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SYNTHESIS OF 2-METHYL-1,3-CYCLOPENTANEDIONE MONOETHYLENE KETAL

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Abstract : Direct ketalization of 2-methyl-1,3-cyclopentanedione **3** led to the corresponding diethylene ketal **2**. Carefully controlled hydrolysis of compound **2** afforded the monoethylene ketal **1** in high yield.

In planning total synthesis in the steroid field, we needed the monoethylene ketal of 2-methyl-1,3-cyclopentanedione **1**. The preparation of this compound (accompanied by a small amount of the corresponding diketal **2**), by direct ketalization of dione **3**, was claimed by a Russian group in 1974[1].

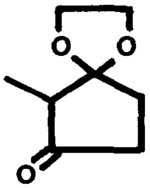
However, this preparation proved to be irreproducible, at least in our hands. Furthermore, we noted several discrepancies between the given spectral data (i.r. and ^{1}H n.m.r.), and those expected for such structures ; we were then compelled to reinvestigate this preparation. The following method readily gave the desired compound **1** *via* the corresponding diketal **2**.

A mixture of 2.8 g (25 mmol) of dione **3**, 45 ml (0.8 mol) of ethylene glycol, 270 ml of toluene, and 100 mg of toluene-*p*-sulphonic acid was refluxed (magnetic stirring) with removal of water (Dean-Stark trap apparatus) ; after 3 h the toluenic layer was separated. To the residual phase was added 270 ml of toluene, 10 ml of ethylene glycol, and 50 mg of toluene-*p*-sulphonic acid ; after 3 h refluxing, the toluenic phase was again separated. The last procedure was repeated two times and the four toluenic fractions were combined, washed with a saturated solution of sodium hydrogen carbonate, and dried over magnesium sulphate. Solvent was then removed under reduced pressure, giving crude diketal **2**, an aliquot of which was purified by molecular distillation (80 °C,0.01 Torr) yielding an oil : ^{1}H n.m.r. (CCl_4, 90 MHz) : δ 0.8 (d, 3H, *J* 6.3 Hz), 1.7 (s, 4H), 2.1 (q, 1H, *J* 6.3 Hz), and 3.8 (m, 8H) ; ^{13}C n.m.r. (C_6D_6) : δ 7.6 (q), 34.8 (t), 49.1 (d), 64.4 (t), 65.0 (t), and 115.8 (s).

Carefully controlled hydrolysis of the crude diketal **2** under heterogeneous conditions[2] [crude diketal **2** in 50 ml of CH_2Cl_2 was stirred at 20 °C under nitrogen with 15g of kieselgel Merck (70-230 mesh), and 1.5 ml of 15 % H_2SO_4, during 2.5 h, followed by filtration, CH_2Cl_2 washing, evaporation, and distillation] led to monoketal **1** (2.7 g, 70 % overall yield from dione **3**) as an oil :b.p. 48 °C (0.01 Torr) ; i.r. (neat) : ν_{max} 1740 cm^{-1} ; ^{1}H n.m.r. (C_6D_6, 200 MHz) : δ 1.14 (d, 3H, *J* 7.1 Hz), 1.6-1.95 (m, 2H), 2.1-2.2 (m, 2H), 2.3 (q, 1H, *J* 7.1 Hz), and 3.5 (m, 4H) ; ^{13}C n.m.r. (C_6D_6) : δ 7.4 (q), 32.1 (t), 36.4 (t), 51.4 (d), 65.0 (t), 65.2 (t), 114.5 (s), and 213.3 (s)^3.

Monoketal **1** is a highly sensitive compound : the cleavage of the ketal ring took place very easily at room temperature, either in basic medium (primary amines), or in acidic medium (acidic $CDCl_3$!), giving quantitatively compound **4** as crystals :m.p. 79 °C (ether) ; i.r. (nujol) : ν_{max} 3380, 1680, and 1620 cm^{-1} ; ^{1}H n.m.r. ($CDCl_3$, 90 MHz) : δ 1.6 (s, 3H), 2.4 (m, 2H), 2.7 (m, 2H), 2.9 (m, 1H), 3.9 (m, 2H), and 4.3 (m, 2H) ; ^{13}C n.m.r. ($CDCl_3$) : δ 6.0 (q), 25.4 (t), 33.4 (t), 61.2 (t), 70.8 (t), 116.3 (s), 184.7 (s), and 206.0 (s).

In spite of this facile ketal ring cleavage, the following nucleophilic reagents added "normally" to the carbonyl group of monoketal **1**, leading to the expected alcohols : diisobutylaluminium hydride, *n*-butyl-lithium (addition in hexane at −78 °C, and then "quenching" by H_2O at this temperature).



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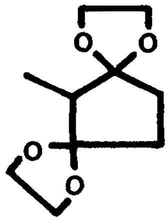

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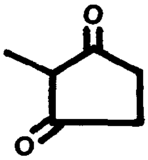

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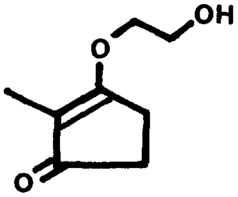

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2 F. Bohlmann and W. Otto, *Liebigs Ann. Chem.*, 1982, 186.

3 Spectral data of compounds **1** and **2** are thus in good agreement with the proposed structures but in strong disagreement with data published by the Russian group [1]. Furthermore these authors described compounds **1** and **2** as solids (m.p. 123-124 °C and 194-195 °C respectively) when both are liquids at room temperature.

"Unfortunately, an exchange of correspondance with Professor I.V. Torgov has failed to resolve the discrepancy"

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