Cyclic Formals of Polyhydroxycyclohexane Compounds

P. V. Bonsignore and M. D. Hurwitz

The Rohm and Haas Company, Bristol, Pennsylvania

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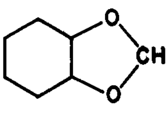
The acid-catalyzed reaction of formaldehyde with *cis*- and *trans*-1,2-cyclohexanediols and with *cis*- and *trans*-3,4-dihydroxycyclohexylmethanols has been investigated. Of particular interest with the latter two compounds was the competition for formaldehyde between the primary and secondary hydroxyl groups. With the *cis*-dihydroxycyclohexylmethanol a high yield of a cyclized intramolecular formal involving only the vicinal secondary glycol group results. The *trans*-dihydroxycyclohexylmethanol yielded thermoset intermolecular polyformals.

It has often been assumed that *trans* fusion of a dioxolane ring and a cyclohexane ring is a highly strained, unstable arrangement, because it had not been possible to prepare cyclic acetals and ketals of *trans*-1,2-cyclohexanediol by the normal acid-catalyzed reaction with aldehydes and ketones. It has been pointed out, by Angyal and MacDonald,[1] that the distance apart of the oxygen atoms in the chair forms of cyclohexane-*cis*- and *trans*-1,2-diol (diequatorial conformation) are the same and that the difference in the ease of acetal and ketal formation is due to the greater number of nonbonded interactions produced when the ring is deformed to bring the oxygen atoms still closer together in the *trans* than in the *cis* case. Head[2] reports that reaction of formaldehyde with *cis*-1,2-cyclohexanediol gives *cis*-hexahydrobenzo-1,3-dioxole (I), whereas the only cyclic product obtained with the *trans*-diol is *trans*-hexahydrobenzo-1,3,5-trioxepin (II). However, the work of Christian, *et al.*,[3] who succeeded in preparing the isopropylidene derivative of *trans*-1,2-cyclohexanediol suggested that the corresponding formal could be synthesized.

It now has been found that the *trans*-hexahydrobenzo-1,3-dioxole (III) can be formed in good yields by the reaction of *trans*-1,2-cyclohexanediol with formaldehyde in the presence of phosphoric acid as catalyst by direct distillation of the reaction mixture. Facile initial formation of II followed by disproportionation in the presence of phosphoric acid was indicated by the fact that formalization reactions in which the phosphoric acid catalyst was neutralized by sodium carbonate resulted in the isolation of II as the main volatile product as reported by Head,[2] and Lichtenberger and Hincky.[4] Compound II was found to disproportionate readily and completely into III and formaldehyde in the presence of phosphoric acid under reaction conditions. The effect of catalysts on the formalization reaction with *trans*-1,2-cyclohexanediol was examined briefly. Sulfuric and *p*-toluenesulfonic acids cause pronounced charring and polymer formation; boric acid was completely ineffectual as a catalyst. Ferric chloride catalysis permitted the isolation of 16% II and 5% III (Head[2] reports 19% II, no III).

