and ether. The ether solution of the product was washed with sodium carbonate solution and concentrated. The crude residual product was evaporatively distilled at 125° (0.4 mm.) to yield 7.8 g. (85%) of crystalline ketone XVI which melted at 44–45°. The analytical sample, recrystallized from methanol–water, had the same melting point.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.50; H, 7.53.

Ketone XVI (1 g.) and sulfur (125 mg.) were heated for 75 minutes under nitrogen at 220°. The mixture was cooled and dissolved in benzene–ether and then this solution was washed with 15% potassium hydroxide solution. Acidification of the alkaline solution yielded the crude naphthol, 1-hydroxy-7-methoxy-6-methylnaphthalene, which was purified by chromatography on neutral alumina. Elution with 50:50 benzene–ethyl acetate removed a brownish oil (400 mg.) which gave a positive ferric chloride test (blue precipitate). This naphthol was methylated by heating with acetone (25 ml.), potassium carbonate (3 g.) and dimethyl sulfate (2 ml.) for 24 hours; during this time three additional portions (1 ml.) of dimethyl sulfate were added at equal intervals of time. The reaction mixture was poured into water and the product extracted with ether. The crude product remaining after evaporation of the ether was chromatographed on basic alumina using hexane as the solvent. The first fraction (63 mg.) crystallized and melted at 72.5–73.5°. The melting point of a mixture of this substance and II prepared by metalation of 1,7-dimethoxynaphthalene was 72–73°.

β-7-(6-Methoxy-1,2,3,4-tetrahydronaphthoyl)-propionic Acid (XVII).[19]—β-6-Methoxy-1,2,3,4-tetrahydronaphthalene (2 g.), prepared by the method of Stork,[20] was allowed to react with succinic anhydride (1.2 g.) and aluminum chloride (3.6 g.) in nitrobenzene (25 ml.) as in the preparation of acid III. The dark-brown product was recrystallized first from benzene–isopropyl alcohol and then from methanol to yield nearly colorless needles which melted at 178–179°.

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.51; H, 7.06.

The ultraviolet spectrum of this acid was quite different, $\lambda_{\max}^{\mathrm{EtOH}}$ 258 mμ (log ε 4.23) and 318 mμ (log ε 3.86), from that of acids III and XIV.

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[19] This structure was assigned rather than the alternate possibility, β-5-(6-methoxy-1,2,3,4-tetrahydronaphthoyl)-propionic acid, because similar Friedel–Crafts reactions in nitrobenzene introduce the substituent into the least sterically hindered position even if there are some opposing electronic factors.

[20] G. Stork, THIS JOURNAL, **69**, 576 (1947).

NEW BRUNSWICK, N. J.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, THE FLORIDA STATE UNIVERSITY]

cis- and *trans*-Bicyclo[3.2.1]octanol-2[1]

BY A. A. YOUSSEF, M. E. BAUM AND H. M. WALBORSKY[2]

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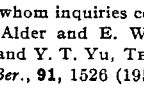
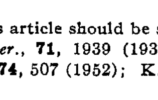
The synthesis and establishment of configuration of *cis*- and *trans*-bicyclo(3.2.1)octanol-2 is described. The rate of saponification of the acetates at 25° was found to be 1.05 × 10⁻³ l. mole⁻¹ sec.⁻¹ for the *trans* isomer and 2.21 × 10⁻³ l. mole⁻¹ sec.⁻¹ for the *cis* isomer. The saponification rate of the acetate of bicyclo(2.2.2)octanol-2 was found to be identical with that of *trans*-bicyclo(3.2.1)octyl-2 acetate. The reduction of bicyclo(3.2.1)octanone-2 by a variety of reducing agents to yield various ratios of *cis*- and *trans*-alcohols is described and the results are discussed.

