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On the Formation of Biacetyl Trimers in Acidic Media

Kai Baldenius[a], P Dallman and John Hudec*
Department of Chemistry, The University, Southampton, SO9 5NH

Abstract - Evidence is presented to show that the tricyclic trimer of biacetyl (1) is formed in acidic media *via* "biacetyl hydrates" rather than the dimeric aldol (2). A new trimer (3) has been isolated as well as a crystalline biacetyl trimer dihydrate.

It has been suggested that the interesting tricyclic trimer (1)[1,2] that can be recrystallised either from water or petroleum ether b.p. 30-40°C, is formed from biacetyl in concentrated hydrochloric acid *via* the aldol dimer (2)[3] (in its open or cyclised form). Indeed, it was suggested that (1), because of its stability to alkali, could be used as a reagent for the protection of α- or δ-diketones[4]. We wish to show that these statements are incorrect.

An investigation of mother liquors from the preparation of (1)[1] yielded small amounts of several crystalline compounds, one of which is an isomeric bicyclic trimer (3), m.p. 88-90°C. The ^1H nmr ($CDCl_3$ in ppm) showed three singlets of equal intensity at 1.38, 1.64 and 2.23; ^{13}C nmr ($CDCl_3$ in ppm) showed signals at 22.0, 23.9 and 25.0 (CH_3 groups), 108.7 and 111.8 (O-C-O) and 205.2 (C=O). The *cis* stereochemistry of the four quaternary methyl groups follows from its reactions. Thus (3) on heating in dilute aqueous NaOH yields only (1) and the pentadeuterated trimer (1a) is obtained when either (1) or (3) is heated with a trace of NaOD in D_2O, indicating that under the above conditions (1) is thermodynamically more stable than (3)[5]. Furthermore, (3) dissolves readily in 100 vol H_2O_2 at room temperature - this solution deposits after 2-3 days fine long needles of the hydrogen peroxide *d, ℓ*-adduct (4).

The fact that we are able to isolate (3) as the only stereoisomer under a variety of conditions of acid concentration, time and temperature and that the presence of water in the reaction is essential, suggests that (1) is formed *via* hydrated forms of biacetyl[6], the last step being the acid catalysed aldol condensation of (3) to (1). Thus a) no trace of (1) is obtained even after 2 weeks on treatment of biacetyl in ether or chloroform saturated with HCl gas under anhydrous conditions and b) only (2) is obtained when biacetyl in dry ether is treated with magnesium bromide etherate[7].

A plausible mechanistic rationalisation that accounts for the formation of (3) and (1) is given in Scheme 1. The preference of biacetyl to hydrate rather than to enolise should not be unexpected as such reaction removes the electrostatic repulsion between the δ+ charges on the adjacent carbonyl carbon atoms. Indeed, this interaction must be responsible for the relative stability of the fused dioxolane system in (1) and (3) in aqueous acid. There are many examples of hydration of carbonyl groups in the literature[8] - the most illustrative one, which shows the directional influence of the δ+ on the adjacent α-carbon atoms on the carbonyl group is the comparison of (5) and (6), the former is hemiketalised in $CHCl_3$/abs.EtOH (9:1) to the extent of 75±5%

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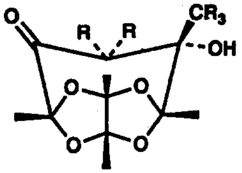
[a] Hamburg University Exchange Student 1985-6.

whilst the latter only 5%[9]. This conformationally dependent σ^*/π^* interaction is conceptually identical to the vertical stabilisation[10], albeit in a destabilising sense on account of the adjacent electron poor σ-bonds.

When the reaction between biacetyl and the acid is carried out in 37% DCl in D_2O, (1) and (3) have deuterium incorporated virtually equally on all hydrogen bearing C atoms to the extent of 5.5 ±0.5%[11]. As might be expected on the basis of general acid catalysis, the reaction in DCl/D_2O is about 2 to 3 times faster than in HCl/H_2O.

We have so far isolated only an oily mixture of hydrates on treatment of biacetyl with water only or with aqueous HCl up to 3 molar solution overall. However, 5M aqueous H_2SO_4 yields a crystalline trimer dihydrate which decomposes between 85 and 100°C (without melting) into yellow liquid. The ^{1}H nmr (1:1 $CDCl_3$/DMSO-d_6 in ppm) showed signals at 1.33, 1.41 and 1.44 (CH_3 groups) and 5.1 and 5.6 (O-H groups); ^{13}C nmr (as for ^{1}H nmr) 20.1, 21.8 and 23.0 (CH_3 groups) and 104.9, 106.0 and 108.5 (O-C-O). The structure is at present unknown; the data would fit two stereoisomers of (7), each with either *cis* or *trans* ring junction, and the *d, ℓ* or either of the two *meso* isomers of (8). The dioxolane structures appear to be more probable by analogy with earlier work on acid catalysed reaction between various alcohols and glyoxal[12]. Further work is in progress. [Compounds (3), (4) and (7)/(8) gave satisfactory analytical data]



