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A STUDY OF THE DIMERIC STRUCTURES OF GLYCOLALDEHYDE SOLUTIONS BY NMR

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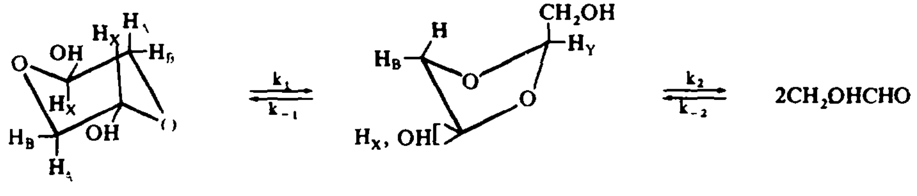
Abstract—The NMR spectra of glycolaldehyde in methanol, acetone and DMSO prove that three different structures, two dimeric and one monomeric exist in solution. The chemical shifts and coupling constants for these structures and their rates of interconversion are reported.

CRYSTALLINE glycolaldehyde is known to be a dimer.[1] In solution dimeric glycolaldehyde undergoes a depolymerization (Scheme 1), the rate of which depends on the solvent and is catalysed by acid and base.[2] The symmetrical dimer, 2,5-dihydroxy-1,4-dioxane (I) has been reported by several authors to exist in fresh solutions of glycolaldehyde.



I II III

SCHEME 1

Spath and Raschik[3] have isolated the intermediate 2-hydroxymethyl-4-hydroxy-1,3-dioxolane (II). Bell and Hirst[4] had proposed the linear structure

$$CH_2OHCH(OH)OCH_2CHO$$

for the depolymerization intermediate. In this paper we present spectroscopic evidence for the existence of the three forms (I–III) in different solvents as well as rates of interconversion of the three species in solution.

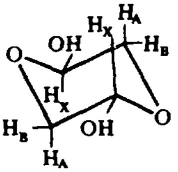
RESULTS AND DISCUSSION

The spectrum of glycolaldehyde in d_6-DMSO is shown in Fig 1. In fresh solution (spectrum *a*) only the symmetrical dimer (I) is present. The spectral parameters are given in Table 1. The assignment of the protons was based on the following arguments: of the geminal protons on C-3, H_A appears at higher field ($\tau = 6\cdot78$) and is assigned the axial position.

TABLE 1. MONOMER CH_2OHCHO

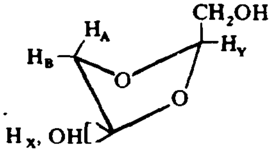
Solvent	$J_{CHO—CH_2}$, c/s	Chemical shift in τ			
d_4-Methanol	5·0[a]	—CH_2	6·42	—$CH(OMe)_2$	5·33[a]
d_6-DMSO	< 1	—CH_2	5·89	—CHO	0·57

Dimer I



Solvent	J_{AB}	J_{AX}	J_{BX}	$J_{X—OH}$	H_A	H_B	H_X	OH
d_4-Methanol	−11·7	5·75	2·5	—	6·58	6·02	5·17	—
d_6-Acetone	−11·5	6·00	2·5	6·25	6·68	6·10	5·20	4·65
d_6-DMSO	−11·5	7·00	2·5	6·25	6·78	6·24	5·33	3·42

Dimer II



Solvent	J_{AB}	J_{AX}	J_{BX}	$J_{Y—CH_2}$	H_A	H_B	H_X	H_Y	CH_2
d_4-Methanol				3·25			4·42	4·88	
d_6-DMSO	−8·5	2·5	4·5	3·75	6·46	6·03	4·55	5·00	6·6

[a] τ and J for acetal proton to α-carbon hydrogen.

Hydrogen H_X on C-2 is coupled by 7·0 c/s to H_A and by 2·5 c/s to H_B and therefore should occupy the axial position.[5] The OH on C-2 is coupled to H_X by 6·25 c/s and is seen at $\tau = 3·42$. After equilibrium is reached the hydroxylic protons move upfield to about $\tau = 6$ as shown in spectrum *b* (Fig 1). Spectrum *b* is a superposition of all three forms. At $\tau = 0·57$ the aldehydic proton of the monomeric form appears. Splitting from the coupling between the aldehydic and α-proton was not observable but the line width was 2 c/s at half-height. The coupling of aldehydic to α-protons is generally small (0–3 c/s).[6] For instance the coupling of the aldehydic proton with the proton in D-lactaldehyde monomer in d_6-DMSO is 1 c/s.