Introduction

Previous syntheses[3] of bicyclo(3.2.1) octanol-2 have not been directed toward the procurement of the geometric isomers which were desired for further study. In contrast to bridged bicyclic systems such as bicyclo(2.2.1)heptane (norbornane) and bicyclo(2.2.2)octane where the six-membered ring is held rigidly in the boat conformation, the bicyclo(3.2.1)octane (I) system is unique in that it is composed of a six-membered ring which can exist in a chair conformation in which two *axial* carbon atoms (C-6 and C-7) are joined to form an ethylene bridge. Evidence which justifies looking upon this molecule as possessing a six-membered ring rather than a seven-membered (C-1 to C-7) can be found from the inspection of the carbonyl absorption in the infrared spectrum of bicyclo(3.2.1)octanone-2. The absorption occurs at 1715 cm.⁻¹ which is typical of a six-membered ring ketone.[4]



I



II

In substituted cyclohexanes a conversion of the ring can occur which transforms an *equatorial* bond into an *axial* bond and the molecule usually exists as an equilibrium mixture of these forms.[5] In the bicyclo(3.2.1)octane system this type of ring conversion is not possible because of the ethylene bridge at C-1 and C-5. The only ring conversion that is possible is a chair–boat interconversion by a flipping of the ring at C-2 and C-4. This type of conversion should be energetically unfavorable since in cyclohexane itself the boat conformation has been calculated to be less stable than the chair by 7–10 kcal.[6] In the bicyclo(3.2.1)octane system (I) the chair conformation should be more stable than the boat (II) by an amount greater than 7–10 kcal. since in the boat conformation there is also an eclipsing of the C-2 and C-4 hydrogen atoms with the C-6 and C-7 methylene groups. Therefore, one can describe this system as being essentially fixed in the chair conformation. On this basis it is possible to assign the *axial* (IIIa) conformation to the hydroxyl

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[1] *cis* and *trans* refers to the position of a substituent with respect to the *ethylene bridge*.

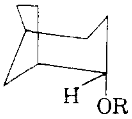
[2] To whom inquiries concerning this article should be sent.

[3] K. Alder and E. Windemuth, *Ber.*, **71**, 1939 (1938); M. S. Newman and Y. T. Yu, THIS JOURNAL, **74**, 507 (1952); K. Alder and Reubke, *Ber.*, **91**, 1526 (1958).

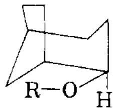
[4] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen Ltd., London, 1954.

[5] For excellent reviews on this subject see H. D. Orloff, *Chem. Revs.*, **54**, 347 (1954); W. Klyne, "Progress in Stereochemistry," Vol. I, Academic Press Inc., New York, N. Y., 1954.

[6] W. G. Dauben and K. S. Pitzer in M. S. Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, 1956, p. 15.



IIIa, R = H
b, R = $\mathrm{C(=O)CH_3}$

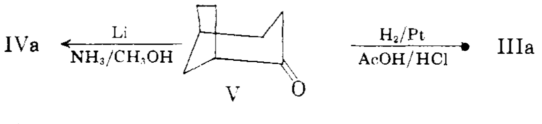


IVa, R = H
b, R = $\mathrm{C(=O)CH_3}$

group in *trans*-bicyclo(3.2.1)octanol-2 and the *equatorial* (IVa) to the *cis* isomer.

Results

Preparation of Isomers.—A convenient precursor for the preparation of the *cis* and *trans* isomers of bicyclo(3.2.1)octanol-2 is the ketone bicyclo(3.2.1)-octanone-2. This ketone was prepared following the procedure of Alder[3] with the modification that the mixture of isomeric alcohols (IIIa and IVa) was oxidized under homogeneous conditions to produce the ketone V in 79% yield.



