Oxidative Cyclization Reactions: Amide Trapping Groups and the Synthesis of Furanones

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Supporting Information

A. Sample Procedure for the Oxidation Reaction

A solution of compound 1a (138 mg, 0.50 mmol) in methanol (15.0 mL) and water (1.7 mL) was placed in a three-neck round bottom flask under an argon atmosphere. To this solution was added $LiClO_4$ (161 mg, 1.51 mmol) and 2,6-lutidine (0.35 mL, 3.0 mmol). A reticulated vitreous carbon anode and a platinum wire cathode were inserted into the reaction mixture, and then the resulting solution was sonicated under an argon atmosphere for 10 minutes. The electrolysis was carried out with a constant current of 8.0 mA until 3.0 F/mol of electricity had been passed. Then, about half of the solvent mixture was removed under reduced pressure. Water and ether were added to the concentrated solution. The mixture was mixed and allowed to separate. The aqueous layer was extracted twice more with ether. The organic layers were combined and concentrated *in vacuo*. The crude product was chromatographed through a silica gel column (hexane/ether, 1:3) to afford compound 2 (103 mg, 83%) as a pale yellow oil. This oil is used directly is subsequent synthetic steps. The oil may also be triturated by dissolving it in a minimal amount of refluxing hexane. Cooling this solution, and then filtering the resulting slurry, produced compound 2 as white crystals for high quality analytical purposes.

A. Spectral Data

5-(2-Methoxy-[1,3]dithian-2-yl)-5-methyl-dihydro-furan-2-one (Compound 2)

The ^{1}H NMR (300 MHz, $CDCl_3$), ^{13}C (75 MHz, $CDCl_3$), and IR (neat/NaCl) match literature values[2].
^{1}H NMR (300 MHz, C_6D_6): δ 3.34 (s, 3H), 2.74-2.65 (m, 1H), 2.57-2.26 (m, 5H), 2.05-1.93 (m, 1H), 1.44 (s, 3H), 1.45-1.35 (m, 1H), 1.31-1.21 (m, 2H)
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.52 (s, 3H), 2.92-2.87 (m, 4H), 2.72-2.62 (m, 2H), 2.59-2.52 (m, 1H), 1.97-1.91 (m, 2H), 1.88-1.81 (m, 1H), 1.57 (s, 3H).
m.p.: 72-73 ºC.

4-Methoxy-4-(2-methoxy-[1,3]dithian-2-yl)-pentanoic acid diethylamide (Compound 6)

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.52 (s, 3H), 3.49 (s, 3H), 3.41-3.31 (m, 4H), 2.95-2.73 (m, 4H), 2.65-2.53 (m, 1H), 2.43-2.30 (m, 2H), 2.22-2.10 (m, 1H), 1.91-1.82 (m, 2H), 1.37 (s, 3H), 1.19 (t, J=7.1 Hz, 3H), 1.12 (t, J=7.1 Hz, 3H)
^{13}C (75 MHz, $CDCl_3$): δ (# attached protons) 172.6 (0), 118.2 (0), 59.7 (0), 53.8 (3), 52.6 (3), 42.3 (2), 40.4 (2), 30.2 (2), 29.4 (2), 28.7 (2), 27.8 (2), 26.7 (2), 21.3 (3), 14.7 (3), 13.4 (3).
IR (neat/NaCl) 3473, 2975, 2930, 1639, 1429, 1150, 1094, 1057, 929 cm^{-1}.
LRMS (EI) m/e (relative intensity) 320.1 (M-CH_3, 10), 304.2 (M-OCH_3, 10), 214.2 (100), 182 (85), 115.1 (100), 100.1 (95). HRMS (EI) calcd. for $C_{14}H_{26}NO_3S_2$ (M-CH_3) 320.1354, found 320.1341.

(3R)-2,3-Dimethyl-pentanedioic acid 1-methyl ester (Compound 19)

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.69 (s, 3H), 2.68 (residual HMPA, d, J=12.0 Hz, 0.04H), 2.65 (residual HMPA, d, J=9.0 Hz, 0.04H), 2.55-2.48 (m, 1H), 2.44(dd, J=15.6 Hz, 5.4 Hz, 1H), 2.39 (dq, J=7.2 Hz, 7.2 Hz, 0.82H), 2.32-2.26 (m. 0.18H), 2.23 (dd, J=15.0 Hz, 8.4 Hz, 1H), 1.16 (d, J=7.2 Hz, 0.55H), 1.13 (d, J=7.2 Hz, 2.45H), 1.05 (starting material, d, J=6.0 Hz, 0.22 H), 1.00 (d, J=7.2 Hz, 0.55H), 0.98 (d, J=7.2 Hz, 2.45H)
^{13}C NMR (75 MHz, $CDCl_3$) for major isomer: δ (# attached protons) 179.1 (0), 176.1 (0), 51.8 (3), 43.8 (1), 39.1 (2), 32.5 (1), 16.6 (3), 13.0 (3).

