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THE STEREOSTRUCTURE OF TWO TRIMERS OF BIACETYL

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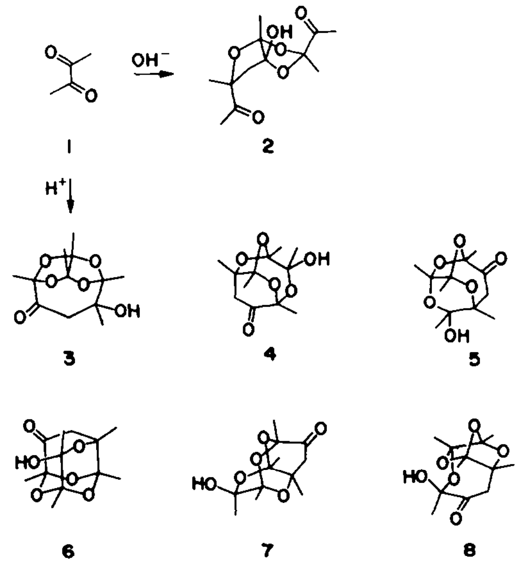
Abstract—Structures of two trimers of biacetyl were determined on the basis of chemical and spectroscopic evidence and the single-crystal X-ray analysis. The compounds are shown to be *exo*-3, *endo*-7-diacetyl-1-hydroxy-*endo*-3,5,*exo*-7-trimethyl-*cis*-2,4,6-*trioxabicyclo*[3.3.0]octane (2) and 11-hydroxy-1,3,5,7,11-pentamethyl-*cis*-2,4,6,8-tetraoxatricyclo[3.3.3.0^{3,7}]undecan-9-one (3).

Two trimeric products have been isolated in crystalline form from self-condensations of biacetyl (1) in the presence of either alkaline or acidic catalysts.[1–3] The bicyclic structure 2 and the tricyclic structure 4 were assigned to the trimers largely on the basis of spectral data and a complex mechanistic rationale.[2] We now wish to report a straightforward structural assignment for the trimers of 1, establishing the structure and stereochemistry of the bicyclic trimer 2, and revising the structure of the tricyclic trimer.

The trimer, m.p. 75°, obtained by mild alkaline catalysis[2,3] readily dissociates into the parent biacetyl and the corresponding dimeric β-ketol. Attempts to prepare carbonyl and hydroxyl derivatives resulted in disproportionation of the labile cyclic hemiketal array, giving in most cases derivatives of two components. The basic skeleton and the substitution pattern of 2 was apparent from ^{1}H and ^{13}C-NMR spectra (Experimental). The intramolecular H-bonding in 2 was originally inferred from an anomalous IR OH band,[2] but the validity of assigning the stereochemistry on this basis is doubtful.[3] In an effort to clarify the situation and to establish the relative stereochemistry of 2, we have carried out a direct single-crystal X-ray structure determination. Our results confirm the structure and stereochemistry of 2. However, there is only an intermolecular H-bonding O(1)—H(1)...O(4) of 2.04 (4) Å and 161 (4)°. An ORTEP drawing of the molecule of 2, presenting the numbering scheme and the H-bonding pattern, is shown in Fig. 1. The atomic parameters which define the crystal structure, bond lengths and angles are given in the Supplementary Material.†

We have also re-examined the other trimer, m.p. 105°, prepared according to Diels and Jost.[1] The compound shows no reducing properties (Tollens' and Fehling's reagent), and is also unaffected by periodate or permanganate. One oxygen atom is contained in a tertiary OH function, for reaction with acetic anhydride afforded the monoacetyl derivative. The trimer gave stable carbonyl derivatives, i.e. a monooxime, semicarbazone, and *p*-nitrophenylhydrazone,[1] but the NMR evidence excluded an acetyl function. The stability of the trimer to alkalis, oxidation and acetolysis, taken in conjunction with the spectral properties, also excluded a 3- or 4-membered ring and a tetrahydrofuranone system. The problem of assigning a structure could then be summarised by two questions: (1) where was the OH group? (2) how were the remaining four ketal linkages arranged in the tetraoxatricycloundecanone system? There are six possible combinations 3–8 when only one of each of the epimers of 4–8 is considered. However, a straightforward structural assignment can be made from a simple heuristic. The structures 4–8 having a cyclic hemiketal array could be dismissed in view of the formation and



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† The atomic co-ordinates for this work are available from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

