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.

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

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.

[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]

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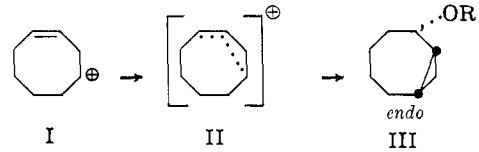
RECEIVED MARCH 3, 1961

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-

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

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

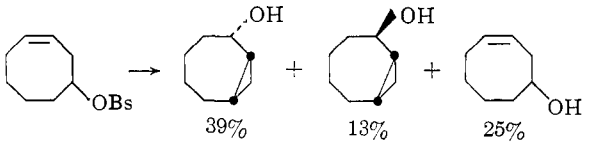
(3) National Institutes of Health Postdoctoral Fellow, 1956–1958.

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

cholestan-6-yl (*i*-cholesteryl) systems,[5] and to support this theory, the identity of the solvolysis products of cholesteryl tosylate and 3,5-cyclocholestan-6β-yl trichloroacetate was taken to indicate a common cationic intermediate analogous to II for the reactions involved.

In order to obtain a clearer understanding of the nature of the intermediate in the solvolysis of 3-cycloöcten-1-yl brosylate, the present study was undertaken to investigate the solvolysis of bicyclo[5.1.0]octan-2-ol and 3-cycloöcten-1-ol derivatives which might occur by SN1 reactions.

Stereochemistry of the Bicyclo[5.1.0]octan-2-ols.—The stereochemistry of the bicyclo[5.1.0]-octan-2-ol obtained from the solvolysis of 3-cyclooctenyl-1-yl brosylate has not been determined, but it was predicted[4] that the alcohol would be principally the *endo* isomer from mechanistic considerations (assuming that the solvolysis was a concerted process or proceeded *via* a bridged ion intermediate). In the present study the bicyclic alcohol obtained from a repetition of the solvolysis of 3-cycloöcten-1-yl brosylate[4] was shown to be a mixture of two components by gas chromatography on Silicone oil. These two components were later identified as *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol. The relative amounts of the *endo* and *exo* isomers were estimated to be 75 and 25%. In addition some 3-cycloöcten-1-ol was obtained as reported previously. The products of solvolysis and yields in which they were obtained in this study are



It was possible to separate the two bicyclic alcohols by chromatography on alumina. The separation was shown to be complete by gas chromatography of the fractions on Silicone oil. It has been reported,[5,6] that the hindered nature of an axial hydroxyl substituent on a cyclohexane ring as compared with an equatorial substituent causes an axial alcohol to be more weakly adsorbed on alumina than its equatorial epimer. Study of models of *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol showed that the hydroxyl group of the *endo* isomer is much more hindered than that of the *exo* isomer. Therefore, the *endo* isomer would be expected to be eluted more easily than the *exo* isomer. Experimentally the epimer formed in larger amount in the solvolysis reaction was eluted more easily and this finding constitutes one portion of the evidence which led to the assignment of the *endo* configuration to this isomer.

The infrared spectra of the isomers supported the assignment of configurations noted above. The spectrum of the *exo* isomer showed a much larger peak at 3100–3600 cm.$^{-1}$ corresponding to a hydrogen-bonded hydroxyl group than did the spectrum of the *endo* isomer. This finding reflects the steric hindrance to hydrogen bonding expected to be present in the *endo* isomer.

Since the *exo* isomer would be predicted to be thermodynamically more stable than the *endo* isomer, it should be possible to convert the *endo* isomer to the more stable *exo* form. In fact, the *endo* isomer was partially converted to the *exo* isomer under Meerwein-Ponndorf conditions to the extent of 65%. However, the amount of the *exo* isomer present at equilibrium is not necessarily 65%. It was not practical to follow the isomerization until equilibrium was reached because continued heating partially converted the bicyclic alcohols to 3-cycloöcten-1-ol.

Additional support for the assignment of configurations to the bicyclic alcohols comes from the work of Simmons and Smith.[7] One of the features of the reaction of an olefin with methylene iodide and zinc-copper couple is that a cyclopropane ring is formed by addition of a methylene group to the less hindered position of the unsaturated compound. Accordingly, it would be predicted that the reaction of 2-cyclohepten-1-yl acetate with methylene iodide and zinc-copper couple would, after hydrolysis, give *exo*-bicyclo[5.1.0]octan-2-ol, in which the methylene group has been added from the side opposite to the acetoxy group. In fact, the product[8] had an infrared spectrum identical with that of the isomer assigned the *exo* configuration on the basis of the other experiments just described.

From the above five criteria, the configurations of *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol were assigned. The skeletal structure of the *exo* isomer is known from the synthesis of this isomer accomplished *via* methylene iodide and zinc-copper couple.[7] In this study a sample of the *endo* isomer was oxidized to the same ketone as that obtained previously[4] from the *exo* isomer and from a mixture of *endo* and *exo* isomers obtained from solvolysis. This demonstrates that both isomers are in fact epimeric bicyclo[5.1.0]octan-2-ols.