The reaction of formaldehyde was extended to the isomeric 3,4-dihydroxycyclohexylmethanols, *cis*-3,4-dihydroxy- (IV) and *trans*-3,4-dihydroxy-(V),[5] the *cis* and *trans* applying only to the glycol configuration. No attempt was made to determine the relation between the $-CH_2OH$ group and the glycol groupings although presumably the $-CH_2OH$ group would be equatorial. With these trihydroxy compounds, *i.e.*, IV and V, it was of interest to determine the site of reaction when both primary and secondary hydroxyl groups compete for a fixed amount of formaldehyde. In addition, the effect of *cis*- *vs.* *trans*-glycol configuration in determining the relative ease of intra- *vs.* intermolecular formalization might be examined. Compounds III and IV, as well as the cyclic formal of IV and its methyl ether, are believed to be new compounds. Reaction of V with an equimolar amount of formaldehyde in the presence of phosphoric acid resulted in extensive polymer formation with little or no volatile material being isolated. What volatile material was produced showed very strong carbonyl absorption in its infrared spectra (most probably pinacol rearrangement products). Washing out of carbonyl compounds by Girard T reagent and distillation resulted in the isolation of a very small amount ($\sim$4%) of an oil whose infrared and n.m.r. spectra as well as *p*-nitrobenzoate derivative was consistent with a *trans*-fused dioxolane structure (VI). Reaction of IV with an equimolar amount of formaldehyde resulted in relatively high yields (50–55%) of a monohydroxy formal whose infrared and n.m.r. spectra and analysis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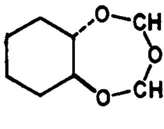
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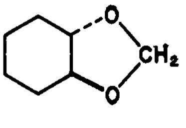
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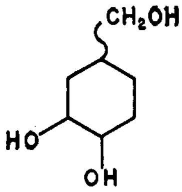
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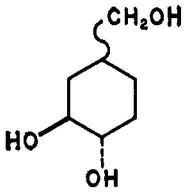
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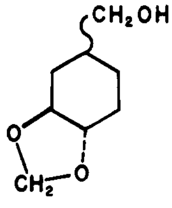
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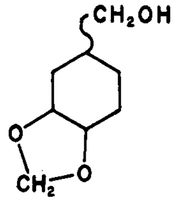
VII

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[1] S. J. Angyal and C. G. MacDonald, *J. Chem. Soc.*, 686 (1952).

[2] F. S. Head, *ibid.*, 1778 (1960).

[3] W. R. Christian, C. J. Gogek, and C. B. Purres, *Can. J. Chem.*, **29**, 911 (1951).

[4] J. Lichtenberger and J. Hincky, *Bull. soc. chim. France*, 854 (1961).

[5] R. Grewe, A. Heinke, and C. Somner, *Ber.*, **89**, 1978 (1956).

were consistent with structure VII. The structure of VII and the position of the formal group was confirmed by methylation of the free hydroxy group followed by acid hydrolysis of the formal group and periodic acid titration of the liberated vicinal glycol group.

The reluctance of V to condense to an intramolecular formal is no doubt due to the resistance of the cyclohexane configuration containing the bulky methylol group to undergo the distortion required to bring the *trans*-hydroxyl groups into the same plane. The thermoset nature of the polymeric formal indicated participation of the primary hydroxyl group.

Experimental

Reaction of *trans*-1,2-Cyclohexanediol with Formaldehyde. A. Direct Distillation of the Reaction Mixture to Yield *trans*-Hexahydrobenzo-1,3-dioxole (III) (Neat Reaction).—In a 50-ml. distillation flask was placed 11.62 g. (0.1 mole) of *trans*-1,2-cyclohexanediol, m.p. 102–103°, 3.50 g. (0.105 mole) of paraformaldehyde (calcd. as 90%), and 0.11 g. (0.002 mole) of sodium methoxide. The flask and its contents were heated in an oil bath at 140° for 20 min. whereupon a clear melt resulted. Phosphoric acid, 0.58 g. (0.005 mole), was added and the oil bath temperature raised to 180–190°. During 2 hr. 2.1 g. of water was collected. The temperature of the oil bath was raised to 240° to remove all volatile material. The distillate was diluted with ether, washed with dilute sodium bicarbonate solution, and the ether solution dried over anhydrous sodium sulfate. After evaporation of the ether solvent, the residue was distilled. One main fraction of *trans*-hexahydrobenzo-1,3-dioxole was collected, b.p. 66–67° (19 mm.), 6.2 g., 48%, $n^{26}\text{D}$ 1.4549, d^{25}_{25} 1.036. Composition and isomeric purity was better than 99.5% as determined by v.p.c.

