-carboxylate (2d) and Methyl 6-hydroxyundecanoate (3d). The reaction of **1a** (142 mg, 1.0 mmol) with hexanal (120 mg, 1.2 mmol), by a procedure similar to that for **2a**, gave the title compound **2d** (197 mg, 81% yield as a mixture of four diastereomers). Treatment of **2d** (125 mg, 0.51 mmol) with an excess of Raney Ni in refluxing MeOH for 1 h gave the title compound **3d** (100 mg, 91% yield).

2d: ^{1}H NMR ($CDCl_3$, 200 MHz) (A mixture of two isomers **2d**-1 and **2d**-2): δ 5.99–5.81 (2 H, m), 4.71–4.66 (1 H, m,), 4.45–4.42 (0.5 H, m), 4.39–4.36 (0.5 H, m), 3.73 (3 H, s), 3.70–3.66 (1 H, m), 1.51–1.34 (2 H, m), 1.33–1.20 (6 H, m), 0.89–0.82 (3 H, m). (A mixture of two isomers **2d**-3 and **2d**-4): 6.03–5.98 (0.5 H, m), 5.93–5.83 (1.5 H, m), 4.83–4.75 (1 H, m), 4.51–4.41 (1 H, m), 3.72 (3 H, s), 3.69–3.55 (1 H, m), 1.49–1.37 (2 H, m), 1.30–1.18 (6 H, m), 0.85 (3 H, t, *J* = 6.1 Hz). **3d**: oil; TLC (EtOAc/hexane, 1:4) R_f = 0.18; IR (neat) 3434, 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.62 (3 H, s), 3.54 (1 H, m), 2.28 (2 H, t, *J* = 7.2 Hz), 1.62–1.54 (3 H, m), 1.44–1.25 (12 H, m), 0.84 (3 H, t, *J* = 6.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.2 (C), 71.5 (CH), 51.4 (CH_3), 37.4 (CH_2), 36.9 (CH_2), 33.9 (CH_2), 31.8 (CH_2), 25.2 (CH_2), 25.1 (CH_2), 24.8 (CH_2), 22.6 (CH_2), 13.9 (CH_3); FAB-MS *m/z* 217 (M^+ + 1); HRMS calcd for $C_{12}H_{24}O_3$: 216.1725; found: 216.1735.

Methyl 5-(1-hydroxynonyl)-2,5-dihydrothiophene-2-carboxylate (2e) and Methyl 6-hydroxytetradecanoate (3e). The reaction of **1a** (142 mg, 1.0 mmol) with nonanal (170 mg, 1.2 mmol), by a procedure similar to that for **2a**, gave the title compound **2e** (210 mg, 73% yield as a mixture of diastereomers). Treatment of **2e** (143 mg, 0.50 mmol) with an excess of Raney Ni in MeOH at 25 °C for 30 min gave the title compound **3e** (116 mg, 90% yield).

2e (a mixture of diastereomers): ^{1}H NMR (CD_3COCD_3, 200 MHz): δ 6.15–6.10 (0.5 H, m), 6.02–5.94 (0.5 H, m), 5.89–5.84 (1 H, m), 4.81–4.71 (1 H, m), 4.38–4.36 (0.5 H, m), 4.35–4.23 (0.5 H, m), 3.70/3.68 (3 H, s), 3.68–3.50 (1 H, m), 1.6–1.2 (12 H, m), 0.89–0.83 (3 H, m). **3e**: oil; TLC (EtOAc/hexane, 1:4) R_f = 0.27; IR (neat) 3428, 1742 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.60 (3 H, s), 3.52 (1 H, m), 2.27 (2 H, t, *J* = 7.2 Hz), 1.89 (1 H, br s), 1.60–1.20 (20 H, m), 0.82 (3 H, t, *J* = 6.3 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 174.2 (C), 71.5 (CH), 51.4 (CH_3), 37.4 (CH_2), 36.9 (CH_2), 33.9 (CH_2), 31.8 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.2 (CH_2), 25.6 (CH_2), 25.1 (CH_2), 24.8 (CH_2), 22.6 (CH_2), 14.0 (CH_3); FAB-MS *m/z* 259 (M^+ + 1), 241 (M^+ + 1– H_2O); HRMS calcd for $C_{15}H_{31}O_3$ (M^+ + 1): 259.2273; found: 259.2281.

Methyl 5-[1-(4-methoxyphenyl)-2-methoxycarbonyl]ethyl-2,5-dihydrothiophene-2-carboxylate (2f) and 3-(4-Methoxyphenyl)octanedioic acid dimethyl ester (3f). A mixture of methyl 2-thiophenecarboxylate (**1a**) (255 mg, 1.8 mmol) and methyl 4-methoxycinnamate (345 mg, 1.8 mmol) was added slowly to the THF solution (40 mL) of SmI_2 (3.6 mmol) and HMPA (16 mmol) at –78 °C. After 3 h the mixture was allowed to warm to 0 °C slowly. The reaction mixture was quenched with saturated aqueous NH_4Cl solution, and then passed through a bed of silica gel to remove HMPA. The crude material was purified by column chromatography (silica gel) with elution of gradients of EtOAc and hexane to give **2f** (332 mg, 55% yield as a mixture of diastereomers). Treatment of **2f** (100 mg, 0.3 mmol) with an excess of Raney Ni in MeOH at 25 °C for 1 h gave the title compound **3f** (80 mg, 87% yield).

2f (a mixture of diastereomers): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.14–7.08 (2 H, m), 6.83–6.76 (2 H, m), 5.83–5.65 (2 H, m), 4.70–4.55 (1 H, m), 4.48–4.45 (1 H, m), 3.75/3.74/3.72 (3 H, s), 3.67/3.65 (3 H, s), 3.53/3.51/3.49 (3 H, s), 3.41–3.34 (1 H, m), 2.94–2.54 (2H, m); MS *m/z* (rel intensity) 334 (M – H_2, 37), 261 (98), 193 (98), 151 (100). **3f**: oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.03 (2 H, d, *J* = 8.5 Hz), 6.78 (2 H, d, *J* = 8.5 Hz), 3.73 (3 H, s), 3.58 (3 H, s), 3.53 (3 H, s), 3.01–2.94 (1 H, m), 2.58–2.43 (2 H, m), 2.18 (2 H, t, *J* = 7.5 Hz), 1.62–1.46 (4 H, m), 1.19–1.09 (2 H, m). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.9 (C), 172.7 (C), 158.1 (C), 135.7 (C), 128.2 (2 CH), 113.8 (2 CH), 55.1 (CH_3), 51.3 (2 CH_3), 41.8 (CH), 41.1 (CH), 35.7 (CH_2), 33.8 (CH_2), 26.7 (CH_2), 24.7 (CH_2); MS *m/z* (rel intensity) 308 (M^+, 34), 151 (100).

