# SYNTHESIS AND PROPERTIES OF THIODIGLYCOLALDEHYDE\*

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## ABSTRACT

Thiodiglycolaldehyde (1) has been synthesised by dehydration of its hemialdal form, *cis*-2,6-dihydroxy-1,4-oxathiane (2a) The hydration and polymerisation of 1 have been studied The composition and conformational population has been established for solutions of 2a in various solvents In aqueous solution, 1, 2a and its *tians* isomer 2b, and the acyclic dihydrate and monohydrate were detected The preferred conformer of 2a has diequatorial OH groups

# INTRODUCTION

Thiodiglycolaldehyde (2,2'-thiobisacetaldehyde) (1), in the form of the cyclic hemialdal 2, has been prepared<sup>1</sup> by acid hydrolysis of thiodiglycolaldehyde bis(dimethyl acetal) (3) or bis(diethyl acetal) (4), but the geometrical isomerism and conformation in the crystalline state or in solution have not been described. We now report a study of these aspects by <sup>1</sup>H-n m r spectroscopy

# **RESULTS AND DISCUSSION**

When <sup>1</sup>H-n m r spectra were obtained for freshly prepared solutions of 2 in Me<sub>2</sub>SO- $d_6$ , cis-2,6-dihydroxy-1,4-oxathiane (2a) was identified on the basis of a multiplet at  $\delta$  4 76 corresponding to the acetal hydrogens coupled with vicinal methylene and OH groups (double resonance) The values (6 7 and 4 3 Hz,  $J_{ax} + J_{bx}$ 



<sup>\*</sup>Derivatives of 3-Hetero-1,5-dialdehydes, Part I

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11 Hz) of  $J_{CH CH_2}$  accord with the *cis* configuration and predominance of the axial disposition of the acetal hydrogens in the conformational equilibrium Chair conformers are assumed for these derivatives, as in 1,4-oxathiane<sup>2</sup> Also detected were small amounts of acyclic forms on the basis of signals between  $\delta$  3 2 and 3 4

After 24 h, the spectra revealed that the proportion of cis isomer had diminished to 61% Signals at  $\delta$  5 25 (CH-CH<sub>2</sub>), with  $J_{ax} + J_{bx} = 8$  Hz, showed the presence of the *trans* isomer 2b (22%) This figure, and that noted above for the *cis* isomer 2a, agree with the corresponding values reported for the related cis- and trans-dioxane derivatives<sup>3 +</sup> The  $J_{ax} + J_{bx}$  value for 2a and 2b indicates<sup>5</sup> a conformational equilibrium relevant to the acetal protons of 87 5% diaxial and 12 5% diequatorial for 2a The set of values  $J_{a}$ , 95.  $J_{a}$ , 25, and  $J_{e}$ , 1.5 Hz was selected, and checked by its application to the *trans* isomer 2b, where N is 0.5 Signals at  $\delta$  9.45 and 3.30 indicate the existence in the solution of 1 (2%) The fact that the signals appear somewhat complicated and the existence of a doublet at  $\delta$  5 87 (J 6 Hz, proton exchangeable with  $D_2O$ ) suggested the presence of the acyclic monohydrate 6 (15%) The integration for acetal hydrogens in the spectra was the same as that for hydroxyl hydrogens, and showed the absence of any appreciable amount of the dihydrate 5 For glutaraldehyde, it has been postulated<sup>6</sup><sup>7</sup> that it is not possible to differentiate between cyclic monomers and such dimers as 8 by  $^{1}$ H-n m r spectroscopy. However, for the stereoisomeric dimers<sup>8</sup> 9. the signals of the acetal hydrogens were more complex than in the corresponding monomeric species. This finding suggests that there is no appreciable amount of dimeric compounds in the solutions of 2a When the temperature was increased, the proportion of free aldehydic forms increased at 120°, the only signals were due to 1 and water If the temperature was decreased, the process was reversed



