of bromine (1.0 g., 0.0062 mole) in the solvent (8–10 ml.) was added slowly through the addition funnel. When the addition was complete, the reaction mixture was heated for an additional hour, then cooled to room temperature and filtered to remove inorganic solids. Residual unreacted acid was extracted into aqueous 5.0 *M* sodium hydroxide. The solution was dried over Drierite and concentrated to about 5 ml. by careful fractionation. The concentrate was examined by vapor phase chromatography. This procedure was used for carbon tetrachloride, bromotrichloromethane, and 1,2-dibromoethane.

The attempted preparations of 1-iodobicyclo[2.2.2]octane followed the same procedure except that iodine (insoluble in these solvents at room temperature) was added as a solid.

General Procedure, Inverse Addition.—For inverse addition, bromine in the appropriate solvent was first placed in the reaction flask. The insolubility of the mercuric oxide–carboxylic acid mixture in carbon tetrachloride or bromotrichloromethane prevented the simple addition of these reagents as a homogeneous phase. However, heating the mixture and rapid shaking made dropwise addition practicable. The reaction mixtures were treated as described for normal addition.

1-Halobicyclo[2.2.2]octanes.—A pure sample of 1-bromobicyclo[2.2.2]octane was prepared by the method of normal addition with 1,2-dibromoethane as solvent. The concentrated solution of the product in the reaction solvent was chromatographed on alumina. The desired bromide was eluted with cyclohexane. The hydrocarbon was evaporated and the residue purified by sublimation at 75° at 2 mm. The yield of purified material was 63%.

Pure samples of these materials were also obtained by preparative vapor phase chromatography. The melting points of 1-chloro-(m.p. 103.5–104.5; lit.,[13] 104–105°) and 1-bromobicyclo-[2.2.2]octane (m.p. 58.5–59.5°; lit.,[13] 64.5–65.5°) were in reasonable agreement and the infrared spectra were identical to those reported for samples prepared from 1-hydroxybicyclo-[2.2.2]octane.[13]

1-Bicyclo[2.2.2]octyl Bicyclo[2.2.2]octane-1-carboxylate.—The ester was prepared by the normal addition procedure with iodine as previously described. A white, waxy solid was isolated in 61% yield. After sublimation at 80° at 2 mm., the material melted sharply at 88.5–89.5° and exhibited a strong absorption at 1740 cm.$^{-1}$ in carbon tetrachloride solution.

Anal.[14] Calcd. for $C_{17}H_{26}O_2$: C, 77.80; H, 9.98. Found: C, 77.89; H, 10.09.

Vapor Phase Chromatography.—Analyses were achieved by examination of the reaction products on 6 ft. × 1/4 in. column of Dow-Corning Hi-Vac grease on firebrick at 90–100° with 80–100 ml. helium min.$^{-1}$. For trapping experiments a 6 ft. × 3/8 in. column was employed. Under these conditions, the reaction solvents were eluted first followed by 1-chlorobicyclo-[2.2.2]octane, hexachloroethane, and 1-bicyclo[2.2.2]octyl bicyclo[2.2.2]octane-1-carboxylate with similar but not identical retention times. 1-Bromobicyclo[2.2.2]octane was considerably separated from these substances.

A typical chromatogram as that obtained for the products of the normal addition of bromine to a mixture of mercuric oxide and the acid in carbon tetrachloride showed a large elution peak for the excess solvent followed by a lesser quantity of bromotrichloromethane. The Simonini ester and hexachloroethane were not observed, but large quantities of 1-chloro- and 1-bromobicyclo[2.2.2]octane were eluted. At long retention times, four additional products representing about 15–20% of the area for the halobicyclo[2.2.2]octanes were detected.

The four products with longer retention times were formed in all experiments involving brominative decarboxylation, regardless of the solvent employed. Only three of these materials could be obtained in quantities sufficient for infrared spectra. No firm assignment of structure can be made. However, the simplicity of the infrared spectra suggested two of these products (liquids) to be similar di- or trihalogenated bicyclo[2.2.2]octanes. The nature of the third substance (a solid) is very uncertain. It exhibited absorptions at frequencies characteristic of the bicyclic nucleus and, in addition, at 1705 and 1720 cm.$^{-1}$ (in carbon tetrachloride solution).

Yields reported for the halobicyclo[2.2.2]octanes were established by the application of *p*-dichlorobenzene as an internal standard.

---

[13] A. A. Sayigh, Thesis, Columbia University Libraries (1952), pp. 55, 59, 79.

