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Note

Preparation of some diglycolaldehyde acetals*

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The reaction of diglycolaldehyde (**1**, 2,2′-oxybisacetaldehyde) with alcohols in acid media at room temperature has been studied in relation to the influence of the degree of α-substitution of the alcohol on the nature of the products[1]. Diglycolaldehyde bis(dimethyl acetal) (**2a**) was the only acetal isolated when methanol was used, but a mixture of *cis*- and *trans*-2,6-di-isopropoxy-1,4-dioxanes (**3d,4d**) was obtained with 2-propanol. Ethanol and 1-propanol yielded a mixture of the acyclic acetals (**2b,2c**) and the corresponding stereoisomers of 2,6-dialkoxy-1,4-dioxanes (**3,4b**, **3,4c**). In each case, the reaction time was so long that it was assumed that equilibrium had been reached, and the results then suggest that the proportion of cyclic acetals increases with increase in α-substitution in the alcohols (see Table I).

The reactions of **1** and these alcohols at reflux temperature have now been

TABLE I

REACTION PRODUCTS FROM DIGLYCOLALDEHYDE (**1**) AND ALCOHOLS IN ACID MEDIA

Alcohols	*Products (%)*[a]		*Time (h)*	
	I (Room temp.)	*II (Refluxing temp.)*	*I*	*II*
MeOH	**2a** (66)[1]	**2a** (74.5)[b]	24	6
EtOH	**2b** (47.5), **3b,4b** (22.7)[1]	**2b** (39), **3b,4b** (13.9)	24	9
PrOH	**2c** (43.6), **3c,4c** (18.5)[1]	**2c** (40.3), **3c,4c** (15.5)	72	9
$\mathrm{Pr^{i}OH}$	**3d,4d** (66)[1]	**2d** (9.9), **3d,4d** (56.8)[c]	72	24
$\mathrm{Bu^{t}OH}$	**3e,4e** (13.6)		216	
$\mathrm{HOCH_2CH_2OH}$		**2f** (53.2)		5

[a] Yields referred to **1**. [b] Water was removed using 2,2-dimethoxypropane. Compound **2a** (70%) was obtained when this reaction was carried out at room temperature for 2 days. After boiling for 6 h, **2a** (65%) was obtained in the absence of 2,2-dimethoxypropane. [c] Water was removed by azeotropic distillation.

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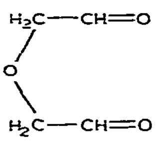
*Derivatives of Diglycolaldehyde, Part XV. For Part XIV, see ref. 2.



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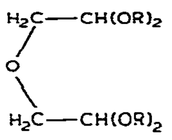

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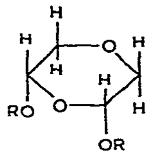
a R = Me d R = Pr^i
b R = Et e R = Bu^t
c R = Pr f R = CH$_2$



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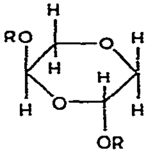

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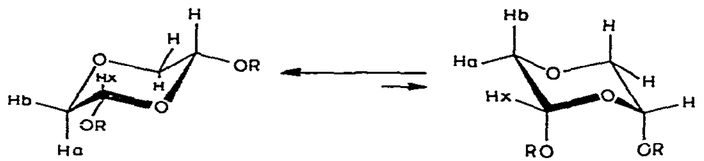
studied. Methanol and primary alcohols gave results similar to those obtained at room temperature. For the derivatives of primary alcohols, the acyclic–cyclic acetal ratios were slightly increased and the overall yields diminished. However, for 2-propanol, in addition to the dioxane derivatives **3d**,**4d**, diglycolaldehyde bis(diisopropyl acetal) (**2d**) was isolated as a new product, and its yield was increased when water was distilled from the reaction mixture. The mixture **3d**,**4d** was partially transformed into **2d** under similar conditions. The reaction between **1** and 2-methyl-2-propanol was carried out at room temperature in order to avoid olefin formation. As expected from steric considerations, the dioxane derivatives **3e** and **4e** were the only products.

In each of the above reactions, the acyclic acetals and the cyclic compounds were separated by distillation, and the mixtures of cyclic isomers were resolved by column chromatography. The relative configurations and conformational equilibria were established by ^{1}H-n.m.r. spectroscopy[1,2]. The chair conformers for the *trans* isomers (**6**) are equivalent, but, for each of the *cis* isomers (**5**), the diequatorial conformer is progressively more favoured as α-substitution increases in *R*, as indicated by the J_{ax} values (Table II).