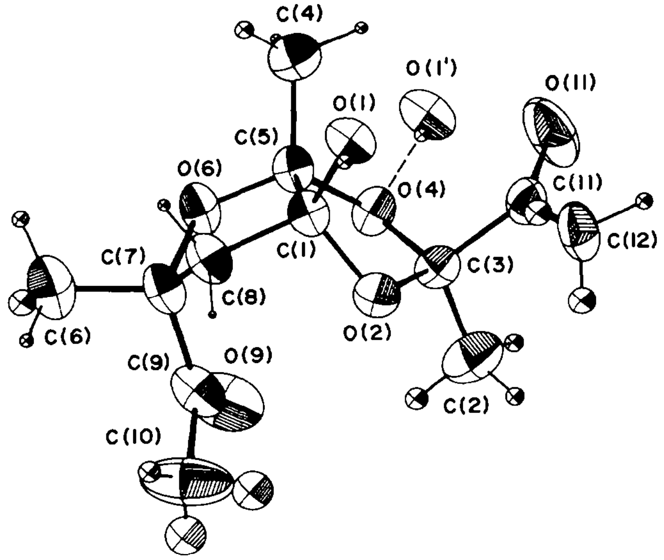

Fig. 1. ORTEP drawing of the structure of **2**.

stability of the mono-oxime after a vigorous treatment with an excess of hydroxylamine. It is well known that cyclic hemiketals do not survive such conditions. The interpretation of all available evidence led to structure **3**. This structure certainly accounts for the tetraoxatricycloundecanone system, the five methyls, and the β-ketol grouping and is entirely in accord with its detailed ^1H and ^{13}C-NMR spectra. The acetylation shift (an α-effect of 6.9 and a β-effect of -6.4 ppm) in the ^{13}C-NMR spectra of the parent trimer and its acetate was consistent with the β-ketol array in **3**. The assessment of the partial β-ketol structure in an eight-membered ring was completed when dihedral angles of 30° and 145° are found in a Dreiding stereomodel for methylene protons and carbonyl oxygen. This is compatible with the small J_{gem} 10.6 Hz observed in **3**.[4]

In order to remove any equivocation about the structural assignment we carried out an X-ray crystallographic structure determination. An ORTEP drawing of the molecule of **3** presenting the numbering scheme is shown in Fig. 2. There is a weak intermolecular interaction O(11)—H(11)...O(2) of 2.50 (5) Å and 163 (6)°. The atomic parameters, bond lengths and angles are given in the Supplementary Material, see footnote on p. 1985.

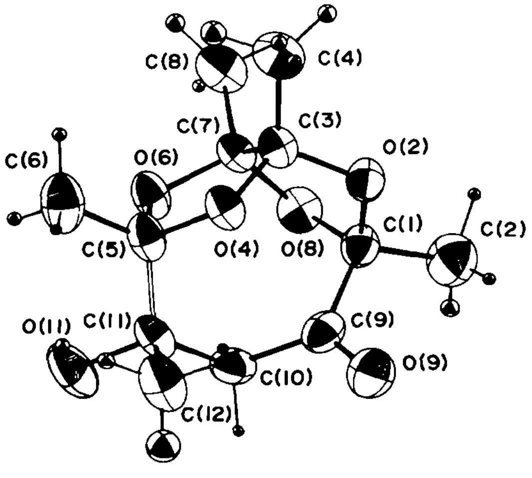

Fig. 2. ORTEP drawing of the structure of **3**.

At the outset of this study, no precedent existed for the ketal array of **3** such as that formed by ketalisation of a δ-diketone with an α-diketone. The ready availability of **3** and its pronounced stability in alkaline media, suggests the utility of this reaction in generating new structural types that could well serve as useful intermediates in organic synthesis; e.g. for the protection of α- or δ-diketones. These studies are currently in progress in our laboratory.

EXPERIMENTAL

M.ps are uncorrected. IR spectra were taken on a Perkin-Elmer 167 grating IR spectrometer. NMR spectra were recorded on Varian T-60 or Bruker WP-80/DS FT NMR spectrometer. Chemical shifts are given in ppm (δ) from an internal TMS and coupling constants are expressed in Hz (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet). Off-resonance decoupling served to distinguish between the primary, secondary, tertiary and quaternary carbons. Mass spectra were determined on a Varian MAT CH-7 instrument at 70 eV and 100 μA.

exo - 3,endo - 7 - *Diacetyl* - 1 - *hydroxy* - endo - 3,5,exo - 7 - *trimethyl* - cis - 2,4,6 - *trioxabicyclo*[3.3.0]*octane* (**2**)