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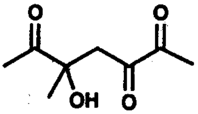
1a R = D



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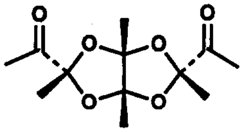

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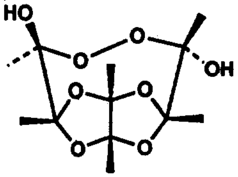

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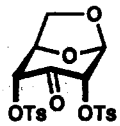

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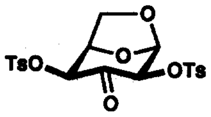

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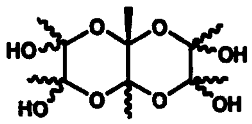

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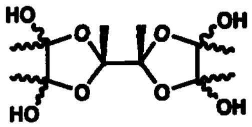

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5. An improved method for the preparation of (3): Freshly distilled biacetyl (2 ml) and c. HCl (3ml) stirred at RT for 1.5 hours. The homogeneous reaction mixture is poured into brine and extracted several times with $CHCl_3$. The extracts (after water washing, drying and evaporation) yield *ca* 0.8 g of oil which is a mixture of (1) and (3), the latter in greater amounts (50-80%). Crystallisation either from water or petroleum ether b.p. 30-40°C yields pure (3).

6. Contrast with the work of Platzer, N. ; Lefebvre, B. ; Temmen, J. ; Mattioda, G. *Bull. Soc. chim. Fr.*, **1981**, 40 where hydration for the control of the stereoselectivity cannot be involved.

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11. Evaluation by ^2H nmr in $CDCl_3$ using an internal deuterated standard.

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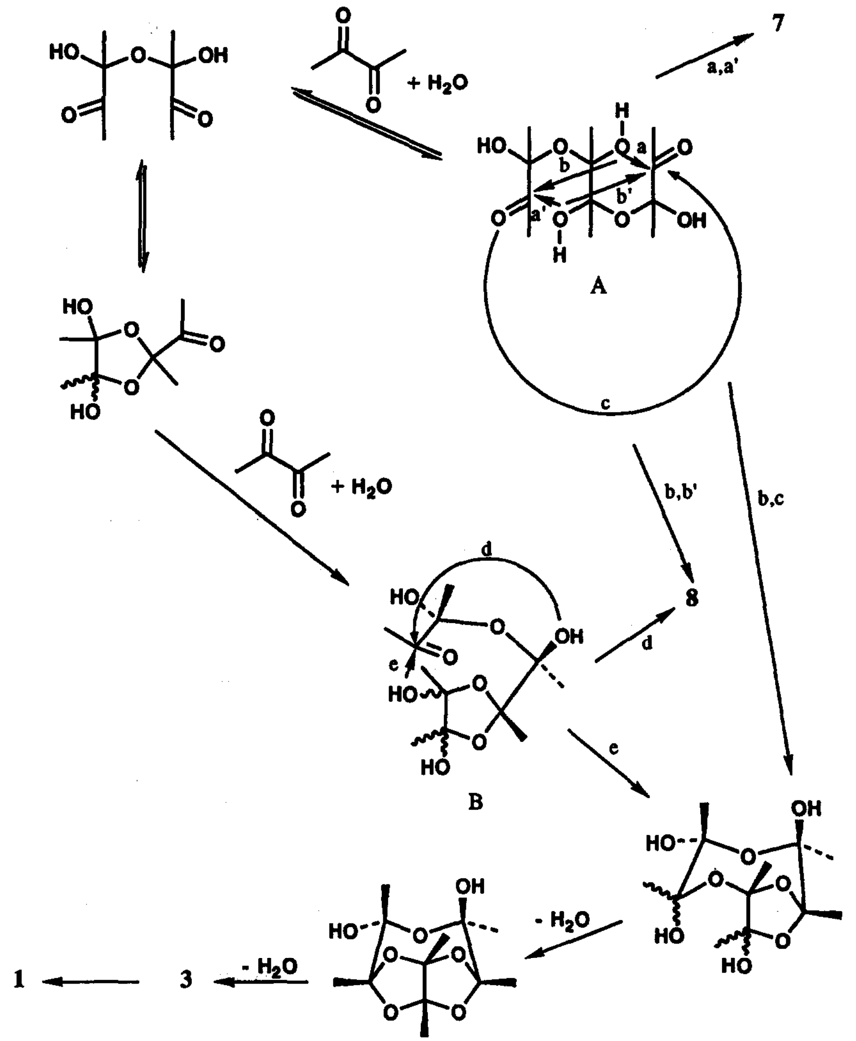
Scheme 1



Arrows marked with a, a', b, b', c, d and e show various modes of cyclisation (the addition of hydroxyl group to a protonated carbonyl group) in the hypothetical intermediates A and B.

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