[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Proximity Effects. X. *cis*-1,4-Cycloheptanediol from Solvolysis of Cycloheptene Oxide[1]

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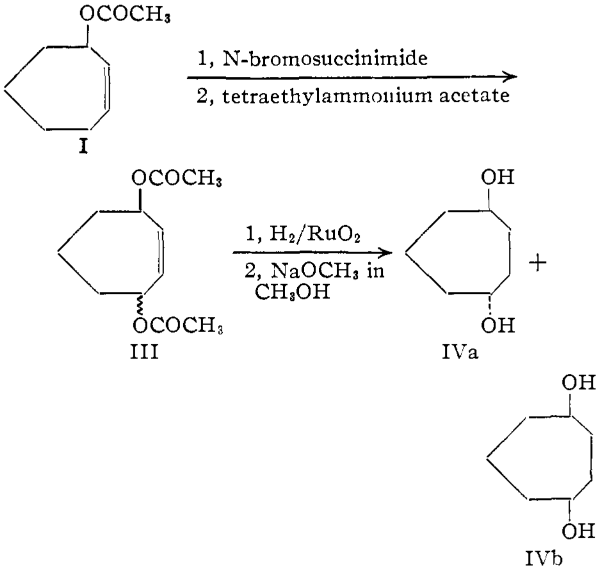
The solvolysis of cycloheptene oxide with dilute hydrochloric acid has been shown to form *cis*-1,4-cycloheptanediol in 2.4% yield, in addition to the previously observed *trans*-1,2-cycloheptanediol and 2,2′-dihydroxydicycloheptyl ether. An authentic sample of *cis*-1,4-cycloheptanediol was prepared by catalytic hydrogenation of 1,4-epidioxycyclohept-2-ene (V). *trans*-1,4-Cycloheptanediol and the two 1,3-cycloheptanediols (*cis* and *trans*) also have been prepared.

Several earlier investigations of the acid-catalyzed solvolysis of cycloheptene oxide have indicated that no products were formed as a result of a "transannular reaction." Prelog, Schenker and Küng[3] reported that only *trans*-1,2-cycloheptanediol was formed when cycloheptene was treated with performic acid. Cope and Baxter[4] hydrolyzed cycloheptene oxide with aqueous formic acid and isolated, after hydrolysis of intermediate formates, *trans*-1,2-cycloheptanediol and 2,2′-dihydroxydicycloheptyl ether. The solvolysis of cycloheptene oxide with both dilute hydrochloric acid[5] and acetic acid[6] also has been reported to form only *trans*-1,2-cycloheptanediol.

The solvolysis of cycloheptene oxide with dilute hydrochloric acid now has been reinvestigated.[7] Cycloheptene oxide was heated with 2% hydrochloric acid to give a mixture of glycols, from which it was possible to separate *trans*-1,2-cycloheptanediol as the isopropylidene ketal by treatment with acetone and cupric sulfate. The mixture of glycols (5.4%) that did not react with acetone to form ketals was then chromatographed on alumina to afford four main fractions, eluted in the following order: (1) 2,2′-Dihydroxydicycloheptyl ether, identified by mixed melting point and comparison of the infrared spectrum witn the spectrum of an authentic sample.[4] (2) A small amount of an oil that could not be crystallized (probably a mixture of (1) and (3)). (3) A solid, $C_7H_{14}O_2$, m.p. 69.0–70.2°, with an infrared spectrum containing a strong band at 3290 cm.$^{-1}$, indicative of a hydrogen-bonded hydroxyl group. The presence of two hydroxyl groups in this material was established by preparation of a bis-phenylurethan, m.p. 141–142°. (4) An unidentified oil containing a glycol $C_7H_{14}O_2$ (see the Experimental part).

The solid (3), m.p. 69.0–70.2°, was different from the known *cis*- and *trans*-1,2-cycloheptanediols, and was therefore believed to be one of the 1,3- or 1,4-cycloheptanediols, resulting from a transannular hydride shift, such as is known to occur in the cyclooctane series.[8] Since the yield of (3) was small (2.4%), its structure was proved by synthesis rather than degradation.

A mixture of *cis*- and *trans*-1,4-cycloheptanediols was prepared according to the reaction scheme



I

III

IVa

IVb

2-Cyclohepten-1-yl acetate (I) was brominated with N-bromosuccinimide in carbon tetrachloride to give a mixture of bromocycloheptenyl acetates in 57% yield. Presumably this mixture consists primarily of *cis*- and *trans*-4-bromocyclohept-2-en-1-yl acetate (II). However, *cis*- and *trans*-2-bromocyclohept-3-en-1-yl acetate also could be present. The intermediate radical formed from I could be brominated in either the 2- or 6-positions, or the allylic bromides might be isomerized on distillation. The bromine atom in II was displaced by an acetate group by treatment with tetraethylammonium acetate in acetone, to form 78% of a mixture containing *cis*- and *trans*-2-cycloheptene-1,4-diol diacetate (III), which partially crystallized on standing at 5°. Apparently the acetate ion also causes a small amount of dehydrobromination, since in the distillation of the diacetate III there was obtained a low-boiling forerun that probably contained 2,4-cycloheptadien-1-yl acetate. The bromide II, in addition to undergoing an SN2 reaction with an acetate anion, could also react in an SN2′ fashion to form either *cis*- or *trans*-cyclohept-3-ene-1,2-diol diacetate.

The mixture of unsaturated diacetates was first hydrogenated with platinum oxide as the catalyst, but extensive hydrogenolysis evidently took place, since 172% of one molar equivalent of hydrogen was

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[2] James Flack Norris Fellow, 1955–1956.

[3] V. Prelog, K. Schenker and W. Küng, *Helv. Chim. Acta*, **36**, 471 (1953).