(3R)-4-Diethylcarbamoyl-2,3-dimethyl-butyric acid methyl ester

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.68 (s, 3H), 3.67 (impurity, s, 0.34H), 3.42-3.27 (m, 4H), 2.55-2.49 (m, 1H), 2.48-2.41 (m, 1H), 2.34 (dd, J=15.2 Hz, 4.8 Hz, 1H), 2.17 (dd, J=15.2 Hz, 8.7 Hz, 1H), 1.18 (t, J=7.5 Hz, 3H), 1.15 (d, J=9.6 Hz, 0.67H), 1.13 (d, J=7.2 Hz, 2.33H), 1.11 (t, J=7.2 Hz, 3H), 1.03 (impurity, d, J=6.0 Hz, 0.34H), 0.96 (d, J=6.6 Hz, 0.67H), 0.95 (d, J=7.2 Hz, 2.33H).
^{13}C NMR (75 MHz, $CDCl_3$) for major isomer: δ (# attached protons) 176.5 (0), 170.9 (0), 51.5 (3), 44.0 (1), 42.0 (2), 40.2 (2), 37.5 (2), 32.8 (1), 16.8 (3), 14.5 (3), 13.2 (3) for 2C.

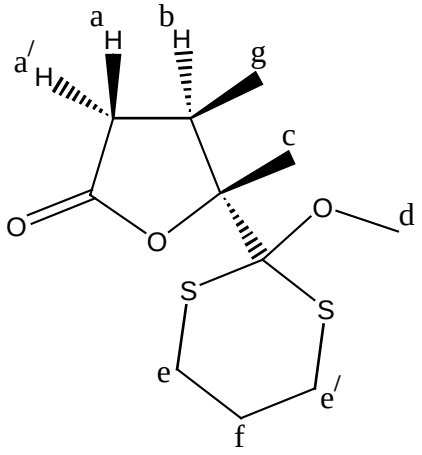
(4R)-4-[1,3]Dithian-2-ylidene-3-methyl-pentanoic acid diethylamide (Compound 20)