For a solution of 2 in acctone- $d_6$  the spectra indicated the *cis*-isomer 2a to be more abundant, but considerable proportions of dialdehyde 1 and its monohydrate 6 were observed The presence of the *trans* isomer was not clearly proved, but signals at  $\delta 5 35$  may be partially ascribed thereto In the conformational equilibrium for 2a, there was ~91% of diaxial character for the acetal hydrogens Addition of a small amount of acetic acid promoted rapid dehydration, to give the dialdehyde 1, which was then the only structure present in solution

For solutions of  $2 \text{ in } D_2O$ , the rate of equilibration between the different forms

was faster than in acetone- $d_6$ , and the dihydrate 5 was clearly observed The nature of the solvent appears not to change appreciably the conformational population, as would be expected if an anomeric effect was operative As in other oxathiane derivatives, the "hockey-stick" effect seems to be more important<sup>5</sup>

Few 3-hetero-1,5-dialdehydes have been obtained in anhydro forms<sup>4 9 10</sup> Muhlstadt and co-workers<sup>11</sup> reported the preparation of 1, but it was not isolated and the acyclic structure was not proved. We have prepared 1 in a pure state in almost quantitative yield, by distillation of the corresponding hemialdal 2a under diminished pressure The stability and easy preparation of 1 contrasts with the situation reported for its oxygenated analogue, diglycolaldehyde The tendency of 1 to hydrate is lower than for diglycolaldehyde, but can be observed by i r spectroscopy by leaving a film of 1 on a NaCl window exposed to moisture. The abscrption at  $1710 \text{ cm}^{-1}$  (C=O) gradually declined in parallel with an increase in the O-H and C-O stretching bands at 3300 and 1176–950 cm<sup>-1</sup>, respectively A freshly prepared sample of 1 showed a band at  $1613 \text{ cm}^{-1}$  that some authors<sup>4 9 12</sup> have ascribed to hemialdal forms in some diglycolic derivatives, and others to hydration water<sup>13</sup> In our case, longer exposure to moisture increased the area of this band but in a proportion lower than those of the two other bands mentioned above These facts, and the absence of this band in the spectrum of the pure hemialdal 2a, point to the latter hypothesis. The <sup>1</sup>H-n m r spectra of 1 in  $D_2O$  showed the rapid formation of the hemialdals 2a and 2b, and the hydrated, acyclic forms 5 and 6, the same signals were observed in the solutions of 2a in D<sub>2</sub>O Consequently, 1 was transformed into 2a (98 5°) by simply removing water from its aqueous solutions

Upon prolonged storage at room temperature in a dry atmosphere, 1 polymerised by a process that could be followed by <sup>1</sup>H-n m r spectroscopy The sharp signals of 1 gradually faded and, simultaneously, broad signals, corresponding to the polymer 10, appeared at  $\delta$  2 20–3 40 (-CH<sub>2</sub>-) and 4 80–5 80 (-CH-) The latter signals consist of two broad signals that correspond to hydrogens with more or less axial or equatorial character Structures such as 10a and 10b can be proposed for the polymer 10 The structure similar to that reported<sup>3</sup> for diglycolaldehyde cannot be considered, because the polymerisation occurred in the absence of water and no ir absorptions for hydroxyl groups were observed The ratio between free and polymeric aldehyde appears to be solvent-dependent After 3 days, the monomer-polymer ratios were 66 34 (neat), 68 32 (acetone- $d_6$ ), and 20 80 (CDCl<sub>3</sub>) Even after a long time, monomer or free formyl groups were present in the solutions The polymer 10, m p  $66-68^{\circ}$ , was stable at room temperature, but could be depolymerised [yielding the monomer (monitoring by  $^{1}$ H-n m r spectroscopy)] by heating it above its m p On the other hand, the monomer 1 can be obtained (75%) from 10 by distillation under diminished pressure Depolymerisation was also promoted by solvents By <sup>1</sup>H-n m r monitoring, 16% of 1 was observed after 2 h in chloroform The polymer 10 was insoluble in water, but, on shaking with water for 3 days at room temperature, depolymerisation occurred with formation of 2a (74%)