[4] A. C. Cope and W. N. Baxter, THIS JOURNAL, **76**, 279 (1954).

[5] J. Böeseken and H. G. Derx, *Rec. trav. chim.*, **40**, 529 (1921).

[6] L. N. Owen and G. S. Saharia, *J. Chem. Soc.*, 2582 (1953).

[7] See A. C. Cope, T. A. Liss and G. W. Wood, *Chem. and Ind.*, 823 (1956).

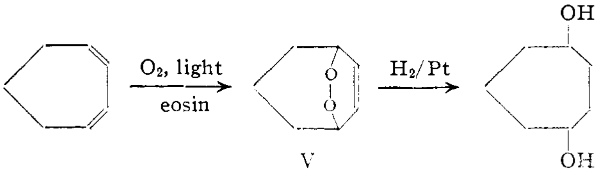
[8] A. C. Cope, S. W. Fenton and C. F. Spencer, THIS JOURNAL, **74**, 5884 (1952).

absorbed. The extent of hydrogenolysis was reduced somewhat by using ruthenium oxide as the hydrogenation catalyst; in this procedure 144% of one molar equivalent was absorbed. The mixture of cycloheptanediol diacetates was not isolated but converted directly to the glycols by treatment with a small amount of sodium methoxide in methanol.

The mixture that was formed, which contained predominantly 1,4-cycloheptanediols, was treated with cupric sulfate and acetone, and the resulting mixture of glycols and isopropylidene ketals was chromatographed on alumina. The following substances, in order of elution, were obtained: (1) a mixture of isopropylidene ketals that was hydrolyzed to the glycols, which in turn were chromatographed to afford crystalline *trans*-1,2-cycloheptanediol as well as a small amount of impure *cis*-1,2-cycloheptanediol; (2) cycloheptanol, formed as a result of partial hydrogenolysis in reduction of the diacetate III; (3) a small unidentified liquid fraction; (4) a glycol IVa, $C_7H_{14}O_2$, m.p. 96.6–98.0°; (5) a glycol IVb, $C_7H_{14}O_2$, m.p. 68.4–70.0°, that was identical with the abnormal glycol obtained in the solvolysis of cycloheptene oxide, as shown by melting point and mixed melting point determinations and comparison of the infrared spectra of the glycols and their bis-phenylurethans.

The glycols IVa and IVb were shown to be stereoisomers by oxidizing each with chromic acid in 98% acetic acid to 1,4-cycloheptanedione, isolated as the 2,4-dinitrophenylhydrazone in 79 and 83% yields. The two 2,4-dinitrophenylhydrazones were identical as shown by melting point and mixed melting point determinations and comparison of their infrared spectra.

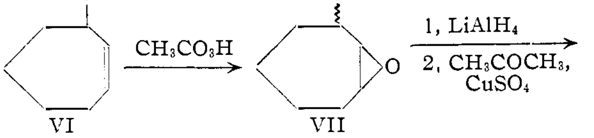
Determination of the sterochemistry of these two glycols, IVa and IVb, has been possible by making use of the synthetic sequence



1,3-Cycloheptadiene was converted to the crystalline peroxide, 1,4-epidioxycyclohept-2-ene (V), in 29% yield by treatment with oxygen, catalyzed by light in the presence of eosin. The peroxide V was hydrogenated employing a platinum catalyst. The oil obtained was chromatographed on alumina and afforded two main fractions: (1) a solid representing 78% of the total amount of glycols, m.p. 68.0–69.4°, which was identical with IVb and (2) an oil representing 22% of the glycols, which was rechromatographed, and was thereby shown to consist of 24% of IVb, m.p. 68.0–69.8°, and 76% of an oil that formed a bis-phenylurethan, m.p. 184.5–185.0°, identical with the bis-phenylurethan of IVa. Thus, the product of the reduction of V consists of at least 83% of IVb, m.p. 68.0–69.4°, which is therefore *cis*-1,4-cycloheptanediol. It has been established in many cases[9] that the reduction of a 1,4-peroxide bridge produces a *cis*-1,4-glycol; for example, ascaridole has been reduced to *cis*-1,4-terpin.[10] The stereoisomer IVa, m.p. 98.6–99.4°, must be *trans*-1,4-cycloheptanediol. It is not clear why any *trans*-1,4-cycloheptanediol is formed at all, since a *trans*-peroxide bridge would not be expected to be possible sterically. It may be possible that some polymeric peroxide was present in the crude (but analytically pure) sample of V which was hydrogenated. The crude peroxide melted below 100°, while a sample recrystallized from ethyl ether melted at 119.0–122.4°. The sample that was hydrogenated did not contain an amount of the isomeric hydroxy ketone detectable by the infrared spectrum, for the spectrum contained neither hydroxyl nor carbonyl bands. A possible way in which the *trans*-glycol IVa could be formed in hydrogenation of the peroxide V would be partial dehydrogenation of one of the secondary alcohol groups in the presence of the catalyst forming a carbonyl group, followed by reduction to a mixture of the stereoisomeric glycols.

The mechanism of formation of *cis*-1,4-cycloheptanediol from cycloheptene oxide on solvolysis is postulated to be similar to that for the corresponding reaction in the cycloöctane series, involving a hydride shift across the ring.

The synthesis of the 1,3-cycloheptanediols was undertaken in order to complete the series of cycloheptanediols as reference compounds for future work. A mixture of *cis*- and *trans*-1,3-cycloheptanediols was prepared according to the scheme



mixture of 1,2-cycloheptanediol isopropylidene ketals and 1,3-cycloheptanediols

2-Cyclohepten-1-ol (VI) was treated with peracetic acid to form 3-hydroxycycloheptene oxide (VII) in 67% yield. The corresponding compound in the cycloöctane series, 3-hydroxycycloöctene oxide, was evidently the *trans* isomer, for it formed only *trans*-1,2-cycloöctanediol and *trans*-1,3-cycloöctanediol[11] on reduction with lithium aluminum hydride.[12] The oxide VII is a mixture of stereoisomers, however, as evidenced by the following. The mixture of isomers obtained on reduction of VII with lithium aluminum hydride was treated with acetone and cupric sulfate to remove the 1,2-isomers as the ketals. These ketals were hydrolyzed with aqueous formic acid to form a mixture of glycols which was chromatographed and thus separated into *cis*- and *trans*-1,2-cycloheptanediol, with the former predominating.

