Synthesis and hydrogenation of acetonylmalonaldehyde bis(ethylene acetal)

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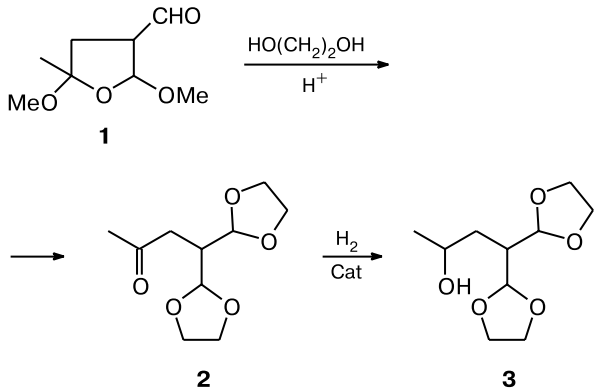
A single-step synthetic route to acetonylmalonaldehyde bis(ethylene acetal) from 2,5-dimethoxy-5-methyltetrahydrofuran-3-carbaldehyde was proposed.

Key words: tetrahydrofurancarbaldehydes, malonaldehyde, bis(ethylene acetals), synthesis.

Malonaldehydes are useful C_3-fragments, which can be transformed in reactions with mono- and bifunctional nucleophiles into open-chain,[1] carbocyclic,[2] or heterocyclic compounds.[3] In the study of the properties of α-substituted 2,5-dimethoxytetrahydrofuran-3-carbaldehydes,[4] we have found that they are hydrolyzed by water to give acetonylmalonaldehyde and its derivatives in virtually quantitative yields.[5,6]

To investigate this further, we studied acid-catalyzed reactions of 2,5-dimethoxy-5-methyltetrahydrofuran-3-carbaldehyde (**1**) with alcohols. Heating of compound **1** with a double amount of ethylene glycol in toluene at 100—120 °C in the presence of the cation-exchange resin KU-2 gave previously unknown acetonylmalonaldehyde bis(ethylene acetal) (**2**) in 65% yield.

Scheme 1



Ketone **2** was smoothly reduced at a nickel catalyst at 70 °C and P_{H_2} = 10 MPa to 2-hydroxypropylmalonaldehyde bis(ethylene acetal) (**3**).

Experimental

IR spectra were recorded on a Specord M-82 instrument (thin film between NaCl plates). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 spectrometer (200 (^{1}H) and 50.3 MHz (^{13}C)) in $CDCl_3$. Chemical shifts are given on the δ scale with reference to the solvent as the internal standard. Mass spectra were recorded on a Kratos MS-300 instrument (EI, 70 eV).

Acetonylmalonaldehyde bis(ethylene acetal) (2). A mixture of freshly distilled 2,5-dimethoxy-5-methyltetrahydrofuran-3-carbaldehyde (**1**)[4] (5.38 g, 31 mmol), ethylene glycol (3.83 g, 62 mmol), and the cation-exchange resin KU-2 (0.8 g) in dry toluene (50 mL) was heated with stirring on an oil bath (100—120 °C) for 3 h in a flask equipped with a fractionating column until a mixture of methanol and water ceased to be liberated. On cooling, the catalyst was filtered off, the filtrate was concentrated under reduced pressure, and the residue was distilled *in vacuo*. The yield of compound **2** as a colorless oily liquid was 4.37 g (65%), b.p. 112—114 °C (1 Torr), d_4^{20} 1.2029, n_D^{20} 1.4735. Found (%): C, 54.91; H, 7.71. $C_{10}H_{16}O_5$. Calculated (%): C, 55.55; H, 7.45. IR, ν/cm^{-1}: 2960, 2892 (CH_3, CH_2); 1716 (C=O); 1150—1040 (intense absorption bands of the dioxolane rings). ^{1}H NMR ($CDCl_3$), δ: 2.16 (s, 3 H, COMe); 2.52 (d, 2 H, $COCH_2$, ^3J = 6.26 Hz); 2.76 (tt, 1 H, CH, ^3J = 4.33 Hz, ^3J = 6.26 Hz); 3.8—4.0 (wm, 8 H, OCH_2CH_2O); 4.97 (d, 2 H, OCHO, ^3J = 4.33 Hz). ^{13}C NMR ($CDCl_3$), δ: 29.8 (Me); 37.35 (CH_2); 41.92 (CH); 64.8 (OCH_2CH_2O); 103.04 (OCHO); 207.15 (CO). MS, m/z (I_{rel} (%)): 216 $[M]^+$(0.7), 215 $[M - H]^+$ (4), 173 $[M - MeCO]^+$ (13.6), 159 $[M - MeCOCH_2]^+$ (28.3), 143 $[M - CHO(CH_2)_2O]^+$ (12.8), 115 (15.1), 113 (20), 99 (24.8), 87 (29.1), 83 (11.8), 73 $[CHO(CH_2)_2O]^+$ (100), 57 $[MeCOCH_2]^+$ (20.1), 55 (33.5), 45 (54.2), 43 $[MeCO]^+$ (45.8).

2-Hydroxypropylmalonaldehyde bis(ethylene acetal) (3). A rotating steel autoclave was charged with ketone **2** (4.37 g, 20 mmol) in methanol (90 mL) and with freshly prepared Raney nickel (1.5 g). The initial hydrogen pressure was 11.2 MPa. Hydrogenation at 70 °C for 2 h gave compound **3** (3.61 g, 82%) as a colorless oily liquid, b.p. 115—117 °C (1 Torr), d_4^{20} 1.2032, n_D^{20} 1.4739. Found (%): C, 55.29; H, 8.45. $C_{10}H_{18}O_5$. Calculated (%): C, 55.04; H, 8.31. IR, ν/cm^{-1}: 3472 (OH); 2964, 2888 (CH_3, CH_2); 1150—1004 (intense absorption bands of the dioxolane rings). ^{1}H NMR ($CDCl_3$), δ: 1.14 (d, 3 H, Me, ^3J = 6.2 Hz); 1.40—1.90 (wm, 3 H, $C\underline{H}_2C\underline{H}$(OH)Me); 2.20 (pseudoquint, 1 H, CH, ^3J = 7.54 Hz); 3.18 (br.s, OH, ^3J = 3.2 Hz); 4.00—3.90, 3.90—3.80 (wm, 8 H, OCH_2CH_2O); 4.94 (dd, 2 H, OCHO, ^3J = 4.25 Hz, ^3J = 1.30 Hz). ^{13}C NMR

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($CDCl_3$), δ: 23.56 (Me); 32.68 (CH_2); 43.01 (CH); 64.97 and 64.74, 64.60 and 64.27 (OCH_2CH_2O); 66.38 (OHCH); 103.95 (OCHO). MS, m/z (I_{rel} (%)): 218 $[M]^+$ (2.8), 203 $[M - Me]^+$ (4.8), 174 (20), 157 (15.3), 143 (1.9), 127 (6.7), 115 (17.3), 99 (25), 73 $[CHO(CH_2)_2O]^+$ (100), 45 $[MeCH(OH)]^+$ (34.6).

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