Solvolyses of Alcohols and Esters.—Several attempts were made to obtain crystalline arylsulfonic acid esters of *endo*-bicyclo[5.1.0]octan-2-ol, all without success. Solvolysis of *endo*- and *exo*-bicyclo[5.1.0]oct-2-yl *p*-nitrobenzoate in acetic acid containing sodium acetate at 120° for forty-eight hours yielded 3-cycloöcten-1-yl acetate. Later, it was shown that these are conditions under which the bicyclo[5.1.0]oct-2-yl acetates, if initially formed, would have rearranged to 3-cycloöcten-1-yl acetate. The solvolysis of *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol at room temperature for twelve hours in acetic acid solution containing 0.5% by weight of 70% aqueous perchloric acid gave principally 3-cycloöcten-1-yl acetate and some 3-cyclooctenyl-1-ol. These products are the ones that would be expected from the solvolysis under reversible (equilibrating) conditions.[9]

(5) E. M. Kosower and S. Winstein, *J. Am. Chem. Soc.*, **78**, 4347 (1956).

(6) (a) S. Winstein and N. J. Holness, *ibid.*, **77**, 5562 (1955); (b) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953); (c) K. Savard, *J. Biol. Chem.*, **202**, 457 (1953).

(7) H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **81**, 4256 (1959).

(8) Prepared by H. E. Simmons and described in ref. 4.

(9) The energy change in the analogous cholesteryl system was estimated to be 9 kcal. in favor of the unsaturated alcohol by Winstein and Kosower; S. Winstein and E. M. Kosower, *J. Am. Chem. Soc.*, **81**, 4399 (1959).

endo-Bicyclo[5.1.0]oct-2-yl acetate was also converted to 3-cycloöcten-1-yl acetate after twelve hours at room temperature in acetic acid containing 0.5% of 70% aqueous perchloric acid. However, it was found that *endo*-bicyclo[5.1.0]oct-2-yl acetate gave major amounts of *exo*-bicyclo[5.1.0]oct-2-yl acetate and 3-cycloöcten-1-yl acetate when it was solvolyzed for only five minutes in the presence of perchloric acid, indicating that the initially formed products of reaction of the acetate were obtained when the reaction was carried out for a short time. In several experiments, the relative amounts of the various products were not reproduced precisely, and some *endo*-bicyclo[5.1.0]oct-2-yl acetate sometimes survived, Accordingly, the solvolyses of *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol were repeated at room temperature for five minutes instead of twelve hours in order to obtain information about the initially formed products.

The results are summarized in Table I. Under these solvolysis conditions, it is unlikely that much simple esterification of the alcohol occurred since cyclohexanol was not esterified under the same conditions. The bicycloöctanols would be expected to esterify at a similar or slower rate, since they are, if anything, more hindered than cyclohexanol. Accordingly, the acetates reported in Table I must arise from the alcohols by a carbonium ion mechanism. The data in Table I indicate that *endo*-bicyclo[5.1.0]octan-2-ol reacts more rapidly than the *exo* isomer, since considerable *exo* alcohol remained unchanged. As discussed in detail by Winstein and Kosower,[9] the higher reactivity of the *endo* isomer (analogous to 3,5-cyclocholestan-6β-ol) is expected both because of the higher ground state energy of the crowded *endo* isomer and because of a more favorable stereoelectronic arrangement (the *p*-orbital vacated by the hydroxyl group is in a position to accept electrons from the cyclopropane ring),

TABLE I

YIELDS OF PRODUCTS FROM SOLVOLYSIS OF *endo*- AND *exo*-BICYCLO[5.1.0]OCTAN-2-OL

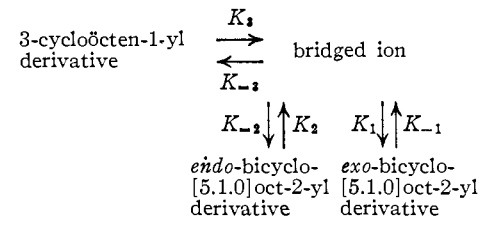
Product	% from *endo*-bicyclo-[5.1.0]-octan-2-ol	% from *exo*-bicyclo-[5.1.0]-octan-2-ol
endo-Bicyclo[5.1.0]octan-2-ol	[a]	[b]
exo-Bicyclo[5.1.0]octan-2-ol	4	25
3-Cycloöcten-1-ol	11	7
endo-Bicyclo[5.1.0]oct-2-yl acetate	15	20
exo-Bicyclo[5.1.0]oct-2-yl acetate	30	31
3-Cycloöcten-1-yl acetate	40	19

[a] The maximum amount that could have been present is 1.5%. [b] The maximum amount that could have been present is 1%.