Methyl 5-(1-methyl-2-methoxycarbonyl)ethyl-2,5-dihydrothiophene-2-carboxylate (2g) and 3-Methyloctanedioic acid dimethyl ester (3g). The reaction of **1a** (255 mg, 1.8

mmol) with methyl acrylate (180 mg, 1.8 mmol), by a procedure similar to that for **2f**, gave the title compound **2g** (260 mg, 60% yield as a mixture of diastereomers). Treatment of **2g** (100 mg, 0.41 mmol) with an excess of Raney Ni in MeOH at 25 °C for 1 h gave the title compound **3g** (72 mg, 81% yield).

2g (a mixture of diastereomers): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.88–5.78 (2 H, m), 4.73–4.68 (1 H, m), 4.42–4.33 (1 H, m), 3.71/3.69 (3 H, s), 3.64/3.62 (3 H, s), 2.51–2.09 (3 H, m), 0.98/0.95 (3 H, d, J = 6.6 Hz); MS *m/z* (rel intensity) 244 (M^+, 70), 182 (81), 169 (94), 111 (100). **3g**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.63 (6 H, s), 2.28 (2 H, t, J = 7.0 Hz), 2.27 (1 H, dd, J = 14.6, 5.4 Hz), 2.04 (1 H, dd, J = 14.6, 7.8 Hz), 2.01–1.85 (1 H, m), 1.59–1.50 (2 H, m), 1.32–1.14 (4 H, m), 0.86 (3 H, d, J = 6.6 Hz). ^{13}CNMR ($CDCl_3$, 75 MHz) δ 174.0 (C), 173.5 (C), 51.3 (CH_3), 51.2 (CH_3), 41.4 (CH_2), 36.1 (CH_2), 33.8 (CH_2), 30.3 (CH), 26.3 (CH_2), 24.9 (CH_2), 19.5 (CH_3).

Methyl 4,5-bis(1-hydroxycyclohexyl)-4,5-dihydrothiophene-2-carboxylate (5a) and Methyl 4,5-bis(1-hydroxycyclohexyl)pentanoate (6a). The reaction of **1a** (142 mg, 1.0 mmol) with cyclohexanone (220 mg, 2.1 mmol), by a procedure similar to that for **2a**, gave the title compound **5a** (310 mg, 91% yield) with *trans* configuration. Treatment of **5a** (120 mg, 0.35 mmol) with an excess of Raney Ni in refluxing MeOH for 6 h gave the title compound **6a** (87 mg, 80% yield).

5a: solid; mp 98–100 °C; TLC (EtOAc/hexane, 3:7) R_f = 0.20; IR (KBr) 3406, 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (1 H, d, J = 3.5 Hz), 3.72 (3 H, s), 3.69 (1 H, d, J = 2.7 Hz), 3.18 (1 H, dd, J = 3.5, 2.7 Hz), 2.55 (2H, br s, 2 OH), 1.69–1.29 (18 H, m), 1.10–1.00 (2 H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.6 (C), 135.1 (C), 134.4 (CH), 74.4 (C), 73.9 (C), 60.6 (CH), 59.8 (CH), 52.1 (CH_3), 35.7 (CH_2), 34.4 (CH_2), 32.0 (CH_2), 30.9 (CH_2), 25.4 (2 CH_2), 21.5 (2 CH_2), 21.2 (2 CH_2); MS *m/z* (rel intensity) 340 (M^+, 56), 144 (100); HRMS calcd for $C_{18}H_{28}O_4S$: 340.1708; found: 340.1704. The *trans* configuration of **5a** was established by an X-ray diffraction analysis. **6a**: oil; TLC (EtOAc/hexane, 1:4) R_f = 0.12; IR (neat) 3373, 1739 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz) δ 3.62 (3 H, s), 3.30 (2 H, br s, 2 OH), 2.43 (1 H, ddd, *J* = 15.9, 9.8, 5.7 Hz), 2.25 (1 H, ddd, *J* = 15.9, 9.2, 6.6 Hz), 1.89–1.71 (2 H, m), 1.63–1.12 (23 H, m); ^{13}C NMR (CDCl$_3$, 50 MHz) δ 174.3 (C), 73.6 (C), 70.1 (C), 51.5 (CH$_3$), 43.1 (CH), 41.6 (CH$_2$), 40.0 (CH$_2$), 36.8 (CH$_2$), 36.1 (CH$_2$), 33.2 (CH$_2$), 30.9 (CH$_2$), 28.2 (CH$_2$), 25.8 (CH$_2$), 25.7 (CH$_2$), 22.3 (CH$_2$), 22.0 (CH$_2$), 21.8 (CH$_2$), 21.2 (CH$_2$); FAB-MS *m/z* 295.1 (M$^+$ + 1 − H$_2$O); HRMS calcd for $C_{18}H_{30}O_3$ (M$^+$ − H$_2$O): 294.2195; found: 294.2184.

Methyl 4,5-bis(1-hydroxycyclopentyl)-4,5-dihydrothiophene-2-carboxylate (5b) and Methyl 4,5-bis(1-hydroxycyclopentyl)pentanoate (6b). The reaction of **1a** (142 mg, 1.0 mmol) with cyclopentanone (186 mg, 2.1 mmol), by a procedure similar to that for **2a**, gave the title compound **5b** (178 mg, 57% yield). Treatment of **5b** (140 mg, 0.45 mmol) with an excess of Raney Ni in refluxing MeOH for 6 h gave the title compound **6b** (103 mg, 81% yield).

