

Anodic Cyclization Reactions: Capitalizing on an Intramolecular Electron Transfer to Trigger the Synthesis of a Key Tetrahydropyran Building Block

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Supporting Information

Example experimental procedure for electrolysis reaction; spectroscopic data for **7, 8, 9, 12a, 14a, 12b, 13b** (5 pages).

General.

Electrolysis reactions were conducted using a model 630 coulometer, a model 410 potentiostatic controller, and a model 420A power supply purchased from the Electrosynthesis Company, Inc. Carbon rods, reticulated vitreous carbon (RVC), and platinum electrodes were also purchased from the Electrosynthesis Co. Tetraethyl ammonium tosylate was purchased from Aldrich and used without purification. Anhydrous methanol was purchased from Aldrich in Sure/Seal bottles and used without further purification. Tetrahydrofuran was distilled from sodium benzophenone ketyl. Gravity flow and flash chromatography were carried out using Natland International Corporation Silica gel (200 - 400 mesh). All proton and carbon magnetic resonance spectra were recorded using a Varian Gemini 300, Varian Mercury 300, or Varian Unity 300 spectrometer using CDCl₃ as solvent. Infrared spectra (IR) were obtained using a Perkin Elmer Spectrum BS FT-IR System Spectrophotometer. High resolution electron

ionization (EI^+) mass spectral data were obtained using a Micromass ZAB-SE spectrometer with and 8 keV acceleration voltage. High resolution fast atom bombardment (FAB) mass spectral data were obtained using a Kratos MS-50 spectrometer.

A. Example experimental procedure for electrolysis reaction.

A solution of 480 mg (1.6mmol) tetraethyl ammonium p-toluene sulfonate in 8 mL of 30% MeOH/THF containing 60 mg (0.16 mmol) of enol ether (**7**) and 0.03 mL (0.24 mmol) 2,6-lutidine was placed in a three necked round bottom flask equipped with a reticulated vitreous carbon anode (suspended from a carbon rod), a platinum wire cathode, and a nitrogen inlet. The reaction was degassed via sonication (10 min), warmed to 45°C, and then electrolyzed at a constant current of 8.0 mA until 38.6 C (2.5 Faradays per mole) of charge had been passed. When complete, the solvent was removed in vacuo and the residue was chromatographed through 20 mL of silica gel packed with 20% ethyl ether in hexane. Elution with the same solvent led to the isolation of 42.1 mg(70%) of **8** and 6.0 mg of **9** (10%).

B. Characterization Data for Electrolysis Substrates and corresponding products

(2S)-1-(benzyloxy)-3-{2-[(2E,Z)-3-methoxyprop-2-enyl]-1,3-dithian-2-yl}propan-2-ol (7**):** (TLC (EtOAc/Hexane (1:1)) $R_f=0.4$; 1H NMR ($CDCl_3/300MHz$) 7.35-7.25 (m, 5H), 6.37(d, $J=12.6Hz$, 0.6H), 6.02(dt, $J_d=6.3Hz$, $J_t=1.2Hz$, 0.4H), 4.77(dt, $J_d=12.6Hz$, $J_t=7.2Hz$, 0.6H), 4.57(d, $J=1.2Hz$, 2H), 4.51(dt, $J_d=6.3Hz$, $J_t=7.2Hz$, 0.4H), 4.23-4.07(m, 1H), 3.56(s, 1.2H), 3.50(s, 1.8H), 3.45(d, $J=5.4Hz$, 2H), 3.26(d, $J=2.7Hz$, 0.4H), 3.16(d, $J=2.4Hz$, 0.6H), 3.00-2.74(m, 5H), 2.60(ddd, $J=1.2Hz$, 7.2Hz, 14.7Hz, 1H), 2.18(ddd,

J=7.2Hz, 8.4Hz, 15.3Hz, 1H), 2.05(d, J=3.3Hz, 1H), 2.03-1.87(m, 2H); ¹³C NMR (CDCl₃/75MHz) 149.9, 148.4, 138.1, 138.0, 128.4, 128.3, 127.7, 127.6, 100.1, 96.1, 74.4, 74.3, 73.3, 73.2, 67.6, 67.5, 59.5, 55.9, 52.2, 41.3, 40.9, 38.2, 33.8, 26.3, 26.0, 26.0, 24.9, 24.9; IR (neat/NaCl) 3467, 2904, 1653, 1452, 1207, 1106, 698 cm⁻¹; LRMS (EI) *m/z* 354.1(M⁺, 2), 323.1(M-OCH₃, 2), 283.1(30), 175.0(35), 91.1(100); HRMS (EI) C₁₈H₂₆O₃S₂(M⁺) calcd 354.1323, found 354.1323.