A second feature of the data in Table I is that both the *endo* and the *exo* acetates are formed in the major amounts from both alcohols. If the reactions of the alcohols occur *via* the ionic intermediate or intermediates involved in the solvolysis of 3-cycloöcten-1-yl brosylate, the *endo* acetate should be formed in larger amount. The large amounts of *endo* acetate that were found suggest that this isomer may be the product first formed in larger amount in both cases, but since the *endo* acetate was shown to rearrange partially to the more stable *exo* isomer under similar reaction conditions, it is not surprising that the *exo* isomer predominates in the products reported in Table I, Presumably, 3-cycloöcten-1-yl acetate is in part the initially formed product and in part the product of rearrangement of initially formed bicyclic acetates.

Mechanisms of the Solvolyses.—The results of the present study can be accommodated by a mechanism similar to that which has been used to explain solvolysis reactions in the cholesteryl system. The principal new result of our study is the discovery of conditions under which a major reaction is conversion of *endo*-bicyclo[5.1.0]octan-2-ol to the corresponding *exo* isomer. Winstein and Kosower[9] have reported the acid-catalyzed rearrangement of the cyclocholestanyl acetates under conditions very similar to those of our alcohol rearrangements in which 30% and 31% of *exo* acetate was found (*cf.* Table I). Similar conversion of the 6β- to the 6α-isomer in their case would probably have led to noticeable deviations in the first-order rate plots, determined polarimetrically, since the α-acetate has a higher positive rotation than the β-acetate.

A bridged ion mechanism in our case, then, must include a reaction path in which the ion gives the *exo* isomer in appreciable amount, as in the following scheme which would be applicable in the rearrangement of the acetates in acetic acid. Expansion of the scheme to include the reactions of the corresponding alcohols is readily envisioned, An essentially equivalent reaction path can be formulated involving classical ions in equilibrium provided their stereochemistry is preserved.



Since the products of solvolysis of 3-cycloöcten-1-yl brosylate are stable under the reaction conditions employed, the reported yields of products may be used to obtain an approximate ratio of rate constants for reaction of the intermediate ion, The results are: $K_{-3}:K_{-2}:K_{-1} = 0.3:0.5:0.2$.

On the other hand, the second experiment of Table I indicates that if a single ion were an intermediate, reaction of the ion to form *exo* acetate was at least 1.5 times as fast as formation of 3-cycloöcten-1-yl acetate. Since an even higher ratio would probably have been found for a smaller over-all percentage of reaction, an ion–solvent molecule pair which specifically reacts only at the 2-position to give *exo* acetate may be involved.

Formation of the alcohols in the solvolysis mixtures can be explained by attack by water (present in small amount) on ions. It is known that water is a better nucleophile than acetic acid.[10]

(10) C. G. Swain, R. B. Mosely and D. E. Brown, *J. Am. Chem. Soc.*, **77**, 3731 (1955).

Experimental[11]

Solvolysis of 3-Cycloöcten-1-yl Brosylate.—The solvolysis of 3-cycloöcten-1-yl brosylate in acetic acid in the presence of excess sodium acetate at room temperature for 12 hours was repeated as described before.[4] From 49 g. of 3-cycloöcten-1-yl brosylate 27.5 g. of crude acetates was obtained. The acetates contained no hydrocarbon as shown by gas chromatography on Silicone oil[12] at 180°.

The acetates were hydrolyzed by stirring with 400 ml. of 10% potassium hydroxide in water–methanol solution for 2 hours at room temperature. The methanol was removed under reduced pressure and the aqueous layer was extracted with two 100-ml. and one 50-ml. portion of ether, and the combined extracts were washed with water and dried over magnesium sulfate. Removal of the ether at atmospheric pressure gave 18.5 g. (theoretical 17.9 g.) of the crude mixture of alcohols. The infrared spectrum of the mixture showed that the hydrolysis was complete, for it contained no acetate carbonyl band. The alcohols were separated into a saturated portion (9.3 g.) and an unsaturated portion (4.5 g.) by silver nitrate extraction.[4] The saturated portion was shown to be a mixture of 75% of the *endo* and 25% of the *exo* isomer of bicyclo[5.1.0]octan-2-ol by gas chromatography on Silicone oil at 180°. The unsaturated portion was shown to be 3-cycloöcten-1-ol by comparison of its infrared spectrum with the spectrum of an authentic sample.