5b: solid; mp 82–84 ^{O}C; TLC (EtOAc/hexane, 3:7) R_f = 0.15; IR (KBr) 3286, 1718, 1600, 1255 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz) δ 6.42 (1 H, d, *J* = 3.5 Hz), 3.90 (1 H, d, *J* = 3.0 Hz), 3.72 (3 H, s), 3.36 (1 H, dd, *J* = 3.5, 3.0 Hz), 2.75 (1 H, br s, OH), 2.63 (1 H, br s, OH), 1.8–1.45 (16 H, m); ^{13}C NMR (CDCl$_3$, 50 MHz) δ 162.6 (C), 135.1 (C), 134.5 (CH), 84.8 (C), 84.4 (C), 60.4 (CH), 58.9 (CH), 52.3 (CH$_3$), 38.4 (CH$_2$), 37.4 (CH$_2$), 36.1 (CH$_2$), 35.8 (CH$_2$), 23.9 (CH$_2$), 23.67 (CH$_2$), 23.63 (CH$_2$), 23.5 (CH$_2$); MS *m/z* (rel intensity) 312 (M$^+$, 52), 144 (100); HRMS calcd for $C_{16}H_{24}O_4S$: 312.1395; found: 312.1396; Anal. calcd. for $C_{16}H_{24}O_4S$: C 61.54, H 7.75; found: C 61.59, H 7.62. **6b**: oil; TLC (EtOAc/hexane, 3:7) R_f = 0.14; IR (neat) 3388, 1736, 1165 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz) δ 3.65 (3 H, s), 3.63 (2 H, br s, OH), 2.50–2.32 (2 H, m), 1.95–1.21 (21 H, m); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 174.5 (C), 85.3 (C), 81.6 (C), 51.6 (CH$_3$), 43.4 (CH), 42.4 (CH$_2$), 41.2 (CH$_2$), 39.3 (CH$_2$), 39.2 (CH_2), 35.9 (CH_2), 32.9 (CH_2), 28.0 (CH_2), 24.3 (CH_2), 24.1 (CH_2), 23.4 (CH_2), 23.3 (CH_2); FAB-MS *m/z* 285.12 (M^+ + 1); HRMS calcd for $C_{16}H_{26}O_3$ ($M^+ - H_2O$): 266.1882; found: 266.1889; Anal. calcd for $C_{16}H_{26}O_3$: C 67.56, H 9.93; found: C 67.16, H 9.96.

Methyl 4-[1-(4-chlorophenyl)-1-hydroxyethyl]-5-[1-hydroxy-(4-methylphenyl)methyl]-4,5-dihydrothiophene-2-carboxylate (5c) and Methyl 4-[1-(4-chlorophenyl)-1-hydroxyethyl]-6-hydroxy-6-(4-methylphenyl)hexanoate (6c). A mixture of methyl 2-thiophenecarboxylate (**1a**) (142 mg, 1.0 mmol) and 4-methylbenzaldehyde (118 mg, 1.0 mmol) in THF (10 mL) were added dropwise to the THF solution (40 mL) of SmI_2 (3.6 mmol) and HMPA (16 mmol) at 0 ^{O}C. The reaction mixture was warmed to room temperature and stirred for 1 h. A solution of 4-chloroacetophenone (156 mg, 1.2 mmol) in THF (5 mL) was added dropwise. The reaction mixture was stirred for 12–15 h, quenched with saturated aqueous NH_4Cl solution, and then passed through a bed of silica gel to remove HMPA. The crude material was purified by column chromatography (silica gel) with elution of gradients of EtOAc and hexane to give the alcohol **5c** (264 mg, 63% yield as a mixture of two diastereomers in a ratio of 43:57). Two isomers were further separated by repeated column chromatography (silica gel). Treatment of minor isomer ($4S^*,5R^*,1'S^*,1''S^*$)-**5c** (65 mg, 0.16 mmol) with an excess of Raney Ni in refluxing MeOH for 3 h gave the title compound ($4R^*,6R^*,1'S^*$)-**6c** (45 mg, 73% yield).

5c-minor isomer ($4S^*,5R^*,1'S^*,1''S^*$) (recrystallized from $CHCl_3$/hexane): solid; mp 150–152 ^{O}C; TLC (EtOAc/hexane, 3:7) R_f = 0.17; IR (neat) 3427, 1707 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.24–7.06 (8 H, m), 6.33 (1 H, d, *J* = 3.4 Hz), 4.60 (1 H, d, *J* = 7.2 Hz), 3.90 (1 H, dd, *J* = 7.2, 4.3 Hz), 3.73 (1 H, dd, *J* = 4.3, 3.4 Hz), 3.69 (3 H, s), 3.28 (2 H, br s, 2 OH), 2.31 (3 H, s), 1.41 (3 H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.3 (C), 143.5 (C), 138.1 (C), 137.2 (C), 135.2 (C), 133.2 (CH), 132.8 (C), 129.1 (2 CH), 128.1 (2 CH), 126.7 (2 CH), 126.6 (2 CH), 76.6 (CH), 76.0 (C), 62.5 (CH), 55.5 (CH), 52.4 (CH_3), 28.0 (CH_3), 21.1

(CH_3); HRMS calcd for $C_{22}H_{23}O_4S^{37}Cl$: 420.0976; found: 420.0975; Anal. calcd. for $C_{22}H_{23}O_4SCl$: C 63.14, H 5.54; found: C 63.06, H 5.60. The stereochemistry of **5c**-minor was established by and X-ray diffraction analysis. **5c**-major isomer (4*S**,5*R**,1'*S**,1"*R**): solid; mp 93–94.5 ^{O}C; TLC (EtOAc/hexane, 3:7) R_f = 0.14; IR (neat) 3458, 1707 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.25-7.10 (4 H, m), 7.04 (2 H, d, *J* = 8.0 Hz), 6.94 (2 H, d, *J* = 8.1 Hz), 6.37 (1 H, d, *J* = 3.4 Hz), 4.28 (1 H, d, *J* = 5.7 Hz), 3.87 (1 H, dd, *J* = 5.7, 3.6 Hz), 3.72 (3 H, s), 3.44 (1 H, dd, *J* = 3.6, 3.4 Hz), 2.95 (1 H, br s, OH), 2.31 (4 H, s, CH_3 + OH), 1.43 (3 H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.4 (C), 143.6 (C), 137.7 (C), 137.0 (C), 135.0 (C), 134.2 (CH), 133.0 (C), 129.0 (2 CH), 128.2 (2 CH), 126.6 (2 CH), 126.1 (2 CH), 76.3 (C), 75.8 (CH), 62.7 (CH), 58.1 (CH), 52.4 (CH_3), 25.4 (CH_3), 21.0 (CH_3); HRMS calcd for $C_{22}H_{23}O_4S^{35}Cl$: 418.1055; found: 418.0998. **6c**, (4*R**,6*R**,1'*S**)-isomer: oil; TLC (EtOAc/hexane, 3:7) R_f = 0.20; IR (neat) 3408, 1734, 1490, 1174 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32 (2 H, d, *J* = 8.6 Hz), 7.25 (2 H, d, *J* = 8.7 Hz), 7.16 (2 H, d, *J* = 8.2 Hz), 7.10 (2 H, d, *J* = 8.0 Hz), 4.55 (1 H, dd, *J* = 10.0, 3.2 Hz), 3.62 (3 H, s), 3.10–2.90 (2 H. br s, 2 OH), 2.33 (3 H, s), 2.30–2.20 (2 H, m), 1.98–1.79 (3 H, m), 1.57 (3 H, s), 1.34–1.25 (2H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.3 (C), 145.1 (C), 141.9 (C), 137.2 (C), 132.6 (C), 129.1 (2 CH), 128.0 (2 CH), 127.4 (2 CH), 125.5 (2 CH), 76.4 (C), 73.3 (CH), 51.7 (CH_3), 46.4 (CH), 39.9 (CH_2), 32.5 (CH_2), 27.9 (CH_3), 26.7 (CH_2), 21.1 (CH_3); MS *m/z* (rel intensity) 390 (M^+, 3), 144 (100); HRMS calcd for $C_{22}H_{27}O_4Cl$: 390.1598; found: 390.1599.