[14] Microanalytical data were obtained by W. Saschek.

Configurations of the 1,3-Cycloheptanediols and the 3-Hydroxycycloheptene Oxides

ARTHUR C. COPE, JAMES K. HEEREN, AND VICTOR SEEMAN

Department of Chemistry, Massachusetts Institute of Technology, Cambridge 39, Massachusetts

Received July 26, 1962

The *cis* and *trans* forms of 3-hydroxycycloheptene oxide have been reduced separately with lithium aluminum hydride to give in each case a mixture of only one 1,2-glycol and one 1,3-glycol. From the identity of the 1,2-cycloheptanediol in each case, the configurations of both the 3-hydroxycycloheptene oxide and the accompanying 1,3-cycloheptanediol were assigned.

In earlier work two 1,3-cycloheptanediols were isolated from the mixture of glycols obtained by lithium aluminum hydride reduction of a mixture of the isomeric forms of 3-hydroxycycloheptene oxide and were designated as α- and β-1,3-cycloheptanediol.[1] In order to determine the configurations of the two 1,3-glycols, *cis*- and *trans*-3-hydroxycycloheptene oxides were separated and each was reduced. Each isomer yielded only one 1,2-glycol and one 1,3-glycol. Since both *cis*- and *trans*-1,2-cycloheptanediol are well characterized compounds,[2] the configurations of both the 3-hydroxycycloheptene oxide and the accompanying 1,3-cycloheptanediol could be assigned once the 1,2-cycloheptanediol formed in each reduction had been identified.

Analysis of the mixtures of 3-hydroxycycloheptene oxides by gas chromatography showed that the isomers (designated as A and B) were formed in the same ratio (2:1 A:B) on epoxidation of 2-cyclohepten-1-ol with monoperphthalic acid or peracetic acid. It is interesting to note that the epoxidation of 2-cycloöcten-1-ol yields the *trans* isomer[3] and that the epoxidation of 2-cyclohexen-1-ol yields the *cis* isomer.[4] Fractional distillation of the mixture of 3-hydroxycycloheptene oxides separated pure isomer A from isomer B containing 2% of A. Infrared spectra of the isomers were different, and the phenylurethans melted at 129.5–130.0° and 134.0–134.5°, respectively, and had different infrared spectra.

Reduction of isomer A with lithium aluminum hydride yielded a mixture of glycols containing 81%

---

[1] A. C. Cope, T. A. Liss, and G. W. Wood, *J. Am. Chem. Soc.*, **79**, 6287 (1957).

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

[3] A. C. Cope, A. H. Keough, P. E. Peterson, H. E. Simmons, Jr., and G. W. Wood, *J. Am. Chem. Soc.*, **79**, 3900 (1957).

[4] H. B. Henbest and R. A. Wilson, *Chem. Ind.* (London), 659 (1956); *J. Chem. Soc.*, 1958 (1957).

of a 1,2-cycloheptanediol and 19% of a 1,3-cycloheptanediol according to gas chromatographic analysis. Treatment of the mixture with acetone and copper sulfate followed by chromatography on alumina separated the 1,2-cycloheptanediol isopropylidine ketal (73% yield) from the 1,3-cycloheptanediol (17%). The isopropylidene ketal was identified as the *cis* isomer by its infrared spectrum, and by treatment with formic acid followed by base, which yielded *cis*-1,2-cycloheptanediol (86%),[2] characterized by its infrared spectrum and by conversion to the bisphenylurethan. The 1,3-cycloheptanediol isolated from the same reduction was shown by similar comparisons to be identical with α-1,3-cycloheptanediol.[1] Therefore this glycol and isomer A of 3-hydroxycycloheptene oxide have the *cis* configuration.

When isomer B of 3-hydroxycycloheptene oxide was reduced with lithium aluminum hydride, the resulting mixture of glycols was shown by gas chromatography to contain 77% of a 1,3-glycol and 23% of a 1,2-glycol. The mixture was treated with copper sulfate and acetone and the resulting isopropylidene ketal and 1,3-glycol mixture was separated by chromatography on alumina. The 1,3-glycol (64%) was shown to be identical with an authentic sample of β-1,3-cycloheptanediol[1] by mixed melting point, by comparison of infrared spectra, and by conversion to an identical bisphenylurethan. The isopropylidene ketal (25%) had an infrared spectrum identical with that of an authentic sample of *trans*-1,2-cycloheptanediol isopropylidene ketal. It was treated with formic acid followed by base and the resulting 1,2-glycol was identified as *trans*-1,2-cycloheptanediol[2] by mixed melting point with an authentic specimen, by comparison of infrared spectra, and by conversion to an identical bisphenylurethan. Thus the configurations of both isomer B of 3-hydroxycycloheptene oxide and β-1,3-cycloheptanediol are *trans*.

