were prepared by the method of McElvain.[8,9] Of these compounds the last three have not been reported in the literature. Fractions were collected over the following boiling ranges: Ethyl orthocaprate, 136–138° (6 mm.); ethyl orthocaprylate, 215–225°; ethyl orthocaproate, 180–189°. Each fraction was contaminated with the corresponding normal ester and amide, but all reacted readily with compound F and were used without further purification or characterization.

The zinc chloride used was J. T. Baker, reagent grade.

1-Ethylcitrinin (1-Ethyl-4,6-dihydro-8-hydroxy-3,4,5-trimethyl-6-oxo-3H-2-benzopyran-7-carboxylic Acid).—A mixture of 1.0 g. of compound F and 2.0 ml. of ethyl orthopropionate was warmed briefly to give a homogeneous solution. A yellow color developed immediately. After standing for 5 min. at room temperature the solution gave a red-brown color with 5% aqueous ferric chloride. Evaporation of the excess orthoester produced a crystalline residue that after two recrystallizations from ethanol yielded 0.90 g. (77%) of lemon-yellow crystals melting at 138.2–139.2°, resolidifying and remelting at 265–268° dec. A mixture of this product with a sample of 1-ethylcitrinin produced by oxidation of 1-ethyldihydrocitrinin melted without depression of the melting point.

Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.86; H, 6.57.

1-Alkylcitrinins (1-Alkyl-4,6-dihydro-8-hydroxy-3,4,5-trimethyl-6-oxo-3H-2-benzopyran-7-carboxylic Acid).—The following general procedure was found most satisfactory for the preparation of the 1-alkyl derivatives of citrinin. To a solution of 1.0 g. (0.0042 mole) of compound F dissolved in 15 ml. of hot ethyl acetate and cooled to room temperature was added 2.0 ml. of the appropriate orthoester. A yellow color developed immediately and gradually darkened. At the end of 15–30 min. the solution gave a red-brown color with 5% aqueous ferric chloride, indicating complete reaction of compound F. After 2 hours the solvent was evaporated on a steam-bath whereupon the residue crystallized spontaneously or when stirred with a little ethanol. Three or four recrystallizations from hot ethanol followed by drying under vacuum over phosphorus pentoxide at elevated temperature yielded a product suitable for analysis. The compounds, their properties, and analytical data are summarized in Table II.

In the case of 1-octylcitrinin and 1-nonylcitrinin, because of their relatively high solubility in the residual orthoester and their low melting points, it was found advantageous to extract them from the reaction mixture with dilute aqueous base. Dilute sodium hydroxide was used for the 1-octyl compound while dilute ammonium hydroxide was found more satisfactory for the 1-nonyl because of the low solubility of its sodium salt. The basic solution was acidified and extracted with ether. Evaporation of the ether after the solution had been dried over anhydrous sodium sulfate yielded a residue that was recrystallized as described above. Methanol proved to be a more effective solvent for 1-nonylcitrinin.

1-Hexylcitrinin (1-Hexyl-4,6-dihydro-8-hydroxy-3,4,5-trimethyl-6-oxo-3H-2-benzopyran-7-carboxylic Acid).—The oxidation of 1-hexyldihydrocitrinin was carried out successfully and was used in lieu of the orthoester synthesis. To a solution of 0.5 g. (0.0015 mole) of 1-hexyldihydrocitrinin in 15 ml. of chloroform was added dropwise 3.0 ml. of 0.5 *M* bromine in chloroform. After 1 hr. at room temperature the solution was evaporated to an oil which crystallized when stirred with ethanol. Three recrystallizations from ethanol yielded lemon-yellow crystals of sufficient purity for analysis. Properties and analytical data are given in Table II.

1-Alkyldihydrocitrinins (1-Alkyl-6,8-dihydroxy-3,4,5-trimethyl-7-isochromancarboxylic Acid).—The following general procedure was used in the preparation of all of the 1-alkyldihydrocitrinin derivatives. To a suspension of 2.0 g. (0.0083 mole) of compound F in 20 ml. of benzene at room temperature was added 4.0 ml. of the appropriate freshly distilled aldehyde and 0.4 g. of zinc chloride. Anhydrous hydrogen chloride was bubbled through for 30 sec. The suspended material dissolved within about 5 min. After standing for 2 hr. the solution was washed twice with water and dried over anhydrous sodium sulfate. Evaporation of the benzene yielded an oil that crystallized when stirred persistently with petroleum ether or with petroleum ether and ethylene bromide.

For the 1-propyl, 1-butyl, 1-pentyl and 1-hexyl derivatives three or four recrystallizations from benzene and one from 10% ethyl acetate–cyclohexane followed by drying over phosphorus pentoxide under vacuum at an elevated temperature yielded products suitable for analysis. The 1-heptyl and 1-nonyl compounds were recrystallized four times from benzene with addition of petroleum ether, and the 1-octyl derivative was recrystallized once from benzene and three times from *n*-heptane. The properties of the compounds and analytical data are summarized in Table I.

Assay for Antibacterial Activity.—The method of Waksman and Reilly[5] as previously described[2] was used. Compounds to be tested were converted to their sodium salts by dissolving them in the minimum of 5% sodium hydroxide with addition of a few drops of acetone and diluting to the appropriate concentrations. The stock solutions were used immediately to prevent possible decomposition of the compounds. The results are summarized in Table III.

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(8) S. M. McElvain and J. W. Nelson, *J. Am. Chem. Soc.*, **64**, 1825 (1942).

(9) S. M. McElvain, R. E. Kent and C. L. Stevens, *ibid.*, **68**, 1922 (1946).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Proximity Effects. XXIII. Synthesis of the Seven Bicyclo[4.2.0]octanols[1,2]

BY ARTHUR C. COPE AND ROBERT W. GLEASON[3]

RECEIVED AUGUST 2, 1960

The preparation of the seven bicyclo[4.2.0]octanols is described and on the basis of the methods of synthesis, rates of oxidation, conformational analysis and infrared spectra, configurations have been assigned to five of them. *endo*-Bicyclo-[4.2.0]octan-7-ol was found to be the bicyclooötanol formed in about 0.1% yield by the treatment of *cis*-cycloöctene oxide with formic acid. It was discovered that the lithium aluminum hydride reduction of bicyclo[4.2.0]oct-7-ene oxide gives in addition to the expected bicyclo[4.2.0]octan-7-ol, a monocyclic alcohol identified as *cis*-2-methylcyclohexanemethanol.

Among the "abnormal" products that have been isolated from reactions of cycloöctane derivatives are several bicycloöctanols. Bicyclo[3.3.0]octan-2-ols are formed on treatment of *cis*- and *trans*-cycloöctene oxides with lithium diethylamide and with phenyllithium,[4] on solvolysis of *cis*- and *trans*-1,2-cycloöctanediol ditosylates and *cis*-1,4-cycloöctanediol ditosylate[5] and on the solvoly-

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(1) Supported in part by a research grant (NSF-G5055) of the National Science Foundation.

(2) Paper XXII, A. C. Cope, G. A. Berchtold, P. E. Peterson and S. H. Sharman, *J. Am. Chem. Soc.*, **82**, 6370 (1960).

(3) National Science Foundation Summer Fellow, 1959.

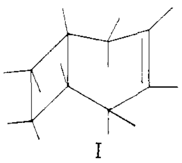
(4) A. C. Cope, H. H. Lee and H. E. Petree, *J. Am. Chem. Soc.*, **80**, 2849 (1958).