(8R,10S)-8-(dimethoxymethyl)-10-(benzyloxymethyl)-9-oxa-1,5-

dithiaspiro[5.5]undecane (8): (TLC (EtOAc/Hexane (1:1)) R_f=0.6; ¹H NMR (CDCl₃/300MHz) 7.35-7.25(m, 5H), 4.58(s, 2H), 4.28(d, J=5.7Hz, 1H), 4.04(ddt, J_t=5.4Hz, J_d=11.1Hz, 2.1Hz, 1H), 3.94(ddd, J=11.7Hz, 5.7Hz, 2.1Hz, 1H), 3.57(A of ABX, J_{ab}=10.2Hz, J_{ax}=5.4Hz, 1H), 3.47(B of ABX, J_{ab}=10.2Hz, J_{bx}=4.8Hz, 1H), 3.43(s, 3H), 3.42(s, 3H), 3.02-2.70(m, 4H), 2.41(dt, J_d=13.8Hz, J_t=2.1Hz, 1H), 2.23(dt, J_d=13.8Hz, J_t=2.1Hz, 1H), 2.06-1.94(m, 2H), 1.72(ddd, J=13.8Hz, 11.2Hz, 6.0Hz, 2H); ¹³C NMR (CDCl₃/75MHz) 138.2, 128.3, 127.7, 127.6, 105.3, 73.4, 73.1, 72.7, 72.0, 55.3, 54.5, 47.5, 40.0, 37.4, 25.9, 25.8, 25.7; IR (neat/NaCl) 2904, 1452, 1100, 737, 698 cm⁻¹; LRMS (EI) *m/z* 384.1(M⁺, 10), 352.1(M-OCH₃, 20), 281.1(25), 91.0(55), 75.0(100); HRMS (EI) C₁₉H₂₈O₄S₂(M⁺) calcd 384.1429, found 384.1427.

(2S,6E,Z)-1-(benzyloxy)-4,4,7-trimethoxyhept-6-en-2-ol (9): (TLC (EtOAc/Hexane (1:1)) R_f=0.45; ¹H NMR (CDCl₃/300MHz) 7.35-7.25(m, 5H), 6.34(d, J=12.6Hz, 0.6H), 5.94(dt, J_d=6.3Hz, J_t=1.5Hz, 0.4H), 4.62(dt, J_d=12.6Hz, J_t=7.2Hz, 0.6H), 4.56(d, J=1.8Hz, 2H), 4.32(dt, J_d=6.3Hz, J_t=7.2Hz, 0.4H), 4.10-3.97(m, 1H), 3.55(s, 1.2H), 3.48(s, 1.8H), 3.42(d, J=5.4Hz, 2H), 3.25(s, 3H), 3.20(s, 1.8H), 3.20(s, 1.2H), 2.47(A of ABX, J_{ab}=14.7Hz, J_{ax}=6.9Hz, 1H), 2.28(B of ABX, J_{ab}=14.7Hz, J_{bx}=8.4Hz, 1H), 1.99-1.73(m, 2H), 1.60(bs, 1H); ¹³C NMR (CDCl₃/75MHz) 149.4, 147.7, 138.2, 128.3, 128.2, 127.6, 127.5, 103.3, 103.1, 100.5, 96.8, 74.4, 74.3, 73.3, 73.2, 66.9, 59.5, 55.8, 48.1, 48.1, 36.4, 35.8, 32.5, 28.9; IR (neat/NaCl) 3480, 2937, 1656, 1453, 1105, 1047, 737, 698 cm⁻¹; LRMS (FAB) *m/z* 317(M+Li, 95), 157(100); HRMS (FAB) C₁₇H₂₆O₅Li(M+Li) calcd 317.1940, found 317.1933.