Experimental[5]

3-Hydroxycycloheptene Oxide.—A solution of 3.0 g. of 2-cyclohepten-1-ol in 20 ml. of ether was added dropwise in 5 min. to 100 ml. of an ether solution of monoperphthalic acid containing 5.45 g. (excess) of the peracid. The mixture was stirred at room temperature and samples were removed periodically treated with sodium bicarbonate solution, dried over magnesium sulfate, and analyzed by gas chromatography. After 19 hr. the analysis indicated that 92% of the 2-cyclohepten-1-ol had reacted and after 22 hr. the analysis was unchanged. The mixture was allowed to settle and the supernatant ether solution was decanted from the phthalic acid, which was then washed by decantation with three 25-ml. portions of ether. The combined ether solutions were washed with two 25-ml. portions of saturated sodium bicarbonate. The aqueous layers were combined and extracted with five 20-ml. portions of ether (because of the solubility of the product in water). The ether solutions were combined and dried over magnesium sulfate. Most of the solvent was removed by distillation through a Widmer column at atmospheric pressure, and the remainder was removed under reduced pressure at room temperature. The residue (3.12 g., 91%) was distilled in a short-path still, yielding 2.90 g. of a colorless oil. Gas chromatographic analysis showed that the product consisted of 1.6% of unchanged 2-cyclohepten-1-ol, 66.3% of 3-hydroxycycloheptene oxide (isomer A) and 32.1% of the other isomer (B).

Pure isomer A, $n^{25}\mathrm{D}$ 1.4890, b.p. 78.0–78.5° (1.4 mm.), was separated by fractional distillation through a 45 × 0.5-cm. spinning band column.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.48; H, 9.45.

The phenylurethan of isomer A formed needles from cyclohexane, m.p. 129.5–130.0°.

Anal. Calcd. for $C_{14}H_{17}O_3N$: C, 67.99; H, 6.93. Found: C, 68.01; H, 6.87.

The purest fraction of isomer B, $n^{25}\mathrm{D}$ 1.4875, b.p. 88.0° (1.9 mm.), was contaminated with 2% of isomer A. The phenylurethan of isomer B was recrystallized from cyclohexane as needles, m.p. 134.0–134.5°.

Anal. Calcd. for $C_{16}H_{17}O_3N$: C, 67.99; H, 6.93. Found: C, 68.14; H, 6.95.

Lithium Aluminum Hydride Reduction of Isomer A.—To a solution of pure isomer A of 3-hydroxycycloheptene oxide (0.784 g.) in ether (25 ml.) was added a suspension of 0.835 g. of lithium aluminum hydride in 25 ml. of ether. The resulting mixture was stirred at room temperature for 5 hr., after which 0.85 ml. of water was added slowly, followed by 0.85 ml. of 15% sodium hydroxide and finally by 4.5 ml. of water.[6] The mixture was stirred for 1 hr., then the salts were collected by filtration, suspended in ether, and filtered again several times, until evaporation of the solvent left no residue. The ether filtrate and washings were combined and the solvent was removed under reduced pressure at room temperature. Gas chromatographic analysis of the solid residue, 0.78 g. (98%) indicated a mixture containing 81% of 1,2- and 19% of 1,3-glycol.

A solution of a mixture of the 1,2- and 1,3-glycols (prepared in a similar manner from 2.0 g. of isomer A) in 20 ml. of dry acetone was stirred with 3.0 g. of anhydrous copper sulfate for 22 hr. The copper sulfate was collected by filtration and washed several times with acetone. The filtrate and washings were combined and most of the solvent was distilled through a Widmer column at atmospheric pressure. The remainder of the acetone was removed under reduced pressure. The residue was dissolved in a mixture of benzene and ether and chromatographed on 95 g. of activity II alumina. The isopropylidene ketal was eluted with pentane. Removal of the pentane under reduced pressure at room temperature gave 1.94 g. (73%) of isopropylidene ketal with an infrared spectrum identical with that of an authentic sample of the isopropylidene ketal of *cis*-1,2-cycloheptanediol.