The material that did not form an isopropylidene ketal was chromatographed. The *cis*- and *trans*-1,3-cycloheptanediols behaved very similarly on the chromatographic column, and their separation proved to be difficult. However, two crystalline

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[9] See G. O. Schenck, *Angew. Chem.*, **64**, 21 (1952).

[10] H. Paget, *J. Chem. Soc.*, 829 (1938).

[11] A. C. Cope, A. H. Keough, P. E. Peterson, H. E. Simmons, Jr., and G. W. Wood, THIS JOURNAL, **79**, 3900 (1957).

[12] The epoxide of 2-cyclohexen-1-ol also is formed as a single stereoisomer but with the *cis* configuration; H. B. Henbest and R. A. L. Wilson, *Chem. and Ind.*, 659 (1956); *J. Chem. Soc.*, 1958 (1957).

isomers, m.p. 48.5–49.5° and 53.6–54.6°, were obtained. It is not possible at present to assign a stereochemical configuration to these 1,3-cycloheptanediols.

A table of the melting points of the isomeric cycloheptanediols and their bis-phenylurethans is compiled for convenience.

TABLE I

ISOMERIC CYCLOHEPTANEDIOLS

Isomer	Glycol, m.p., °C.	Bis-phenylurethan, m.p., °C.
cis-1,2	49.6–51.0[a]	173.6–174.5
trans-1,2	64–65[b]	219.5–220.6
α-1,3	48.5–49.5	169.2–170.6
β-1,3	53.6–54.6	134.8–136.2
cis-1,4	68.4–70.0	141.4–143.0
trans-1,4-	96.6–98.0	184.8–185.8

[a] Ref. 6 reports m.p. 46–47° for this glycol. [b] Ref. 6 reports m.p. 64–65°.

Experimental[13]

cis-1,2-Cycloheptanediol.—The procedure for the preparation of this compound is included because substantially higher yields were obtained than those reported by oxidation of cycloheptene with potassium permanganate, osmic acid and hydrogen peroxide, or osmic acid and sodium chlorate.[6] Cycloheptene was obtained in 75% yield by gradually heating a mixture of cycloheptanol and boric acid to 195°. To a solution of 0.379 g. of cycloheptene and 1.5 ml. of pyridine in 30 ml. of anhydrous ether was added a solution of 1.0 g. of osmium tetroxide in 30 ml. of ether. The resulting mixture was allowed to stand at room temperature for 22 hr. The brownish complex which had formed immediately was collected on a filter and briefly air-dried.to give 1.91 g. (96%) of residue. This complex was partially dissolved in 50 ml. of ethanol, and to the resulting suspension was added a solution of 8.1 g. of sodium sulfite in 40 ml. of water. This mixture was heated under reflux in a boiling-water bath for about 90 min. The liquid was filtered from the black solid and then concentrated under reduced pressure to remove ethanol. The aqueous solution was diluted with water to about 75 ml. and continuously extracted with chloroform overnight. The chloroform was removed by distillation, and the residue was crystallized from dry ether to give 0.230 g. of *cis*-1,2-cycloheptanediol, m.p. 48.0–49.7°. The mother liquor was concentrated and then sublimed to give a semi-solid that was recrystallized from ethyl acetate to provide an additional 0.094 g. (total of 0.324 g., 63%). Both portions were combined and crystallized from ethyl acetate to give *cis*-1,2-cycloheptanediol as a mica-like solid, m.p. 49.6–51.0° (lit.[6] m.p. 46–47°).

cis-1,2-Cycloheptanediol **Bis-phenylurethan.**—A mixture of 0.053 g. of *cis*-1,2-cycloheptanediol and 0.139 g. of phenyl isocyanate was allowed to stand at room temperature overnight in a well-stoppered flask. The excess phenyl isocyanate was then removed at about 60° and 1 mm., and the residue was dissolved in hot carbon tetrachloride and filtered to remove diphenylurea. The carbon tetrachloride was evaporated and the residue was crystallized from aqueous methanol to afford 0.118 g. (79%) of the bis-phenylurethan of *cis*-1,2-cycloheptanediol, m.p. *ca.* 135°. After one crystallization from aqueous methanol the yield was 0.092 g., with m.p. 172.0–174.4°, and after two more crystallizations from aqueous methanol the bis-phenylurethan melted at 173.6–174.5°.

Anal. Calcd. for $C_{21}H_{24}O_4N_2$: C, 68.46; H, 6.57; N, 7.61. Found: C, 68.43; H, 6.60; N, 7.70.

***trans*-1,2-Cycloheptanediol bis-phenylurethan** was prepared from *trans*-1,2-cycloheptanediol (from the solvolysis of cycloheptene oxide described below) and after five crystallizations from ethyl acetate had m.p. 219.5–220.6°.

Anal. Calcd. for $C_{21}H_{24}O_4N_2$: C, 68.46; H, 6.57; N, 7.61. Found: C, 68.75; H, 6.54; N, 7.50.