2-(3-Methoxy-allyl)-2-(7-methoxy-hept-6-enyl)-[1,3]dithiane (12a): (TLC (Et₂O/Hexane (1:2)) R_f=0.6; ¹H NMR (CDCl₃/300MHz) 6.36(d, J=12.6Hz, 0.6H), 6.27(d, J=12.6Hz, 0.5H), 6.02(ddd, J=1.5Hz, 2.4Hz, 6.3Hz, 0.5H), 5.86(ddd, J=1.5Hz, 3.0Hz, 6.3Hz, 0.4H), 4.74(dt, J_t=7.5Hz, J_d=12.6Hz, 0.6H), 4.71(dt, J_t=7.5Hz, J_d=12.6Hz, 0.5H), 4.44(dt, J_t=7.5Hz, J_d=6.3Hz, 0.5H), 4.32(dt, J_d=6.3Hz, J_t=7.5Hz, 0.4H), 3.60, 3.57, 3.57, 3.55, 3.50(5s, 6H), 2.96-2.76(m, 4H), 2.73(dt, J_d=7.5Hz, J_t=1.8Hz, 1H), 2.52(ddd, J=1.2Hz, 2.7Hz, 7.8Hz, 1H), 2.10-1.78(m, 6H), 1.52-1.25(m, 6H); ¹³C NMR (CDCl₃/75MHz) 149.2, 148.2, 146.9, 146.8, 146.0, 145.9, 106.8, 106.7, 102.9, 102.8, 100.8, 96.8, 96.8, 59.5, 59.4, 55.8, 55.8, 53.2, 53.2, 38.5, 37.8, 37.8, 36.6, 36.6, 32.3, 31.5, 30.5, 30.4, 29.5, 29.5, 29.4) IR (neat/NaCl) 2932, 2829, 1654, 1450, 1208, 1108, 934 cm⁻¹; LRMS (EI) m/z 245(M⁺-CH₂CHCHOCH₃, 98), 71(CH₂CHCHOCH₃, 100) ; HRMS (EI) C₁₂H₂₁OS₂(M⁺- CH₂CHCHOCH₃) calcd 245.1034, found 245.1042.

1,4,4,11-Tetramethoxy-undeca-1,10-diene (14a): (TLC (Et₂O/Hexane (1:1)) R_f=0.5; ¹H NMR (CDCl₃/300MHz) 6.34(dt, J_t=1.5Hz, J_d=12.9Hz, 0.17H), 6.27(dt, J_t=1.5Hz, J_d=13.8Hz, 0.76H), 5.96(dt, J_t=1.5Hz, J_d=6.3Hz, 0.83H), 5.86(dt, J_t=1.5Hz, J_d=6.3Hz, 0.24H), 4.72(dt, J_t=7.2Hz, J_d=12.9Hz, 0.83H), 4.57(dt, J_t=7.5Hz, J_d=12.9Hz, 0.17H), 4.32(dt, J_t=7.2Hz, J_d=6.3Hz, 0.24H), 4.27(dt, J_t=7.5Hz, J_d=6.3Hz, 0.76H), 3.59, 3.57, 3.53, 3.50(4s, 6H), 3.17(s, 6H), 2.39(dd, J=1.5Hz, 7.5Hz, 1.7H), 2.22(m, 0.3H), 2.1-2.0(m, 0.4H), 1.95-1.88(m, 1.6H), 1.62-1.52(m, 2H), 1.43-1.21(m, 6H); ¹³C NMR (CDCl₃/75MHz) 147.8, 146.9, 103.3, 100.6, 59.5, 55.9, 47.9, 33.0, 30.6, 29.2, 27.5, 23.3; IR (neat/NaCl) 2934, 2856, 1128, 1060, 907 cm⁻¹; LRMS (EI) m/z 272(M⁺, 35), 129(20), 95(30), 75(100); HRMS (EI) C₁₅H₂₈O₄(M⁺) calcd 272.1988, found 272.1977.