The hemialdal 2a shows the normal reactivity of these compounds, yielding thiodiglycolaldehyde bis(semicarbazone) (11), bis(*p*-nitrophenylhydrazone) (12), and bis(2,4-dinitrophenylhydrazone) (13). The spectra and elemental analyses were in agreement with the acyclic structures

11 R =  $CO^{M}H_{2}$ 12 R =  $p - NO_{2} - C_{6}H_{4}$ 13 R = 2 4 - d1NO<sub>2</sub> - C<sub>6</sub>H<sub>3</sub>

### **EXPERIMENTAL**

General methods — Solvents were evaporated under diminished pressure at  $<40^{\circ}$  I.r spectra were recorded for films on NaCl windows or KBr discs with Pye-Unicam SP 1000 or Perkin-Elmer 137 (Infracord) spectrometers <sup>1</sup>H-N m r spectra were obtained for solutions in various solvents (internal Me<sub>4</sub>Si or DDS) with Perkin-Elmer-Hitachi R-20B (60 MHz) or R-32 (90 MHz) spectrometers Chemical shifts (first order) are given on the  $\delta$  scale with first-order coupling in Hz Melting points were obtained with an Electrothermal Melting Point apparatus and are uncorrected

Thiodiglycolaldehyde bis(dimethyl acetal)<sup>14</sup> (3). — This compound was prepared from Na<sub>2</sub>S 9H<sub>2</sub>O (719 g) and bromoacetaldehyde dimethyl acetal (389 g) in ethanol-water (195 mL, 132.63) After boiling under reflux for 20 h, the solvent

(100 mL) was removed and anhydrous  $K_2CO_3$  (50 g) was added The mixture was extracted with ether, and the extract was concentrated, to yield 3 (90%), b p 136–138°/12 mmHg,  $v_{max}$  (selected bands) 1195, 1125, 1065, and 965 cm<sup>-1</sup>. <sup>1</sup>H-n m r (CDCl<sub>3</sub>) data  $\delta$  4 39 (t, 1 H, J 5 5 Hz), 3 26 (s, 6 H), and 2 68 (d, 2 H, J 5 5 Hz)

Theodigly colaidehy de bis(diethyl acetal)<sup>1</sup> (4) — This compound, prepared (93.6%) in a manner analogous to that described above, had b p 115–119°/13 mmHg,  $v_{max}$  (selected bands) 1207, 1162, 1117, 1058, and 1015 cm<sup>-1</sup> <sup>1</sup>H-n m r (CDCl<sub>3</sub>) data  $\delta$  4.55 (t, 1 H, J 5.5 Hz), 3.53 (m, 4 H, J 6.5 Hz), 2.72 (d, 2 H, J 5.5 Hz) and 1.20 (t, 6 H, J 6.5 Hz)

cis-2,6-Dihydroxy-1,4-oxathiane<sup>1</sup> (2a) — When 3 or 4 was hydrolysed by acetic acid in water at 50°, >90% of 2a was obtained Purification by recrystallisation from ether or washing with cold chloroform gave material (88%) having mp 73°,  $v_{mx}^{\text{kBr}}$ 3500–3000, 1150, 1099, 1064, 1015, 966, 797, 784, 772, and 760 cm<sup>-1</sup>, <sup>1</sup>H-n m r (Me<sub>2</sub>SO-d<sub>6</sub>) data  $\delta$  5 62 (d, 1 H, J 6 8 Hz), 4 76 (m, 1 H), and 2 50 (m, 2 H), immediately after the sample had dissolved (Found C, 35 5; H, 59, S, 23 4, C<sub>4</sub>H<sub>8</sub>O<sub>3</sub>S, calc C, 35 2, H, 59 S, 23 5)

