STEREOCHEMISTRY OF THE PRODUCTS OF BASE CATALYZED SELF-CONDENSATION OF BIACETYL

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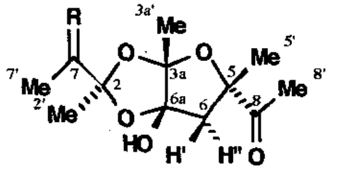
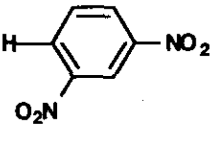
Abstract - The structures of the base catalyzed trimer and dimer of biacetyl have been determined.

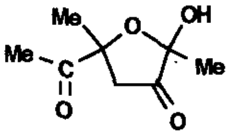
Introduction

Biacetyl readily undergoes self-condensation to give **1**[1] and **3**[2-4] under base catalyzed conditions and **4**[5,6] and **5**[6] under acid catalyzed conditions. The structure of **1** rests on early nmr and ir H-bonding studies[1] and the stereochemistry of the anomers of **3** ($3a \rightleftharpoons 3b$) has not been determined. Accordingly, systems **1** and **3a** $\rightleftharpoons$ **3b** were selected for study.



1 R = O
2 R = NNH





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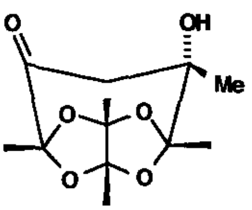

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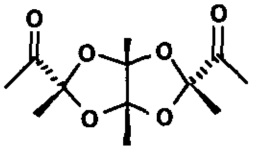

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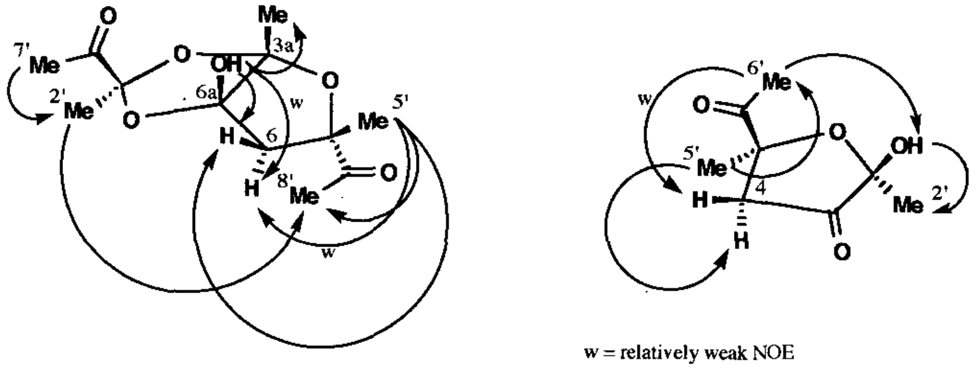
Results and Discussion

*The structure of the base catalyzed trimer: perhydro-2-*exo*-5-*endo*-diacetyl-2-*endo*-3a',5-*exo*-trimethyl-6a-hydroxyfurano[2,3-*d*]dioxolan* (**1**) - The structure of **1** had previously[1] been assigned on the basis of intramolecular hydrogen bonding in **1** and free hydroxy group in the derived mono-2,4-dinitrophenylhydrazone. This latter was assigned structure (**2**) since it gave rise to the mono-2,4-dinitrophenylhydrazone of biacetyl on standing in ethanolic solution. Accordingly a *cis*-relationship between the angular hydroxyl and the carbonyl group attached to C2 was assigned. The complete structure of **1** was established on X-ray data.[7]

This paper describes the structural arrangement on detailed nmr evidence. The assignment of the methyl singlet resonances at δ 0.98, 1.42, 1.15, 1.67 and 2.22 in the ^{1}H nmr spectrum (C_6D_6) was aided by differential NOE experiments (Figure 1). The two relatively downfield (δ 2.22 and 1.67) methyl resonances were characteristic of those adjacent to carbonyl groups. The methyl singlet at δ 0.98 was assigned to C(5')Me on the basis of observed NOEs between the COMe signal at δ 2.22 and the AB quartet (δ 1.82 and 3.45, $J = -13.2$ Hz) of the C6 methylene protons. An anticlinal arrangement between the C(5')Me and C6 proton giving rise to the downfield doublet was indicated by a relatively weaker NOE. Similar differential NOEs between the C6 methylene proton signals and the broad hydroxyl signal at δ 4.82 established a *cis* stereochemistry between the hydroxyl group, C(5')Me and the C6 proton absorbing at δ 1.82. The C(3a')Me group was also shown to be *cis* to the hydroxyl group after obtaining a NOE differential from irradiation of the O*H* signal.