7-Methoxy-1-[2-(3-methoxy-allyl)-[1,3]dithian-2-yl]-hept-6-en-2-ol (12b): (TLC (Et₂O/Hexane (1:1)) R_f=0.25; ¹H NMR (CDCl₃/300MHz) 6.29(d, J=12.9Hz, 0.4H), 6.22(dd, J=1.2Hz, 11.4Hz, 0.6H), 5.98(dt, J_t=1.2Hz, J_d=6.3Hz, 0.6H), 5.81(ddd, J=1.8Hz, 3.6Hz, 6.3Hz, 0.4H), 4.69(dt, J_t=7.5Hz, J_d=12.3Hz, 0.4H), 4.65(dt, J_t=7.2Hz, J_d=12.9Hz, 0.6H), 4.42(dt, J_t=7.2Hz, J_d=6.3Hz, 0.6H), 4.27(ddt, J_t=7.2Hz, J_d=1.2,

6.3Hz, 0.4H), 3.96-3.86(m, 1H), 3.54, 3.51, 3.50, 3.48, 3.43(5s, 6H), 3.40-3.22(m, 1H), 2.97-2.72(m, 4H), 2.70(dd, J=1.2, 7.5Hz, 1H), 2.52(ddd, J=7.2, 14.7, 14.7Hz, 1H), 2.15(ddt, Jt=1.8Hz, Jd=9.3Hz, 14.1Hz, 1H), 2.05-1.79(m, 5H), 1.50-1.27(m, 4H); ¹³C NMR (CDCl₃/75MHz) 149.9, 148.5, 147.2, 147.1, 146.2, 146.1, 106.7, 106.5, 102.8, 102.7, 99.9, 96.1, 68.3, 68.2, 59.6, 59.4, 56.0, 55.8, 52.3, 52.2, 44.7, 44.7, 44.2, 44.2, 38.4, 38.4, 37.4, 37.3, 37.2, 37.1, 34.0, 27.6, 27.6, 26.6, 26.4, 26.1, 26.0, 25.6, 25.6, 24.9, 24.9, 23.7, 23.6; IR (neat/NaCl) 3462, 2933, 2857, 1654, 1440, 1208, 1109, 1069, 935 cm⁻¹; LRMS (EI) *m/z* 332(M⁺, 17), 300(M-HOCH₃, 15), 261(M⁺-CH₂CHCHOCH₃, 100); HRMS (EI) C₁₆H₂₈O₃S₂(M⁺) calcd 332.1480, found 332.1477.

8-Dimethoxymethyl-10-(5-methoxy-pent-4-enyl)-9-oxa-1,5-dithia-spiro[5.5]undecane (13b): (TLC (Et₂O/Hexane (1:1)) R_f=0.45; ¹H NMR (CDCl₃/600MHz) 6.26(d, J=12.0Hz, 0.7H), 5.85(d, J=6.6Hz, 0.3H), 4.69(dt, Jt=7.2Hz, Jd=12.6Hz, 0.7H), 4.31(dt, Jt=7.2Hz, Jd=6.6Hz, 0.3h), 4.22(d, J=5.4Hz, 1H), 3.85(dd, J=5.4, 10.8Hz, 1H), 3.75-3.70(m, 1H), 3.55(s, 0.9H), 3.48(s, 2.1H), 3.40(s, 6H), 3.01-2.68(m, 4H), 2.42(d, J=6.9Hz, 1H), 2.15-1.89(m, 5H), 1.66(t, J=6.3Hz, 1H), 1.55(t, J=6.3Hz, 1H), 1.52-1.24(m, 4H); ¹³C NMR (CDCl₃/150MHz) 147.2, 146.2, 106.5, 105.3, 102.7, 73.1, 72.5, 72.4, 59.4, 55.8, 55.1, 54.0, 53.9, 47.8, 45.9, 43.4, 37.7, 35.1, 35.0, 27.6, 26.6, 25.9, 25.8, 25.5, 23.6; IR (neat/NaCl) 2934, 2908, 1655, 1440, 1208, 1105, 952 cm⁻¹; LRMS (EI) *m/z* 362(M⁺, 7), 330(M⁺-OCH₃, 75), 287(M⁺-CH(OCH₃)₂, 35), 259(60), 127(85), 75(100); HRMS (EI) C₁₇H₃₀O₄S₂(M-OCH₃) calcd 362.1586, found 362.1587.