Catalytic reduction in acid media generally leads to a preponderance of the *axial* isomer[7] IIIa; Eliel[8] has found that a mixture of acetic acid–hydrogen chloride to be advantageous, and when this procedure was applied to V rapid reduction ensued. The infrared spectrum of the crude alcohol showed strong absorption at 1015 cm.$^{-1}$ and a weak absorption at 1065 cm.$^{-1}$. After purification *via* the *p*-nitrobenzoate derivative the resultant alcohol showed an absorption band at 1015 cm.$^{-1}$ and the 1065 cm.$^{-1}$ was no longer present. Since isomerization of bicyclo(3.2.1)octanol-2 to bicyclo(2.2.2)octanol-2 is possible[9] under the acid conditions used in the reduction, the alcohol was reoxidized to the ketone and isolated as its 2,4-dinitrophenylhydrazone. Careful chromatography on an alumina column and the isolation of only one product, m.p. and mixed m.p. 137.5–139°,[3] indicates that no isomerization occurred during the reduction.

Reduction of V by lithium in a mixture of liquid ammonia and methanol[10] yielded a crude alcohol which initially absorbed weakly at 1015 cm.$^{-1}$ and strongly at 1065 cm.$^{-1}$ in the infrared. Upon purification of the crude alcohol *via* the *p*-nitrobenzoate derivative the absorption at 1015 cm.$^{-1}$ disappeared. From the method of synthesis[10] this hydroxyl group has been assigned the *equatorial* conformation.

The absorption band at 1065 cm.$^{-1}$ has been assigned to the *equatorial* C–O stretching vibration and the absorption at 1015 cm.$^{-1}$ to the *axial* C–O. These assignments are in agreement with the values cited recently[11] for the *equatorial* C–O stretching vibration in *trans*-4-*t*-butylcyclohexanol (1062 cm.$^{-1}$) and the assignment of the 1015 cm.$^{-1}$ to the *axial* C–O is in perfect line with the values cited for axially-substituted hydroxyl groups in the steroids.[12]

Saponification of *cis* and *trans*-Bicyclo(3.2.1)-octyl-2 Acetates.—Barton[13] originally pointed out the importance of conformation on the esterification of hydroxyl groups and saponification of ester groups in substituted cyclohexanes; that hydroxyl groups are esterified and ester groups are saponified more easily in the *equatorial* than in the axial position, due to the greater steric interactions in the latter. Eliel[14] has suggested that in a mobile substituted cyclohexane system where the two possible chair conformations are readily interconvertible (thereby causing a substituent to be in equilibrium between its *axial* and *equatorial* conformation) both conformations must be taken into account in determining reactivity. Winstein and Holness[15] have confirmed the suggestion of Eliel and have shown how this type of conformation equilibrium constant can be determined.

Inspection of the saponification rates of 2-alkylcyclohexyl esters indicates that when the alkyl group is relatively small so that a mobile system exists which permits a conformational equilibrium then the ratio of the rates of saponification of the epimeric esters is small. For example, when the alkyl group is methyl then the ratio of *cis* to *trans* is 1.77[16] and for ethyl, propyl and butyl it is 3.7. On the other hand, if the substituent is large or the system is rigid then the saponification rate ratio is large as in *cis*- and *trans*-2-isopropylcyclohexyl phthalate (34) and *trans*-α-decalyl phthalates series I and II (21). One might expect that since the *cis*- and *trans*-bicyclo(3.2.1)octyl system is a rigid one the ratio of the saponification rates of these isomers would also be large. As seen from the data in Table I this is not the case; the ratio of *cis* to *trans* is 2.1. Examination of molecular models reveals that although the acetoxy group in *trans*-bicyclo(3.2.1)octyl-2 acetate is hindered as in *axial*-cyclohexyl acetate it also shows that the equatorial acetoxy group (IV) is also somewhat hindered by the ethylene bridge. This may account for the small ratio that is observed. A similar observation

TABLE I

RATES OF SAPONIFICATION OF ACETATES IN AQUEOUS ETHANOLIC SODIUM HYDROXIDE

Acetate	Temp., °C.	Acetate 10^2 *M*	NaOH 10^2 *M*	$10^3 k_2$, l. mole^{-1} sec.$^{-1}$
trans-Bicyclo(3.2.1)	25.0	1.23	1.23	1.02
octyl-2 (IIIb)	25.0	1.23	1.23	1.07
cis-Bicyclo(3.2.1)octyl-	25.0	1.13	1.13	2.17
2 (IVb)	25.0	1.13	1.13	2.26
Bicyclo(2.2.2)octyl-2	25.0	1.23	1.23	1.04
	25.0	1.23	1.23	1.05
	25.0	1.23	1.23	1.04

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(7) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).