(5) A. C. Cope, S. Moon and P. E. Peterson, *ibid.*, **81**, 1650 (1959).

sis of 4-cycloöcten-1-yl brosylate and treatment of 1,5-cycloöctadiene with acids.[6] *endo*-Bicyclo-[5.1.0]octan-2-ol is formed in the solvolysis of 3-cycloöcten-1-yl brosylate.[7] In addition a bicycloöctanol of heretofore unknown structure is formed by the treatment of *cis*-cycloöctene oxide with formic acid.[8] Operating on the premise that this alcohol might have the bicyclo[4.2.0]octane ring system and, in order to characterize the seven bicyclo[4.2.0]octanols for reference purposes, the synthesis of these alcohols was undertaken.[9]

Bicyclo[4.2.0]octan-3-ols.—Bicyclo[4.2.0]oct-3-ene was prepared in an over-all yield of 35% from diethyl tetrahydrophthalate.[10] This olefin was converted to the epoxide in 69% yield using a 40% solution of peracetic acid in glacial acetic acid. Analysis of the bicyclo[4.2.0]oct-3-ene oxide by gas chromatography showed that the material was a mixture of two compounds comprising 87 and 13% of the total. Later information, discussed below, showed that the two components of the mixture are isomers, and that the one amounting to 87% of the mixture is *exo*-bicyclo[4.2.0]-oct-3-ene oxide and that the other is the *endo* isomer.

Because of the double bond and the fusion of a four-membered ring opposite the double bond, the six-membered ring of bicyclo[4.2.0]oct-3-ene is forced into a boat form. There are, however, two conformations possible in this ring system in which the six-membered ring is in the boat form. They are depicted as I and II. Examination of Dreiding and Stuart–Briegleb models shows that approach to the double bond of I is relatively unhindered from either side, so one might expect that epoxidation of I would yield a mixture of nearly equal amounts of the *endo* and *exo* isomers. On the other hand, it is easily seen in the models that approach of the oxidizing species to the *endo* side of the double bond of II is seriously hindered by the four-membered ring and the hydrogen atoms of its methylene groups. From this conformation one would expect a large preponderance of the *exo* isomer upon epoxidation. Since a mixture of isomers in unequal amounts (87:13) was obtained from the epoxidation of bicyclo-[4.2.0]oct-3-ene, it is believed that II is the more stable conformation. The models show that II has two less hydrogen–hydrogen non-bonded interactions than I. This lends support to the conclusion. Thus 87% of the mixture of the bicyclo[4.2.0]oct-3-ene oxides is the *exo* isomer and 13% is the *endo* isomer.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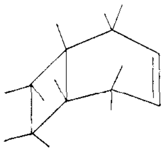
II

Reduction of bicyclo[4.2.0]oct-3-ene oxide (a mixture of the two isomers) with lithium aluminum hydride gave a mixture of *exo*- and *endo*-bicyclo-[4.2.0]octan-3-ols in 89% yield. Since this mixture could not be separated into its components using gas chromatography, quantities of *endo*- and *exo*-bicyclo[4.2.0]oct-3-ene oxide sufficient for characterization and reduction to the alcohols were separated by gas chromatography. Reduction of the *exo*-bicyclo[4.2.0]oct-3-ene oxide with lithium aluminum hydride gave *exo*-bicyclo[4.2.0]-octan-3-ol in 80% yield, and reduction of the *endo*-oxide gave *endo*-bicyclo[4.2.0]octan-3-ol in 61% yield.

Bicyclo[4.2.0]octan-3-one was prepared in 67% yield by the chromic anhydride oxidation of a mixture of *endo*- and *exo*-bicyclo[4.2.0]octan-3-ols. Reduction of this ketone over Adams platinum catalyst in an acidic medium gave a 70% yield of a product that, as indicated by its infrared spectrum and the fact that a phenylurethan prepared from it was identical to the phenylurethan of *endo*-bicyclo[4.2.0]octan-3-ol, was predominantly *endo*-bicyclo[4.2.0]octan-3-ol. This was expected since the methylene groups of the four-membered ring would make adsorption of the *endo* side of the carbonyl function on the catalyst unfavorable. This result is in accord with the generally accepted view that the catalytic reduction of cyclohexanones in acidic media affords the less stable of the two possible cyclohexanols.[11]

Further evidence that the stereochemical assignments in the case of the bicyclo[4.2.0]octan-3-ols are correct was obtained by the hydroboration of bicyclo[4.2.0]oct-3-ene followed by oxidation.[12] This procedure, which is known to give predominantly *exo*-norborneol with norbornene,[12] gave a product that was shown by its infrared spectrum to be principally *exo*-bicyclo[4.2.0]octan-3-ol.

An attempt to further substantiate the stereochemical assignments by determining the relative rates of oxidation of the two bicyclo[4.2.0]octan-3-ols according to the procedure of Schreiber and Eschenmoser[13] gave results from which it is impossible to draw conclusions concerning the stereochemistry of the hydroxyl groups[13,14] (see Table I, Experimental section).

Bicyclo[4.2.0]octan-2-ols.—Monoepoxides of both cycloöctatetraene dibromide and cycloöctatetraene dichloride have been prepared,[15] and in the case of the oxide of cycloöctatetraene dichloride isomers were separated. As seen in III, one of the carbon–oxygen bonds in these monoepoxides is allylic and it has been demonstrated[6,16] that the allylic bond is the more labile of the two and that

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[6] A. C. Cope and P. E. Peterson, *J. Am. Chem. Soc.*, **81**, 1643 (1959).

[7] A. C. Cope, S. Moon and P. E. Peterson, *ibid.*, **84**, 1935 (1962).

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

[9] The *trans* fused bicyclo[4.2.0]octane system appears to be unknown. The ring fusion of bicyclo[4.2.0]octane derivatives discussed in this paper shall be understood to be *cis*.

[10] K. Alder and H. A. Dortmann, *Chem. Ber.*, **87**, 1492 (1954)

[11] W. Klyne, "Progress in Stereochemistry," W. Klyne, Ed., Academic Press, Inc., New York, N. Y., 1954, p. 74.

[12] H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **81**, 247 (1959).

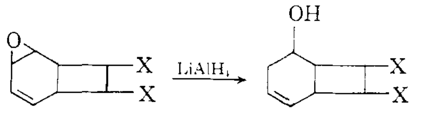
[13] J. Schreiber and A. Eschenmoser, *Helv. Chim. Acta*, **38**, 1529 (1955).

[14] H. Kwart and P. S. Francis, *J. Am. Chem. Soc.*, **81**, 2116 (1959).

[15] W. Reppe, O. Schlichting, K. Klager and T. Toepel, *Ann.*, **560**, 1 (1948).

[16] (a) T. A. Crabb and K. Schofield, *Chemistry & Industry*, 102 (1958); (b) C. A. VanderWerf, R. Y. Heisler and W. E. McEwen, *J. Am. Chem. Soc.*, **76**, 1231 (1954).

it should break preferentially upon lithium aluminum hydride reduction (eq. 1).



III IV (1)

Cycloöctatetraene dibromide and cycloöctatetraene dichloride[17] were converted to the monoepoxides in 16 and 60% yields, respectively, following the procedure of Reppe[15] with the exception that 40% peracetic acid was substituted for perbenzoic acid as the oxidizing agent. By careful distillation the monoepoxide of cyclooctatetraene dichloride was separated into a solid isomer and a liquid isomer or mixture of isomers. During this distillation a great deal of polymerization occurred, and it was later found[18] that introduction of hydroquinone and calcium carbonate into the distilling flask greatly improved the recovery.