Solvolysis of Cycloheptene Oxide.—Cycloheptene oxide (8.0 g.) was heated on a steam-bath with 300 ml. of 2% hydrochloric acid for a period of 3 hr. The mixture was concentrated under reduced pressure to a volume of 100 ml. and continuously extracted with chloroform for 20 hr. The chloroform was removed, and the solid residue of 7.0 g. was dissolved in 300 ml. of dry acetone and stirred with 10 g. of anhydrous curpic sulfate in a stoppered flask for 18 hr. The cupric sulfate and acetone were removed, yielding a residue that was diluted with 30–60° petroleum ether and chromatographed on 100 g. of activity III alumina. Elution with 500 ml. of 30–60° petroleum ether afforded, after removal of the solvent and distillation of the residue, 7.0 g. of *trans*-1,2-cycloheptanediol isopropylidene ketal, b.p. 94° (24 mm.), $n^{25}D$ 1.4519 (lit.[14] $n^{18}D$ 1.4543). Elution with ether-methanol (4:1) then yielded 0.500 g. of a viscous oil. This oil was dissolved in ether and chromatographed on 50 g. of activity III alumina.

Fraction	Volume, ml.	Solvent, ether : methanol	Weight, g.
11–13	150	99:1	0.038
14–22	450	99:1	.112
23–32	500	98:2	.223
33–35	350	2:1	.121

Fractions 11–13 were crystallized from ethyl acetate and gave 2,2′-dihydroxydicycloheptyl ether, m.p. 85.6–86.5°, undepressed on admixture with an authentic specimen.[4] Fractions 14–22 could not be crystallized. Fractions 23–32 were recrystallized from ethyl acetate as needles, m.p. 69.0–70.2°. Evidence cited below establishes the structure of this compound as *cis*-1,4-cycloheptanediol.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.59; H, 10.84. Found: C, 64.55; H, 10.67.

The bis-phenylurethan of *cis*-1,4-cycloheptanediol after several recrystallizations from aqueous methanol had m.p. 141–142°.

Anal. Calcd. for $C_{21}H_{24}O_4N_2$: C, 68.46; H, 6.57; N, 7.61. Found: C, 68.60; H, 6.75; N, 7.53.

Fractions 33–35 were treated with phenyl isocyanate and formed a crystalline bis-phenylurethan (0.118 g.), which was dissolved in benzene and chromatographed on 25 g. of Grade "H" alumina (Peter Spence and Sons, Widnes, England). Elution with benzene:ether (3:1) gave 0.042 g. of a bis-phenylurethan that had m.p. 186.5–188.0° after four recrystallizations from aqueous methanol.

Anal. Calcd. for $C_{21}H_{24}O_4N_2$: C, 68.46; H, 6.57. Found: C, 68.41; H, 6.81.

This bis-phenylurethan was not identified. It may be derived from a glycol $C_7H_{14}O_2$ with a rearranged carbon skeleton.

2-Cyclohepten-1-yl Bromide.—A mixture of 30.0 g. of cycloheptene, 55.5 g. of N-bromosuccinimide and 0.4 g. of benzoyl peroxide in 200 ml. of carbon tetrachloride was heated under nitrogen on a steam-bath in a flask fitted with a reflux condenser. After the exothermic reaction subsided (15–20 min.), the mixture was heated for an additional period of 15 min. The succinimide was removed by filtration, and the filtrate was washed with 5% sodium bicarbonate solution and water and dried over magnesium sulfate. The solution was concentrated by distillation under reduced pressure through a Vigreux-type Claisen head, and the residue was distilled at 1 mm. The distillate was fractionally distilled through a Vigreux column (26 × 1.4 – cm.), to give 30.1 g. (55%) of 2-cyclohepten-1-yl bromide, b.p. 59° (5.2 mm.), $n^{25}D$ 1.5304 (lit.[15] $n^{20}D$ 1.5323).

2-Cyclohepten-1-yl Acetate (I).—A suspension of 42 g. of silver acetate in 120 ml. of glacial acetic acid was added in

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[13] Melting points are corrected and boiling points are uncorrected. We are indebted to Dr. S. M. Nagy and his associates for analyses. Infrared spectra were determined with a Baird double beam recording spectrometer (model B), with a sodium chloride prism. Merck alumina was neutralized by washing with ethyl acetate and methanol and reactivated by heating under reduced pressure to the activities on the Brockmann scale [H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1941)], indicated for the various chromatograms. Many of the filtrations involved in the crystallizations described below were carried out by the method of Craig [L. L. Craig and O. W. Post, *Ind. Eng. Chem., Anal. Ed.*, **16**, 413 (1944)], and only very small quantities of solvent were used in many cases, especially in the case of the cycloheptanediols.

[14] H. G. Derx, *Rec. trav. chim.*, **41**, 331 (1921).

[15] E. Pesch and S. L. Friess, THIS JOURNAL, **72**, 5756 (1950).

portions to a slightly cooled, stirred solution of 29.1 g. of 2-cyclohepten-1-yl bromide in 90 ml. of glacial acetic acid. The mixture was stirred for an additional hour at room temperature and allowed to stand in the dark at room temperature for about 36 hr. After filtration, the residue was washed with 75 ml. of acetic acid and with ether, and the filtrate was poured into 350 ml. of water. The aqueous layer was extracted successively with 250- and 150-ml. portions of ether; the combined ether layers were washed with six 100-ml. portions of water and two 100-ml. portions of 5% sodium bicarbonate solution, dried over magnesium sulfate and concentrated. The residue was distilled through a semimicro column, affording 20.9 g. (82%) of colorless liquid. A small portion of this distillate was fractionally distilled and provided an analytical sample of I, b.p. 70° (6 mm.), $n^{25}\text{D}$ 1.4610, d^{20}_4 0.9966.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.09; H, 9.15. Found: C, 70.01; H, 9.20.