Anal. Calcd. for $C_7H_{12}O_2$: C, 66.37; H, 9.44; hydrolyzable formaldehyde, 23.6. Found: C, 66.10, 66.29; H, 9.49, 9.57; hydrolyzable formaldehyde, 22.3, 23.7.

A sample of the *trans*-hexahydrobenzodioxole, 0.5 g., was dissolved in 5 ml. of acetone and 5 ml. of water; 5 drops of concentrated HCl was added and the solution heated on a steam bath for 1 hr. Evaporation to dryness left a brown crystalline sludge which was purified by dissolving it in hot ethyl acetate and treating the solution with decolorizing charcoal. Slow evaporation of the clear liquor left white crystals which melted at 100°, m.m.p. 101° with authentic *trans*-1,2-cyclohexanediol (m.p. 101°), m.m.p. 73–75° with *cis*-1,2-cyclohexanediol (m.p. 97–98°).

B. Neutralization of Acid Formalization Catalyst to Yield *trans*-Hexahydrobenzo-1,3,5-trioxepin (II) (Phosphoric Acid Catalysis).—The reaction of formaldehyde with *trans*-1,2-cyclohexanediol was carried out as in procedure A with the exception that, after removal of the water of reaction over a period of 2 hr., the reaction mixture was neutralized with excess sodium carbonate solution (5%) and subjected to steam distillation. The steam distillate was extracted with chloroform and the chloroform layer dried over anhydrous sodium sulfate. After removal of the solvent the residue was distilled yielding two fractions: 0.52 g. (4%) of *trans*-hexahydrobenzo-1,3-dioxole, b.p. 63–66° (12 mm.), $n^{26}\text{D}$ 1.4573; and 1.55 g. (13%) of *trans*-hexahydrobenzo-1,3,5-trioxepin, b.p. 92° (16 mm.), $n^{26}\text{D}$ 1.4661; lit.[2] b.p. 97° (20 mm.), $n^{20}\text{D}$ 1.4686.

C. Disproportionation of *trans*-Hexahydrobenzo-1,3,5-trioxepin (II).—In a microdistillation apparatus was placed 3.0 g. (0.019 mole) of II, b.p. 94° (20 mm.), and 5 drops of 85% phosphoric acid. A slow stream of nitrogen was bubbled through the reaction mixture while the flask was heated in an oil bath at 185°. White clouds of paraformaldehyde quickly built up throughout the condenser. After 1 hr. the reaction mixture was distilled under vacuum and one fraction of *trans*-hexahydrobenzo-1,3-dioxole was obtained, 1.33 g. (55% b.p. 58–61° (18 mm.), $n^{26}\text{D}$ 1.4552. The infrared spectrum of this material was superimposable on that of authentic *trans*-hexabenzo-1,3-dioxole.

Reaction of Formaldehyde with *cis*- and *trans*-3,4-Dihydroxycyclohexylmethanols. A. Preparation of *trans*-3,4-Dihydroxycyclohexylmethanol (V).—In a 500-ml. flask was placed 33.6 g. (0.3 mole) of 1,2,5,6-tetrahydrobenzyl alcohol (Shell Development Corp.) and 200 ml. of 98% formic acid. Hydrogen peroxide, 35.5%, 28.8 g. (0.3 mole), was added in one portion and the temperature held at 40° for 1 hr. and then raised to 55° for an additional hour. At the end of this time a test for peroxides was negative. Formic acid was stripped off under water aspirator vacuum and the residual viscous hydroxyformate ester hydrolyzed by stirring with 200 ml. of water at steam bath temperature for 16 hr., whereupon a clear solution resulted. The hydrolyzed formic acid and water were removed under vacuum and the residual oil was redissolved in water and passed through a mixed bed ion exchange column to remove final traces of formic acid. After removal of water, the residual oil was vacuum distilled to yield 27.5 g. (63%) of *trans*-3,4-dihydroxycyclohexylmethanol, b.p. 175° (0.10 mm.), lit.[5] b.p. 160–170° (0.06 mm.).