Separation of *endo*- and *exo*-Bicyclo[5.1.0]octan-2-ol.—A mixture (2.0 g.) of *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol was passed through a water-cooled column (35 × 1.8 cm.) of 100 g. of acid-washed activity II alumina packed in pentane. The column was eluted with pentane and the eluent was gradually changed to 10, 20, 30, 40 and 50% ether–pentane mixtures. The fractions eluted with 0–40% ether–pentane mixtures contained pure *endo*-bicyclo[5.1.0]octan-2-ol, and the fraction eluted with a 50% ether–pentane mixture was a mixture of *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol, estimated to be present in equal amounts from the relative peak areas obtained by gas chromatography on Silicone oil at 180°. The fractions eluted with 50–100% ether contained pure *exo*-bicyclo[5.1.0]octan-2-ol. The *endo* alcohol showed a strong band in the infrared spectrum at 1025 cm.$^{-1}$ and medium bands at 1065, 995, 960 and 875 cm.$^{-1}$; the *exo* alcohol exhibited strong bands at 1055, 1015 cm.$^{-1}$, and weak bands at 835 and 735 cm.$^{-1}$. Both epimeric alcohols had bands at 3070 and 2990 cm.$^{-1}$, characteristic of a methylene group in a cyclopropane ring.

endo-Bicyclo[5.1.0]octan-2-ol was a crystalline solid, m.p. 42.8–43.6° after two recrystallizations from pentane.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.07; H, 11.27.

endo-Bicyclo[5.1.0]oct-2-yl **phenylurethan** was recrystallized twice from pentane; m.p. 75.4–76.0°. *Anal.* Calcd. for $C_{15}H_{19}O_2N$: C, 73.44; H, 7.81. Found: C, 73.28; H, 7.83.

endo-Bicyclo[5.1.0]oct-2-yl *p*-**nitrobenzoate** was recrystallized three times from pentane; m.p. 63.5–64.3°. *Anal.* Calcd. for $C_{15}H_{17}O_4N$: C, 65.44; H, 6.22. Found: C, 65.49; H, 6.40.

exo-Bicyclo[5.1.0]octan-2-ol was a colorless liquid. An analytical sample was obtained by gas chromatography on Silicone oil at 180°; $n^{25}D$ 1.4870. *Anal.* Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.18; H, 11.49.

exo-Bicyclo[5.1.0]oct-2-yl **phenylurethan** was recrystallized three times from pentane; m.p. 123.0–124.0°. *Anal.* Calcd. for $C_{15}H_{19}O_2N$: C, 73.44; H, 7.81. Found: C, 73.44; H, 7.59.

exo-Bicyclo[5.1.0]oct-2-yl *p*-**nitrobenzoate** was recrystallized twice from pentane; m.p. 110.5–111.5°. *Anal.* Calcd. for $C_{15}H_{17}O_4N$: C, 65.44; H, 6.22. Found: C, 65.25; H, 6.13.

Equilibration of *endo*-Bicyclo[5.1.0]octan-2-ol.—A mixture of 100 mg. of *endo*-bicyclo[5.1.0]octan-2-ol, 100 mg. of freshly distilled aluminum isopropoxide, 1 ml. of anhydrous isopropyl alcohol and 0.07 ml. of anhydrous acetone was heated at 100° for 7 days. The mixture was cooled, 1 ml. of cold dilute hydrochloric acid was added, and the mixture was extracted with ether. After the extracts were dried and the ether had been removed, the residue was found to be a mixture of *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol, identified by comparison of its infrared spectrum with the spectra of authentic samples. The composition of the mixture was shown to be 35% of *endo*- and 65% of *exo*-bicyclo[5.1.0]octan-2-ol by gas chromatography on Silicone oil at 180°.

3-Cycloöcten-1-yl Acetate.—A solution of 1.0 g. of 3-cycloocten-1-ol and 1.6 g. of acetic anhydride in 7 ml. of anhydrous pyridine was allowed to stand at room temperature for 24 hours and diluted with water and extracted with ether. The ether extracts were washed with water, 6 *N* hydrochloric acid, water, 5% sodium bicarbonate solution and water, and dried over magnesium sulfate. Concentration of the solution gave 0.8 g. of 3-cycloöcten-1-yl acetate, b.p. 56° (0.50–0.65 mm.), $n^{25}D$ 1.4693.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.37; H, 9.52.

4-Cycloöcten-1-yl Acetate.—4-Cyclöcten-1-ol (1.0 g.) was treated with acetic anhydride in pyridine as described for the preparation of 3-cycloöcten-1-yl acetate. The yield of 4-cycloöcten-1-yl acetate, b.p. 55° (0.65 mm.), $n^{25}D$ 1.4686, was 0.8 g. (60%).

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.40; H, 9.54.

***endo*-Bicyclo[5.1.0]oct-2-yl Acetate.**—A solution of 150 mg. of *endo*-bicyclo[5.1.0]octan-2-ol and 300 mg. of acetic anhydride in 1.5 g. of anhydrous pyridine was allowed to stand at room temperature for 24 hours. The product was isolated as described for the preparation of 3-cycloöcten-1-yl acetate. The crude product was distilled in a short-path still (at 0.5 mm. with a bath temperature of 80°), giving 60 mg. of the acetate, $n^{25}D$ 1.4675.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.25; H, 9.63.

***exo*-Bicyclo[5.1.0]oct-2-yl Acetate.**—A solution of 100 mg. of *exo*-bicyclo[5.1.0]octan-2-ol and 200 mg. of acetic anhydride in 1 ml. of anhydrous pyridine was allowed to stand at room temperature for 24 hours. The crude product, 114 mg., was isolated as described for the preparation of 3-cycloöcten-1-yl acetate. The analytical sample, $n^{25}D$ 1.4625, was collected by gas chromatography on Silicone oil at 165°.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.46; H, 9.66.

