REVERSING THE POLARITY OF ENOL ETHERS: AN ANODIC ROUTE TO TETRAHYDROFURAN AND TETRAHYDROPYRAN RINGS

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Supporting Information

Example procedure for the electrolysis reaction; spectroscopic and analytical data for **1a,b,d, 2a-d, 3a,b, 4a,b, 8, 9, 10,** and NOESY data for compounds **2a** and **4a**. (8 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, retriculated vitrious 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 $CDCl_3$ as solvent. Infrared spectra (IR) were obtained using a Mattson Polaris FT-IR, an Analect FX-6160 FT-IR, or 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.

A. Example experimental procedure for electrolysis reaction.

A solution of 1.16 g tetraethyl ammonium p-toluene sulfonate in 130 mL of 30% MeOH/THF containing .400 g (3.0 mmol) of enol ether **(1a)** and 2.7 mL (22.8 mmol) 2,6-lutidine was placed in a three necked round bottom equipped with a retriculated vitreous carbon anode (suspended from a carbon rod), a platinum wire cathode, and a nitrogen inlet. The reaction was degassed via sonnication (10 min), and electrolyzed at a constant current of 8.0 mA until 732 C (2.5 F/ mole) of charge had been passed. When complete, the solvent was removed in vacuo and the residue was chromatographed through 100 mL of silica gel packed with ethyl ether. Elution with ethyl ether led to the isolation of .470 g (96%) of **2a.**

B. Characterization Data for Electrolysis Substrates

1-methoxy-3-methyl-(E,Z)-1-penten-5-ol (1a): The spectral data are reported for a 7/3 mixture of enol ether isomers. ^1H NMR (300 MHz, $CDCl_3$) δ 6.30 (d, 12.4 Hz, .7H), 5.92 (d, J = 6.3 Hz, .3H), 4.60 (dd, J = 12.7, 8.8 Hz, .7H), 4.15 (dd, J= 9.6, 6.2 Hz, .3H), 3.68-3.63 (m, 2H), 3.59 (s, .9H), 3.50 (s, 2.1H), 2.85-2.74 (bs, O<u>H</u>), 2.27-2.17 (m, 1H),

1.79-1.20 (m,2H), 1.03 and 1.00 (two d, J = 6.8 Hz, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.4, 145.7, 112.2, 108.7, 61.2, 61.1, 59.6, 55.9, 40.6, 39.9, 29.8, 25.2, 22.4, 21.7; IR (neat, NaCl) 3351b, 2931, 1654, 1454, 1209, 1153, 1104, 1051, 936 cm^{-1}; HRMS (EI) *m/z* calcd for C_5H_9O (M-C_2H_5O) 85.0653, found 85.0645.

3-benzyl-1-methoxy-(E,Z)-1-penten-5-ol (1b): The data are reported for a 3/1 ratio of isomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.11 (m,5H), 6.16 (d, J = 12.7 Hz, .75H), 5.92 (d, J= 7.1 Hz, .25H), 4.51 (dd, J = 12.6, 9.6 Hz, .75H), 4.17 (dd, J = 9.7, 6.3 Hz, .25H), 3.70-3.60 (m, 2H), 3.50 (s, .25H), 3.46 (s, .75H), 3.11-2.96 (m, O<u>H</u>), 2.70-2.57 (m, 2H), 2.40-2.29 (m, 1H), 1.83-1.67 (m,1H), 1.50-1.21 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.4, 146.6, 140.1, 129.3, 128.0, 127.9, 125.8, 110.0, 106.1, 61.3, 61.0, 56.0, 43.7, 42.5, 38.0, 37.4; IR (neat, NaCl) 3381b, 3029, 1651, 1590, 1496, 1455, 1216, 1145 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{13}H_{18}O_2$ (M) 206.1307, found 206.1306.