After the monoepoxides were separately reduced with lithium aluminum hydride yielding IV or a mixture of stereoisomers of IV in high yields, it was necessary to reduce IV to the unsubstituted bicyclo[4.2.0]octan-2-ol.

Crude 7,8-dibromobicyclo[4.2.0]oct-2-en-5-ol (IV, X = Br) was reduced over Raney nickel at 80° and 2000 p.s.i. yielding 62% of impure product. Careful distillation gave analytically pure bicyclo-[4.2.0]octan-2-ol. Most of the work on the bicyclo[4.2.0]octan-2-ols described herein was done on materials prepared from the monoepoxides of cycloöctatetraene dichloride by a similar series of reductions.

It was found that the bicyclo[4.2.0]octan-2-ols obtained from the solid cycloöctatetraene dibromide monoepoxide and the solid cycloöctatetraene dichloride monoepoxide were identical and that they showed only one peak on gas chromatography. We have assigned this alcohol the *exo* configuration, for reasons described below.

The product obtained from the liquid isomer or mixture of isomers of cycloöctatetraene dichloride monoepoxide was found to be a mixture of *endo*- and *exo*-bicyclo[4.2.0]octan-2-ols in which *endo*-bicyclo[4.2.0]octan-2-ol predominated. Although the presence of a mixture could be demonstrated using gas chromatography, separation using this technique was not practical.

A mixture of *endo*- and *exo*-bicyclo[4.2.0]octan-2-ols was oxidized with chromic anhydride in pyridine to bicyclo[4.2.0]octan-2-one in 60% yield. Upon catalytic reduction in an acidic medium a 76% yield of *endo*-bicyclo[4.2.0]octan-2-ol was obtained. Since a single symmetrical peak was observed upon gas chromatography the reduction must have been essentially stereospecific.

The assignment of the *endo* configuration to this alcohol and the *exo* configuration to the alcohol obtained from the solid oxides of cycloöctatetraene dichloride and cycloöctatetraene dibromide is based on four facts.

First, catalytic reduction of cyclohexanones in acidic media generally affords the less stable cyclohexanol,[11] in this case presumably the *endo*-alcohol.

Second, the infrared spectrum of the *endo* isomer has a much less intense hydrogen-bonded hydroxyl absorption band than does the spectrum of the *exo* isomer. Models show that the hydroxyl group of the *endo* isomer is considerably shielded by close-neighboring carbon and hydrogen atoms. For this reason one would predict that the *endo* isomer would have a less intense associated-hydroxyl absorption band in the infrared than would the *exo* isomer.

Third, further examination of the infrared spectra of the two bicyclo[4.2.0]octan-2-ols gives additional evidence that the alcohol obtained by the reduction of bicyclo[4.2.0]octan-2-one is the *endo* isomer. Since an X-ray or an electron diffraction study of the bicyclo[4.2.0]octane system has not been reported its exact geometry is not known. However, it is reasonable to assume that the steric restrictions placed upon the cyclohexane ring by the cyclobutane ring in bicyclo[4.2.0]octane would closely resemble the restrictions imposed upon the cyclohexane ring in cyclohexene oxide. An electron diffraction study of cyclohexene oxide has shown that the cyclohexane ring in this compound exists in a pseudo chair form.[19] Assuming that the cyclohexane ring in bicyclo[4.2.0]octane is also a pseudo chair, the hydroxyl group of the bicyclo[4.2.0]octan-2-ols can exist in two conformations, pseudo axial and pseudo equatorial. Pickering and Price[20] have shown that in the infrared spectrum of cyclohexanol the absorption at 1069 cm.$^{-1}$ is due to an equatorial carbon–oxygen bond and the absorption at 955 cm.$^{-1}$ is caused by an axial carbon–oxygen bond. Assuming that a pseudo axial hydroxyl group would cause absorption at a lower wave number than a pseudo equatorial hydroxyl group, the infrared spectra of the two isomeric alcohols were compared in the 1000 cm.$^{-1}$ region. The infrared spectrum of *endo* bicyclo[4.2.0]octan-2-ol has only weak absorption below 1000 cm.$^{-1}$, while the *exo* isomer has fairly strong absorption at 990 cm.$^{-1}$. This is interpreted as indicating that in the *endo* isomer the four-membered ring prevents the interconversion of pseudo equatorial and pseudo axial hydroxyl groups while in the *exo* isomer, where the four-membered ring has little or no influence, the normal equilibrium between equatorial and axial conformations is approached.

Fourth, when the relative rates of oxidation of *endo*- and *exo*-bicyclo[4.2.0]octan-2-ol with chromic anhydride in 90% acetic acid were determined spectrophotometrically[13] it was found that the *endo* isomer was oxidized approximately 1.5 times faster than the *exo* isomer. These findings support the stereochemical assignments.[13,14]

Bicyclo[4.2.0]octan-7-ols.—Cycloöctatetraene dibromide was converted to bicyclo[4.2.0]oct-7-ene according to the procedure of Vogel.[21] Bicyclo-

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[17] A. C. Cope and M. Burg, *J. Am. Chem. Soc.*, **74**, 168 (1952).

[18] J. M. Grisar, unpublished research.

[19] B. Ottar, *Acta Chem. Scand.*, **1**, 283 (1947).

[20] R. A. Pickering and C. C. Price, *J. Am. Chem. Soc.*, **80**, 4931 (1958).

[21] E. Vogel, *Angew. Chem.*, **65**, 346 (1953).

[4.2.0]oct-7-ene oxide, prepared in a 68% yield from bicyclo[4.2.0]oct-7-ene and peracetic acid, was reduced with lithium aluminum hydride in 83% yield to a mixture of two compounds present in nearly equal amounts (45 and 55% as shown by gas chromatography). Fractional distillation separated the mixture into its components. The lower boiling material, comprising 55% of the mixture, was identified by its index of refraction, the preparation of two crystalline derivatives and its infrared spectrum as *cis*-2-methylcyclohexanemethanol.[22] The other component was assumed to be bicyclo[4.2.0]octan-7-ol.

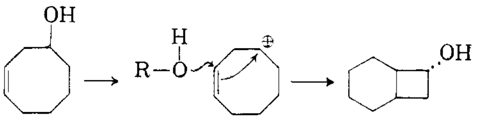
This assumption was validated by the preparation of bicyclo[4.2.0]octan-7-ol by the hydroboration of bicyclo[4.2.0]oct-7-ene followed by oxidation.[12] This reaction produced in a yield of 96% a product that showed a single peak on gas chromatography and that for reasons discussed above[12] was assigned the structure of *exo*-bicyclo[4.2.0]-octan-7-ol. The infrared spectrum of this compound and the infrared spectrum of the higher-boiling component of the mixture produced by the lithium aluminum hydride reduction of bicyclo-[4.2.0]oct-7-ene oxide are identical. Further proof that the alcohols are identical was obtained by a comparison of their phenylurethans (m.p., mixed m.p. and infrared spectra).

exo-Bicyclo[4.2.0]octan-7-ol was oxidized according to the procedure of Nenitzescu[23] to bicyclo-[4.2.0]octan-7-one in 74% yield. The presence of a carbonyl group in a four-membered ring was demonstrated by the strong absorption in the infrared at 1780 cm.$^{-1}$; cyclobutanone itself absorbs at 1775 cm.$^{-1}$.[24] This ketone was reduced in acetic acid over Adams platinum catalyst, yielding 59% of *endo*-bicyclo[4.2.0]octan-7-ol.