Anal. Calcd. for $C_7H_{14}O_3$: C, 57.45; H, 9.83. Found: C, 57.24; H, 9.70.

B. Formalization of *trans*-3,4-Dihydroxycyclohexylmethanol (V).—In a typical experiment 26.5 g. (0.18 mole) of V was allowed to react with 6.05 g. (0.182 mole) of paraformaldehyde and 0.2 g. of sodium methoxide at 140° for 40 min. Phosphoric acid, 1.0 g., was added and the heating bath temperature raised to 190°. Water, 3.0 g., distilled in 2 hr. Vacuum (~0.15 mm.) was applied and the temperature of the oil bath raised. No volatile products distilled up to a bath temperature of 290°. The residue in the flask was a hard resin.

Several experiments in which the ratio of formaldehyde to V was varied also resulted in thermoset resin.

In one experiment where high vacuum was immediately applied after addition of the phosphoric acid catalyst, about 2 g. of volatile material was obtained for an initial charge of 0.11 mole of V. This material showed very strong carbonyl absorption in its infrared spectrum. Repeated washing of a chloroform solution of this material with Girard T reagent resulted in a product which distilled over the range 89–95° (0.10 mm.) but still showed strong carbonyl absorption in its infrared spectrum, 1.03 g. (4%).

Anal. Calcd. for $C_8H_{14}O_3$ (VI): C, 60.74; H, 8.92; O, 30.34. Found: C, 59.87; H, 9.20; O, 29.90.

The n.m.r. spectrum of this material was essentially consistent with the proposed structure (VI).

From 0.94 g. of this material there was obtained 0.55 g. of recrystallized *p*-nitrobenzoate ester, m.p. 108–109°.

Anal. Calcd. for $C_{15}H_{17}O_6N$: C, 58.62; H, 5.58; N, 4.56. Found: C, 58.54; H, 5.80; N, 4.65.

C. *cis*-3,4-Dihydroxycyclohexylmethanol (IV).—The catalytic procedure of Vogel[6] for the *cis*-hydroxylation of a double bond based on the Milas reagent was used.

In a 300-ml. flask was placed 70 mg. of osmium tetroxide in a small amount of anhydrous *t*-butyl alcohol. To this was added 250 ml. of the hydrogen peroxide reagent in *t*-butyl alcohol (6.3% at 0°). During 0.75 hr., 1,2,5,6-tetrahydrobenzyl alcohol, 44.8 g. (0.4 mole), was added. The reaction was stirred at 0–5° for 8 hr. then at room temperature overnight. After removal of the solvent and unchanged starting material, the residue was distilled to yield 23 g. (38% yield) of *cis*-3,4-dihydroxycyclohexylmethanol, b.p. 150–155° (0.10 mm.), $n^{25}\text{D}$ 1.5094.

Anal. Calcd. for $C_7H_{14}O_3$: C, 57.45; H, 9.83. Found: C, 57.64; H, 9.55.

The infrared spectrum showed contamination by a small quantity of carbonyl containing impurity.

D. Formalization of *cis*-3,4-Dihydroxycyclohexylmethanol (IV).—In a microdistillation flask was placed 8.3 g. (0.057 mole) of IV, 1.90 g. (0.057 mole) of paraformaldehyde, and 0.05 g. of sodium methoxide. The reaction mixture was heated in an oil bath at 140° for 30 min., 0.25 g. phosphoric acid added, and the temperature raised to 190°. After a reaction period of 1 hr., vacuum from a water aspirator was applied for 15 min. to remove water of reaction. Vacuum distillation of the reaction mixture yielded one main fraction of 4.6 g. (50%) of 5-hydroxymethylhexahydrobenzo-*cis*-1,3-dioxole (VII), b.p. 102° (0.15 mm.), $n^{25}\text{D}$ 1.4853.