TABLE II

Hx CHEMICAL SHIFTS AND COUPLING CONSTANTS FOR *cis*- AND *trans*-2,6-DIALKOXY-1,4-DIOXANES (5 AND 6) (CDCl$_3$)

Compound	*R*	*δ Hx*	J_{ab} *(Hz)*	J_{ax} *(Hz)*
3b	Et	4.65	3.0	7.5
3c	Pr	4.66	3.0	8.2
3d	Pr^i	4.75	3.0	8.2
3e	Bu^t	4.80	3.0	8.5
4b	Et	4.89	3.0	4.5
4c	Pr	4.85	3.0	4.5
4d	Pr^i	4.99	3.0	4.5
4e	Bu^t	5.12	2.8	4.4



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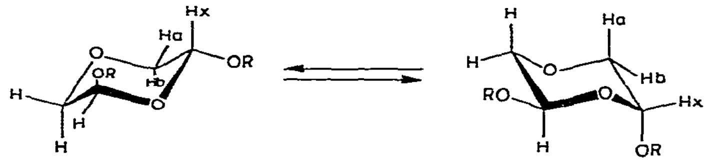

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Diglycolaldehyde bis(ethylene acetal) (**2f**) was the only compound obtained from the reaction between **1** and 1,2-ethanediol in acid media under the various conditions.

EXPERIMENTAL

General methods. — Organic solutions were dried over anhydrous Na_2SO_4. Solvents were evaporated under diminished pressure at <40°. Column chromatography was carried out on Silica Gel 60 (Merck, 70–230 mesh, ASTM). Melting points (uncorrected) were obtained with an Electrothermal melting-point apparatus. I.r. spectra were recorded for films on NaCl or KBr discs with a Pye–Unicam SP 1000 spectrometer. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Perkin–Elmer–Hitachi R-20 B spectrometer. Chemical shifts are given on the δ scale and couplings in Hz.

α,α'-Diglycerol[3] [3,3'-oxybis(propane-1,2-diol)], prepared (15–25%) from glycerol, had b.p. 230–235°/0.5 mmHg. Diglycolaldehyde[3] (**1**, ~100%) was prepared in a polymeric state when α,α'-diglycerol (15 g) was treated with aqueous $NaIO_4$ (39 g in 585 mL). This material can be prepared in a pure state by acid hydrolysis of **2a**.

Reactions between diglycolaldehyde (**1**) *and alcohols in acid media.* — (*a*) *Methanol.* A mixture of **1** [from α,α'-diglycerol (15 g)], 2,2-dimethoxypropane (35 mL), methanol (100 mL), and conc. H_2SO_4 (1 g) was boiled under reflux for 6 h, cooled, basified (MeONa–MeOH), and concentrated. The residue was treated with ether (50 mL) for 10 min, filtered, and concentrated, to give diglycolaldehyde bis(dimethyl acetal) (**2a**; 13.0 g, 74.5%), b.p. 106–110°/16 mmHg, ν_{max} 1123 and 1072 cm^{-1}. ^{1}H-N.m.r. data: δ 4.45 (t, 1 H, J 5.2 Hz), 3.49 (d, 2 H, J 5.2 Hz), and 3.42 (s, 6 H) (Found: C, 49.5; H, 9.3. $C_8H_{18}O_5$ calc.: C, 49.4; H, 9.3%).

When 2,2-dimethoxypropane was omitted from the mixture, 65% of **2a** was obtained.

In the absence of 2,2-dimethoxypropane and at room temperature, 66% of **2a** was obtained[1] after 24 h. In the presence of 2,2-dimethoxypropane, 70% of **2a** was isolated after 2 days.

(*b*) *Ethanol*. A mixture of **1** [from α,α'-diglycerol (15 g)], ethanol (145 mL), and conc. H_2SO_4 (1 g) was boiled under reflux for 9 h, cooled, basified (KOH–MeOH), and concentrated. A solution of the residue in water (20 mL) was extracted with ether (2 × 50 mL), and the combined extracts were dried, filtered, and concentrated. Distillation of the residue yielded, first, a mixture (2.2 g, 13.9%), b.p. 59–64°/0.6 mmHg, of *cis*- and *trans*-2,6-diethoxy-1,4-dioxane (**3b** and **4b**); and then diglycolaldehyde bis(diethyl acetal) (**2b**; 8.78 g, 39%), b.p. 99–107°/0.6 mmHg, ν_{max} 1117 and 1063 cm^{-1}. ^{1}H-N.m.r. data for **2b**: δ 4.48 (t, 1 H, *J* 5.2 Hz), 3.75–3.25 (m, 6 H), and 1.12 (t, 6 H) (Found: C, 57.6; H, 10.2. $C_{12}H_{26}O_5$ calc.: C, 57.6; H, 10.5%).