4-Bromocyclohept-2-en-1-yl Acetate (II).—A mixture of 11.7 g. of I, 13.5 g. of N-bromosuccinimide and 0.2 g. of benzoyl peroxide in 175 ml. of carbon tetrachloride was heated to the reflux temperature on a steam-bath for a period of about 30 min. The product was isolated in the manner described above for 2-cyclohepten-1-yl bromide. The residue obtained after removal of the carbon tetrachloride was distilled under nitrogen and then redistilled through a semimicro column, giving 10.0 g. (57%) of a colorless mixture containing the *cis* and *trans* isomers of II, b.p. 70–79.5° (0.3 mm.), $n^{25}\text{D}$ 1.5130–1.5164. A small portion of the above product was redistilled, affording an analytical sample, $n^{25}\text{D}$ 1.5153.

Anal. Calcd. for $C_9H_{13}O_2Br$: C, 46.37; H, 5.62; Br, 34.29. Found: C, 46.55; H, 5.72; Br, 34.05.

2-Cycloheptene-1,4-diol Diacetate (III).—To a stirred, ice–water cooled solution of 14.1 g. of tetraethylammonium acetate in 50 ml. of acetone was added dropwise over a period of about 45 min. 8.85 g. of II dissolved in 20 ml. of acetone. The mixture was stirred with cooling for an additional 60 min., then at room temperature for 3 hr. and allowed to stand overnight. The precipitated tetraethylammonium bromide (7.59 g., 95%) was removed by filtration and washed with acetone until colorless. The acetone was removed from the filtrate under reduced pressure; to the residue was added 50 ml. of water, and the resulting mixture was extracted with four 20-ml. portions of ether. The extracts were dried over magnesium sulfate, concentrated and distilled under nitrogen through a semimicro column, giving 6.30 g. (78%) of a mixture containing the *cis* and *trans* isomers of III, b.p. 80–86° (0.4 mm.), $n^{25}\text{D}$ 1.4704–1.4671. Some of the fractions on standing at 5° overnight partially crystallized to long needles. A low-boiling fore-run (not investigated further) that collected over the range 36–80° (0.4 mm.) probably contains 2,4-cycloheptadien-1-yl acetate, formed by elimination of hydrogen bromide from II.

A portion of the above-described mixture containing 2-cycloheptene-1,4-diol diacetates was redistilled, giving an analytical sample, $n^{25}\text{D}$ 1.4672.

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.16; H, 7.45.

Mixture of *cis*- and *trans*-1,4-Cycloheptanediol.—Ruthenium dioxide (100 mg.) in 10 ml. of 95% ethanol was pre-reduced with hydrogen; to this catalyst was then added 5.50 g. of III dissolved in 30 ml. of 95% ethanol. Hydrogenation resulted in the absorption of 971 ml. (144% of one mole) of hydrogen. (A similar hydrogenation employing pre-reduced platinum oxide as the catalyst resulted in the absorption of 172% of one mole of hydrogen.) The hydrogenation mixture was filtered and concentrated to a residue of about 5 ml., to which was added a solution of 0.4 g. of sodium in 40 ml. of dry methanol. The solution was allowed to stand at room temperature overnight and then concentrated to a residue of about 10 ml. This residue was poured into 50 ml. of water, and the resulting mixture was continuously extracted with chloroform for 20 hr. The chloroform layer was dried over magnesium sulfate and concentrated; the dark residue was subjected to short-path distillation with a heating block temperature of 80–110° at 0.8 mm., giving a colorless distillate of 1.9 g. This distillate was stirred with 50 ml. of anhydrous acetone and 6 g. of anhydrous cupric sulfate for 14 hr. at room temperature. The solid was then removed by centrifugation; the residue (2.25 g.) remaining after removal of the acetone from the organic layer was dissolved in 150 ml. of benzene and chromatographed on 200 g. of activity III alumina.

Fraction	Volume, ml.	Solvent	Weight, g.
3–6	280	Benzene	0.536
8–16	630	Ether–methanol (99:1)	.226
18–20	210	Ether–methanol (98:2)	.133
21–24	280	Ether–methanol (97:3)	.409
25–33	630	Ether–methanol (95:5)	.696

Fractions 3–6 were treated with formic acid (for procedure see below); the diols obtained were chromatographed on activity III alumina. There was isolated a crystalline compound which melted at 62.0–63.1° after two recrystallizations from ethyl acetate, which did not depress the melting point of an authentic sample of *trans*-1,2-cycloheptanediol. In addition there was obtained a small amount of an oil that was eluted just before *trans*-1,2-cycloheptanediol and hence probably is, at least in part, *cis*-1,2-cycloheptanediol (see the chromatography of a mixture of 1,2-cycloheptanediols described below). Fractions 8–16 contained cycloheptanol, as indicated by index of refraction and behavior on the chromatographic column. Fractions 18–20 were oils that could not be crystallized. Fractions 22–23 were sublimed and then recrystallized twice from ethyl acetate, giving crystals, m.p. 96.6–98.0°. Similar material obtained in a preparation in which III was reduced in the presence of platinum oxide was analyzed. Evidence cited below establishes the identity of this isomer as *trans*-1,4-cycloheptanediol.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.52; H, 10.86.

The bis-phenylurethan of the above diol after three recrystallizations from aqueous methanol had m.p. 184.8–185.8°.

Anal. Calcd. for $C_{21}H_{24}O_4N_2$: C, 68.46; H, 6.57; N, 7.61. Found: C, 68.23; H, 6.74; N, 7.37.

Fractions 26–32 were sublimed and then crystallized four times from ethyl acetate, giving needles of *cis*-1,4-cycloheptanediol, m.p. 68.4–70.0°. A mixed melting point with the "abnormal" diol obtained in the solvolysis of cycloheptene oxide showed no depression, and the infrared spectra of the two specimens were identical. The bis-phenylurethan after three recrystallizations from aqueous methanol had m.p. 141.4–143.0°. A mixed melting point with the bis-phenylurethan of the transannular product showed no depression, and their infrared spectra were identical.