The intermediate form II as well as the linear dimer (proposed by Bell and Hirst[4]) are dissymmetric. The spectrum should contain the diasteroisomers of either the 1,3-dioxolane intermediate or the linear dimer which could exist as any of six rotamers. Fig 2 shows the partial 100 Mc spectrum of glycolaldehyde solution in d_6-DMSO at equilibrium. The stick spectrum of form I is the calculated spectrum for 2,5-dihydroxy-1,4-dioxane. The multiplet at $\tau = 5·33$ is assigned to proton H_X of the dioxane ring. In Fig 1*a* the simulated spectrum agrees with the experimental, representing H_X only in the axial position. As the reaction proceeds (opening and closing of the dioxane

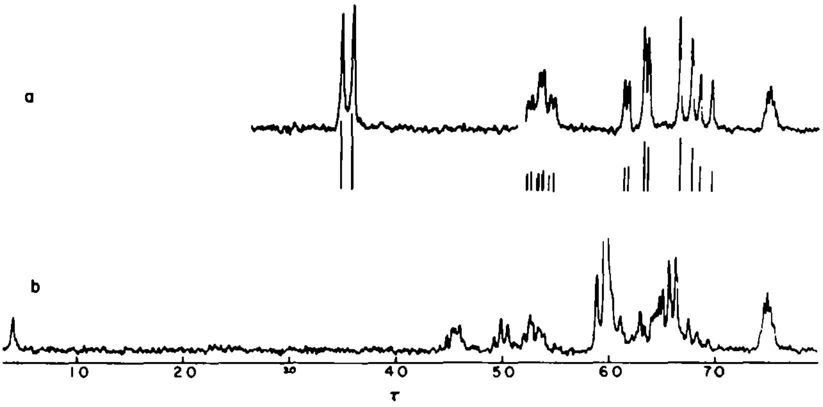


FIG 1. 60 Mc spectrum of glycolaldehyde in d_6-DMSO; *a*. immediately after preparation of solution; *b*. after equilibrium is reached by addition of traces of DCl. Underneath *a* is shown the stick spectrum obtained from computer calculations.

ring) H_X could also occupy the equatorial position. This is probably why the multiplet at $\tau = 5{\cdot}33$ in Fig 2 and Fig 1*b* has more lines than expected. The peak at $\tau = 5{\cdot}89$ belongs to the CH_2 of the monomer (the aldehydic proton is not shown on this spectrum, but see spectrum *b*, Fig 1). The multiplets at $\tau = 4{\cdot}55$ and $5{\cdot}00$ belong to