The 1,3-glycol was eluted with ether–methanol (4:1). Sublimation of the crude glycol at 120° (1.0 mm.) gave 0.345 g. (17%) of a viscous, colorless oil. A portion of this oil crystallized from ethyl acetate–ether as needles, m.p. 47.0–48.5°. This glycol was identical (infrared spectrum, m.p. and mixed m.p.) with α-1,3-cycloheptanediol.[1] The bisphenylurethan, after recrystallization from methanol-water, melted at 169.5–170.5° and did not depress the melting point of a sample of the bisphenylurethan of α-1,3-cycloheptanediol.[1] The infrared spectra of the derivatives were identical.

A 1.0-g. sample of the isopropylidene ketal described above was treated with 30 ml. of 90% formic acid at 100° for 2 hr.

At the end of this time 100 ml. of 20% sodium hydroxide was added with stirring until the solution was alkaline. The aqueous mixture was then extracted with six 50-ml. portions of ether. Removal of the ether under reduced pressure left 0.66 g. (86%) of a solid which on sublimation at 110° gave colorless crystals, m.p. 47.0–48.0°. The bisphenylurethan of this material was recrystallized from methanol–water, m.p. 171.5–173.5°, undepressed on admixture with an authentic sample of the bisphenylurethan of *cis*-1,2-cycloheptanediol. The infrared spectra of the two derivatives were identical.

Lithium Aluminum Hydride Reduction of Isomer B.—A 1.2-g. sample of 3-hydroxycycloheptene oxide (isomer B) was treated with 1.28 g. of lithium aluminum hydride. The resulting crude mixture of glycols, 1.27 g., consisted of 77.5% of 1,3-glycol and 22.5% of 1,2-glycol, by gas chromatographic analysis. The mixture was dissolved in 20 ml. of dry acetone and stirred with 3.0 g. of anhydrous copper sulfate for 96 hr. The copper sulfate was collected on a filter and washed several times with acetone. The filtrate and washings were combined and the solvent was removed at room temperature under reduced pressure. The residue (1.25 g.) was dissolved in ether and chromatographed on 50 g. of activity I alumina. Elution with ether–pentane (1:1) gave 0.41 g. (25%) of isopropylidene ketal. The 1,3-glycol was

---

(5) Melting points are corrected and boiling points are uncorrected. Gas chromatographic analyses were carried out at 170° using 190 × 0.8 cm. Pyrex columns packed with 30% by weight of Dow-Corning silicone oil no. 550 on 48–100-mesh sodium hydroxide-washed fire brick. The authors wish to thank Dr. S. M. Nagy for microanalyses and Mrs. N. Alvord for infrared spectra.

(6) V. M. Micovic and M. L. Mihailovic, *J. Org. Chem.*, **18**, 1190 (1953).

eluted with ether–methanol (4:1) and was then sublimed at 110° (0.5 mm.). The sublimate (0.77 g., 64%) was recrystallized from ether–ethyl acetate, m.p. 53.0–54.0°. A mixed melting point with an authentic sample of β-1,3-cycloheptanediol[1] was undepressed, and the infrared spectra of the two samples were identical. A portion of the glycol was converted to the bisphenylurethan, m.p. 134.5–135.0° (from cyclohexane–ethyl acetate), undepressed on admixture with an authentic sample of the bisphenylurethan of β-1,3-cycloheptanediol. The infrared spectra of the derivatives were identical.

The isopropylidene ketal was treated with 10 ml. of 90% formic acid at 100° for 2 hr. At the end of this time, 25 ml. of water was added followed by sodium hydroxide pellets (with cooling) until the mixture was alkaline. It was extracted with six 10-ml. portions of ether. Removal of the ether under reduced pressure left 0.20 g. (91%) of a viscous yellow oil. This was sublimed at 130° (1.5 mm.), and the sublimate was recrystallized from ether–cyclohexane, m.p. 57.0–58.0°, undepressed on admixture with authentic *trans*-1,2-cycloheptanediol. The infrared spectra of the two were identical. The bisphenylurethan, m.p. 213.0–214.0° (from methanol–ethyl acetate), did not depress the melting point of an authentic sample of the bisphenylurethan of *trans*-1,2-cycloheptanediol. The infrared spectra of the two were identical.

Proximity Effects. XXXI. Ring Contraction of *trans*-Cycloöctene Oxide[1]

ARTHUR C. COPE, PETER SCHEINER,[2a] AND MARY J. YOUNGQUIST[2b]

Department of Chemistry, Massachusetts Institute of Technology, Cambridge 39, Massachusetts

Received July 25, 1962

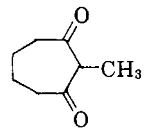
The structures of two glycols formed by ring contraction during the solvolysis of *trans*-cycloöctene oxide in formic acid have been established and confirmed by synthesis. The formation of these compounds contrasts with the absence of ring contraction in the solvolysis of *cis*-cycloöctene oxide. Possible paths leading to these glycols are considered.