Biacetyl (**1**, 86 g) was kept for 5 days at room temp in contact with either an anion-exchange resin (Amberlite CG-400, OH-form)[2] or alkalinised powdered glass[3] to give **2** in a 25–35% yield. The same compound separates as long needles from old specimens of **1**. Repeated crystallisations from ether gave colourless needles, m.p. 75°. IR (KBr) 3390, 1728, 1723, 1432, 1382, 1374, 1360, 1324, 1201, 1178, 1165, 1143, 1135, 1110, 1079, 1061, 1015, 967, 936, 931 cm^{-1}. MS, *m/e* (relative intensity) 259 (M + 1, 0.1), 241 (0.3), 215 (48), 171 (1), 156 (5), 151 (52), 130 (11), 129 (92), 113 (6), 112 (9), 111 (40), 88 (15), 87 (57), 86 (23), 85 (86), 84 (7), 69 (17), 59 (10), 44 (10), 43 (100).

^1H-NMR ($CDCl_3$), δ 4.78 (s, 1H, OH), 3.22, 1.91 (dd, 2H, CH_2, J = 13.5), 2.34 (s, 3H, COMe), 2.24 (s, 3H, COMe), 1.44 (s, 3H, Me), 1.41 (s, 3H, Me), 1.34 (s, 3H, Me). ^1H-NMR (DMSO-d_6), δ 7.42 (s, 1H, OH), 3.03, 1.82 (dd, 2H, CH_2, J = 13.5), 2.26 (s, 3H, COMe), 2.15 (s, 3H, COMe), 1.33 (s, 3H, Me), 1.27 (s, 3H, Me), 1.26 (s, 3H, Me); the spectrum gradually changed and additional signals, due to disproportionation of **2** to **1** and 5 - acetyl - 2 - hydroxy - 2,5 - dimethyl - tetrahydrofuran - 3 - one, appeared at δ 2.29 (biacetyl) and δ 6.83 (s, OH), 3.23, 2.25 (dd, CH_2, J = 19.2), 2.27 (s, COMe), 1.38 (s, Me), 1.35 (s, Me). ^{13}C-NMR ($CDCl_3$), δ 210.7 (s, *exo*-CO), 208 (s, *endo*-CO), 114.8 (s, C-3), 112.4 (s, C-5), 108.9 (C-1), 87.7 (s, C-7), 44.9 (t, C-8), 25.2 (q, COMe), 25.0 (q, COMe), 24.8 (q, Me), 21.4 (q, Me), 21.1 (q, Me).

11 - *Hydroxy* - 1,3,5,7,11 - *pentamethyl* - cis - 2,4,6,8 - *tetraoxatricyclo*[3.3.3.$0^{3,7}$]*undecan* - 9 - *one* (**3**)

The compound was obtained in a 50% yield by HCl-catalysed trimerization of **1** (50 g) and work-up according to Diels and Jost.[1] Analytical sample was prepared by recrystallisation from water; m.p. 105°. IR (KBr) 3500, 1712, 1394, 1216, 1202, 1155, 1130, 1036, 980, 972, 961 cm^{-1}. MS, *m/e* (relative intensity) 259 (M + 1, 0.2), 241 (0.1), 231 (1), 230 (10), 174 (3), 172 (4), 170 (6), 156 (4), 155 (4), 131 (4), 130 (44), 129 (8), 114 (6), 112 (5), 111 (5), 101 (17), 88 (52), 87 (55), 85 (29), 84 (14), 69 (22), 59 (21), 45 (12), 44 (20), 43 (100).

^{1}H-NMR ($CDCl_3$), δ 3.33, 2.45 (dd, 2H, CH_2, J = 10.6), 2.49 (s, 1H, OH), 1.58 (s, 3H, Me), 1.55 (s, 3H, Me), 1.43 (s, 3H, Me), 1.39 (s, 3H, Me), 1.28 (s, 3H, Me). ^{13}C-NMR ($CDCl_3$), δ 211.8 (s, C-9), 112.9 (s, C-1), 112.2 (s, C-7), 111.9 (s, C-3), 106.2 (s, C-5), 81.2 (s, C-11), 47.2 (t, C-10), 23.9 (q, Me), 22.1 (q, Me), 21.4 (q, Me), 20.9 (q, Me), 20.2 (q, Me).