The stereochemistry of the bicyclo[4.2.0]octan-7-ols was assigned on the basis of the syntheses; namely, the hydroboration of an olefin followed by oxidation to give predominately the *exo* isomer[12] (gas chromatography showed that the product was essentially homogeneous), and the catalytic reduction in acidic medium of the corresponding ketone.[11] In addition the rates of oxidation of the two bicyclo[4.2.0]octan-7-ols with chromic anhydride in 90% acetic acid were compared. It was found in two separate determinations that the ratio of the rate of oxidation of the *endo* isomer to the rate of oxidation of the *exo* isomer was 1.9 and 2.6. These findings support the stereochemical assignments.[13,14]

A comparison of the infrared spectrum of *endo*-bicyclo[4.2.0]octan-7-ol with the spectrum of the bicyclic alcohol obtained in the formic acid solvolysis of *cis*-cyclooöctene oxide[8] indicated that they are identical. A comparison (m.p., mixed m.p. and infrared spectra) of the phenylurethans confirmed this indication.

The formation of bicyclo[4.2.0]octan-7-ol in the formic acid solvolysis of *cis*-cyclooöctene oxide[8] can be explained through the sequence of changes in eq. 2. This sequence is capable of explaining the *endo* configuration of the product. As illustrated in Fig. 1, *trans* addition of formic acid (R = HCO) or water (R = H) and of the positive center in the 3-cyclooöcten-1-yl carbonium ion to the *cis* double bond would give *endo*-bicyclo[4.2.0]-octan-7-ol as the bridged product.[6] Since 3-cyclooöcten-1-ol is a major product of the solvolysis reaction,[8] it is reasonable to assume that it is an intermediate.



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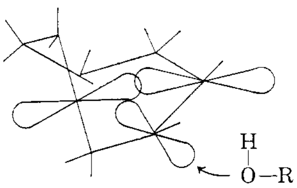

Fig. 1.—Stereospecific formation of *endo*-bicyclo[4.2.0]octan-7-ol.

In eq. 2 the solvent is shown attacking the doubly-bonded carbon atoms in a way that would lead to bicyclo[4.2.0]octan-7-ol; it should be pointed out that it has been demonstrated[6,7] that upon solvolysis with acetic acid at room temperature 3-cyclooöcten-1-yl brosylate yields predominantly *endo*-bicyclo[5.1.0]octan-2-ol. However, it is also significant that *endo*-bicyclo[5.1.0]octan-2-ol on treatment with acetic acid at elevated temperatures rearranges completely to 3-cyclooöcten-1-ol.[7] The possibility remains that during the formic acid solvolysis of *cis*-cyclooöctene oxide at 100°[8] the product formed by solvent attack at the other doubly-bonded carbon atom in the middle figure of eq. 2 reverted to starting material, while the small amount of material formed as shown in eq. 2 was relatively stable under the reaction conditions and remained in the reaction mixture.

The formation of *cis*-2-methylcyclohexanemethanol in the lithium aluminum hydride reduction of bicyclo[4.2.0]oct-7-ene oxide was completely unexpected. An investigation to ascertain how this transformation occurred began with the analysis of bicyclo[4.2.0]oct-7-ene oxide by gas chromatography. This showed that the oxide was a mixture, 87% of which was *exo*-bicyclo[4.2.0]oct-7-ene oxide and 13% of which was *endo*-bicyclo-[4.2.0]oct-7-ene oxide. These two isomers were separated by gas chromatography and separately reduced with lithium aluminum hydride. In the case of the *exo* isomer the products of the reduction, identified by their infrared spectra, were *cis*-2-methylcyclohexanemethanol (55%) and *exo*-bicyclo[4.2.0]octan-7-ol (45%). The lithium aluminum hydride reduction of the *endo* isomer gave a mixture 46% of which was *endo*-bicyclo[4.2.0]-octan-7-ol and 54% of which was *cis*-2-methylcyclohexanemethanol, based on analysis by gas chromatography. It was thus demonstrated that both *endo*- and *exo*-bicyclo[4.2.0]oct-7-ene oxides undergo the anomalous ring opening with equal facility, within the limits of experimental error.

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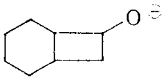
[22] A. K. Macbeth, J. A. Mills and D. H. Simmonds, *J. Chem. Soc.*, 1011 (1949).

[23] M. Avram, C. D. Nenitzescu and M. Maxim, *Chem. Ber.*, **90**, 1424 (1957).

[24] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p. 149.

In order to investigate the possibility that the alcohols themselves were transformed to the monocyclic product in a manner similar to that proposed[25] for the conversion of *trans*-cycloöctene oxide to hexahydro-*o*-tolualdehyde, the pure *endo*- and *exo*-bicyclo[4.2.0]octan-7-ols were subjected to the conditions of the lithium aluminum hydride reduction. In both cases only the original alcohol was recovered.

It is obvious then that the first step in the conversion of bicyclo[4.2.0]oct-7-ene oxide to *cis*-2-methylcyclohexanemethanol cannot be the hydride cleavage of the carbon–oxygen bond of the oxide ring, which would lead to the same anions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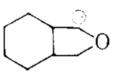
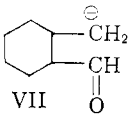

VI



VII

(V) formed by treating the pure alcohols with lithium aluminum hydride. This leads to the conclusion that the carbon–carbon bond of the oxide ring is first attacked by the reagent forming VI which in some way is converted to *cis*-2-methylcyclohexanemethanol. It has been suggested[26] that VII is a tautomeric form of VI and that this form would be reduced under the conditions of the reaction to *cis*-2-methylcyclohexanemethanol.

Bicyclo[4.2.0]octan-1-ol.—The seventh alcohol in the series was prepared by the ozonization of bicyclo[4.2.0]octane. A solution of pure (one peak on gas chromatography) bicyclo[4.2.0]octane in carbon tetrachloride was ozonized according to the procedure of Adkins.[27] When the ozonide was hydrolyzed and the neutral products were isolated it was found that eight components were present (as indicated by gas chromatography). Using gas chromatography the two major products (comprising 43 and 31% of the mixture) were collected. One (31%) was identified as bicyclo[4.2.0]-octan-2-one by its infrared spectrum, and the other (43%) was an alcohol, the infrared spectrum of which was different from the spectra of all of the six previously characterized bicyclo[4.2.0]octanols. The infrared spectra of *cis*-bicyclo[3.3.0]octan-1-ol[28] and an alcohol thought to be *trans*-bicyclo-[3.3.0]octan-1-ol[29] were also different from the spectrum of the ozonolysis product.

Further, an examination of the infrared spectrum of the ozonolysis product showed no absorption bands in the 3000 cm.$^{-1}$ region that could be attributed to unsaturation or to a cyclopropane ring. Thus by considering the elemental analysis, which indicates a saturated bicycloöctanol or a cyclooctenol, and by eliminating the other possible systems, the conclusion that the bicyclo[4.2.0]-octane ring system is present becomes inescapable. The alcohol was proved to be tertiary by the fact that it was not oxidized by chromic anhydride in 90% acetic acid (observed spectrophotometrically).