(8) E. L. Eliel and R. S. Ro, THIS JOURNAL, **79**, 5993 (1957).

(9) K. Alder, H. Krieger and H. Weiss, *Ber.*, **88**, 144 (1955).

(10) F. Sondheimer, O. Mancera, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **75**, 1282 (1953).

(11) R. Pickering and C. Price, *ibid.*, **80**, 4931 (1958).

(12) R. N. Jones, *et al.*, *ibid.*, **73**, 3215 (1951); **75**, 1498 (1953); **74**, 2828 (1952); H. C. Cole and L. L. Estes, *J. Chem. Soc.*, 4969 (1952).

(13) D. H. R. Barton and R. C. Cookson, *Quart. Revs.*, **10**, 44 (1956).

(14) E. L. Eliel, *Experientia*, **9**, 91 (1953); E. L. Eliel and C. A. Lukach, THIS JOURNAL, **79**, 5986 (1957).

(15) S. Winstein and N. J. Holness, *ibid.*, **77**, 5562 (1955).

(16) W. Hückel, *et al.*, *Ann.*, **533**, 128 (1937); G. Vavon, *Bull. soc. chim.*, [4] **49**, 989 (1931).

has been made[17] in the rate of esterification of *cis-* and *trans-*sabinene hydrate. In this case the ratio was near unity.

As can be seen from Table I the expected trend for the rate constant that an ester group in the *equatorial* conformation (IVb) reacts faster than one in the *axial* (IIIb) is observed. This is a further confirmation of the assignment of conformation for the isomers of bicyclo(3.2.1)octanol-2. It is interesting to note that bicyclo-(2.2.2)octyl-2 acetate saponifies at a rate identical with *trans-*bicyclo(3.2.1)octyl-2 acetate.

Reduction of V.—The reduction of alicyclic ketones by metal hydrides or catalytic means has been the subject of many recent investigations.[8,18a–f] None of the cyclohexanone derivatives studied possessed a substituent which was fixed in the *axial* position adjacent to the carbonyl group. Since ketone V possessed this characteristic (the CH$_2$ group of the ethylene bridge is *axially* situated) it was of interest to determine the effect such a structure would have on the reduction of the carbonyl function. Table II summarizes the results of a variety of reducing agents on ketone V.

TABLE II

No.	Type of reduction	Wt. of subst. in mg./1. ml. CS$_2$	Optical density[a,c] (av. value)	% *cis*	% *trans*
1	Lithium in liq. ammonia	12.5	0.400	97	3
2	Catalytic reduction	15.1	.255[b]	46	54
3	Ring expansion	12.5	.372	90	10
4	Equilibration I[d]	12.6	.390	94	6
5	Equilibration II[e]	12.2	.382	95	5
6	LiAl(*t*-BuO)$_3$H	12.5	.380	92	8
7	NaBH$_4$	12.9	.380	89	11
8	LiAlH$_4$	12.4	.368	90	10

[a] The calculations were made by comparing these optical densities with an optical density of 0.370 obtained from a sample of pure *cis-*bicyclo(3.2.1)octanol-2 (11.2 mg./1 ml. CS$_2$). [b] In this case this value was compared with an optical density of 0.255 obtained from a sample of pure *cis-*alcohol (7 mg./1 ml. CS$_2$). [c] In all cases the absorption band at 1065 cm.$^{-1}$ was used. [d] Composition of starting alcohol was 90% *cis*. [e] Composition of starting alcohol was 46% *cis*.