Chromatography (3:1 hexane–ether) of the mixture **3b**,**4b** gave, first, **3b**; ν_{max} 982, 951, 911, and 881 cm^{-1}. ^{1}H-N.m.r. data: δ 4.65 (dd, 1 H, *J* 7.5 and 3.0 Hz), 4.2–3.1 (m, 4 H), and 1.2 (t, 3 H). Eluted second was **4b**; ν_{max} 891, 876, 835, and 771 cm^{-1}. ^{1}H-N.m.r. data: δ 4.89 (dd, 1 H, *J* 4.5 and 3.0 Hz), 4.05–3.3 (m, 4 H), and 1.25 (t, 3 H) (Found for **3b** + **4b**: C, 54.3; H, 9.4. $C_8H_{16}O_4$ calc.: C, 54.5; H, 9.1%).

At room temperature, **2b** (47.5%) and the **3b**,**4b** mixture (22.7%) were obtained[1].

(*c*) *1-Propanol*. This reaction was carried out at the boiling point, using essentially the method in (*b*), with 1-propanol (186 mL) and conc. H_2SO_4 (1 g). Distillation of the crude product yielded, first, a mixture (2.85 g, 15.5%), b.p. 79–82°/1 mmHg, of *cis*- and *trans*-2,6-dipropoxy-1,4-dioxane (**3c** and **4c**); and then diglycolaldehyde bis(dipropyl acetal) (**2c**; 11.5 g, 40.3%), b.p. 100–110°/1 mmHg, ν_{max} 1123 and 1075 cm^{-1}. ^{1}H-N.m.r. data for **2c**: δ 4.58 (t, 1 H, *J* 5.2 Hz), 3.8–3.2 (m, 6 H), 1.57 (m, 4 H), and 0.91 (t, 6 H) (Found: C, 63.0; H, 10.8. $C_{16}H_{34}O_5$ calc.: C, 62.7; H, 11.2%).

Chromatography (2:1 hexane–ether) of the **3c**,**4c** mixture gave, first, **3c**; ν_{max} 1112, 1042, 936, and 905 cm^{-1}. ^{1}H-N.m.r. data: δ 4.66 (dd, 1 H, *J* 8.25 and 3.0 Hz), 4.05–3.22 (m, 4 H), 1.58 (m, 2 H), and 0.94 (t, 3 H). Eluted second was **4c**; ν_{max} 894, 844, 797, and 745 cm^{-1}. ^{1}H-N.m.r. data: δ 4.85 (dd, 1 H, *J* 4.5 and 3.0 Hz), 3.95–3.22 (m, 4 H), 1.58 (m, 2 H), and 0.94 (t, 3 H) (Found for **3c** + **4c**: C, 58.5; H, 9.9. $C_{10}H_{20}O_4$ calc.: C, 58.8; H, 9.9%).

At room temperature, **2c** (43.6%) and the **3c**,**4c** mixture (18.5%) were obtained[1].

(*d*) *2-Propanol*. A mixture of **1** [from the acid hydrolysis of **2a**[3] (11.5 g)], 2-propanol (180 mL), conc. H_2SO_4 (1 g), and benzene (50 mL) was boiled under reflux, with azeotropic removal of water, for 24 h, and then cooled, basified (KOH–MeOH), and concentrated. A solution of the residue in ether (150 mL) was washed with water (10 mL), dried, filtered, and concentrated to dryness. Distillation of the residue gave, first, a mixture (6.88 g, 56.8%), b.p. 93–104°/14 mmHg of *cis*- and *trans*-2,6-di-isopropoxy-1,4-dioxane (**3d** and **4d**); and then a mixture of several compounds (3.28 g), b.p. 131–135°/14 mmHg. A solution of this latter mixture in ether (50 mL) was washed with water (6 × 10 mL) and concentrated, and the residue was distilled, to give diglycolaldehyde bis(di-isopropyl acetal) (**2d**; 1.8 g, 9.9%), b.p. 140–142°/14 mmHg, ν_{max} 1128 and 1040 cm^{-1}. ^{1}H-N.m.r. data: δ 4.60 (t, 1 H, J 5.1 Hz), 3.82 (h, 2 H, J 6 Hz), 3.40 (d, 2 H, J 5.1 Hz), 1.12 (d, 6 H, J 6 Hz), and 1.10 (d, 6 H, J 6 Hz) (Found: C, 62.9; H, 11.2. $C_{16}H_{34}O_5$ calc.: C, 62.7; H, 11.2%).