Experimental[30]

Bicyclo[4.2.0]oct-3-ene Oxide.—According to the procedure of Alder and Dortmann[10] 8.06 g. (35%) of bicyclo-[4.2.0]oct-3-ene was prepared from 60 g. of diethyl tetrahydrophthalate. To a solution of 11 g. of bicyclo[4.2.0]-oct-3-ene in 3 ml. of glacial acetic acid was added with vigorous stirring a mixture of 25.3 g. of commercial 40% peracetic acid and 5.6 g. of sodium acetate trihydrate. During the addition, which required 0.5 hr., and until the exothermic reaction subsided (1.3 hr.) the temperature of the reaction mixture was maintained below 29°. The mixture was cooled to 0°, neutralized in the cold with 35% sodium hydroxide and extracted with five 50-ml. portions of ether. The extracts were dried (magnesium sulfate), concentrated and the residue distilled under reduced pressure through a semi-micro column. The yield of bicyclo-[4.2.0]oct-3-ene oxide, b.p. 90–92.5° (38 mm.), $n^{25}\mathrm{D}$ 1.4820–1.4840, was 8.85 g. (69%). A sample with $n^{25}\mathrm{D}$ 1.4822 was analyzed.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.46; H, 9.87.

When a sample of bicyclo[4.2.0]oct-3-ene oxide was subjected to gas chromatography at 135° using a column packed with 30% 1,2,3-tris-(2-cyanoethoxy)-propane (T-CEP) on base-washed firebrick it was found that the sample was a mixture of 87% *exo*- and 13% *endo*-bicyclo[4.2.0]-oct-3-ene oxides. Collection using gas chromatography followed by short-path distillation at 12 mm. with a bath temperature of 90° gave *endo*-bicyclo[4.2.0]oct-3-ene oxide, $n^{25}\mathrm{D}$ 1.4848.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.46; H, 9.61.

exo-Bicyclo[4.2.0]oct-3-ene oxide was isolated in the same way; $n^{25}\mathrm{D}$ 1.4814.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.44; H, 9.85.

***exo*-Bicyclo[4.2.0]octan-3-ol.**—To a suspension of 0.150 g. of lithium aluminum hydride in 5 ml. of anhydrous ether was added dropwise with stirring a solution of 0.250 g. of *exo*-bicyclo[4.2.0]oct-3-ene oxide in 3 ml. of ether. After the addition was completed the reaction mixture was refluxed for 1 hr., cooled in an ice-bath and treated with 1 ml. of water followed by enough 20% sulfuric acid to dissolve precipitated salts. The aqueous layer was separated and extracted with three 5-ml. portions of ether. The extracts were combined with the original ether layer and after drying (magnesium sulfate) the solution was concentrated and the residue was distilled under reduced pressure in a short-path still at 12 mm. with a bath temperature of 90°, yielding 0.202 g. (80%) of *exo*-bicyclo[4.2.0]octan-3-ol, $n^{25}\mathrm{D}$ 1.4885.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.13; H, 11.17.

The phenylurethan was prepared and after three recrystallizations from pentane had m.p. 67.5–69.5°.

Anal. Calcd. for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.50; H, 8.02.

The 3,5-dinitrobenzoate was prepared and after several recrystallizations from ethanol had m.p. 68.5–69.5°.

Anal. Calcd. for $C_{15}H_{16}N_2O_6$: C, 56.25; H, 5.04; N, 8.75. Found: C, 56.29; H, 5.06; N, 8.67.

***endo*-Bicyclo[4.2.0]octan-3-ol.**—Using a procedure similar to that described for the *exo* isomer, 0.048 g. (61%) of *endo*-bicyclo[4.2.0]octan-3-ol was prepared from 0.078 g. of *endo*-bicyclo[4.2.0]oct-3-ene oxide by reduction with 0.100 g. of lithium aluminum hydride. The product had $n^{25}\mathrm{D}$ 1.4888.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.08; H, 11.24.

The phenylurethan was prepared and after three recrystallizations from pentane had m.p. 82.5–83.5°.

Anal. Calcd. for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.48; H, 7.70.

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

[26] W. R. Moore, private communication.

[27] R. Durland and H. Adkins, *J. Am. Chem. Soc.*, **61**, 429 (1939).

[28] A. C. Cope, J. M. Grisar and P. E. Peterson, *ibid.*, **82**, 4299 (1960).

[29] J. Martin Grisar, Ph.D. Thesis, Massachusetts Institute of Technology, 1959.

[30] Melting points are corrected and boiling points are uncorrected. We are indebted to Dr. S. M. Nagy and his associates for analyses.

The 3,5-dinitrobenzoate was prepared and after several recrystallizations from ethanol had m.p. 102.5–104.5°.

Anal. Calcd. for $C_{15}H_{16}N_2O_6$: C, 56.25; H, 5.04; N, 8.75. Found: C, 56.15; H, 4.93; N, 8.63.

Bicyclo[4.2.0]octan-3-one.—A mixture of *endo*- and *exo*-bicyclo[4.2.0]octan-3-ol was prepared in 89% yield by the reduction of 8.05 g. of bicyclo[4.2.0]oct-3-ene oxide with 3.5 g. of lithium aluminum hydride according to the procedure described above for the reduction of the pure isomers. The product was collected by distillation under reduced pressure through a semi-micro column and had b.p. 76.0–76.5° (4 mm.), $n^{25}D$ 1.4904–1.4908.

A solution of 1.5 g. of this mixture in 25 ml. of pyridine was added dropwise with stirring to the complex formed from 4.5 g. of chromic anhydride and 22.5 ml. of pyridine. The reaction mixture was stirred at room temperature for 2 days and poured into a mixture of 150 ml. of water and 50 ml. of ether. The brown solid that separated was collected by filtration and triturated with ether. The filtrate was extracted with three 30-ml. portions of ether and the extracts were combined with the extracts of the brown solid. The resulting ether solution was washed with dilute hydrochloric acid until the washings were acidic. Dissolved hydrochloric acid was removed by washing with dilute sodium bicarbonate solution and the ether solution was dried over magnesium sulfate. The solution was concentrated and the residue was distilled under reduced pressure through a semi-micro column. The yield of bicyclo[4.2.0]octan-2-one, b.p. 104–106° (34 mm.), $n^{25}D$ 1.4802–1.4816, was 0.99 g. (67%).

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.19; H, 9.51.

The 2,4-dinitrophenylhydrazone was recrystallized twice from ethanol and had m.p. 120.5–122.0°.

Anal. Calcd. for $C_{14}H_{16}N_4O_4$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.51; H, 5.22; N, 18.57.

Catalytic Reduction of Bicyclo[4.2.0]octan-3-one.—A solution of 2.72 g. of bicyclo[4.2.0]octan-3-one in 30 ml. of glacial acetic acid, to which 6 drops of concentrated hydrochloric acid had been added, was reduced over 0.5 g. of Adams platinum catalyst at room temperature and atmospheric pressure. After 7.7 hr. 98% of 1 molar equivalent of hydrogen had been absorbed. The catalyst was removed from the reaction mixture by filtration and washed with 50 ml. of 50% methanol. The diluted reaction mixture was treated with excess methanolic sodium hydroxide and refluxed for 4 hr. The reaction mixture was extracted with four 100-ml. portions of ether, and the combined extracts were dried over magnesium sulfate. The solution was concentrated and the residue distilled under reduced pressure through a semi-micro column, yielding 1.93 g. (70%) of *endo*-bicyclo[4.2.0]octan-3-ol, b.p. 74–76° (3.7 mm.), $n^{25}D$ 1.4900.

The phenylurethan was prepared and after four recrystallizations from pentane had m.p. 82.5–83.5°. The melting point of a mixture of this compound and the phenylurethan of *endo*-bicyclo[4.2.0]octan-3-ol described above was not depressed.