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.11; H, 9.04.

The infrared spectrum showed the presence of carbonyl containing contaminants but the n.m.r. spectrum was entirely consistent with the proposed structure VII.

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[6] A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd Ed. Longmans Green and Co., New York, N. Y., 1956, p. 895.

A typical duplicate run yielded 52.5% of VII, b.p. 94–97° (0.10 mm.), $n^{26}\text{D}$ 1.4853.

E. **Proof of Structure for the Cyclic Formal of *cis*-3,4-Dihydroxycyclohexylmethanol (IV).** 1. **Methylation of 5-Hydroxymethylhexahydrobenzo-*cis*-1,3-dioxole (VII).**—In a microreaction flask was heated 0.6 g. (0.026 g.-atom) of sodium metal in 30 ml. of toluene. To the sodium at reflux was added dropwise over 45 min. a solution of 4.00 g. (0.0254 mole) of VII in 20 ml. of toluene (N_2 atmosphere). The formation of the alkoxide was allowed to proceed overnight. After 14 hr., dimethyl sulfate, 3.2 g. (0.025 mole) in 10 ml. of toluene, was added over 15 min. and the reaction mixture allowed to reflux 2 hr. Methanol, 10 ml., was added and the resulting toluene solution washed with dilute ammonia water and dried over anhydrous sodium sulfate. After removal of the solvent the residue was distilled. One main fraction was collected, 3.0 g. (73% yield), of 5-methoxymethylhexahydrobenzo-*cis*-1,3-dioxole, b.p. 58° (0.1 mm.), $n^{27}\text{D}$ 1.4605.

Anal. Calcd. for $C_9H_{16}O_3$: C, 62.76; H, 9.34. Found: C, 62.45; H, 9.37.

2. **Hydrolysis of the Methylated Formal of IV and Determination of 1,2-Glycol Content.**—A 0.2811-g. sample of the methylated formal of IV, 50 ml. of water, and 5 drops of concentrated HCl were heated on a steam bath overnight. The resultant homogeneous solution was diluted quantitatively to 100 ml. and the concentration of 1,2-glycol structure determined by periodic acid titration.[7] Aliquots of the hydrolyzed glycol took up 98–110% of the theoretical amount of periodic acid after a 1-hr. reaction time at 25°.

Acknowledgment.—The *trans*-hexahydrobenzo-1,3-dioxole was synthesized for the first time by Dr. Newman M. Bortnick of the Rohm and Haas Company.

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(7) R. A. B. Bannard and L. R. Hawkins, *Can. J. Chem.*, **36**, 1254 (1958).

Synthesis and Polymerization of Propanesultam

ARTHUR D. BLISS, WARREN K. CLINE, CHESTER E. HAMILTON, AND ORVILLE J. SWEETING

Packaging Division Film Operations, Olin Mathieson Chemical Corporation, New Haven, Connecticut

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Propanesultam has been prepared by addition of thiolacetic acid to allyl chloride, oxidation of the adduct with aqueous chlorine to 3-chloropropanesulfonyl chloride, reaction with ammonia, and cyclization of the resulting 3-chloropropanesulfonamide in alcoholic base. Chromatographically pure propanesultam had m.p. 23.1–23.2°, b.p. 156–157 (2 mm.), $n^{22}\text{D}$ 1.4826; the N-benzoyl derivative melted at 171–172°. Polymerization of propanesultam of 99.1% purity has been investigated using a variety of catalysts. Basic catalysts such as sodium hydride, sodium and potassium hydroxides, potassium phenoxide, or tetramethylguanidine are effective in producing polymer of high molecular weight, m.p. 257–260°, $[\eta]$ 0.77 dl./g., particularly when used with an N-alkane- or N-arenesulfonyl-1,3-propanesultam as cocatalyst, as for example, N-(*p*-toluenesulfonyl)-1,3-propanesultam. Lewis acids were ineffective under a variety of conditions. Octadecylamine hydrochloride, aniline hydrochloride, picric acid, *p*-toluenesulfonic acid, mesitylenesulfonic acid, and benzenesulfonyl chloride effected polymerization, but only polymer of low molecular weight was produced.