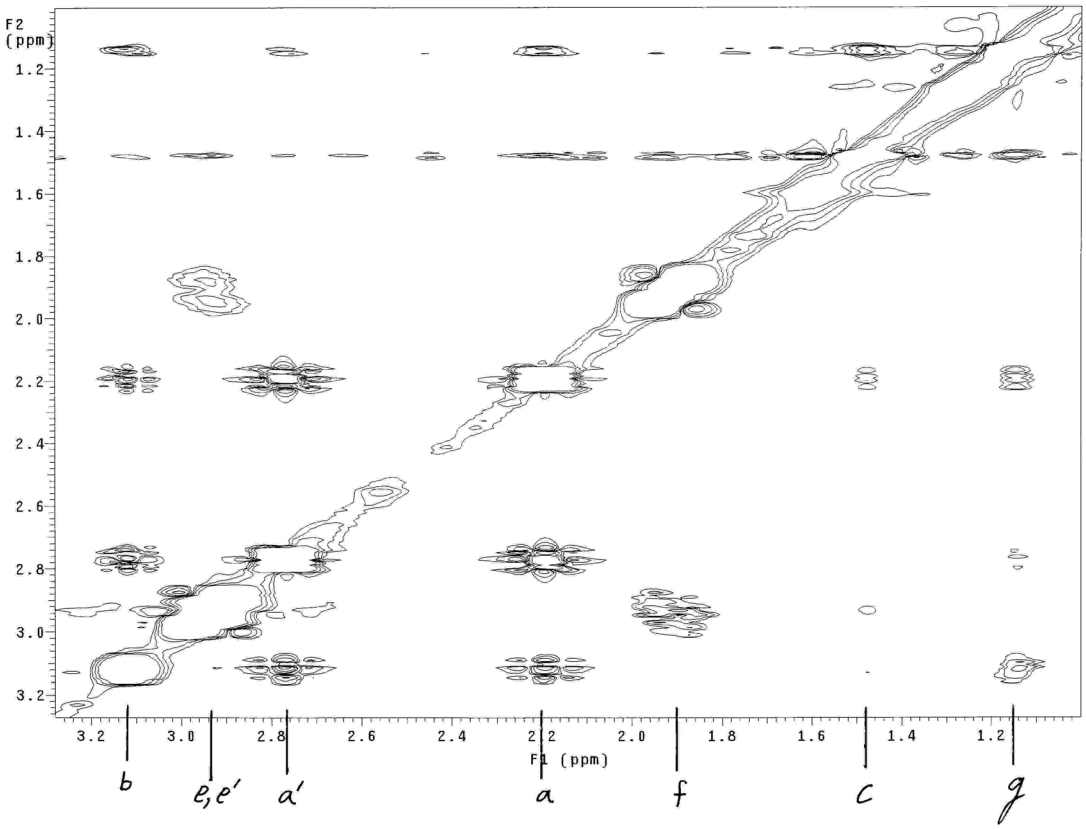
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.75-3.70 (m, 1H), 3.418-3.292 (m, 4H), 2.91-2.83 (m, 4H), 2.36-2.26 (m, 2H), 2.15-2.09 (m, 2H), 1.83 (s, 3H), 1.18 (t, J=7.2 Hz, 3H), 1.11 (t, J=7.2 Hz, 3H), 1.05 (d, J=6.6 Hz, 3H).
^{13}C (75 MHz, $CDCl_3$): δ (# attached protons) 170.6 (0), 141.9 (0), 120.2 (0), 42.1 (2), 40.0 (2), 38.4 (2), 34.9 (1), 30.3 (2), 30.0 (2), 25.1 (2), 18.2 (3), 15.3 (3), 14.6 (3), 13.2 (3).
IR (neat/NaCl) 3467, 2968, 2931, 1639, 1459, 1425, 1378, 1278, 1071 cm^{-1}.
LRMS (EI) m/e (rel. intensity) 287 (M^+, 30), 180 (100), 173 (M^+-CH_2CONEt_2, 85).
HRMS (EI) calcd for $C_{14}H_{25}NOS_2$ (M^+) 287.1378, found 287.1375.
$[\alpha]_D^{20}$= -4.1˚ (c=0.1 g/ml, CH_2Cl_2).

(4R, 5R)-5-(2-Methoxy-[1,3]dithian-2-yl)-4,5-dimethyl-dihydro-furan-2-one (Compound 21)

^{1}H NMR (600 MHz, $CDCl_3$): δ 3.54 (s, 3H), 3.14-3.09 (m, 1H), 3.00-2.96 (m, 1H), 2.94-2.92 (m, 2H), 2.91-2.86 (m, 1H), 2.77 (dd, J=9.0, 4.8 Hz, 1H), 2.19 (dd, J=9.0, 4.8 Hz, 1H), 1.97-1.92 (m, 1H), 1.91-1.85 (m, 1H), 1.48 (s, 3H), 1.14 (d, J=3.6 Hz, 3H).
^{13}C (75 MHz, $CDCl_3$): δ (# attached protons) 175.2 (0), 102.2 (0), 94.4 (0), 52.7 (3), 37.0 (2), 34.5 (1), 27.7 (2), 27.5 (2), 22.5 (2), 17.1 (3), 17.1 (3).
IR (nujol/NaCl) 1762, 1463, 1378, 1354, 1086, 975, 722 cm^{-1}.
m.p.: 122-123 ºC with some apparent polymerization.
LRMS (EI) m/e 262.0 (M^+), 149.0 (-$COCH_3SCH_2CH_2CH_2S$), 113.0 (-$OCOCH_2CHCH_3CHCH_3$)
LRMS (FAB) m/e 269.1 (M+Li)
HRMS (FAB) calcd. for $C_{11}H_{18}O_3S_2Li$ (M+Li) 269.0857, found 269.0857.
$[\alpha]_D^{20}$= -29.9˚ (c=0.01 g/ml, CH_2Cl_2). Relative stereochemistry was verified by NOESY NMR.

500 MHz NOESY NMR Spectra for Compound 21





500 MHz NOESY NMR Spectra for Compound 21 (continued)

Proton Cross-Peak Interaction	Volume Integral
b-g	-127
a-g	-99
a′-g	-29
a-a′	-300
b-a	-3
b-a′	-18
c-g	-190
c-b	-25
c-a	-62
c-a′	0