Methyl 4,5-bis[1-hydroxy-1-(4-methylphenyl)ethyl]-4,5-dihydrothiophene-2-carboxylate (5d) and Methyl 6-hydroxy-4-[1-hydroxy-1-(4-methylphenyl)ethyl]-6-(4-methylphenyl)heptanoate (6d). The reaction of **1a** (142 mg, 1.0 mmol) with 4-methylacetophenone (280 mg, 2.1 mmol), by a procedure similar to that for **2a**, gave the title compound **5d** (252 mg, 62% yield as a mixture of two diastereomers in a ratio of 46:54). Treatment of **5d** [(4*S**,5*R**,1'*S**,1"*R**)-isomer, 153 mg, 0.37 mmol] with an excess of Raney

Ni at 25 ^{o}C for 5 h gave the title compound **6d** [(4*R**,6*S**,1'*S**)-isomer, 107 mg, 75% yield].

5d-minor isomer (4*S**,5*R**,1'*S**,1"*S**): oil; TLC (EtOAc/hexane, 3:7) R_f = 0.32; IR (neat) 3442, 1707 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz) δ 7.29 (2 H, d, *J* = 8.2 Hz), 7.15–7.02 (6 H, m), 6.30 (1 H, d, *J* = 3.5 Hz), 3.98 (1 H, d, *J* = 3.3 Hz), 3.71 (3 H, s), 3.63 (1 H, dd, *J* = 3.5, 3.3 Hz), 2.88 (1 H, s, OH), 2.64 (1 H, s, OH), 2.33 (3 H, s), 2.30 (3 H, s), 1.62 (3 H, s), 1.24 (3 H, s); ^{13}C NMR (CDCl$_3$, 50 MHz) δ 162.3 (C), 142.2 (C), 141.1 (C), 136.8 (C), 136.2 (C), 134.9 (C), 134.7 (CH), 128.7 (2 CH), 128.6 (2 CH), 125.7 (2 CH), 124.7 (2 CH), 76.3 (C), 76.2 (C), 61.8 (CH), 60.7 (CH), 52.2 (CH$_3$), 27.7 (CH$_3$), 25.7 (CH$_3$), 20.9 (CH$_3$), 20.8 (CH$_3$); HRMS calcd for $C_{24}H_{26}O_3S$ ($M^+ - H_2O$): 394.1603; found: 394.1602. **5d**-major isomer (4*S**,5*R**,1'*S**,1"*R**): oil; TLC (EtOAc/hexane, 3:7) R_f = 0.26; IR (neat) 3472, 1707 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz) δ 7.28 (2 H, d, *J* = 8.0 Hz), 7.26 (2 H, d, *J* = 8.2 Hz), 7.11 (2 H, d, *J* = 8.2 Hz), 7.09 (2 H, d, *J* = 8.0 Hz), 6.29 (1 H, d, *J* = 3.5 Hz), 4.20 (1 H, d, *J* = 3.0 Hz), 3.68 (3 H, s), 3.61 (1 H, dd, *J* = 3.5, 3.0 Hz), 2.98 (1 H, s, OH), 2.61 (1 H, s, OH), 2.33 (3 H, s), 2.31 (3 H, s), 1.46 (3 H, s), 1.29 (3 H, s); ^{13}C NMR (CDCl$_3$, 50 MHz) δ 162.3 (C), 142.5 (C), 142.4 (C), 136.6 (2 C), 135.1 (C), 134.9 (CH), 128.8 (4 CH), 125.2 (2 CH), 125.0 (2 CH), 76.6 (C), 76.1 (C), 61.3 (CH), 60.6 (CH), 52.2 (CH$_3$), 26.5 (CH$_3$), 25.0 (CH$_3$), 20.8 (2 CH$_3$); HRMS calcd for $C_{24}H_{26}O_3S$ ($M^+ - H_2O$): 394.1603; found: 394.1597. **6d**, (4*R**,6*S**,1'*S**)-isomer: oil; TLC (EtOAc/hexane, 1:4) R_f = 0.13; IR (neat) 3264, 1736, 1436, 819 cm^{-1}; ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.31 (2 H, d, *J* = 8.0 Hz), 7.26 (2 H, d, *J* = 8.0 Hz), 7.13–7.09 (4 H, m), 5.00 (1 H, br s, OH), 4.01 (1 H, br s, OH), 3.51 (3 H, s), 2.32 (3 H. s), 2.31 (3 H, s), 2.04 (1 H, dd, *J* = 15.3, 6.0 Hz), 1.84–1.68 (2 H, m), 1.57 (3 H, s), 1.47 (3 H, s), 1.50–1.40 (2 H, m), 1.30 (1 H, d, *J* = 15.3 Hz), 0.89–0.83 (1 H, m); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 174.1 (C), 144.8 (C), 142.2 (C), 136.2 (C), 135.6 (C), 128.6 (2 CH), 128.3 (2 CH), 126.5 (2 CH), 125.3 (2 CH), 76.5 (C), 73.3 (C), 51.2 (CH$_3$), 44.4 (CH), 44.3 (CH$_2$), 31.6 (CH$_3$), 31.2 (CH$_2$), 29.1 (CH$_3$), 28.4 (CH$_2$), 20.9 (2 CH$_3$); Anal. calcd for $C_{24}H_{32}O_4$: C 74.90, H 8.39; found: C 74.67, H 8.19. The (4*R**,6*S**,1'*S**) stereochemistry of **6d** was established by an X-ray diffraction analysis.