A reasonable approach to the understanding of the stereochemical results of metal hydride reductions has been proposed by Dauben.[17d] One factor to consider is the "steric approach control" which involves competitive attacks from a sterically favored or unfavored side of the carbonyl and the other factor is the "product development control" which involves the relative stabilities of the final products. One characteristic feature of ketone V is that both factors are operating in the same direction. Consequently, as can be seen from Table II, the metal hydride reductions all give values which are comparable to those obtained from the equilibration experiments. This cannot be interpreted as a "product development control" since the "steric approach control" will also predict the same results.

The equilibration data establishes the fact that the *cis* isomer is the thermodynamically more stable one. This is reflected in the high value of the equilibrium constant which is calculated to be 19 and which corresponds to a free energy difference of −2.12 kcal./mole with reference to isopropyl alcohol at 89° as a solvent.[8]

Based on the general theory of catalytic reduction as postulated by Farkas,[19] Linstead[20] and Seigal,[21] Wicker[22] has predicted that if the methyl group in 2-methylcyclohexanone was frozen in the *axial* position then equal amounts of *cis-* and *trans-*alcohols would be formed. Since ketone V can be looked upon as a 2-methyl substituted cyclohexanone in which the substituent is fixed in the axial position an isomer ratio as predicted by Wicker should be expected. As can be seen in Table II this prediction has been confirmed.

The treatment of *endo-*2-aminomethylbicyclo-(2.2.1) heptane with nitrous acid yields as the main product bicyclo(3.2.1) octanol-2.[23] This reaction, which involves a ring expansion, leads to the formation (90%) of the thermodynamically more stable *cis-*alcohol.

Acknowledgment.—This work was supported in part by a grant from the Florida State University Research Council.

Experimental[24]

Bicyclo(3.2.1)octanone-2.—The oxidation of bicyclo-(3.2.1)octanol-2 in water (inhomogeneous) with potassium dichromate as described by Alder[3] was incomplete even at 100°. Five grams of crude oxidation product chromatographed on 60 g. of alumina was eluted with 600 ml. of petroleum ether (30–60°) to give 3.8 g. of ketone, m.p. 125–128°, followed by elution with ether to give 0.8 g. of crude alcohol, m.p. 158–162°.

To a solution of 63.0 g. (0.50 mole) of bicyclo(3.2.1) octanol-2 in 170 ml. of acetic acid was added a solution of 39.2 g. (0.392 mole) of chromic anhydride in 24 ml. of water and 190 ml. of acetic acid over a period of 1.2 hours with cooling to maintain the temperature below 25°. After 24 hours at room temperature, the reaction was heated on the steam-bath for one hour, followed by dilution with 1.5 l. of water and exhaustive extraction with pentane. After neutralization of the extracts with solid sodium carbonate, drying over anhydrous sodium sulfate and stripping of the solvent there remained a residue of 50.0 g. (79%) of crude bicyclo(3.2.1)octanone-2.

The ketone was converted to the semicarbazone, m.p. 171–172° (lit.[3] 171°), in 69% yield and back to the ketone in 82% yield by steam distillation from 3 *N* hydrochloric acid, m.p. 127–129° (lit.[3] 129°).

Bicyclo(3.2.1)octanol-2. (a) **Catalytic Reduction.**—A solution of 6.70 g. (0.054 mole) of bicyclo(3.2.1) octanone-2 in 25 ml. of glacial acetic acid containing 1.5 g. of hydrogen chloride was reduced in the presence of 0.25 g. of platinum oxide at 50 lb./sq. in. of hydrogen pressure. A total of 4.4 lb. (102%) of hydrogen was absorbed in 30 minutes. The mixture was poured into 40 ml. of water and 40 g. of ice and extracted five times with 50-ml. portions of pentane. Any acid was removed by standing over anhydrous sodium carbonate, and the solution was finally dried over anhydrous

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[17] J. W. Daly, F. C. Green and R. H. Eastman, THIS JOURNAL, **80**, 6330 (1958).