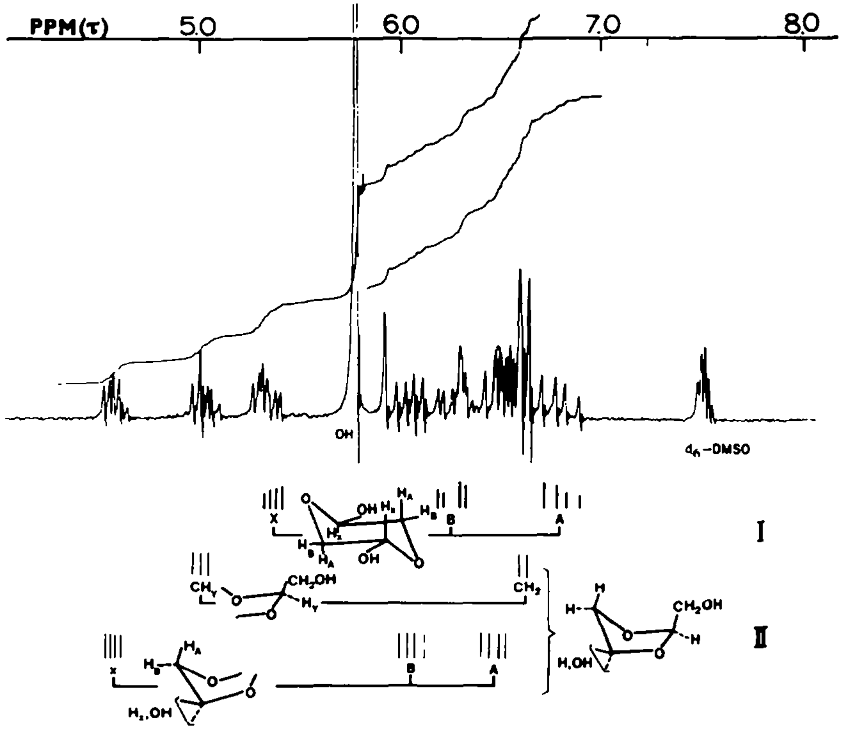


FIG 2. 100 Mc spectrum (partial) of glycolaldehyde in d_6-DMSO after equilibrium is reached.

the intermediate form II, hydrogens on C-4 and C-2 respectively (H_X and H_Y of formula II Fig 2). The methylene groups of the hydroxymethyl group and the methine proton on C-2 give the expected A_2Y spectrum.

The protons on C-5 and C-4 give the expected ABX spectrum. The assignment for the 1,3-dioxolane form (II) was based on spin decoupling experiments. The CH_2 doublet at $\tau = 6{\cdot}6$ collapses when H_Y on C-2 is irradiated (Difference frequency $-95{\cdot}5$ c/s). Selective decoupling of proton H_B on C-5 is observed when H_X on carbon-4 is irradiated (Difference frequency -92 c/s). Both diastereoisomers of 2-hydroxymethyl-4-hydroxyl-1,3-dioxolane are present and the multiplets at 4·55 τ and 5·00 τ are the superposition of the two forms. A dioxolane structure has also been reported to exist in solutions of glyoxal.[8]

The linear form $CH_2OHCH(OH)—O—CH_2CHO$, 2-(α,β-dihydroxyethoxy)ethanal proposed by Bell and Hirst can be excluded on the basis of the above data and the following additional evidence: (a) All protons geminal to OH groups show a (H—OH) coupling. The coupling disappears upon addition of acid or base or by exchange with deuterium. In the case of the linear dimer all hydrogens of the group should couple with the OH in the absence of exchange. However, in the 1,3-dioxolane form,

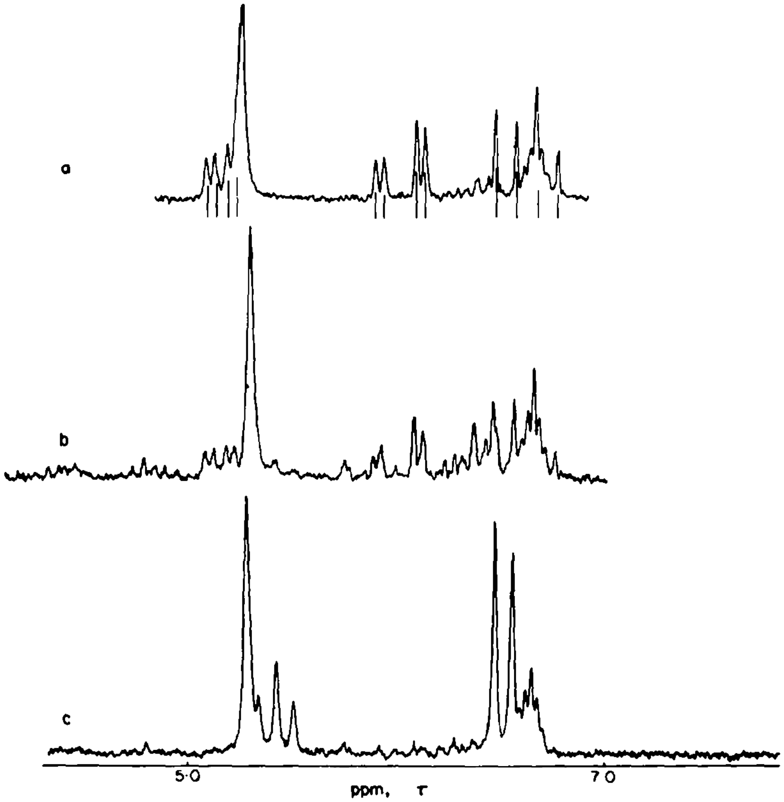


FIG 3. NMR spectrum of glycolaldehyde in d_4-Methanol; *a*. immediately after preparation of solution (stick spectrum also given); *b*. after 30 min; *c*. after 100 min.