1,3-Cycloheptadiene.—The preparation of 1,3-cycloheptadiene from 2-cyclohepten-1-yldimethylamine by exhaustive methylation has been described previously.[15,16]

2-Cyclohepten-1-yl bromide (25.0 g.) was added to 37 g. of quinoline cooled in an ice-water-bath. The flask was fitted with a simple distillation head and gradually heated to about 180°, during which time the yellow product distilled at about 115°. The crude product (13.2 g., 98%) was dissolved in 75 ml. of ether, and the ethereal solution was extracted with 5% hydrochloric acid, water and dried over magnesium sulfate. The residue after removal of the ether was distilled under nitrogen through a semimicro column (foaming occurred), giving 8.67 g. (64%) of 1,3-cycloheptadiene, b.p. 55° (75 mm.), $n^{25}\text{D}$ 1.4940–1.4950 (lit.[15] $n^{20}\text{D}$ 1.4972).

1,4-Epidioxycyclohept-2-ene (V).[17]—A solution of 4.20 g. of 1,3-cycloheptadiene and 0.30 g. of the sodium salt of eosin in 950 ml. of absolute ethanol into which a stream of oxygen was passed through a fritted-glass disk was irradiated by two clear-glass lamps with tungsten filaments (a total of 350 watts) for a period of 144 hr. Pyrex glass windows were inserted between the lamps and the flask, so that the temperature of the reaction mixture did not exceed 39°. Although the flask was fitted with a reflux condenser, it was necessary periodically to add absolute ethanol to the mixture in order to maintain the original volume. The progress of the reaction was followed by removing 1-ml. aliquots and observing the decrease in the absorption of cycloheptadiene at its wave length of maximum absorption, 264 mμ. Such

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(16) E. P. Kohler, M. Tishler, H. Potter and H. T. Thompson, THIS JOURNAL, 61, 1057 (1939).

(17) *Cf.* the preparation of 1,4-epidioxycyclohex-2-ene, Houben-Weyl, "Methoden der Organischen Chemie," Vol. VIII, 4th Ed., Georg Thieme, Stuttgart, 1952, p. 16.

measurements indicated the disappearance of 84% of the cycloheptadiene at the end of 144 hr.

The reaction mixture was worked up in two parts because of the possibility of explosive decomposition of the peroxide. The ethanol was removed by distillation under reduced pressure, during which time the water-bath was maintained at 35–40°. The bright red crystalline residue was sublimed at 0.3 mm. and 40° onto a Dry Ice-cooled cold finger. The total weight of the white, mealy sublimate was 1.65 g. (29%). Analysis of the sublimate without further purification gave the correct values shown.

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.62; H, 7.99. Found: C, 66.80; H, 8.24.

The peroxide V had a strong, characteristic odor, was quite volatile and as obtained above melted below 100°. A small amount was recrystallized by dissolving it in a small amount of dry ether, in which it was very soluble, cooling the solution in an acetone–Dry Ice-bath and filtering rapidly in a Craig tube, m.p. 119.0–122.4°. The peroxide V seemed to be stable indefinitely when maintained at 5°.

Reduction of V.—To 0.080 g. of platinum oxide catalyst which had been pre-reduced with hydrogen in 30 ml. of absolute ethanol was added 0.500 g. of V; this mixture was stirred with hydrogen and absorbed 155 ml. (80% of two equivalents) of hydrogen in 65 min. The mixture was allowed to stir overnight and absorbed some additional hydrogen. The hydrogenation mixture was filtered and concentrated to an oily residue which was sublimed at 0.2 mm. The semisolid sublimate, 0.431 g. (84%), was dissolved in 80 ml. of dry ether and chromatographed on 50 g. of alumina (activity III). The glycols were eluted with ether–methanol (98:2), and there was only one detectable peak. Fractions 8–16 (30-ml. fractions were collected), consisting of 0.336 g. (78% of the glycols obtained), were crystallized individually first, after which they were combined and crystallized three times from ethyl acetate to give needles of *cis*-1,4-cycloheptanediol, m.p. 68.0–69.4°. The infrared spectrum was identical with the spectrum of the abnormal diol obtained in the solvolysis of cycloheptene oxide, and a mixed melting point of the two samples showed no depression. A bis-phenylurethan of a portion of fractions 8–16 was also prepared, m.p. 141.2–142.3°; a mixed melting point with the bis-phenylurethan of the abnormal glycol obtained in the solvolysis of cycloheptene oxide showed no depression.

Fractions 6–7, consisting of 0.093 g. (22% of the glycols obtained) could not be crystallized; they were dissolved in 15 ml. of ether and chromatographed on 15 g. of alumina (activity III). The material in fractions 15′–17′ (24%) solidified on a cold finger when sublimed and after one crystallization from ethyl acetate was identified as *cis*-1,4-cycloheptanediol, m.p. 68.0–69.4°. Fractions 5′–14′ (76%) contained an oil that could not be crystallized; therefore fractions 6′–10′ were treated with phenyl isocyanate to form the bis-phenylurethan. After the excess phenyl isocyanate was removed, the residue was treated with carbon tetrachloride. The carbon tetrachloride-soluble portion, after one crystallization from aqueous methanol, melted at 155–170°. After two further recrystallizations from aqueous methanol, however, it had m.p. 184.5–185.0°; a mixed melting point with *trans*-1,4-cycloheptanediol bis-phenylurethan showed no depression, and the infrared spectra of the two bis-phenylurethans were identical. The carbon tetrachloride-insoluble portion was shown by the infrared spectrum to contain *trans*-1,4-cycloheptanediol bis-phenylurethan contaminated by diphenylurea.