11 - *Acetoxy* - 1,3,5,7,11 - *pentamethyl* - cis - 2,4,6,8 - *tetraoxatricyclo*[3.3.3.$0^{3,7}$]*undecan* - 9 - *one* (**3** - *acetate*)

Treatment of **3** (12 g) with boiling Ac_2O for 5 hr and subsequent work-up according to the original procedure[1] gave **3**-acetate (11 g, 79%); m.p. 94–95°. MS, *m/e* 300 (M^+). IR (KBr) 1738, 1727 cm^{-1}. ^{1}H-NMR ($CDCl_3$), δ 3.46, 3.37 (dd, 2H, CH_2, J = 11.0), 2.06 (s, 3H, OAc), 1.63 (s, 3H, Me), 1.60 (s, 3H, Me), 1.58 (s, 3H, Me), 1.42 (s, 3H, Me), 1.40 (s, 3H, Me). ^{13}C-NMR ($CDCl_3$), δ 209.5 (s, C-9), 169.7 (s, $MeCO_2$), 111.9 (s, C-1), 111.7 (s, C-3), 111.3 (s, C-7), 106.1 (s, C-5), 88.1 (s, C-11), 40.8 (t, C-10), 22.5 (q, Me), 22.2 (q, Me), 21.1 (q, Me), 20.9 (q, Me), 20.8 (q, $MeCO_2$), 20.1 (q, Me).

Reaction of **3** *with an excess of hydroxylamine*

3-*Oxime*. To a suspension of finely powdered **3** (2.58 g, 0.01 mol) in 5% Na_2CO_3 (50 ml) hydroxylamine hydrochloride (2.1 g, 0.03 mol) was added and the mixture was heated under reflux for 3 hr. Colourless needles that separated were collected and recrystallised from water to give 3-oxime (2.6 g, 95%); m.p. 174–175° (lit.[1] m.p. 174–175°). IR (KBr) 3460, 3320 cm^{-1}. ^{1}H-NMR (DMSO-d_6), δ 10.99 (s, 1H, NOH), 4.85 (s, 1H, OH), 2.92, 2.56 (dd, 2H, CH_2, J = 11.7), 1.52 (s, 3H, Me), 1.47 (s, 3H, Me), 1.44 (s, 3H, Me), 1.27 (s, 3H, Me), 1.13 (s, 3H, Me).

Crystallography

Lattice dimensions and intensity data were measured on a Philips PW 1100 computer controlled automatic diffractometer (graphite monochromatised MoK_α radiation). Corrections for the absorption, Lorentz and polarisation effects were applied. The structure was solved by direct methods,[5] using program MULTAN and refined by full-matrix least-squares procedure.

Crystal data. Crystals of **2**, $C_{12}H_{18}O_6$, $M = 258.3$, are monoclinic, space group $P2_1/n$, with $a = 14.902(5)$, $b = 15.858(7)$, $c = 5.566(5)$ Å, $\beta = 93.37(6)$°, $V = 1312.98$ Å^3, $D_c = 1.306$ g cm^{-3}, $Z = 4$, MoK_α radiation, $\lambda = 0.7107$ Å, $\mu = 1.13$ cm^{-1}.

A prism-shaped specimen of **2** (0.750 × 0.090 × 0.075) was used for intensity data collection. Intensities were measured within the interval of $5.1° < 2\theta < 50.0°$ and 1355 reflections were used in subsequent calculations. Final refinement gave $R = 0.052$ ($R_w = 0.048$).

Crystal data. Crystals of **3**, $C_{12}H_{18}O_6$, $M = 258.3$, are monoclinic, space group $P2_1/n$, with $a = 10.831$ (8), $b = 15.724(9)$, $c = 7.591(5)$ Å, $\beta = 110.13(2)$°, $V = 1271.39$ Å^3, $D_c = 1.349$ g cm^{-3}, $Z = 4$, MoK_α radiation, $\lambda = 0.7107$ Å, $\mu = 1.16$ cm^{-1}.

A prism-shaped specimen of **3** (0.180 × 0.600 × 0.060) was in a glass capillary during the data collection. Intensities were measured within the interval of $4.8° < 2\theta < 62.4°$ and 1131 reflections were used in the structure determination and refinement. The final refinement gave $R = 0.053$ ($R_w = 0.052$).

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[3] J. A. Yankeelov, Jr. and C. D. Mitchell, *J. Am. Chem. Soc.* **90**, 1664 (1968); m.p. 112.5–114° was obtained for **2** employing cover glasses dealkalinised with 1 N HCl. The authors also reported significant IR bands in the solid state (KCl) at 3496 and 1718 cm^{-1}. However, similar concentration-independent bands (CCl_4) at 3460 and 1724 cm^{-1} have been used to demonstrate the intramolecular hydrogen-bonding in **2** (Cresswell *et al.*).[2]

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