the methine proton on C-2 should be free of such coupling. Indeed, the multiplet at $\tau = 5{\cdot}00$ is unaffected by either deuterium exchange or the presence of acid or base. (b) The kinetics of the depolymerization were studied by following the rate of disappearance of I and the formation of II and III. At no time could the intensity of the appearing aldehydic proton at $\tau = 0{\cdot}57$ correspond to the intensities of the protons assignable to the linear dimer. It was found that in d_6-DMSO at equilibrium (after 3-days in the presence of acid) a solution of glycolaldehyde 1·46 molar showed the following ratio of the different species:

$$\text{III/II} = 0{\cdot}142 \text{ and II/I} = 1{\cdot}615$$

It is difficult to decide on the conformation of the substituents on C-4 of the dioxolane ring. It has been accepted that the dioxolane ring has an envelope conformation [9, 10] with ϕ (4a 5e) about 35° and $J_{gem} = -7{\cdot}5$ c/s, $J_{cis} = 7{\cdot}1$ c/s and $J_{trans} = 6{\cdot}0$ c/s. Frazer *et al.*[11] have calculated the spectra for 4-alkyl-2,2-dimethyldioxolane derivatives and found $J_{gem} = -8{\cdot}3$ c/s, $J_{cis} = 7{\cdot}6$ and $J_{trans} = 6{\cdot}8$ c/s. On the other hand the coupling constants for 2,2,4,5-tetramethyldioxolanes[12] are $J_{cis} = 5{\cdot}85$ and $J_{trans} = 8{\cdot}35$ c/s. Our values of J_{AX} and J_{BX} of 2·5 and 4·5 c/s for vicinal coupling are smaller because of the electronegativity of the OH substituent on C-4. Examples in the literature show that the vicinal coupling in 5-membered rings are affected both by substituents and geometry.[13, 14]

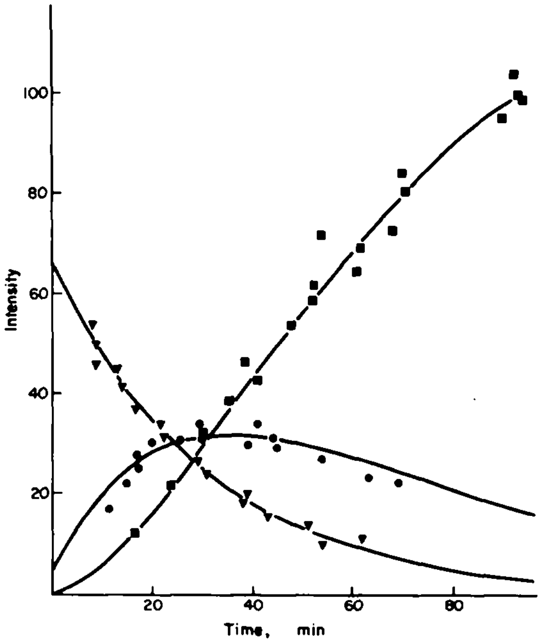


FIG 4. Variation with time of the concentrations of dimeric and monomeric structures of glycolaldehyde 0·72 M solution in d_4-Methanol. Solid lines are the calculated curves for $k_1 = 3{\cdot}37$ min^{-1}, $k_2 = 2{\cdot}16$ min^{-1} and initial signal intensity of intermediate = 3 on the NMR integration scale; ▲ 2,5-dihydroxy-1,4-dioxane; ● 2-hydroxymethyl-4-hydroxy-1,3-dioxolane; ■ glycolaldehyde methylacetal.

The depolymerization of glycolaldehyde in d_4-methanol presents a much clearer picture. In this solvent the reaction is fast and the final product is the methylacetal of glycoaldehyde. Fig 3 shows the spectrum of glycoaldehyde in d_4-methanol at different times. Spectrum *a* agrees well with the calculated spectrum for the 1,4-dioxane. Spectrum *c* corresponds to the methylacetal of glycolaldehyde and this explains the increase in vicinal coupling (5 c/s) between the acetal proton and the protons on the α-carbon.