5-[1-Hydroxy-(4-methoxyphenyl)methyl]-2-(2-methoxycarbonyl)ethylidene-5*H*-thiophene (7a) and Methyl 8-hydroxy-8-(4-methoxyphenyl)octanoate (8a). The reaction of methyl 3-(thien-2-yl)acrylate (**1b**) (168 mg, 1.0 mmol) with 4-methoxybenzaldehyde (163 mg, 1.2 mmol), by a procedure similar to that for **2a**, gave the title compound **7a** (239 mg, 78%) as a mixture of two diastereomers in a ratio of 40:60. Treatment of **7a** (230 mg, 0.75 mmol) with an excess of Raney Ni in MeOH at 25 °C for 2 h gave the title compound **8a** (181 mg, 86% yield).

7a (a mixture of two isomers): oil; TLC (EtOAc/hexane, 3:7) $R_f = 0.16$; IR (neat) 3464, 1735 cm^{-1}; ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.25–7.19 (2 H, m), 6.85–6.80 (2 H, m), 6.28–6.22 (1 H, m), 6.09 (0.4 H, dd, *J* = 6.0, 2.7 Hz), 5.66 (0.6 H, dd, *J* = 6.0, 2.8 Hz), 5.60 (0.6 H, t, *J* = 7.2 Hz), 5.58 (0.4 H, t, *J* = 7.3 Hz), 4.70–4.67 (1 H, m), 4.59–4.55 (1 H, m), 3.74 (3 H, s), 3.63 (1.8 H, s), 3.61 (1.2 H, s), 3.08 (1.2 H, d, *J* = 7.1 Hz), 3.02 (0.8 H, d, *J* = 7.3 Hz), 2.92 (1 H, br s); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 171.6 (2C), 159.3 (2C), 146.6 (C), 146.5 (C), 133.8 (CH), 133.7 (CH), 133.6 (C), 133.5 (CH), 133.4 (CH), 133.3 (CH), 127.5 (2 CH), 127.3 (2 CH), 113.8 (2 CH), 113.6 (2 CH), 109.7 (CH), 109.3 (CH), 76.4 (CH), 75.9 (CH), 65.3 (CH), 63.6 (CH), 55.1 (2 CH$_3$), 51.8 (2 CH$_3$), 36.1 (2 CH$_2$); MS *m/z* (rel intensity) 306 (M$^+$, 4), 265 (7), 137 (100), 135 (44), 110 (20); HRMS calcd for $C_{16}H_{18}O_4S$: 306.0926; found: 306.0929. **8a**: oil; TLC (EtOAc/hexane, 3:7) $R_f = 0.24$; IR (neat) 3457, 1736, 1247, 1035 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz) δ 7.23 (2 H, dd, *J* = 8.5, 2.0 Hz), 6.85 (2 H, dd, *J* = 8.5, 2.0 Hz), 4.57 (1 H, t, *J* = 6.7 Hz), 3.78 (3 H, s), 3.63 (3 H, s), 2.25 (2 H, t, *J* = 7.3 Hz), 1.81–1.53 (5 H, m), 1.40–1.20 (6 H, m); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 174.2 (C), 159.0 (C), 137.0 (C), 127.1 (2 CH), 113.8 (2 CH), 74.2 (CH), 55.2 (CH$_3$), 51.4 (CH$_3$), 38.8 (CH$_2$), 34.0 (CH$_2$), 29.1 (CH$_2$), 29.0 (CH$_2$), 25.6 (CH$_2$), 24.8 (CH$_2$); MS *m/z* (rel intensity) 280 (M$^+$, 3), 262 (5), 147 (17), 137 (100); HRMS calcd for $C_{16}H_{24}O_4$: 280.1674; found: 280.1679.

5-(1-Hydroxynonyl)-2-(2-methoxycarbonylethylidene)-5*H*-thiophene (7b) and Methyl 8-hydroxyhexadecanoate (8b). The reaction of **1b** (168 mg, 1.0 mmol) with nonanal (142 mg, 1.0 mmol), by a procedure similar to that for **2a**, gave the title compound **7b** (212 mg, 76%) as a mixture of diastereomers. The reaction of **7b** (156 mg, 0.56 mmol) with an excess of Raney Ni in MeOH at 25 °C for 2 h gave the title compound **8b** (127 mg, 79% yield).

7b (a mixture of diastereomers): oil; TLC (EtOAc/hexane, 2:8) R_f = 0.34; ^{1}H NMR (CD_3COCD_3, 200 MHz) δ 6.42–6.08 (2 H, m), 5.59 (1 H, t, *J* = 7.0 Hz), 4.52-4.40 (2 H, m), 3.05 (2 H, d, *J* = 7.0 Hz), 1.28 (14 H, br s), 0.87 (3 H, s); ^{13}C NMR (CD_3COCD_3, 50 MHz) δ 172.0, 148.4/148.2, 136.6/135.8, 134.1/133.3, 109.8/109.7, 75.4/74.6, 65.2/64.4, 52.2, 37.0, 36.0/35.9, 31.3 (2 CH_2), 30.1/29.7, 26.8/26.6, 23.6 (2 CH_2), 14.6. **8b**: oil; TLC (EtOAc/hexane, 1:4) R_f = 0.29; IR (neat) 3463, 1741 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.62 (3 H, s), 3.54 (1 H, m), 2.27 (2 H, t, *J* = 7.5 Hz), 1.69–1.23 (24 H, m), 0.85 (3H, t, *J* = 6.3 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 174.3 (C), 71.9 (CH), 51.4 (CH_3), 37.5 (CH_2), 37.3 (CH_2), 34.0 (CH_2), 31.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.2 (2 CH_2), 29.1 (CH_2), 25.6 (CH_2), 25.4 (CH_2), 24.8 (CH_2), 22.6 (CH_2), 14.0 (CH_3); FAB-MS *m/z* 269.1 (M^+ + 1 – H_2O); HRMS calcd for $C_{17}H_{32}O_3$ (M^+ – H_2): 284.2351; found: 284.2350.