Solvolysis of *endo*-Bicyclo[5.1.0]octan-2-ol. (a).—A solution of 30 mg. of *endo*-bicyclo[5.1.0]octan-2-ol in 0.3 ml. of glacial acetic acid was heated at 120° for 24 hours. The solution was diluted with water and extracted with ether. The ether extracts were washed with water, 5% sodium bicarbonate solution and water, dried over magnesium sulfate and concentrated, yielding 30 mg. of material, which gave a single peak on gas chromatography on Silicone oil at 180°. The infrared spectrum of the product after purification by chromatography on alumina (eluted with pentane) was identical with the spectrum of authentic 3-cycloöcten-1-yl acetate.

(b).—A solution of 100 mg. of *endo*-bicyclo[5.1.0]octan-2-ol in 1 ml. of glacial acetic acid (containing 0.5% by weight of 70% aqueous perchloric acid) was allowed to stand at room temperature for 15 hours. The product (112 mg.) was isolated as described above. Gas chromatography on Silicone oil at 180° and 1,2,3-tris-(2-cyanoethoxy)-propane at 150° showed a major peak and a minor peak, later identified as 3-cycloöcten-1-yl acetate and 3-cycloöcten-1-ol, respectively. The relative amounts of these components were estimated from the peak areas to be 92 and 8%. These components were separated by chromatography on neutral activity II alumina. The acetate was eluted with pentane and the alcohol eluted with an ether–pentane mixture. The compounds were identified by comparison of their infrared spectra with the spectra of authentic samples.

(c).—A solution of 300 mg. of *endo*-bicyclo[5.1.0]octan-2-ol in 3 ml. of acetic acid (containing 0.5% by weight of 70% aqueous perchloric acid) was allowed to stand at room temperature for 5 minutes. The products were isolated as described above, yielding 370 mg. of the crude reaction mixture. Gas chromatography of the mixture on Silicone oil at 180° and 1,2,3-tris-(2-cyanoethoxy)-propane at 150° showed that there were present at least five components, later identified as the following compounds, present in the relative amounts shown (estimated from peak areas): *exo*-bicyclo[5.1.0]octan-2-ol (4%), 3-cycloöcten-1-ol (11%), *endo*-(15%)

(11) Melting points are corrected and boiling points are uncorrected.

(12) Reference 4, footnote 24, describes the conditions and equipment used for gas chromatography.

and *exo*-bicyclo[5.1.0]oct-2-yl acetate (30%) and 3-cycloocten-1-yl acetate (40%). The crude solvolysis product (390 mg.) was passed through a water-cooled column (15 × 1.0 cm.) of 5 g. of acid-washed activity II alumina. The acetate fraction (260 mg.), essentially free from the alcohols as shown by gas chromatography on Silicone oil at 180°, was eluted with pentane. The alcohol fraction (85 mg.) containing a small amount of the acetates, as shown by gas chromatography on Silicone oil at 180°, was eluted with a 50% ether–pentane mixture.

Treatment of the acetate fraction (260 mg.) with lithium aluminum hydride in ether at room temperature gave 150 mg. of the corresponding alcohols. A solution of the alcohols in ether was extracted with 20% aqueous silver nitrate solution. Addition of an equal volume of concd. ammonium hydroxide to the silver nitrate layer gave 20 mg. of 3-cycloocten-1-ol, identified by comparison of its infrared spectrum with the spectrum of an authentic sample.

The saturated alcohols (55 mg.) obtained by evaporation of the ether layer from the silver nitrate extraction were passed through a water-cooled column (5 × 0.7 cm.) of 1 g. of acid-washed activity II alumina. The fraction eluted with 10% ether–pentane was *endo*-bicyclo[5.1.0]octan-2-ol. The fraction eluted with 20% ether–pentane was a mixture of *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol, estimated to be present in equal amounts by gas chromatography on Silicone oil at 180°, and the fraction eluted with 30% ether–pentane was *exo*-bicyclo[5.1.0]octan-2-ol. The alcohols were identified by comparison of their infrared spectra with the spectra of authentic samples and by gas chromatography on Silicone oil at 180°.

The alcohol fraction (86 mg.) of the solvolysis products was passed through a water-cooled column (10 × 0.7 cm.) of 2 g. of acid-washed activity II alumina. The fraction eluted with 5% ether–pentane was 3-cycloöcten-1-ol, the fraction eluted with 10% ether-pentane mixture was a mixture of 3-cycloöcten-1-ol and *exo*-bicyclo[5.1.0]octan-2-ol and the fraction eluted with 15–30% ether–pentane mixture was *exo*-bicyclo[5.1.0]octan-2-ol, as shown by comparison of the infrared spectra of the fractions with the spectra of authentic samples and by gas chromatography on Silicone oil at 180°.