Bicyclo[4.2.0]octan-3-ol by the Hydroboration of Bicyclo[4.2.0]oct-3-ene Followed by Oxidation.—Under an atmosphere of nitrogen and at 0° an excess of diborane was bubbled into a solution of 5.9 g. of bicyclo[4.2.0]oct-3-ene in 80 ml. of tetrahydrofuran. The diborane was generated over a period of 1 hr. by dropping a solution of 1.5 g. of sodium borohydride in 100 ml. of diglyme into a solution of 8.0 g. of boron trifluoride etherate in 40 ml. of diglyme. The exit gases were passed through acetone to destroy excess diborane. The reaction mixture was allowed to come to room temperature over a period of 1 hr. and treated with several small pieces of ice, after which it was cooled in an ice-bath and treated with 20 ml. of 3 *N* sodium hydroxide. At 0° and with mechanical stirring 10 ml. of 30% hydrogen peroxide was added dropwise, after which the reaction mixture was allowed to come to room temperature and stirred overnight. The aqueous layer was separated and extracted with four 50-ml. portions of ether. The ether extracts were combined with the original non-aqueous layer, washed with two 10-ml. portions of brine, and dried over magnesium sulfate. The ether solution was concentrated and the residue was distilled under reduced pressure through a semi-micro column. After a sizable forerun containing about 3.5 g. of olefin, 1.28 g. (19%) of bicyclo[4.2.0]octan-3-ol (predominantly the *exo* isomer as indicated by the infrared spectrum) was obtained.

***exo*-Bicyclo[4.2.0]octan-2-ol.**—According to the procedure of Cope and Burg,[17] 107 g. (70%) of cycloöctatetraene dibromide was prepared from 60 g. of cycloöctatetraene and 91.5 g. of bromine. Following the procedure of Reppe,[15] 44.7 g. of cycloöctatetraene dibromide was converted to 7.8 g. (16%) of the monoepoxide with 42 ml. of commercial peracetic acid.

A solution of 12 g. of the monoepoxide of cycloöctatetraene dibromide in 100 ml. of anhydrous ether was added dropwise with stirring to a suspension of 1.9 g. of lithium aluminum hydride in 100 ml. of anhydrous ether. After the addition was completed (1.3 hr.) the reaction mixture was refluxed for 5.5 hr. and stirred overnight. The reaction mixture was cooled and treated with 15 ml. of water followed by enough 20% sulfuric acid to dissolve the lithium and aluminum salts. The aqueous layer was separated and extracted with five 50-ml. portions of ether. The ether extracts were combined with the original ether layer and dried over magnesium sulfate. After evaporation of the ether in a rotary evaporator there remained 10.8 g. (89%) of a yellow oil.

A solution of 5 g. of the crude oil in 15 ml. of methanol was placed in a 50-ml. stainless steel bomb with a mixture of 1.7 g. of potassium hydroxide, 2 ml. of water and 0.4 g. of Raney nickel. With an initial hydrogen pressure of 2040 p.s.i. the bomb was heated to 80° and rocked for 18 hr. The contents of the bomb were removed by rinsing with ether and water and the catalyst was removed by filtration. The aqueous layer was separated and extracted with four 50-ml. portions of ether. The extracts were combined with the original ether washings and washed with 10% hydrochloric acid followed by 5% sodium bicarbonate. After drying over magnesium sulfate the solution was concentrated and the residue was distilled through a semi-micro column, yielding 1.38 g. (62%) of *exo*-bicyclo[4.2.0]-octan-2-ol, b.p. 80–81° (5.5 mm.). Fractionation through a 31 × 0.75-cm. spinning-band column gave an analytical sample, $n^{25}D$ 1.4895.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.01; H, 11.16.

The phenylurethan was recrystallized three times from aqueous ethanol and had m.p. 76.5–77.5°.

Anal. Calcd. for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.45; H, 7.74.

***exo*-Bicyclo[4.2.0]octan-2-ol from Cycloöctatetraene Dichloride Monoepoxide.**—Cycloöctatetraene dichloride was prepared in 93% yield from 125 g. of freshly distilled cyclooctatetraene and 110 g. of chlorine.[17] The dichloride was converted to its monoepoxide with peracetic acid in 60% yield and separated into a solid isomer and a liquid isomer or mixture of isomers according to the procedure of Reppe.[15]

exo-Bicyclo[4.2.0]octan-2-ol was prepared in 79% yield from the solid monoepoxide of cycloöctatetraene dichloride by a procedure identical to that described above. Similar treatment of the liquid isomer or mixture of isomers gave a 76% yield of a mixture of two components (presumably *endo*- and *exo*-bicyclo[4.2.0]octan-2-ols) that could not be separated practically using gas chromatography on silicone oil or TCEP columns at 170°.

Bicyclo[4.2.0]octan-2-one.—To the cooled complex formed from 2.5 g. of chromic anhydride and 25 ml. of pyridine was added dropwise with stirring a solution of 1.01 g. of *exo*-bicyclo[4.2.0]octan-2-ol in 10 ml. of pyridine. The reaction mixture was allowed to stir at room temperature for 8 days (24 hr. is probably sufficient) and was poured into 150 ml. of ice-water. The mixture was extracted with two 50-ml. and four 30-ml. portions of ether. The ether extracts were combined and by following the procedure outlined above for bicyclo[4.2.0]octan-3-one, 0.59 g. (60%) of bicyclo[4.2.0]octan-2-one, b.p. 89–91° (18 mm.), $n^{25}D$ 1.4790–1.4800, was obtained.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.29; H, 9.83.

The 2,4-dinitrophenylhydrazone was recrystallized repeatedly from absolute ethanol and had m.p. 179.5–180°.

Anal. Calcd. for $C_{14}H_{16}N_4O_4$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.18; H, 5.17; N, 18.43.

***endo*-Bicyclo[4.2.0]octan-2-ol.**—A solution of 2.3 g. of bicyclo[4.2.0]octan-2-one in 30 ml. of acetic acid to which 6 drops of concentrated hydrochloric acid had been added was reduced over 0.5 g. of platinum oxide (prereduced) at room temperature and atmospheric pressure. After 28 hr. 90% of 1 molar equivalent of hydrogen had been absorbed. The reaction mixture was filtered and the catalyst was washed with methanol. Treatment of the resulting solution according to the procedure described under the catalytic reduction of bicyclo[4.2.0]octan-3-one gave 1.78 g. (76%) of *endo*-bicyclo[4.2.0]octan-2-ol, b.p. 72–73.5° (3.7 mm.), the last two fractions of which had $n^{25}\text{D}$ 1.4911.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.06; H, 11.23.

The phenylurethan, recrystallized from aqueous methanol, had m.p. 92.8–93.8°.

Anal. Calcd. for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.25; H, 7.81.

Bicyclo[4.2.0]oct-7-ene Oxide.—Cycloöctatetraene dibromide[17] was converted to bicyclo[4.2.0]oct-7-ene in 56% yield according to the procedure of Vogel.[21] To a solution of 1.83 g. of bicyclo[4.2.0]oct-7-ene in 3 ml. of glacial acetic acid, 7.5 ml. of 40% peracetic acid, to which 1.8 g. of sodium acetate trihydrate had been added, was added over a period of 15 min. with vigorous stirring. During the addition and for 2 hr. afterward the temperature of the reaction mixture was maintained between 22° and 29°. The mixture was diluted with 15 ml. of water, neutralized at 0° with 25% sodium hydroxide, and allowed to come to room temperature. The product was extracted with four 50-ml. portions of ether. The combined extracts were washed with water and brine and dried over magnesium sulfate. After distillation of the ether the residue was fractionated under reduced pressure through a semi-micro column yielding 1.54 g. (68%) of bicyclo[4.2.0]oct-7-ene oxide, b.p. 82.0–84.5° (26 mm.). The last two fractions had $n^{25}\text{D}$ 1.4780.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.11; H, 9.90.