3-benzyl-1-methoxy-(E,Z)-1-hexene-6-ol (1d): The data are reported for a 3/1 ratio of isomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.24 (m, 2H), 7.20-7.11 (m, 3H), 6.12 (d, J = 12.6 Hz, .75H), 5.86(d, J = 6.3 Hz, .25H), 4.49 (dd, J = 12.6, 9.6 Hz, .75H), 4.14 (dd, J = 9.6, 6.2 Hz, .25H), 3.59 (t, J = 6.3 Hz, 2H), 3.46 (s, 2.25H), 3.44 (s, .75H), 2.92-2.80 (m, O<u>H</u>), 2.71-2.52 (m, 2H), 2.22-2.09 (m, .5H), 1.71-1.40 (m, 2.5H), 1.31-1.13 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1, 146.1, 140.6, 140.4, 129.2, 129.1, 127.9, 127.8, 125.6, 125.5, 110.7, 106.4, 63.1, 62.9, 59.4, 55.9, 43.5, 42.3, 40.4, 35.6, 31.4, 31.1, 30.6, 30.5; IR (neat, NaCl) 3351b, 3084, 3026, 2932, 1655, 1603, 1495, 1452, 1208, 1141, 1101, 1056, 934, 746, 700 cm^{-1}.

2,3-dimethyl-1-methoxy-(E, Z)-1-penten-5-ol (3a): The data are reported for an 85/15 ratio of isomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.58 (bs, 1H), 3.61-3.55 (m, 5H), 2.58-2.49 (m, .15H), 2.24-2.12 (m, .85H), 1.73-1.40 (m, 5H), 1.01 (d, J = 6.9 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 141.7, 115.2, 61.9, 59.3, 37.3, 34.0, 20.2, 8.7; IR (neat, NaCl) 3368b, 2932, 1680, 1457, 1376, 1238, 1205, 1134, 1050, 9999, 969, 839 cm^{-1}; HRMS (EI) *m/z* calcd for $C_8H_{16}O_2$ (M) 144.1150, found 144.1138.

2,3-dimethyl-1-methoxy-(E, Z)-1-hexen-6-ol (3b): The data are reported for a 60/40 ratio of isomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81 (s, .6H), 5.75 (s, .4H), 3.61-3.66 (m, 2H), 3.56 (s, 1.8H), 3.52 (s, 1.2H), 2.88-2.80 (m, .4H), 2.17-1.96 (m, .6H), 1.55-1.31 (m, 7H), 1.01 (d, J = 6.8 Hz, 1.8H), 0.98 (d, J = 7.1 Hz, 1.2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.7, 141.4, 117.8, 117.5, 99.9, 63.0, 62.9, 59.1, 37.0, 30.8, 30.7, 30.5, 20.0, 18.8, 12.3, 8.6; IR (neat, NaCl) 3359b, 2933, 2872, 1680, 1458, 1384, 1233, 1206, 1131, 1058, 1032, 1008, 834 cm^{-1}; HRMS (EI) *m/z* calcd for $C_6H_{11}O$ (M-C_3H_7O) 99.0810, found 99.0804.

3-benzyl-1-methoxy-1-trimethylsilyl-(E, Z)-1-penten-5-ol (8): The data are reported for a 7/3 ratio of isomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.13 (m, 5H), 4.96 (d, J = 10.3 Hz, .7H), 4.82 (d, J = 9.8 Hz, .3H), 3.67-3.56 (m, 2H), 3.48 (s, .7H), 3.37 (s, .3H), 3.22-3.08 (m, ΘH), 2.73-2.54 (m, 2H), 1.91-1.67 (m, 1H), 1.53-1.18 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3, 140.0, 129.5, 129.2, 128.1, 127.9, 125.9, 125.8, 116.9, 61.7 60.8, 54.5, 44.1, 42.4, 38.5, 37.1, 36.4, 33.3, -0.4, -0.6; IR (neat, NaCl) 3368b, 3027, 2934, 1604, 1495, 1452, 1248, 1192, 1112, 1081, 1056, 973, 952, 842, 759, 700 cm^{-1}; HRMS (EI) *m/z* calcd for $C_9H_{19}O_2Si$ (M-CH_2Ph) 187.1154, found 187.1142.

J = 6.8 Hz, 1.5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.9, 108.8, 79.6, 77.9, 61.5, 61.2, 59.1, 57.3, 56.9, 56.5, 33.9, 33.3, 28.1, 27.0, 26.0, 21.7, 17.4, 16.2, 14.7, 12.7; HRMS (EI) *m/z* calcd for $C_7H_{13}O$ (M-$CH(OCH_3)_2$) 113.0966, found 113.0966.