No conclusive evidence was obtained for the presence of *endo*-bicyclo[5.1.0]octan-2-ol, but the maximum amount that could have been present, as shown by gas chromatography would correspond to a yield of less than 1.5%.

Solvolysis of *endo*-Bicyclo[5.1.0]oct-2-yl Acetate. (a).—A solution of 30 mg. of *endo*-bicyclo[5.1.0]oct-2-yl acetate in 0.3 ml. of glacial acetic acid was heated at 120° for 23 hours. The product was isolated as described for the solvolysis of *endo*-bicyclo[5.1.0]octan-2-ol, and amounted to 26 mg. of 3-cycloöcten-1-yl acetate. The acetate was identified by comparison of its infrared spectrum with the spectrum of an authentic sample, and by gas chromatography on Silicone oil at 180°. A reaction carried out in the presence of sodium acetate gave a similar result.

(b).—A solution of 32 mg. of *endo*-bicyclo[5.1.0]oct-2-yl acetate in 0.3 ml. of glacial acetic acid was allowed to stand at room temperature for 13 hours. The product was isolated as described for the solvolysis of *endo*-bicyclo[5.1.0]-octan-2-ol, and amounted to 25 mg. of *endo*-bicyclo[5.1.0]-oct-2-yl acetate, identified by comparison of its infrared spectrum with the spectrum of an authentic sample, and by gas chromatography on Silicone oil at 180°.

(c).—A solution of 35 mg. of *endo*-bicyclo[5.1.0]oct-2-yl acetate in 0.3 ml. of acetic acid (containing 0.5% by weight of 70% aqueous perchloric acid) was allowed to stand at room temperature for 13 hours. The product was isolated as described for the solvolysis of *endo*-bicyclo[5.1.0]octan-2-ol, and amounted to 13 mg. of 3-cycloöcten-1-yl acetate, identified by comparison of its infrared spectrum with the spectrum of an authentic sample, and by gas chromatography on Silicone oil at 180°.

(d).—A solution of 0.5 g. of *endo*-bicyclo[5.1.0]oct-2-yl acetate in 5 ml. of acetic acid (containing 0.5% by weight of 70% aqueous perchloric acid) was allowed to stand at room temperature for 5 minutes. The product was isolated as described for the solvolysis of *endo*-bicyclo[5.1.0]octan-2-ol, and amounted to 450 mg. of material. Gas chromatography on Silicone oil at 165° of this material showed that there were at least three components, present in relative amounts of 8, 32 and 60%, respectively. Each peak was isolated by gas chromatography on Silicone oil at 165°. The first peak was principally 3-cycloöcten-1-ol, the second peak was *exo*-bicyclo[5.1.0]oct-2-yl acetate and the third peak was 3-cycloöcten-1-yl acetate, identified by comparison of their infrared spectra with the spectra of authentic samples.

Solvolysis of *exo*-Bicyclo[5.1.0]octan-2-ol. (a).—A solution of 50 mg. of *exo*-bicyclo[5.1.0]octan-2-ol in 0.5 ml. of acetic acid (containing 0.5% by weight of 70% aqueous perchloric acid) was allowed to stand at room temperature for 12 hours. The product (51 mg.) was isolated as described for the solvolysis of *endo*-bicyclo[5.1.0]octan-2-ol. Gas chromatography on Silicone oil at 180° showed that this material had two components, later identified as 3-cycloocten-1-yl acetate and 3-cycloöcten-1-ol. The relative amounts of these components were estimated from the peak areas to be 88 and 12%. The two components were separated by chromatography on acid-washed activity II alumina. The acetate was eluted with pentane and the alcohol was eluted with an ether–pentane mixture. The products were identified by comparison of their infrared spectra with the spectra of authentic samples and by gas chromatography on Silicone oil at 180°.

(b).—A solution of 300 mg. of *exo*-bicyclo[5.1.0]octan-2-ol in 3 ml. of acetic acid (containing 0.5% by weight of 70% aqueous perchloric acid) was allowed to stand at room temperature for 5 minutes. The products (370 mg.) were isolated as described for the solvolysis of *endo*-bicyclo[5.1.0]-octan-2-ol. Gas chromatography on Silicone oil at 180° and 1,2,3-tris-(2-cyanoethoxy)-propane at 150° showed that there were present at least five components, later identified as *exo*-bicyclo[5.1.0]octan-2-ol (25%), 3-cycloöcten-1-ol (7%), *endo*-bicyclo[5.1.0]oct-2-yl acetate (20%), *exo*-bicyclo-[5.1.0]oct-2-yl acetate (31%) and 3-cycloöcten-1-yl acetate (19%).