1,4-Cycloheptanedione Bis-2,4-dinitrophenylhydrazone.—To a solution of 0.020 g. of *cis*-1,4-cycloheptanediol in 2 ml. of glacial acetic acid maintained at 16° was added dropwise with stirring over a period of 20 min. a solution of 0.031 g. of chromic acid in 1 ml. of 98% acetic acid. After 5 hr. at room temperature there was added 0.3 ml. of methanol to destroy unreacted chromic acid. The reaction mixture was diluted with 6 ml. of water and extracted with three 20-ml. portions of methylene chloride. The combined extracts were washed successively with sodium bicarbonate solution and water, dried over sodium sulfate and concentrated. An immediate yellow precipitate formed when a solution of 2,4-dinitrophenylhydrazine and hydrochloric acid in methanol was added to the residue, yield 0.062 g. (83%). After five crystallizations from a mixture of nitrobenzene and ethanol, the bis-2,4-dinitrophenylhydrazone had m.p. 242.0–242.4° (dec., sample inserted into bath at 230°).

Anal. Calcd. for $C_{19}H_{18}N_8O_8$: C, 46.91; H, 3.73. Found: C, 47.24; H, 3.99.

The oxidation was repeated as described above, using 0.020 g. of *trans*-1,4-cycloheptanediol; the yield of the derivative was 0.059 g. (79%). After four crystallizations from a mixture of nitrobenzene and ethanol, the bis-2,4-dinitrophenylhydrazone had m.p. 242.4–242.8° dec. A mixed melting point with the bis-2,4-dinitrophenylhydrazone derived from *cis*-1,4-cycloheptanediol showed no depression, and the infrared spectra of the two samples were the same within experimental error.

2-Cyclohepten-1-ol (VI).—A solution of 20.3 g. of I and 20 g. of sodium hydroxide in 75 ml. of water and 200 ml. of methanol was heated under gentle reflux for 90 min. and then poured into 400 ml. of cold water. The resulting mixture was extracted with two 200-ml. and two 100-ml. portions of ether; the ether extracts were dried over magnesium sulfate and concentrated. Final drying was accomplished by adding portions of benzene to the residue and distilling the benzene until the residue was clear. The residue was distilled through a semimicro column and afforded 13.3 g. (90%) of colorless VI, $n^{25}D$ 1.4888. Fractionation of a portion of this distillate afforded an analytical sample, b.p. 72° (7 mm.), $n^{25}D$ 1.4890, $d^{20}{}_4$ 1.0028.

Anal. Calcd. for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.90; H, 10.73.

3-Hydroxycycloheptene Oxide (VII).—A 40% solution of peracetic acid (13.5 ml.), to which 1.65 g. of anhydrous sodium acetate had been added, was added dropwise with stirring to 5.02 g. of VI. The temperature was maintained at 10–15° during the 30 min. required for addition. The mixture was stirred at room temperature for about 4 hr. and allowed to stand overnight at room temperature. To this mixture was added with stirring and cooling 6 *N* sodium hydroxide (approximately 40 ml.) until neutrality was reached and then an additional 8 ml. The resulting mixture was stirred at room temperature for 6 hr., after which it was extracted with four 50-ml. portions of ether. The ethereal extracts were dried over magnesium sulfate, concentrated, and the residue was distilled through a semimicro column, giving 3.83 g. (67%) of VII, b.p. 71–74° (0.8 mm.). Redistillation of a portion of this material for analysis gave VII as a colorless liquid with $n^{25}D$ 1.4857–1.4879. An analytical sample had $n^{25}D$ 1.4875.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.39; H, 9.29.

Lithium Aluminum Hydride Reduction of VII.—To a solution of 6.38 g. of VII in 100 ml. of absolute ether contained in a three-necked flask equipped with a mercury sealed stirrer, reflux condenser and separatory funnel was added dropwise with stirring a slurry of 7.2 g. of lithium aluminum hydride in 120 ml. of ether. After about one-fourth of the lithium aluminum hydride had been added (about 30 min.), the mixture was allowed to stir for 30 min. The remainder of the slurry as then added rapidly (10 min.), and stirring was then continued under gentle reflux for 4 hr. The excess lithium aluminum hydride was destroyed by the addition of ethyl acetate, after which 6 *N* hydrochloric acid was added to hydrolyze the inorganic salts. The ether layer was removed, and the aqueous layer was continuously extracted with chloroform for 24 hr. The combined organic layers were concentrated, and the residue was sublimed onto a Dry Ice-cooled cold finger; the glassy sublimate was an oil at room temperature and amounted to 5.80 g. (90%).

Separation of 1,2- and 1,3-Cycloheptanediols.—The mixture of glycols obtained above was dissolved in 60 ml. of dry acetone and stirred at room temperature in a tightly stoppered flask with 8 g. of anhydrous cupric sulfate for 16 hr. The solid was removed by centrifugation and triturated with ether and recentrifuged. The combined organic layers were concentrated, and the residue was dissolved in a mixture of benzene and ether and chromatographed on 200 g. of activity II alumina. The mixture of 1,2-cycloheptanediol isopropylidene ketals was eluted with ether; it amounted to 4.06 g. (equivalent to 3.11 g. of glycols). The mixture of 1,3-cycloheptanediols was eluted with ether–methanol (70:30) and amounted to 2.49 g. Thus, the mixture of glycols consisted of 56% of the 1,2-cycloheptanediols and 44% of the 1,3-cycloheptanediols. In a similar experiment the percentages were 49 and 51%, respectively.

Chromatography of the Mixture of 1,3-Cycloheptanediols.—A mixture of 2.49 g. of 1,3-cycloheptanediols was dissolved in 150 ml. of ether and chromatographed on 250 g. of activity III alumina.