Chromatography (5:1 hexane–ether) of the **3d**,**4d** mixture gave, first, **3d**; ν_{max} 967, 928, 898, and 828 cm^{-1}. ^{1}H-N.m.r. data: δ 4.75 (dd, 1 H, J 8.2 and 3.0 Hz), 4.03 (h, 1 H, J 6 Hz), 3.45 (m, 2 H), 1.27 (d, 3 H, J 6 Hz), and 1.20 (d, 3 H, J 6 Hz). Eluted second was **4d**; ν_{max} 891, 861, 829, and 758 cm^{-1}. ^{1}H-N.m.r. data: δ 4.99 (dd, 1 H, J 4.5 and 3.0 Hz), 3.98 (h, 1 H, J 6 Hz), 3.58 (m, 2 H), 1.30 (d, 3 H, J 6 Hz), and 1.20 (d, 3 H, J 6 Hz) (Found for **3d** + **4d**: C, 59.0; H, 9.9. $C_{10}H_{20}O_4$ calc.: C, 58.8; H, 9.9%).

At room temperature and omitting the benzene, the **3d**,**4d** mixture (66%) was obtained[1].

Compound **2d** and methanol reacted in acid media to give **2a** (93.2%).

A mixture of **3d**,**4d** (8.1 g), 2-propanol (70 mL), conc. H_2SO_4 (1 g), and benzene (50 mL) was boiled under reflux, with azeotropic removal of water, for 48 h. Compound **2d** (2.40 g, 20%) and starting material (56.5%) were obtained when the product was distilled.

(*e*) *2-Methyl-2-propanol*. A mixture of **1** [from α,α'-diglycerol (15 g)], 2-methyl-2-propanol (230 mL), conc. H_2SO_4 (1 g), and $CuSO_4$ (5 g) was left at room temperature for 9 days, filtered, basified (KOH–MeOH), and concentrated. Aqueous 30% K_2CO_3 (50 mL) was added, the mixture was extracted with ether (3 × 50 mL), and the combined extracts were dried, filtered, and concentrated. A solution of the residue in hexane (75 mL) was treated with sodium (3 g) and then boiled under reflux for 3 h, cooled, filtered, stirred with a small amount of silica gel, filtered, and concentrated to dryness. A mixture (2.85 g, 13.8%), b.p. 110–113°/14 mmHg of *cis*- and *trans*-2,6-di-(*tert*-butoxy)-1,4-dioxane (**3e** and **4e**) was obtained (Found: C, 62.0; H, 10.5. $C_{12}H_{24}O_4$ calc.: C, 62.0; H, 10.4%).

Chromatography (5:1 hexane–ether) of this mixture gave, first, **3e**, m.p. 50–51° (from hexane); ν_{max} 1125, 1042, 928, and 870 cm^{-1}. ^{1}H-N.m.r. data: δ 4.80 (dd, 1 H, J 8.5 and 3.0 Hz), 3.45 (dd, 1 H, J 11.1 and 3.0 Hz), 3.05 (dd, 1 H, J 11.1 and 8.5 Hz), and 1.22 (s, 9 H). Eluted second was **4e**, m.p. 68–69° (from hexane); ν_{max} 880, 840, 800, and 700 cm^{-1}. ^{1}H-N.m.r. data: δ 5.12 (dd, 1 H, J 4.4 and 2.8 Hz), 3.65 (dd, 1 H, J 11.2 and 2.8 Hz), 3.34 (dd, 1 H, J 11.2 and 4.4 Hz), and 1.28 (s, 9 H).

The mixture **3e**,**4e** and methanol reacted in acid media to give **2a** (60%).

(*f*) *1,2-Ethanediol*. A mixture of **1** [from the acid hydrolysis of **2a** (11.5 g)], 1,4-dioxane (100 mL), 1,2-ethanediol (13 g), conc. H_2SO_4 (1 g), and benzene (50 mL) was boiled under reflux, with azeotropic removal of water, for 5 h, cooled, basified (KOH–MeOH), and concentrated. Aqueous 50% K_2CO_3 (25 mL) was added, and the mixture was then extracted with $CHCl_3$ (4 × 50 mL). The combined extracts were dried, filtered, and concentrated to dryness, to give diglycolaldehyde bis(ethylene acetal) (**2f**; 9.1 g, 53.2%), b.p. 115–117°/1.5 mmHg; ν_{max} 1122, 1035, 940, and 865 cm^{-1}. ^{1}H-N.m.r. data: δ 5.02 (t, 1 H, J 3.7 Hz), 3.90 (m, 4 H), and 3.55 (d, 2 H, J 3.7 Hz) (Found: C, 50.3; H, 7.4. $C_8H_{14}O_5$ calc.: C, 50.5; H, 7.4%).

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