*Thuodigly colaldehy de* (1) — Compound 2a (5 92 g) was heated at 100° under atmospheric pressure After cooling to room temperature, the non-crystalline residue was distilled at 70–71°/04 mmHg to give 1 (4 52 g, 88 1%),  $v_{max}$  (selected bands) 2785, 2688, 1710, 1608, and 1030 cm<sup>-1</sup>, <sup>1</sup>H-n m r (CDCl<sub>3</sub>) data  $\delta$  9 50 (t, 1 H, J 2 75 Hz) and 3 22 (d, 2 H, J 2 75 Hz) (Found C, 40 4, H, 5 3, S, 27 1 C<sub>4</sub>H<sub>6</sub>O<sub>2</sub>S calc C, 40 6, H, 5 1, S, 27 1)

When a solution of 1 (3 g) in water (3 mL) was concentrated in a desiccator over KOH to constant weight, 2a (3 4 g) was obtained

When 1 was stored in a desiccator in a dry atmosphere for 2 months, the weight remained constant and a vitreous solid 10. mp 66-68°, was formed with  $v_{mix}^{KBr}$  (selected bands) 2940, 1720, 1100, 1040, and 960 cm<sup>-1</sup> <sup>1</sup>H-N m r (CDCl<sub>3</sub>) data  $\delta$  5 70–4 80 (2 bm, 1 H) and 3 20–2 20 (bm, 2 H) The <sup>1</sup>H-n m r spectrum showed the presence of ~5% of 1 The polymer 10 was sparingly soluble in water, methanol, ethanol, acetone, and carbon tetrachloride, and soluble in methyl sulphoxide and chloroform (Found C, 40 3 H, 5 3 (C<sub>4</sub>H<sub>6</sub>O<sub>2</sub>S)<sub>n</sub> calc C, 40 6. H, 5 1)

When 10 (4 g) was melted and then distilled under diminished pressure, 1 (3 0 g, 75%) was obtained

When 10 (0 5 g) was shaken for 3 days with water (10 mL) at room temperature and, after removal of 5% of unreacted polymer, the aqueous solution was concentrated under diminished pressure at 40°, 2a (0 45 g, 74%) was obtained

Theodigly colaldehyde bis(semicarbazone) (11) bis(p-nitiophenylhydiazone) (12), and bis(2,4-dinitiophenylhydiazone) (13) — These compounds were prepared from 2a in the usual manner

Compound 11 (97 5%) had m p 201–202° (from water) <sup>1</sup>H-n m r (Me<sub>2</sub>SO- $d_6$ ) data  $\delta$  9 90–9 50 (s, 1 H, proton exchangeable with D<sub>2</sub>O), 7 10 (t, 1 H, J 6 Hz), 6 6–6.0 (m, 2 H, proton exchangeable with D<sub>2</sub>O), and 2 70 (d, 2 H, J 6 Hz) (Found

C, 30 9 H, 5 2. N, 35 9, S, 14 1,  $C_6H_{12}N_6O_2S$ , calc C, 31 0, H, 5 2, N, 36 1, S, 13 8)

Compound 12 (95%) had mp 229–230° (from 14-dioxane), <sup>1</sup>H-n mr (Me<sub>2</sub>SO- $d_6$ ) data  $\delta$  120 (bs, 2 H), 805–610 (m, 5 H), and 345 (m, 2 H) (Found C, 49.2. H, 44, S, 81. C<sub>16</sub>H<sub>16</sub>N<sub>6</sub>O<sub>4</sub>S calc C, 49.4 H, 41, S, 82)

Compound 13 (quantitative yield) had m p 228–229° (from *N*,*N*-dimethylformamide–methanol) lit <sup>1+ 15</sup> m p 219–221° and 220–222°, <sup>1</sup>H-n m r (Me<sub>2</sub>SO) data  $\delta$  11.72 (s, 1 H). 8 10–7 50 (m, 3 H), 7 36 (t, 1 H, *J* 6 Hz), and 3 50 (d, 2 H, *J* 6 Hz) (Found. C. 39 9. H, 2 9. N, 23 6. S, 6 4 C<sub>16</sub>H<sub>14</sub>N<sub>8</sub>O<sub>8</sub>S calc C, 40 1, H, 2 9 N, 23.4 S, 6 7)

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