w = relatively weak NOE

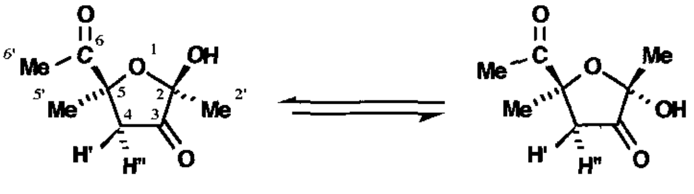
Figure 1 Structures of **1** and **3a** showing nuclear Overhauser enhancements

The proximity of the C(5')Me and the C(8')Me (δ 2.22) was confirmed after irradiation of the C(8')Me, and this also gave an enhancement of the signal at δ 1.15 [C(2')Me]. Irradiation of the latter signal produced a NOE on the C(7')Me signal at δ 1.67 and established a *trans* relationship between the two acetyl groups.

The ^{13}C nmr DEPT spectrum (C_6D_6) shows the expected five methyl resonances (δ 20.8, 21.6, 24.6, 24.6, 24.7), one methylene carbon (δ 45.0), as well as six quaternary carbons (δ 108.5, 87.6, 113.2, 114.9, 209.2, 207.5). The two most downfield absorbances are characteristic of carbonyl carbons and these were assigned unambiguously after low power selective decoupling of all protons in turn and observing changes in the ^{13}C-^{1}H couplings. The result of irradiating the most upfield methyl proton resonance (δ 0.98) and the downfield methyl proton resonance (δ 2.22) altered the shape of the ^{13}C resonance at δ 209.2 from a broad signal to a sharper multiplet. Similarly, irradiation of Me-2' (δ 1.15) and Me-7' (δ 1.67) changed the shape of the ^{13}C resonance at δ 207.5 from a multiplet to a broad quartet. These irradiations permitted the assignment of the δ 209.2 and δ 207.5 signals to C8 and C7, respectively. The remaining quaternary ^{13}C resonances were similarly distinguished.

Treatment of **1** with 2,4-dinitrophenylhydrazine gave an orange coloured mono-2,4-dinitrophenylhydrazone[1] and from the establised stereochemistry of the diketone, the hydrazine is expected to have reacted with the unhindered C2 acetyl group. Confirmation of this was obtained from differential NOE experiments. Irradiation of the methyl singlet absorbing at δ 1.44 showed NOEs on the broad singlet (OH, δ 3.65) and one of the aromatic ring proton signals (δ 7.90, J = 9.5 Hz). The methyl signal was thus clearly identifiable as that arising from the C(3a')Me protons. For this enhancement to be possible the phenylhydrazine moiety has to be situated above the plane of the bicyclic ring. Furthermore, a strong NOE was obtained between the N*H* of the hydrazine group and a resonance at δ 2.01 showing this to arise from Me-7'. All the other NOEs confirmed the original assignment for **1**. The ^{13}C nmr assignments for **2** were assisted by the use of DEPT and comparison of the assignments made for **1**.

The structure of the base catalysed dimer : 5-acetyl-2,5-dimethyl-2-hydroxy-tertrahydrofuran-3-one (**3**) - Distillation of the viscous oil remaining after the distillation of a sample of biacetyl gave an oil. The ^{1}H (nmr) spectrum of this showed it to be a mixture of the anomers (**3**a) and (**3**b) with two AB quartets for the C-4 methylene protons at δ 3.36 and 2.24 (J = –19.1 Hz) and δ 2.93 and 2.61 (J = –19.1 Hz). On allowing the mixture to stand at 10 °C the liquid crystallized to give a single anomer **3**a.



3a **3b**

The ^{1}H nmr spectrum of this anomer showed three methyl singlets (δ 2.34, 1.51 and 1.50), a slightly broad singlet at δ 3.76 and an isolated AB quartet (δ 3.36 and 2.24, J = –19.1 Hz). The signal resonating at δ 2.34 was readily assigned to a methyl group of an acetyl moiety, and that at δ 3.76 to the -*OH* proton. The stereochemistry of the crystalline anomer was shown to be **3**a (5-acetyl-2,5-*cis*-dimethyl-2-

hydroxy-tetrahydrofuran-3-one) on the basis of the observed NOE between C(6')Me and the -O*H* signal (Figure 1).

EXPERIMENTAL

^{1}H and ^{13}C nmr spectra were recorded at room temperature in either $CDCl_3$ or C_6D_6 solution in 5 mm tubes, on a JEOL GSX-270 (^{1}H, ^{13}C) FT spectrometer at 270.16(^{1}H) and 67.97 (^{13}C) MHz, using the deuterium signal of the solvent as the lock and TMS as internal standard. The most important measurement parameters were as follows : spectral width 3 kHz (^{1}H) and 18 kHz (^{13}C), pulse width 3 μs (^{1}H) and 4.2 μs (^{13}C) (*ca.*40° and 45° flip angle, respectively), acquisition time 5.46 or 0.90s, number of scans 16-32 (^{1}H) and 300-2500 (^{13}C) and computer memory 32 K.