***trans*-3-benzyl-2-dimethoxytrimethylsilylmethyltetrahydrofuran (9):** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.22 (m, 2H), 7.21-7.17 (m, 3H), 3.86-3.73 (m, 3H), 3.34 (s, 3H), 3.26 (s, 3H), 3.08 (dd, J = 13.5, 4.4 Hz, 1H), 2.67-2.57 (m, 1H), 2.43 (dd, J = 13.3, 10.5 Hz, 1H), 2.00-1.89 (m, 1H), 1.69-1.59 (m, 1H) 0.22 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.9, 128.9, 128.2, 125.8, 104.2, 8606, 66.7, 51.6, 48.2, 41.8, 39.8, 32.2, -0.24; IR (neat, NaCl) 3027, 5953, 2828, 1604, 1496, 1455, 1246, 1130, 1101, 1079, 1044, 906, 842, 754, 700, 628 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{14}H_{19}O_3$ (M-$Si(CH_3)_3$) 235.1334, found 235.1333.

trans-3-benzyl-2-acetatetetrahydrofuran (10): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.20 (m, 5H), 4.19 (d, J = 5.4 Hz, 1H), 4.06-3.97 (m, 2H), 3.73 (s, 3H), 3.04-2.97 (m, 1H), 2.73-2.62 (m, 2H), 2.07-1.97 (m, 1H), 1.77-1.65 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 139.4, 128.8, 128.4, 126.3, 81.3, 68.8, 52.1, 45.8, 39.3, 31.5; IR (neat, NaCl) 3369 broad and shallow, 3027, 2951, 2888, 1750, 1604, 1496, 1454, 1278, 1208, 1109, 1016, 928, 747, 702cm^{-1}; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_3$ (M) 220.1099, found 220.1095.

cis-3-benzyl-2-acetatetetrahydrofuran (10`): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.18 (m, 5H), 4.72-4.69 (m, 1H), 4.04,-3.79 (m, 2H), 3.35 and 3.29 (two s, 3H), 2.93-2.28 (m, 3H), 2.13-2.02 (m, .5H), 1.95-1.76 (m, 1H), 1.64-1.43 (m, .5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0, 128.7, 128.6, 128.3, 128.2, 126.1, 125.8, 108.8, 104.6, 66.9, 66.6,

C. Characterization Data for Electrolysis Products:

2-dimethoxymethyl-3-methyltetrahydrofuran (2a): The spectral data are reported for a 7/3 ratio of isomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.32 (d, J = 7.4 Hz, .3H), 4.24 (d, J = 5.9 Hz, .7H), 4.01-3.92 (m, .3H), 3.88-3.77 (m, 1.7H), 3.51 (t, J = 6.1 Hz, 1H), 3.44, 3.43 and 3.41(three s, 6H), 2.41-2.31 (m, .3H), 2.25-2.10 (m, .7H), 2.15-2.01 (m, 1H), 1.68-1.49(m, 1H), 1.11 (d, J = 6.7 Hz, 2.2H), 1.00 (d, J = 7.1 Hz, .76H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 105.9, 103.4, 84.4, 79.6, 67.7, 66.8, 55.3, 53.7, 53.0, 35.3, 34.8, 34.5, 34.0, 18.5, 14.3; IR (neat, NaCl) 2974, 2874, 2833, 1455, 1377, 1188, 1089, 970, 927; HRMS (EI) *m/z* calcd for $C_7H_{13}O_2$ (M-CH_3O) 129.0916, found 129.0917.

3-benzyl-2-dimethoxymethyltetrahydrofuran (2b): The data are reported for a 9:1 mixture of isomers. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.28 (m, 2H), 7.19-7.23 (m, 3H), 4.46 (d, J = 6.8 Hz, .1H), 4.22 (d, J = 5.6 Hz, .9H), 4.04-3.95 (m, .2H), 3.92-3.80 (m, 1.8H), 3.73 (t, J = 5.7 Hz, 1H), 3.48, 3.45 and 3.44 (three s, .7H), 3.43and 3.42 (two s, 5.3H), 2.99 (dd, J = 12.9, 4.9 Hz, 1H), 2.57 (dd, J = 12.9, 9.8 Hz, 1H), 2.51-2.43 (m,1H), 2.00-1.89 (m, 1H), 1.71-1.60 (m,1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6, 128.9, 128.8, 128.2, 125.9, 11.2, 105.9, 82.6, 67.8, 55.4, 54.1, 42.4, 39.6, 32.1; IR (neat, NaCl) 3029, 1610, 1496, 1455, 1188, 1089, 927cm^{-1}; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_2$ (M-CH3OH) 204.1150, found 204.1155.