Kinetics of the depolymerization

The kinetics of depolymerization were studied by following the rate of disappearance of I and formation of II and III. This was done by measuring the area of proton X for compound I, protons X and Y for compound II and the aldehydic or acetal protons for III (Scheme I).

The depolymerization of glycolaldehyde in solution was found to follow a two step first-order, consecutive process $A \rightarrow B \rightarrow 2C$. The experimental data were treated according to the method given by Frost and Pearson.[15] Fig 4 shows the calculated and experimental results for a 0·72 molar solution of glycolaldehyde in d_4-methanol. (Molarity is calculated on the m.w. of monomeric glycolaldehyde, 60). The following rate equations were used.[17]

$$A = A_0 e^{-k_1 t} \quad B = A_0 \frac{k_1}{k_2 - k_1}(e^{-k_1 t} - e^{-k_2 t}) + B_0 e^{-k_2 t}$$

and

$$C = 2A_0 \left(1 - \frac{k_2 e^{-k_1 t} - k_1 e^{-k_2 t}}{k_2 - k_1}\right) + B_0(1 - e^{-k_2 t})$$

where A_0 and B_0 are the initial concentrations of I and II.

The rate constants k_1 and k_2 (scheme I) are given in Table II.

TABLE 2

Solvent	Initial conc. (Molarity of I)	β_{max}	k_1 min^{-1}	k_2 min^{-1}	$\kappa = k_2/k_1$
d_4-Methanol	1·46	0·45	$5{\cdot}8 \times 10^{-2}$	$3{\cdot}9 \times 10^{-2}$	0·68
	0·88	0·46	$4{\cdot}2 \times 10^{-2}$	$2{\cdot}8 \times 10^{-2}$	0·66
	0·72	0·47	$3{\cdot}4 \times 10^{-2}$	$2{\cdot}2 \times 10^{-2}$	0·64
d_6-Acetone	0·27		$2{\cdot}9 \times 10^{-3}$	—	
d_6-DMSO	0·74		$7{\cdot}9 \times 10^{-4}$	—	

Values for k_2 in d_6-acetone and d_6-DMSO were not given because the process II → 2 (III) is extremely slow in the absence of acid or base. In d_6-DMSO in the absence of acid after 71 hr no aldehydic proton was observed at $\tau = 0{\cdot}57$. In the presence of acid after 3 days the ratio III/II was 0·143. A solution of glycolaldehyde in acetone showed no trace of dissociation for three weeks.[16]

From Table 2 it can be seen that the rate of depolymerization depends on the solvent. At comparable concentrations the ratio is 100-times faster in methanol than in DMSO. The maximum concentration β_{max} of the intermediate II in methanol solution shows no appreciable change with initial concentration of I. The rates of depolymerization in methanol did not seem to depend appreciably on concentration. McCleland[16] studied the depolymerization in water using the cryoscopic method and found that the rate for a range of concentrations (0·35–0·05 M) changed only by a factor of two. Glycolaldehyde is very soluble in water. A series of solutions were prepared from 0·1 M–8 M in D_2O. In concentrated solutions all three forms were detected by NMR in the beginning of the reaction. In very dilute solutions (0·1 M) only the monomeric form (III), as the hydroxyacetal, was observed. The depolymerization in water is extremely fast.

EXPERIMENTAL

Glycolaldehyde (Fluka) was recrystallized from EtOH and dried over P_2O_5 in vacuum (m.p. 92°). Deuteration of the OH group was achieved by repeatedly dissolving glycolaldehyde in D_2O and evaporating the solvent. A Varian A-60-A spectrometer equipped with Spin-Decoupler Model V-6058A. The 100 Mc spectrum was recorded using a Varian XL-100 spectrometer by Dr. F. Wehrli of Varian A.G. Zuerich to whom our thanks are extended.

Theoretical spectra were calculated using LACN3 a computer program by A. A. Bothner-By and S. M. Castellano for the analysis of high-resolution NMR spectra.

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