The solvolysis products were separated into an acetate fraction and an alcohol fraction by chromatography on alumina, as described for the solvolysis of *endo*-bicyclo[5.1.0]-octan-2-ol. Treatment of the acetate fraction (220 mg.) with lithium aluminum hydride in ether at room temperature gave 150 mg. of the corresponding alcohols. The alcohols were separated into a saturated and an unsaturated portion by the silver nitrate extraction method. The unsaturated portion was 3-cycloöcten-1-ol, identified by comparison of its infrared spectrum with the spectrum of an authentic sample. The saturated portion contained *endo*- and *exo*-bicyclo[5.1.0]octan-2-ol, separated by chromatography on alumina, as described for the solvolysis of *endo*-bicyclo[5.1.0]-octan-2-ol, and identified by comparison of their infrared spectra with the spectra of authentic samples, and by gas chromatography on Silicone oil at 180°.

The alcohol fraction of the solvolysis products was separated by the silver nitrate method into fractions identified as bicyclo[5.1.0]octan-2-ol and 3-cycloöcten-1-ol by comparison of their infrared spectra with the spectra of authentic samples.

No conclusive evidence was obtained for the presence of *ndo*-bicyclo[5.1.0]octan-2-ol, but the maximum amount that could have been present, as shown by gas chromatography on Silicone oil at 180°, would correspond to a yield of less than 1%.

Solvolysis of *exo*-Bicyclo[5.1.0]octan-2-ol Derivatives.—A number of solvolyses carried out in the case of the acetate and *p*-nitrobenzoate gave results similar to those reported for the *endo*-bicyclo[5.1.0]octan-2-ol derivatives.

Solvolysis of Cyclohexanol.—A solution of 0.5 g. of cyclohexanol in 5 ml. of acetic acid (containing 0.5% by weight of 70% aqueous perchloric acid) was allowed to stand at room temperature for 15 hours. The product (0.61 g.) was isolated as described for the solvolysis of *endo*-bicyclo[5.1.0]-octan-2-ol. Gas chromatography of this material on Silicone oil at 165° gave two peaks. The two components were isolated by gas chromatography and identified as cyclohexanol (33%) and cyclohexyl acetate (67%) by their infrared spectra.

Repetition of the above solvolysis at room temperature for 5 minutes gave only the original alcohol.

Phenylurethans.—The phenylurethans of the various alcohols prepared during this study were obtained by heating the corresponding alcohols with phenyl isocyanate on a steam-bath for a few minutes and dissolving the crude derivatives in pentane and filtering to remove any diphenylurea present. The crude phenylurethans were recrystallized from the solvents named.

p-**Nitrobenzoates.**—The *p*-nitrobenzoates were obtained by heating the corresponding alcohols on a steam-bath with 20% excess *p*-nitrobenzoyl chloride in pyridine for a few minutes and pouring the product into water. The crude *p*-nitrobenzoates were isolated by filtration and were recrystallized from pentane.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY, NEW YORK 53, N. Y.]

Stereochemistry of (+)-(S)-2-Propanol-1-d_3. Partial Asymmetric Reduction of 4',1''-Dimethyl-1,2,3,4-dibenzcyclohepta-1,3-diene-6-one[1]

BY KURT MISLOW, ROBERT E. O'BRIEN AND HANS SCHAEFER

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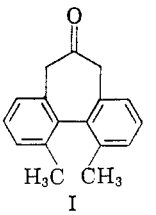
The synthesis of (+)-(*S*)-2-propanol-1-d_3 from (+)-(*S*)-lactic acid is described. The asymmetric Meerwein–Ponndorf–Verley reductions by a number of (*S*)-alkylmethylcarbinols of ketone I demonstrate the utility of this system as a device for estimating relative kinetic size. Use of (+)-2-propanol-1-d_3 in this asymmetric reduction does not reveal the operation of an isotope effect: methyl and trideuteriomethyl appear to have indistinguishable kinetic sizes by this particular criterion.

By virtue of the higher zero-point energy of the lighter isotope, X–H bonds are expected to have higher vibrational amplitudes than the corresponding X–D bonds; the difference in amplitudes, corresponding to the respective van der Waals radii, is estimated[2] at 0.01–0.02 Å.

It might thus be foreseen that protium and deuterium differ in non-bonded potential; evidence exists for corresponding effects in the ground state.[3] A classification of the source of secondary deuterium isotope effects[4] recognizes the possibility that effects may originate in changes in non-bonded interaction which accompany the change of reagents from the ground to the transition state of a reaction[5]; calculations[6] indicate that such effects need not be negligible. Indeed, a number of secondary deuterium isotope effect have recently been uncovered which may conceivably be regarded as reflecting, at least in part, the incursion of kinetic size factors.[7]

The present paper describes an attempt to isolate such factors from effects arising out of differences in ground state energies, by resorting to comparisons of suitable *diastereomeric transition states* in the following experimental approach.

The partial asymmetric reduction of (±)-4',1''-dimethyl-1,2,3,4-dibenzcyclohepta-1,3-diene-6-one (I)[8] by the method described earlier



I

for analogous ketones[9] affords $\Delta\Delta F^{\ddagger}$ values which show the expected[9] response to increasing differences in kinetic bulk between methyl and alkyl (Table I).