2-dimethoxymethyltetrahydropyran (2c): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.22 (d, J = 5.8 Hz, 1H), 4.07 (dt, J = 11.5, 2.2 Hz, 1H), 3.51-3.34 (m, 8H), 1.91-1.28 (m, 6H); ^{13}C

NMR (75 MHz, $CDCl_3$) δ 105.8, 68.6, 54.8, 54.3, 26.6, 25.9, 22.8. Product **2c** was not characterized further due to volatility.

3-benzyl-2-dimethoxymethyltetrahydropyran (2d): In this case, the major product contains 19% of a second diastereomer. The data for the minor product are not reported. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.15 (m, 5H), 4.48 (d, 2.7 Hz, 1H), 4.06-4.00 (m, 2H), 3.49 (s, 3H), 3.44 (s, 3H), 3.27 (dd, J = 9.3, 2.7 Hz, 1H), 3.03 (dd, J = 13.4, 4.4 Hz, 1H), 2.20 (dd, J = 9.9, 13.3 Hz, 1H), 2.01-1.89 (m, 1H), 1.71-1.48 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 129.2, 128.2, 125.8, 104.8, 81.9, 68.3, 56.0, 37.9, 37.8, 28.8, 25.6; IR (neat, NaCl) 3026, 2935, 2846, 1746, 1603, 1495, 1452, 1378, 1314, 1264, 1193, 1115, 1069, 948, 849, 751, 701 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{12}H_{15}O$ (M-$CH(OCH_3)_2$) 175.1123, found 175.1124.

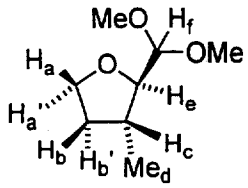
2-dimethoxymethyl-2,3-dimethyltetrahydrofuran (4a): In this case, the product contains 20% of a second diastereomer. The peaks for the minor product have not been included. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.02 (s,1H), 3.89-3.82 (m,1H), 3.70-3.65 (m,1H), 3.51 (s, 3H), 3.5 (s, 3H), 2.36-2.25 (m, 1H), 2.09-1.99 (m, 1H), 1.65-1.51 (m, 1H), 1.03 (s, 3H), 1.01 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 111.4, 108.7, 85.4, 66.3, 66.2, 57.7, 57.4, 42.6, 37.1, 34.8, 20.9, 17.1, 15.3, 14.5; IR (neat, NaCl) 2963, 2877, 2831, 1449, 1379, 1192, 1109, 1085, 987, 866 cm^{-1}; HRMS (EI) *m/z* calcd for $C_6H_{11}O$ (M-$CH(OCH_3)_2$) 99.0810, found 99.0810.

2-dimethoxymethyl-2,3-dimethyltetrahydropyran (4b): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.14 (s, 1H), 3.80-3.70 (m, 2H), 3.58, 3.53, 3.52, and 3.49 (four s, 6H), 2.03-1.84 (m, 1H), 1.77-1.27 (m, 4H), 1.25 (s, 1.5H), 1.13 (s, 1.5H), 1.03 (d, J = 7.1 Hz, 1.5H), 0.84 (d,

54.7, 54.6, 46.7, 46.3, 38.5, 34.8, 29.6, 29.2.

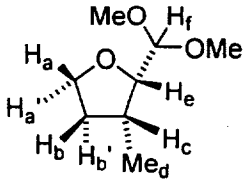
D. ^{1}H NMR NOSEY Data for Tetrahydrofurans 2a and 4a:

Tetrahydrofuran 2a (The numbers reported are the volume integrals obtained for the NOESY cross peaks)



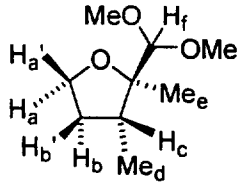
d – b'	-35	c – e	-9
d – b	-10	d – e	-41
c – b	-37	f – c	-37
c – b'	-14	f – b	-9
c – d	-35	f – d	-10

Tetrahydrofuran 2a' (minor isomer)



f – d	-20	c – d	-15	d – b'	-22
a – b'	-14	c – e	-14	d – b	-7
a – b	-6	c – b	-14		
a – d	-7	c – b'	nill		

Tetrahydrofuran 4a



f – c	-26	c – b'	-32
f – g	-110	b – b'	-193
f – Me_c	-53	c - Me_d	-53
a – a'	-189	b' - Me_d	-33
a – b	-46	b - Me_d	-61
		a - Me_d	-24
		a – b'	-23
		a' - b'	-43
		a' - b	-15
		a' - c	-14
		OMe – $Me_{c\&d}$	-48