Gas chromatography (30% silicone oil column at 170°) indicated that the product was a mixture of *endo*- and *exo*-bicyclo[4.2.0]oct-7-ene oxides present as 13 and 87% of the total, respectively. The two isomers were collected using gas chromatography. The *exo* isomer had $n^{25}\text{D}$ 1.4781.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.18; H, 9.74.

Lithium Aluminum Hydride Reduction of Bicyclo[4.2.0]-oct-7-ene Oxide.—A solution of 5.7 g. of bicyclo[4.2.0]-oct-7-ene oxide in 50 ml. of ether was added dropwise to a stirred suspension of 1.65 g. of lithium aluminum hydride in 100 ml. of ether. After the addition was completed (0.5 hr.) the reaction mixture was refluxed for 3 hr. and excess lithium aluminum hydride was destroyed by the cautious addition of 5 ml. of water. The precipitated salts were dissolved by the addition of 20% sulfuric acid and the aqueous layer was separated and extracted with four 30-ml. portions of ether. The combined ether solutions were dried and concentrated and the residue was fractionated under reduced pressure through a semi-micro column, yielding 4.84 g. (83%) of product, b.p. 86–88° (5 mm.), $n^{25}\text{D}$ 1.4697–1.4792. Fractionation through a 100 × 0.5-cm. spinning-band column separated the mixture into *cis*-2-methylcyclohexanemethanol (phenylurethan m.p. 47.5–49.5°, lit.[22] 47–48°; 3,5-dinitrobenzoate m.p. 93–94°, lit.[22] 92–93°) and bicyclo[4.2.0]octan-7-ol, $n^{25}\text{D}$ 1.4852.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 75.95; H, 10.98.

The phenylurethan was repeatedly recrystallized from pentane and had m.p. 128–129°.

Anal. Calcd. for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.29; H, 7.57.

Analysis by gas chromatography (30% TCEP column at 140°) showed that the initial mixture was composed of 55% *cis*-2-methylcyclohexanemethanol and 45% bicyclo-[4.2.0]octan-7-ol.

Bicyclo[4.2.0]octan-7-one.—To the cooled complex prepared from 25 g. of chromic anhydride and 250 ml. of pyridine was added dropwise with stirring a solution of 10.4 g. of bicyclo[4.2.0]octan-7-ol in 100 ml. of pyridine. After the addition was completed (1 hr.) the reaction mixture was stirred for 4 days at room temperature and then at 45° for 3 hr. The reaction mixture was poured into 1500 ml. of ice-water and extracted with five 300-ml. portions of ether. The ether extracts were combined and by following the procedure outlined above for bicyclo[4.2.0]octan-3-one, 7.6 g. (74%) of bicyclo[4.2.0]octan-7-one, b.p. 89–90.5° (25 mm.), $n^{25}\text{D}$ 1.4723–1.4730, was obtained.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.15; H, 9.78.

The 2,4-dinitrophenylhydrazone, recrystallized several times from absolute ethanol, had m.p. 114–115°.

Anal. Calcd. for $C_{14}H_{16}N_4O_4$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.05; H, 5.33; N, 18.27.

***endo*-Bicyclo[4.2.0]octan-7-ol.**—A solution of 7.58 g. of bicyclo[4.2.0]octan-7-one in 75 ml. of glacial acetic acid to which 15 drops of concentrated hydrochloric acid had been added was reduced over 1.2 g. of platinum oxide (prereduced) at room temperature and atmospheric pressure. After 4 hr., when 108% of 1 molar equivalent of hydrogen had been absorbed, the reaction mixture was filtered and neutralized with aqueous sodium hydroxide. A 1.5 molar excess of sodium hydroxide was added and the mixture was refluxed for 8 hr. The reaction mixture was extracted with four 200-ml. portions of ether and the combined extracts were washed with brine and dried over magnesium sulfate. After the ether had been distilled the residue was fractionated under reduced pressure through a semi-micro column yielding 4.54 g. (59%) of *endo*-bicyclo[4.2.0]octan-7-ol, b.p. 81–82.5° (5 mm.), $n^{25}\text{D}$ 1.4892.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.23; H, 11.14.

The phenylurethan (m.p. 119.5–120°) was reported in a previous publication.[8]

***exo*-Bicyclo[4.2.0]octan-7-ol by the Hydroboration of Bicyclo[4.2.0]oct-7-ene Followed by Oxidation.**—Following the procedure described above for bicyclo[4.2.0]octan-3-ol, a solution of 5.40 g. of bicyclo[4.2.0]oct-7-ene in 60 ml. of tetrahydrofuran was treated with the diborane produced from 1.0 g. of sodium borohydride in 60 ml. of diglyme and 5.5 g. of boron trifluoride etherate in 20 ml. of diglyme. The solution of the trialkylborane was cooled to 0°, made basic by the addition of 15 ml. of 15% sodium hydroxide, and treated with 8 ml. of 30% hydrogen peroxide. Following the procedure outlined above, 6.01 g. (96%) of *exo*-bicyclo[4.2.0]octan-7-ol, b.p. 100–102.5° (13 mm.), was obtained from the reaction mixture. This material was shown to be homogeneous by gas chromatography at 170° on a TCEP column (conditions known to separate the *endo* and *exo* isomers). The fact that the alcohol prepared in this way and the bicyclic alcohol prepared by the lithium aluminum hydride reduction of bicyclo[4.2.0]oct-7-ene oxide are identical was demonstrated by a comparison of the infrared spectra and the phenylurethans (m.p., mixed m.p. and infrared spectra).

Reaction of *endo*- and *exo*-Bicyclo[4.2.0]octan-7-ol with Lithium Aluminum Hydride.—To a suspension of 0.2 g. of lithium aluminum hydride in 10 ml. of ether a solution of 0.250 g. of *endo*-bicyclo[4.2.0]octan-7-ol in 3 ml. of ether was added dropwise with stirring. The reaction mixture was refluxed for 2 hr., cooled to 0°, and treated with 1 ml. of water and enough 20% sulfuric acid to dissolve the precipitated salts. The aqueous layer was separated and extracted with three 15-ml. portions of ether. The extracts were combined with the original ether layer and washed successively with sodium bicarbonate solution, water and brine. After drying over magnesium sulfate the ether was distilled leaving a small residue, which upon distillation in a short-path still yielded 0.20 g. (84%) of the starting material, *endo*-bicyclo[4.2.0]octan-7-ol, identified by its infrared spectrum.

Similar treatment of 0.250 g. of *exo*-bicyclo[4.2.0]octan-7-ol with 0.2 g. of lithium aluminum hydride afforded 0.180 g. (72%) of the unchanged starting material, identified by its infrared spectrum.