TABLE I

RESULT OF PARTIAL ASYMMETRIC REDUCTION OF I BY (+)-(*S*)-ALKYLMETHYLCARBINOLS AT 63° IN DIOXANE

Alkyl group	k_R/k_S	$\Delta\Delta F^{\ddagger}$, cal./mole	Alkyl group	k_R/k_S	$\Delta\Delta F^{\ddagger}$, cal./mole
CH_3	1.00	0 (std.)	*n*-C_6H_{13}	1.59	310
C_2H_5	1.29	170	Neo-C_5H_{11}	1.8*i*	420
n-C_3H_7	1.31	180	*i*-C_3H_7	1.92	440
i-C_4H_9	1.58	310	*t*-C_4H_9	2.91	720

The use of I as a sensitive reagent had been indicated by the fortuitous circumstance that specific rotations of I are very high in the near ultraviolet and visible region in which the ketone is virtually non-absorbent.[8] This makes possible the measurement of extremely high rotations under conditions

(1) Communicated in preliminary form: *J. Am. Chem. Soc.*, **82**, 5512 (1960). A Fulbright travel grant (H. S.) and fellowship support by the Alfred P. Sloan Foundation (K.M.) and by the Trubek Laboratories (R.E.O. and H.S.) are gratefully acknowledged.

(2) A. R. Ubbelohde, *Trans. Faraday Soc.*, **32**, 525 (1936). The simple harmonic oscillator approximation is employed; the results satisfy conditions for C–H, N–H and O–H bonds with $\tilde{\nu}$ *ca.* 3000–3500 cm.$^{-1}$ and are in harmony with recent electron diffraction data on CH_4 and CD_4 (L. S. Bartell, K. Kuchitou and R. J. DeNeui, *J. Chem. Phys.*, **33**, 1254 (1960)).

(3) (a) The ratio of molal volumes of C_6H_6 and C_6D_6 is 1.008 at 17.2° (G. R. Clemo and A. McQuillen, *J. Chem. Soc.*, 1220 (1935)). (b) The ratio of molal volumes of H_2 and D_2 is 1.13 at $T < 18$°K. (K. Clusius and E. Bartholomé, *Z. physik. Chem.*, **B30**, 237 (1935); E. Bartholomé, *ibid.*, **B33**, 387 (1936)) and 1.08 for benzene solutions at 25° and 1 atm. (J. Walkley and J. H. Hildebrand, *J. Am. Chem. Soc.*, **81**, 4439 (1959)). (c) The edge of the cubic lattice of LiH diminishes from 4.080 to 4.060 on substitution of deuterium (E. Zintl and A. Harder, *Z. physik. Chem.*, **B28**, 478 (1935); J. M. Robertson, "Organic Crystals and Molecules," Cornell Univ. Press, Ithaca, N. Y., 1953, p. 235).

(4) V. Shiner, *Tetrahedron*, **5**, 243 (1959).

(5) Qualitatively, increased crowding in the transition state is expected to result in a negative, and relief from crowding in a positive, isotope effect k_H/k_D if the kinetic size of X–H significantly exceeds that of X–D. The assignment of van der Waals radii depends on the method of measurement. Kinetic studies (as of the ratio of rates in a competitive reaction system) often give evidence of differential steric effects: since, however, these effects may reflect factors not included in crystallographic parameters, it is advisable to specify kinetic "size" as such.

(6) L. S. Bartell, *Tetrahedron Letters*, **No. 6**, 13 (1960); *J. Am. Chem. Soc.*, **83**, 3567 (1961).

(7) (a) K. T. Leffek, J. A. Llewellyn and R. E. Robertson, *Chemistry & Industry*, 588 (1960); *J. Am. Chem. Soc.*, **82**, 6315 (1960); *Can. J. Chem.*, **38**, 1505, 2171 (1960); K. T. Leffek, R. E. Robertson and S. E Sugamori, *Chemistry & Industry*, 259 (1961); (b) V. Prelog, *Bull soc. chim. France*, 1433 (1960); (c) P. L. Love, R. W. Taft, Jr., and T. Wartik, *Tetrahedron*, **5**, 116 (1959); (d) J. M. Jones and M. L. Bender, *J. Am. Chem. Soc.*, **82**, 6322 (1960); M. L. Bender and M. S. Feng, *ibid.*, **82**, 6318 (1960).

(8) Synthesis and stereochemistry of I and of the derived alcohol (6-ol) have been described by K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg and C. Djerassi, *ibid.*, **82**, 4740 (1960); K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg, J. Weiss and C. Djerassi, *ibid.*, **84**, 1455 (1962).

(9) P. Newman, P. Rutkin and K. Mislow, *ibid.*, **80**, 465 (1958); K. Mislow and F. A. McGinn, *ibid.*, **80**, 6036 (1958).