5-[1-Hydroxy-1-(4-methylphenyl)ethyl]-2-(2-methoxycarbonylethylidene)-5*H*-thiophene (7c) and Methyl 8-hydroxy-8-(4-methylphenyl)nonanoate (8c). The reaction of **2** (168 mg, 1.0 mmol) with 4-methylacetophenone (168 mg, 1.2 mmol), by a procedure similar to that for **2a**, gave the title compound **7c** (210 mg, 69%) as a mixture of two diastereomers in a ratio of 50:50. Two isomers were separated by repeated column chromatography (silica gel). The reaction of **7c** (a mixture of diastereomers, 110 mg, 0.36 mmol) with an excess of Raney Ni in MeOH at 25 °C for 2 h gave the title compound **8c** (62 mg, 62% yield), accompanied by a partially reduced product, methyl 8-hydroxy-8-(4-methylphenyl)-5-nonenoate (15mg, 16%). Compound **8c** was purified by HPLC (Merck Lichro CART 250-10 Cat. 16816 Lichrosorb Si 60, 7μm, EtOAc/hexane, 1:9).

7c (more polar isomer): oil; TLC (EtOAc/hexane, 1:9) R_f = 0.07; IR (neat) 3494, 1739, 1171 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31 (2 H, d, *J* = 8.1 Hz), 7.14 (2 H, d, *J* = 8.1 Hz), 6.33 (1 H, dd, *J* = 6.2, 1.8 Hz), 6.05 (1 H, dd, *J* = 6.2, 2.7 Hz), 5.63 (1 H, t, *J* = 7.0 Hz), 5.02 (1 H, d, *J* = 1.2 Hz), 3.65 (3 H, s), 3.06 (2 H, d, *J* = 7.0 Hz), 2.60 (1 H, s), 2.33 (3 H, s), 1.59 (3 H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.5 (C), 146.1 (C), 144.0 (C), 136.9 (C), 134.2 (CH), 133.1 (CH), 129.0 (2 CH), 124.7 (2 CH), 110.2 (CH), 75.2 (C), 69.2 (CH), 51.9 (CH_3), 36.2 (CH_2), 26.5 (CH_3), 20.9 (CH_2); MS *m/z* (rel intensity) 286 (13, $M^+ - H_2O$), 119 (100); HRMS calcd for $C_{17}H_{18}O_2S$ ($M^+ - H_2O$): 286.1028; found: 286.1014. **7c** (more polar isomer): TLC (EtOAc/hexane, 1:9) R_f = 0.12; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35 (2 H, d, *J* = 8.1 Hz), 7.16 (2 H, d, *J* = 8.1 Hz), 6.23 (1 H, dd, *J* = 6.2, 1.9 Hz), 5.67–5.61 (2 H, m), 4.88 (1 H, d, *J* = 1.1 Hz), 3.68 (3 H, s), 3.15 (2 H, d, *J* = 7.2 Hz), 2.55 (1 H, s), 2.33 (3 H, s), 1.58 (3 H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.5 (C), 146.4 (C), 141.9 (C), 136.7 (C), 134.2 (CH), 133.3 (CH), 128.9 (2 CH), 124.8 (2 CH), 110.1 (CH), 75.0 (C), 69.4 (CH), 51.9 (CH_3), 36.3 (CH_2), 29.4 (CH_3), 20.9 (CH_3). **8c**: oil; IR (neat) 3484, 1734 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.28 (2 H, d, *J* = 8.2 Hz), 7.12 (2 H, d, *J* = 8.2 Hz), 3.62 (3 H, s), 2.31 (3 H, s), 2.23 (2 H, t, *J* = 7.5 Hz), 1.88–1.64 (3 H, m), 1.58–1.45 (2 H, m), 1.50 (3 H, s), 1.25–1.01 (6 H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.2 (C), 145.1 (C), 136.0 (C), 128.8 (2 CH), 124.7 (2 CH), 74.5 (C), 51.4 (CH_3), 44.1 (CH_2), 34.0 (CH_2), 30.1 (CH_3), 29.5 (CH_2), 29.0 (CH_2), 24.8 (CH_2), 23.8 (CH_2), 20.9 (CH_3); HRMS calcd for $C_{17}H_{26}O_3$: 278.1891; found: 278.1901.

2-(2-Methoxycarbonylethylidene)-5-[2-methoxycarbonyl-1-(4-methoxyphenyl)ethyl]-5*H*-thiophene (7d) and 3-(4-Methoxyphenyl)decanedioic acid dimethyl ester (8d). The reaction of **2** (168 mg, 1.0 mmol) with methyl 4-

methoxycinnamate (192 mg, 1.0 mmol), by a procedure similar to that for **2a**, gave the title compound **7d** (254 mg, 70%) as a mixture of two diastereomers in a ratio of 50:50. The reaction of **7d** (82 mg, 0.23 mmol) with an excess of Raney Ni in MeOH at 25 ^{o}C for 2 h gave the title compound **8d** (64 mg, 83% yield).