*Perhydro-2-*exo-5-endo-*diacetyl-2-*endo-*3a',5-*exo-*trimethyl-6a-hydroxyfurano[2,3-*d*]dioxolan* (**1**)[1] : ^{1}H Nmr ($CDCl_3$) δ 1.43 (Me3a'), 1.45 (Me2'), 1.36 (Me5'), 2.26 (Me7'), 2.36 (Me8'), 1.94 (d, J = –13.2, H6'), 3.24 (d, J = –13.2, H6"), 4.95 (OH); (C_6D_6) δ 1.42 (Me3a'), 1.15 (Me2'), 0.98 (Me5'), 1.67 (Me7'), 2.22 (Me8'), 1.82 (d, J = –13.2, H6'), 3.45 (d, J = –13.2, H6"), 4.82 (OH); (acetone-d_6) δ 1.45 (Me3a'), 1.33 (Me2'), 1.29 (Me5'), 2.17 (Me7'), 2.29 (Me8'), 1.91 (d, J = –13.2, H6'), 3.13 (d, J = –13.2, H6"), 6.20 (OH). ^{13}C Nmr ($CDCl_3$) δ 108.3 (C2), 20.9 (C2'), 114.3 (C3a), 21.3 (C3a'), 87.3 (C5), 25.1 (C5'), 111.8 (C6a), 44.5 (C6), 208.1 (C7), 24.9 (C7'), 210.6 (C8), 24.9 (C8'); (C_6D_6) δ 108.5 (C2), 20.8 (C2'), 114.9 (C3a), 21.6 (C3a'), 87.6 (C5), 24.7 (C5'), 113.2 (C6a), 45.0 (C6), 207.5 (C7), 24.6 (C7'), 209.2 (C8), 24.6 (C8'); (acetone-d_6) δ 109.3 (C2), 21.3 (C2'), 114.9 (C3a), 21.9 (C3a'), 88.3 (C5), 25.5 (C5'), 111.8 (C6a), 45.3 (C6), 206.8 (C7), 25.1 (C7'), 210.5 (C8), 25.0 (C8'). Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.8; H, 7.0 %. Found : C, 55.9; H, 6.9.

2,4-Dinitrophenylhydrazone of **1** (**2**) : **2** was prepared by the reported[1] method. ^{1}H Nmr (DMSO-d_6) 1.44 (Me3a'), 1.37 (Me2'), 1.26 (Me5'), 2.01 (Me7'), 2.31 (Me8'), 1.82 (d, J = –13.2, H6'), 3.02 (d, J = –13.2, H6"), 3.65 (OH), 10.69 (NH), 7.90 (d, J = 9.5, Ar-H), 8.44 (dd, J = 2.6, 9.5, Ar-H), 8.87 (d, J = 2.6, Ar-H). ^{13}C Nmr (DMSO-d_6) δ 107.8 (C2), 23.3* (C2'), 114.0 (C3a), 21.9* (C3a'), 87.1 (C5), 24.8 (C5'), 110.5 (C6a), 44.9 (C6), 144.8 (C7), 12.4 (C7'), 210.2 (C8), 24.8 (C8'), 157.4 (Ar-C), 137.3 (Ar-C), 130.2 (Ar-CH), 129.6 (Ar-C), 122.8 (Ar-CH), 116.1 (Ar-CH). Anal. Calcd for $C_{18}H_{22}N_4O_9$: C, 49.3; H, 5.0; N, 12.8 . Found : C, 49.0; H, 4.9; N, 12.7.

5-Acetyl-2,5-dimethyl-2-hydroxy-tertahydrofuran-3-one (**3**) : The residual viscous oil remaining after distillation of a sample of biacetyl was distilled to give an oil bp 104 °C at 0.8 mmHg). The anomer (**3**a) crystallized, mp 53 °C, upon allowing this oil to stand at 10 °C. ^{1}H Nmr **3a** : ($CDCl_3$) δ 1.50 (Me2'), 1.51 (Me5'), 2.34 (Me6'), 3.36 (d, J = –19.1, H4'), 2.24 (d, J = –19.1, H4"), 3.76 (OH). **3b** : ($CDCl_3$) δ 1.48* (Me2'), 1.60* (Me5'), 2.29 (Me6'), 2.93 (d, –19.1, H4'), 2.61 (d, –19.1, H4"). ^{13}C Nmr **3a** : ($CDCl_3$) δ 98.7* (C2), 24.2~ (C2'), 208.6+ (C3a), 40.8 (C4), 84.1* (C5), 24.6~ (C5'), 211.2+ (C6), 21.6~ (C6'). Anal. Calcd for $C_8H_{12}O_4$: C, 55.8; H, 7.0 . Found : C, 55.7; H, 6.9.

*+~ respective nmr signals may be interchanged

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