Fraction	Volume, ml.	Solvent, ether–methanol	Weight, g.
9–17	630	99:1 to 98:2	0.096
24–32	630	195:5 to 193:7	0.536
33–44	840	193:7 to 90:10	1.330

Fractions 9–17 were oils that were not examined further and probably contained 1,2-cycloheptanediols which were not completely removed in the treatment with cupric sulfate and acetone. A portion of fractions 24–32 was crystallized from ethyl acetate; m.p. 46.8–48.3°. Similar material from another chromatogram was crystallized five times from ethyl acetate, after which it had m.p. 48.5–49.5° (this 1,3-cycloheptanediol of unknown configuration is designated as the α-form).

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.39; H, 10.91.

A bis-phenylurethan was prepared from the above glycol in the fashion described earlier (it was rather insoluble in carbon tetrachloride) and was crystallized three times from aqueous methanol, m.p. 169.2–170.6°.

Anal. Calcd. for $C_{21}H_{24}N_2O_4$: C, 68.46; H, 6.57. Found: C, 68.48; H, 6.80.

Fractions 37–44 formed a glass when sublimed onto a cold finger and solidified when allowed to stand at room temperature. A portion of this material was crystallized as a solid mass from ethyl acetate; fine, white crystals were obtained when the glycol was crystallized from a mixture of ether and ethyl acetate, m.p. 53.6–54.6° (this is designated as the β-isomer of 1,3-cycloheptanediol).

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.87; H, 10.61.

A mixture of this glycol with the other 1,3-cycloheptanediol described above (m.p. 48.5–49.5°) had a melting range of 33–53° immediately after being formed and became liquid on standing at room temperature.

A bis-phenylurethan of the β-1,3-cycloheptanediol, m.p. 53.6–54.6°, had m.p. 134.8–136.2° after three crystallizations from aqueous methanol.

Anal. Calcd. for $C_{21}H_{24}N_2O_4$: C, 68.46; H, 6.57; N, 7.61. Found: C, 68.64; H, 6.60; N, 7.71.

Hydrolysis of the 1,2-Cycloheptanediol Isopropylidene Ketals and Chromatography of the Glycols.—A mixture of 0.508 g. of the 1,2-cycloheptanediol isopropylidene ketals prepared from the mixture of glycols obtained by lithium aluminum hydride reduction of VII and 15 ml. of 88% formic acid was stirred at 100° for 2 hr. To this mixture was added at room temperature with stirring about 30 ml. of 20% sodium hydroxide solution (until basic); stirring was continued at room temperature for 30 min., after which the solution was extracted continuously with chloroform overnight. The residue from these extracts was dissolved in 100 ml. of dry benzene and chromatographed on 45 g. of activity III alumina (50-ml. fractions were collected). Fractions 24–32 (0.161 g.) were eluted with ether–methanol (97:3). A portion of this material that was crystallized twice from ethyl acetate, m.p. 46–47°, had an infrared spectrum identical with the spectrum of authentic *cis*-1,2-cycloheptanediol. Its bis-phenylurethan, m.p. 173.2–174.4°, did not depress the melting point of authentic *cis*-1,2-cycloheptanediol bis-phenylurethan, and the spectra of the two samples were identical. Fractions 33–49 (0.115 g.) were eluted with ether–methanol (97:3 to 70:30) and could not be crystallized. However, the bis-phenylurethan that was prepared from a portion of the corresponding fractions in a similar chromatogram had m.p. 215.0–216.4°, and its infrared spectrum was identical with the spectrum of *trans*-1,2-cycloheptanediol bis-phenylurethan.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Proximity Effects. XI. Reaction of *trans*-1,2-Dibromocycloheptane with Silver Acetate[1]

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The reaction of *trans*-1,2-dibromocycloheptane with silver acetate in acetic acid has been shown to form 2-cyclohepten-1-yl acetate, *trans*-1,2-cycloheptanediol diacetate and a product which is the cyclic ketal of *trans*-2-acetoxycycloheptyl acetoacetate with *cis*-1,2-cycloheptanediol.

It became of interest to study the reaction of *trans*-1,2-dibromocycloheptane with silver acetate in glacial acetic acid when the solvolysis of cycloheptene oxide with dilute hydrochloric acid[3] was shown to form *cis*-1,4-cycloheptanediol in 2.4% yield. The normal product, *trans*-1,2-cycloheptanediol, and some 2,2′-dihydroxydicycloheptyl ether were obtained in that reaction in addition to the non-vicinal glycol, which can have arisen only from a "transannular reaction." In the cycloöctane series it had been found that the reaction between *trans*-1,2-dibromocycloöctane and silver acetate in acetic acid gave rise to a larger proportion of abnormal products than did the solvolysis of *cis*-cycloöctene oxide with dilute hydrochloric acid.[4] By analogy, it seemed likely that transannular effects might also be more prominent in the reaction of *trans*-1,2-dibromocycloheptane with silver acetate than in the solvolysis of cycloheptene oxide.

trans-1,2-Dibromocycloheptane was treated with silver acetate in hot anhydrous acetic acid, and it was found that the product separated into three distinct fractions on distillation: an unsaturated monoacetate fraction (I), a diacetate fraction (II) and a high-boiling residue (III). Fraction I was saponified and treated with phenyl isocyanate. Chromatography of the resulting mixture of phenylurethans separated the monophenylurethan (70%) from some *trans*-1,2-cycloheptanediol bis-phenylurethan (24%) that also was present. The monophenylurethan fraction on further chromatography yielded 2-cyclohepten-1-yl phenylurethan as the only identifiable component. Comparison of the infrared spectrum of I with the spectrum of an authentic sample of 2-cyclohepten-1-yl acetate[3] showed that fraction I was composed principally of this allylic acetate.

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[3] A. C. Cope, T. A. Liss and G. W. Wood, THIS JOURNAL, **79**, 6287 (1957).

[4] A. C. Cope and G. W. Wood, *ibid.*, **79**, 3885 (1957).