7d (a mixture of two isomers): oil; TLC (EtOAc/hexane, 1:9) R_f = 0.14; IR (neat) 1736 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.16–7.10 (2 H, m), 6.83–6.78 (2 H, m), 6.23–6.19 (1 H, m), 5.95 (0.5 H, dd, *J* = 6.0, 2.8 H), 5.77 (0.5 H, dd, *J* = 6.0, 2.8 Hz), 5.60 (0.5 H, t, *J* = 7.0 Hz), 5.56 (0.5 H, t, *J* = 7.0 Hz), 4.73–4.70 (0.5 H, m), 4.66–4.62 (0.5 H, m), 3.74 (3 H, s), 3.66 (1.5 H, s), 3.64 (1.5 H, s), 3.51 (1.5 H, s), 3.49 (1.5 H, s), 3.40–3.37 (1 H, m), 3.09 (1 H, d, *J* = 7.0 Hz), 3.04 (1 H, d, *J* = 7.0 Hz), 2.86 (0.5 H, dd, *J* = 15.5, 5.1 Hz), 2.75–2.71 (1 H, m), 2.60 (0.5 H, dd, *J* = 15.5, 5.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.3 (C), 172.2 (C), 171.5 (2 C), 158.6 (C), 158.5 (C), 146.6 (C), 146.5 (C), 135.7 (CH), 133.7 (CH), 133.4 (CH), 133.2 (C), 132.7 (C), 132.5 (CH), 128.8 (2 CH), 128.5 (2 CH), 113.9 (2 CH), 113.7 (2 CH), 109.4 (CH), 109.2 (CH), 63.1 (CH), 62.0 (CH), 55.1 (2 CH_3), 51.8 (CH_3), 51.7 (CH_3), 51.5 (CH_3), 51.4 (CH_3), 46.7 (CH), 46.0 (CH), 37.3 (CH_2), 36.3 (CH_2), 36.2 (CH_2), 36.1 (CH_2); MS *m/z* (rel intensity) 362 (M^+, 2), 288 (100); HRMS calcd for $C_{19}H_{22}O_5S$: 362.1188; found: 362.1199. **8d**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.06–7.01 (2 H, m), 6.81–6.76 (2 H, m), 3.77 (3 H, s), 3.55 (3 H, s), 3.49 (3 H, s), 3.03–2.93 (1 H, m), 2.59–2.43 (2 H, m), 2.22 (2 H, t, *J* = 7.6 Hz), 1.63–1.47 (4 H, m), 1.31–1.06 (6 H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.2 (C), 172.9 (C), 158.0 (C), 136.0 (C), 128.2 (2 CH), 113.7 (2 CH), 55.1 (CH_3), 51.3 (2 CH_3), 41.8 (CH_2), 41.2 (CH), 36.1 (CH_2), 33.9 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 27.1 (CH_2), 24.8 (CH_2). MS *m/z* (rel intensity) 336 (M^+, 3), 119 (100); HRMS calcd for $C_{19}H_{28}O_5$: 336.1948; found: 336.1942.

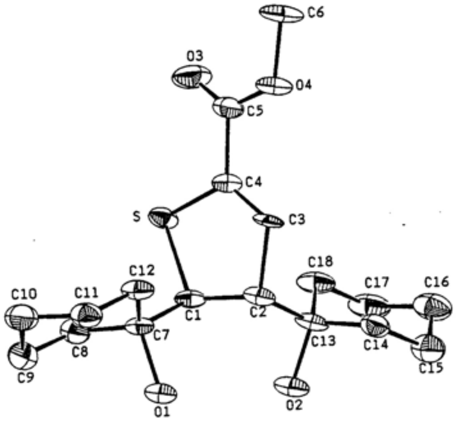
Methyl 4’,5’-bis(1-hydroxycyclohexyl)-5,2’-bithiophene-2-carboxylate (10). A THF solution of 2,2’-bithiophene (498 mg, 3 mmol) was treated with LDA (3.6 mmol) and chloroformate (2.3 mmol) at −78 °C to give methyl 5,2’-bithiophene-2-carboxylate (**1c**, 386 mg, 75%). The reaction of **1c** (224 mg, 1.0 mmol) with cyclohexanone (245 mg, 2.5 mmol), by a procedure similar to that for **2a**, gave *trans*-**10** (132 mg, 31%), *cis*-**10** (50 mg, 12%) along with **1c** (25% recovery) and other products **12** (10%), **13** (6%) and **14** (14%). *Trans*-**10**: Solid, mp 137–139 °C; TLC (EtOAc/hexane (25:75)) $R_f = 0.20$; IR (KBr) 3426, 1721 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.63 (1 H, d, $J = 3.9$ Hz), 7.00 (1 H, d, $J = 3.9$ Hz), 5.88 (1 H, d, $J = 3.6$ Hz), 3.85 (3 H, s), 3.82 (1 H, d, $J = 2.8$ Hz), 3.24 (1 H, m), 1.73–1.13 (20 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.3 (C), 143.4 (C), 135.0 (C), 133.7 (CH), 132.1 (C), 126.0 (CH), 120.9 (CH), 74.6 (C), 73.8 (C), 60.9 (CH), 60.7 (CH), 52.2 (CH_3), 35.8 (CH_2), 34.3 (CH_2), 32.6 (CH_2), 32.0 (CH_2), 25.6 (2 CH_2), 21.6 (2 CH_2), 21.4 (2 CH_2); MS *m/z* (rel intensity) 423 (M^+ + 1, 100), 405 (M^+ - H_2O + 1, 65). HRMS calcd for $C_{22}H_{31}O_4S_2$ (M^+ + 1): 423.1586. Found: 423.4648. The *trans* configuration was established by an X-ray diffraction analysis. *Cis*-**10**: Solid, mp 149–151 °C; TLC (EtOAc/hexane (25:75)) $R_f = 0.13$; IR (KBr) 3529, 1704 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.63 (1 H, d, $J = 3.9$ Hz), 7.00 (1 H, d, $J = 3.9$ Hz), 5.87 (1 H, d, $J = 2.5$ Hz), 3.86 (3 H, s), 3.71 (1 H, s), 3.51 (1 H, br s), 1.73–0.98 (20 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.4 (C), 143.0 (C), 134.6 (C), 133.8 (CH), 132.5 (C), 126.3 (CH), 122.1 (CH), 73.7 (C), 71.1 (C), 63.0 (CH), 54.2 (CH), 52.2 (CH_3), 37.6 (2 CH_2), 33.6 (CH_2), 33.4 (CH_2), 25.8 (2 CH_2), 25.6 (CH_2), 22.2 (2 CH_2), 21.5 (CH_2); MS *m/z* (rel intensity) 423 (M^+ + 1, 100), 405 (M^+ - H_2O +1, 65).

Side product **12**, 7-oxa-6,6-pentamethylene-2-thia-3-(thien-2-yl)bicyclo[3.3.0]octa-3-en-8-one. An oil; TLC (EtOAc/hexane (25:75)) $R_f = 0.40$; IR (KBr) 1767 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.22 (1 H, d, $J = 5.1$ Hz), 7.05 (1 H, d, $J = 3.5$ Hz), 6.96 (1 H, dd, $J = 3.5, 5.1$ Hz), 5.66 (1 H, d, $J = 2.7$ Hz), 4.50 (1 H, d, $J = 9.4$ Hz), 3.91 (1 H, dd, $J = 9.4, 2.7$ Hz), 1.90–1.23 (10 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.9 (C), 136.7 (C), 135.5 (C), 127.5 (CH), 127.1 (CH), 126.1 (CH), 113.6 (CH), 88.9 (C), 59.8 (CH), 49.6 (CH), 38.5 (CH_2), 34.3 (CH_2), 24.8 (CH_2), 22.5 (2 CH_2); MS *m/z* (rel intensity) 293 (M^+ + 1, 100). HRMS calcd for $C_{15}H_{16}O_2S_2$: 292.0592. Found: 292.0591.