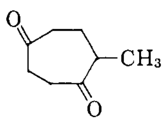
The isolation of six products from the solvolysis *trans*-cycloöctene oxide in formic acid has been reported.[3] Four of these compounds were identified as *trans*-1,4-cycloöctanediol, *trans*-1,3-cycloöctanediol, 4-cycloöcten-1-ol, and hexahydro-*o*-tolualdehyde. The two remaining products, isomeric glycols A and B ($C_8H_{16}O_2$), each had one C-methyl group and each gave a negative periodate test. This paper reports the structures of glycols A and B.

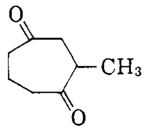
Repetition of the formolysis of *trans*-cycloöctene oxide[3] gave glycols A and B in yields of 4 and 7%, respectively. The glycols were only partially separated by chromatography on alumina, and, therefore, were converted to diacetates which were separated by gas chromatography. The infrared spectra of the glycols obtained by treating the corresponding diacetates with lithium aluminum hydride were identical to those of glycols A and B obtained previously.[3]

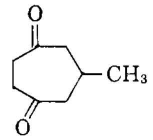
The carbon skeleton of the glycols was established by lithium aluminum hydride reduction of the ditosylates. A mixture of the ditosylates of A and B gave in over 90% yield only one hydrocarbon, methylcycloheptane. Thus methylcycloheptanediol structures were established for A and B.

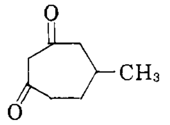
Oxidation of A and B produced the corresponding diketones, A′ and B′. Excluding the 1,2-diketones on the basis of the negative periodate test, there are six possible methylcycloheptanedione structures to be considered (I–IV). To distinguish between these possibilities, the nuclear magnetic resonance spectra of diketones A′ and B′ were obtained. The spectrum of A′ was compatible only with I. The tertiary hydrogen atom resonance appeared as a well resolved quartet centered at $\tau = 6.33$. A doublet at $\tau = 8.95$ was attributed to the methyl protons split by the single tertiary proton. Two multiplets of equal intensity corresponding to the α-methylene protons ($\tau = 7.57$) and the β-methylene protons ($\tau = 8.05$) comprised the remainder of the spectrum.

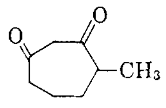

I. A′


II. B′


III


IV


V


VI

The n.m.r. spectrum of diketone B′ was less conclusive. However, lack of resonance below $\tau = 7.5$ excluded the 1,3-diketone structures V and VI. Structure IV also was eliminated because the intensity of the β proton signal indicated the presence of more than one β proton. The remaining possible structures, II and III, could not be differentiated on the basis of the spectrum.

Chemical evidence for the structure of glycol B was obtained by pyrolysis of the diacetate. The resulting mixture of dienes exhibited ultraviolet absorption at 248 mμ, indicating the presence of a 1,3-cycloheptadiene unsubstituted on the chromophore.[4] This suggested structure II for the diketone (B′) derived from glycol B, since the conjugated diene derived from structure III would have a methyl substituent on the chromophore.

Structures I and II for the diketones were confirmed by synthesis. The mixture of glycols obtained by the reaction of 3-hydroxycycloheptene oxide[5] (a mixture of *cis* and *trans* isomers) with methyllithium was treated with acetone and copper sulfate and the resulting mixture of isopropylidene ketal and 1,3-glycol was

---

[1] Supported in part by a research grant (NSF-G5055) of the National Science Foundation. Paper XXX, A. C. Cope, S. Moon, C. H. Park, and C. L. Woo, *J. Am. Chem. Soc.*, **84**, 4865 (1962).

[2] (a) National Institutes of Health Postdoctoral Fellow, 1961–1962; (b) National Institutes of Health Predoctoral Fellow, 1960–1961.

[3] A. C. Cope, A. Fournier, Jr., and H. E. Simmons, Jr., *J. Am. Chem. Soc.*, **79**, 3905 (1957).

[4] A. E. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold Ltd., London, 1958, p. 96.

[5] A. C. Cope, T. A. Liss, and G. W. Wood, *J. Am. Chem. Soc.*, **79**, 6287 (1957).