Reduction of *endo*- and *exo*-Bicyclo[4.2.0]oct-7-ene Oxide with Lithium Aluminum Hydride.—A solution of 0.143 g. of *exo*-bicyclo[4.2.0]oct-7-ene oxide in 3 ml. of ether was added dropwise with stirring to a suspension of 0.15 g. of lithium aluminum hydride in 10 ml. of ether. The reaction mixture was refluxed for 1 hr., cooled, and treated with 1 ml. of water and enough 20% sulfuric acid to dissolve the precipitated salts. The aqueous layer was separated and extracted with three 10-ml. portions of ether. The ether extracts were combined with the original ether layer and washed successively with sodium bicarbonate solution, water and brine. After drying over magnesium sulfate

TABLE I

RELATIVE RATES OF OXIDATION OF *endo*- AND *exo*-BICYCLO-[4.2.0]OCTAN-X-OLS

X	Concn. CrO_3, *M*	Concn. ROH, *M*	Half-time *exo*/half-time *endo*
3[a]	0.00107	0.00073	1.02
3[a]	.00071	.0097	1.3
3[b]	.00081	.0013	1.04
3[b]	.00054	.0017	1.0
2	.000908	.00109	1.43
2	.000605	.00145	1.55
7	.00117	.000638	1.9
7	.000782	.000426	2.6

[a] The *endo*- and *exo*-bicyclo[4.2.0]octan-3-ols were obtained by the lithium aluminum hydride reduction of pure *endo*- and *exo*-bicyclo[4.2.0]oct-3-ene oxides. [b] The *endo*-bicyclo[4.2.0]octan-3-ol was obtained by the catalytic reduction of bicyclo[4.2.0]octan-3-one; the *exo*-bicyclo-[4.2.0]octan-3-ol was obtained by the lithium aluminum hydride reduction of a mixture of *endo*-(13%) and *exo*-bicyclo[4.2.0]oct-3-ene (87%) oxides.

the solution was concentrated and the residue was distilled in a short-path still at 10 mm. with a bath temperature of 120° yielding 0.110 g. (76%) of colorless liquid. Separation of the product into its two components by gas chromatography at 170° on a TCEP column and identification of the components by their infrared spectra showed that the mixture was composed of 55% of *cis*-2-methylcyclohexanemethanol and 45% of *exo*-bicyclo[4.2.0]octan-7-ol.

Following a similar procedure 0.032 g. of *endo*-bicyclo-[4.2.0]oct-7-ene oxide[31] was treated with 0.060 g. of lithium aluminum hydride. Due to the small scale of the reaction, the product was analyzed by gas chromatography. This analysis indicated that the product contained 54% of *cis*-2-methylcyclohexanemethanol and 46% of *endo*-bicyclo[4.2.0]-octan-7-ol.

Relative Rates of Oxidation of *endo* and *exo* Isomers in the Bicyclo[4.2.0]octanol Series.—According to the procedure of Schreiber and Eschenmoser,[13] the relative rates of oxidation of *endo*- and *exo*-bicyclo[4.2.0]octanols with chromic anhydride in 90% acetic acid were determined spectrophotometrically. The results are summarized in Table I.

Bicyclo[4.2.0]octan-1-ol.—7,8-Dichlorobicyclo[4.2.0]-octane was prepared in 84% yield from cycloöctatetraene.[21] This material was catalytically reduced over Raney nickel in 65% yield to bicyclo[4.2.0]octane.[15] A solution of 6.0 g. of bicyclo[4.2.0]octane in 45 ml. of carbon tetrachloride was ozonized at 0° with an oxygen flow rate of approximately 75 ml. per min. containing approximately 5% ozone. After 24 hr. the clear viscous oil that collected on the surface of the solution was removed and the reaction tube was washed with acetone. The carbon tetrachloride solution was returned to the reaction tube and the ozonization was continued for another 20 hr. The carbon tetrachloride solution and the viscous ozonide on the surface were dissolved in acetone and this solution was combined with the acetone solution of the ozonide previously collected. The solvents were removed with a rotary evaporator leaving 6.8 g. of a yellow oil. This oil was heated with 100 ml. of water at 60° for 3 hr. and allowed to stand at room temperature overnight. The mixture was extracted with three 50-ml. portions of ether. The combined extracts were washed with 10 ml. of water, three 10-ml. portions of 20% sodium carbonate solution, water and brine, and then dried over magnesium sulfate. The solution was concentrated and the residue was fractionated under reduced pressure through a semi-micro column, yielding 1.42 g. of material boiling between 58° (50 mm.) and 82° (1.5 mm.). Two fractions boiling at 84° (10 mm.) totaling 0.472 g. had infrared spectra that showed the presence of hydroxyl and carbonyl groups. Upon gas chromatography it was found that these two fractions were mixtures of at least eight components. The major component amounting to approximately 43% of the mixture was collected by gas chromatography, yielding 94 mg. (1.3%) of bicyclo[4.2.0]octan-1-ol as a semi-solid material, which, after two sublimations at 100° (atmospheric pressure), had m.p. 52–53°.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.05; H, 11.20.

The phenylurethan was recrystallized to a constant melting point from aqueous ethanol and had m.p. 116.5–117.5°.

Anal. Calcd. for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.29; H, 8.02.

The second largest component of the mixture (31%) was also collected using gas chromatography and identified by its infrared spectrum as bicyclo[4.2.0]octan-2-one.

Attempted Oxidation of Bicyclo[4.2.0]octan-1-ol.—A solution of 0.59 mg. of bicyclo[4.2.0]octan-1-ol in 1 ml. of 90% acetic acid was treated with 2 ml. of 0.000629 *M* chromic anhydride in 90% acetic acid. The optical density of the reaction mixture at 348 mμ as observed with a Beckman DU spectrophotometer did not change appreciably over a period of 2.3 hr.

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[31] This compound was homogeneous according to gas chromatography (silicone oil at 170°), but was not obtained in sufficient quantity for elemental analysis.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Proximity Effects. XXIV. *endo*- and *exo*-Bicyclo[5.1.0]octan-2-ol and Solvolyses of their Derivatives[1,2]

BY ARTHUR C. COPE, SUNG MOON AND PAUL E. PETERSON[3]

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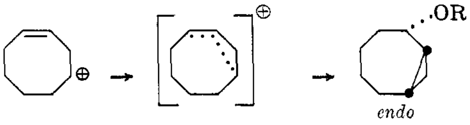
endo- and *exo*-Bicyclo[5.1.0]octan-2-ol were obtained from the solvolysis of 3-cycloöcten-1-yl brosylate and separated by chromatography on alumina. Their configurations have been established. Solvolysis of the alcohols in acetic acid containing perchloric acid gave *exo*-bicyclo[5.1.0]octan-2-ol, 3-cycloöcten-1-ol, *endo*- and *exo*-bicyclo[5.1.0]oct-2-yl acetate and 3-cycloöcten-1-yl acetate. These products are similar to those obtained from the solvolysis of 3-cycloöcten-1-yl brosylate. Possible reaction mechanisms including one involving intervention of a bridged carbonium ion intermediate are discussed.

The solvolysis of 3-cycloöcten-1-yl brosylate yields bicyclo[5.1.0]octan-2-ol in addition to the normal product, 3-cycloöcten-1-ol.[4] A mechanism can be written for the formation of these products, in which a bridged carbonium ion II is formed



I II III

The existence of such a hybrid carbonium ion has been proposed in the cholesteryl and 3,5-cyclo-

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[2] Paper XXIII, A. C. Cope and R. W. Gleason, *J. Am. Chem. Soc.*, **84**, 1928 (1962).

[3] National Institutes of Health Postdoctoral Fellow, 1956–1958.

[4] A. C. Cope and P. E. Peterson, *J. Am. Chem. Soc.*, **81**, 1643 (1959).