Recently, the results of a study by Libby[1] of the polymerization of propanesultam have appeared. At the time, we were investigating the same reaction and both our studies and Libby's have shown that propanesultam polymerizes readily in the presence of a strong base as a catalyst and an N-acylpropanesultam as an initiator by a mechanism analogous to that proposed for the base-catalyzed polymerization of 2-pyrrolidinone.[2,3]

Our work on base-catalyzed sultam polymerization has confirmed the results reported by Libby. We have in addition investigated the previously unknown and much less facile polymerization of propanesultam in the presence of acid catalysts.

Best results have been obtained with sodium hydride as the basic catalyst in conjunction with N-benzenesulfonyl-1,3-propanesultam, but other strong bases may be used (Table I). Sodium hydroxide and potassium hydroxide are only slightly less effective, and potassium phenoxide is also quite effective. The alkali metal salts of 1,3-propanesultam itself may be used as catalysts in the polymerization. In general, amines do not give good results, but tetramethylguanidine did.

It has been found that sodium hydride and other basic catalysts should be used in concentrations of 0.3–1.0 mole % based on monomer. An excess of catalyst over initiator is needed to prevent chain transfer reactions which result in products of low molecular weight. Usually about two moles of base have been employed per mole of initiator, and best results have been obtained when the initiator was used in a concentration of 0.25–0.50 mole % based on the amount of monomer used.

Wide variation in the structure of the initiator is permissible. In general, any N-alkane- or N-arenesulfonyl-1,3-propanesultam is effective, as, *e.g.*, N-(*p*-toluenesulfonyl)-1,3-propanesultam, N-(2,5-dimethylbenzenesulfonyl)-1,3-propanesultam, N-(1-naphthalene sulfonyl)-1,3-propanesultam, or N-(2-naphthalenesulfonyl)-1,3-propanesultam. It also is possible to employ an alkane- or arenesulfonyl halide in conjunction with a strong base, in which case the active N-alkane-

TABLE I

POLYMERIZATION OF 1,3-PROPANESULTAM

Catalyst	Weight %	Temp., °C.	Time, hr.	% conversion	M.p. of polymer, °C.
NaH[a]	0.3	130	18	64.4	257–260
NaOH[a]	0.5	120	5	23.4	243–250
KOH[a]	0.7	130	3.5	35.8	240–244
C_6H_5OK[a]	0.3	127	5	29.1	238–246
$(Me_2N)_2C:NH$[a]	0.3	110	4.5	33.8	236–242
Octadecylamine hydrochloride	0.5	164	22	4.5	252–255
Octadecylamine hydrochloride	1.5	190	18	22.9	250–257
Aniline hydrochloride	0.4	165	22	1.5	228–232
Aniline hydrochloride	0.4	190	21	14.6	250–255
Picric acid	0.5	160	18	Trace	
Picric acid	0.5	190	20	13.0	230–242
p-Toluenesulfonic acid	0.7	130	20	Trace	
p-Toluenesulfonic acid	0.7	160	22	7.1	238–242
Mesitylenesulfonic acid	0.7	130	22	Trace	
Mesitylenesulfonic acid	0.7	160	22	10.8	232–236
Benzenesulfonyl chloride	0.7	160	18	9.5	223–228

[a] N-Benzenesulfonyl-1,3-propanesultam was added as an initiator.

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(1) W. H. Libby, U. S. Patent 2,983,713 (May 9, 1961).

(2) H. K. Hall, Jr., *J. Am. Chem. Soc.*, **80**, 6404 (1958).

(3) G. Champetier and H. Sekiguchi, *Compt. rend.*, **249**, 108 (1959).