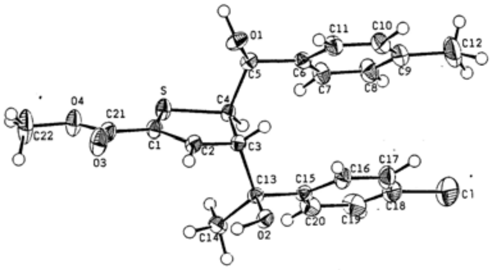
Side product **13,** 1-hydroxycyclohexyl-7-oxa-6,6-pentamethylene-2-thia-3-(thien-2-yl)bicyclo[3.3.0]oct-3-en-8-one. Solid, mp 130–132 °C; TLC (EtOAc/hexane (25:75)) R_f = 0.43; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.22 (1 H, d, *J* = 5.1 Hz), 7.06 (1 H, d, *J* = 3.6 Hz), 6.97 (1 H, dd, *J* = 3.6 Hz, 5.1 Hz), 5.59 (1 H, d, *J* = 3.8 Hz), 3.50 (1 H, d, *J* = 3.8 Hz), 2.94 (1 H, br s), 2.23 (1 H, d, *J* = 13.2 Hz), 1.87 (2 H, t, *J* = 13.2 Hz), 1.80–1.52 (14 H, m), 1.45 (1 H, dt, *J* = 4.1, 12.4 Hz), 1.80–1.52 (2 H, m), 1.30–1.00 (1 H, m). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.9 (C), 136.8 (C), 135.2 (C), 127.7 (CH), 126.8 (CH), 126.0 (CH), 114.8 (CH), 87.7 (C), 74.7 (C), 73.7 (C), 61.8 (CH), 39.0 (CH_2), 34.3 (CH_2), 31.6 (CH_2), 29.8 (CH_2), 25.4 (CH_2), 24.9 (CH_2), 22.6 (CH_2), 22.2 (CH_2), 21.4 (CH_2), 20.9 (CH_2). MS *m/z* (rel intensity) 391 (M^+ + 1, 100), 373 (M^+ - H_2O +1, 100). HRMS calcd for $C_{21}H_{27}O_3S_2$ (M^+ + 1): 391.1323. Found: 391.1396.

Side product **14**, methyl 2',3'-dihydro-3'-(1-hydroxycyclohexyl)-5,2'-bithiophene-2-carboxylate. An oil; TLC (EtOAc/hexane (25:75)) R_f = 0.33; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58 (1 H, d, *J* = 3.8 Hz), 6.95 (1 H, d, *J* = 3.8 Hz), 6.35 (1 H, dd, *J* = 6.1 Hz), 5.47 (1 H, dd, *J* = 6.1, 3.0 Hz), 5.14 (1 H, d, *J* = 3.8 Hz), 3.82 (3 H, s), 3.21 (1 H, dd. *J* = 3.8, 3.0 Hz), 1.67–1.23 (10 H, m).^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.6 (C), 158.0 (C), 133.5 (CH), 131.6 (C), 127.5 (CH), 124.5 (CH), 119.0 (CH), 74.3 (C), 69.4 (CH), 52.0 (CH_3), 46.9 (CH), 35.3 (CH_2), 33.8 (CH_2), 25.5 (CH_2), 21.6 (CH_2), 21.5 (CH_2). MS *m/z* (rel intensity) 325 (M^+ + 1, 100), 307 (M^+ - H_2O + 1, 97), HRMS calcd for $C_{16}H_{21}O_3S_2$ (M^+ + 1): 325.0854 Found: 325.0938.

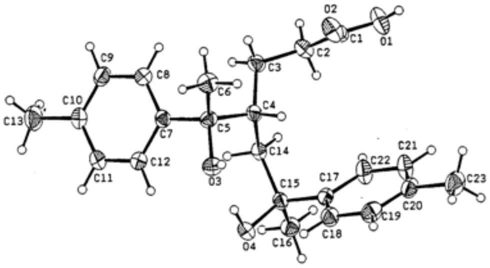
Methyl 9-cyclohexylidene-8-(1-hydroxycyclohexyl)nonanoate (11). Compound *trans*-**10** (23 mg) was treated with an excess of Raney Ni in refluxing EtOH for 16 h to give **11** (16 mg, 85%). An oil; TLC (EtOAc/hexane (25:75)) R_f = 0.45; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.83 (1 H, d, *J* = 10.5 Hz), 3.64 (3 H, s), 2.28 (2 H, t, *J* = 7.5 Hz), 2.25–2.10 (5 H, m), 1.70–1.15 (22 H, m), 1.15–0.82 (4 H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.2 (C), 143.1 (C), 121.8 (CH), 73.2 (C), 51.4 (CH_3), 47.8 (CH), 37.8 (CH_2), 34.7 (CH_2), 34.4 (CH_2), 34.1 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 28.97 (CH_2), 27.93 (CH_2), 27.90 (CH_2), 26.9 (CH_2), 26.0 (CH_2), 25.0 (CH_2), 22.0 (CH_2), 21.8 (CH_2); MS *m/z* (rel intensity) 350 (M^+, 13), 342 (M^+ - H_2O + 1, 55). HRMS calcd for $C_{22}H_{38}O_3$: 350.2821 Found: 350.2816.



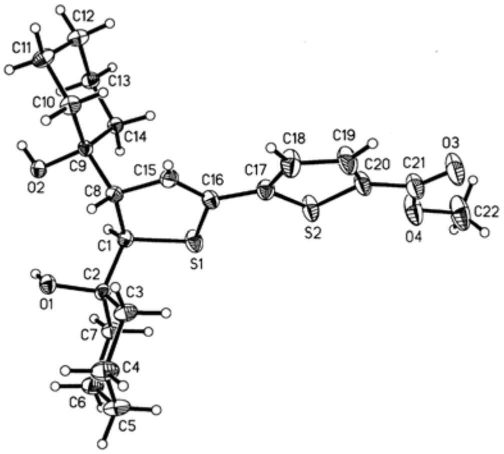
ORTEP drawing of compound **5a** (*trans*)



ORTEP drawing of compound **5c**-minor (4*S**,5*R**,1'*S**,1"*S**)



ORTEP drawing of compound **6d** (4*R**,6*S**,1'*S**)



ORTEP drawing of compound **10** (*trans*)