[18] (a) D. S. Noyce and D. G. Denney, *ibid.*, **72**, 5743 (1950); (b) J. B. Umland and M. I. Jefraim, *ibid.*, **78**, 2788 (1956); (c) H. R. Nace and G. L. O'Connor, *ibid.*, **73**, 5824 (1951); (d) W. G. Dauben, G. J. Fonken and D. S. Noyce, *ibid.*, **78**, 2579 (1956); (e) W. G. Dauben, E. J. Blanz, J. Jui and R. A. Micheli, *ibid.*, **78**, 3752 (1956); (f) O. H. Wheeler and J. L. Mateos, *Chemistry & Industry*, 395 (1957).

[19] A. Farkas and L. Farkas, *Trans. Faraday Soc.*, **33**, 837 (1937).

[20] R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine and R. R. Whetstone, THIS JOURNAL, **64**, 1985 (1942).

[21] S. Seigal, *ibid.*, **75**, 1317 (1953).

[22] R. J. Wicker, *J. Chem. Soc.*, 2165 (1956).

[23] K. Alder, *Suomen Kemist.*, **31B**, 71 (1958).

[24] Melting points and boiling points are uncorrected. Analyses were performed by E. Thommen, Basel, Switzerland. Infrared spectra were run in carbon disulfide solution on a Perkin-Elmer model 21 instrument.

sodium sulfate. The solvent was removed and the oily residue (smelling strongly of bicyclo(3.2.1)octyl-2 acetate) was taken up in 25 ml. of anhydrous ether. The ether solution was added to 2.0 g. (0.053 mole) of lithium aluminum hydride in 25 ml. of anhydrous ether and stirred for 3 hours at room temperature. About 7 ml. of water was added and the ether was decanted. The solids were washed several times with ether and the combined extracts were evaporated to dryness, after standing over anhydrous sodium sulfate. A sample, m.p. 184–190°, was sublimed for infrared analysis; strong absorption occurred at 1015 cm.$^{-1}$, but at 1065 cm.$^{-1}$ only a weak band occurred.

Fractional crystallization of the crude alcohol from pentane gave 1.1 g. (16.2%), m.p. 199–200°; 1.1 g. (16.2%) m.p. 196–198°; 1.5 g. (22%), m.p. 182–186°; and 0.9 g. of lower melting fractions.

A *p*-nitrobenzoate derivative was prepared in the usual way from 1.4 g. (0.0111 mole) of alcohol, m.p. 196–200°, dissolved in 4.2 ml. of anhydrous pyridine, and 2.32 g. (0.0125 mole) of *p*-nitrobenzoyl chloride. One gram (31%) of product, m.p. 94–95°, was obtained after several crystallizations from pentane.

Anal. Calcd. for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.23; N, 5.09. Found: C, 65.79; H, 6.22; N, 5.24.

A suspension of 1.0 g. (0.0036 mole) of the *p*-nitrobenzoate, m.p. 94–95°, in 0.43 ml. of 50% potassium hydroxide (0.0055 mole, 50% excess) was heated on the steam-bath for 10 minutes. To increase the volume, 2.0 ml. of methanol and 1.0 ml. of water was added which also took some of the oil into solution. The mixture was refluxed for three hours, and the clear solution was poured into 125 ml. of water, and extracted with ether. The ether was dried over anhydrous sodium sulfate, and the solvent removed *in vacuo*. The alcohol was crystallized twice from pentane to give 0.22 g. (48%) of shiny plates m.p. 200–201°. The infrared spectrum shows strong absorption at 1015 and none at 1065 cm.$^{-1}$.

One gram of alcohol IIIa was oxidized by chromic anhydride in acetic acid and the ketone isolated as its 2,4-dinitrophenylhydrazone derivative (2.1 g., 86%). A sample (0.5 g.) was chromatographed on an alumina column and of the twenty fractions taken, twelve contained material. Each fraction was recrystallized separately and the m.p.'s of the fractions ranged from 137.5–139° (lit.[3] 137–138°). The combined weight of the recrystallized fractions was 0.4 g. (80%).

(b) **Lithium in Liquid Ammonia.**—To 400 ml. of liquid ammonia were added 66 ml. of anhydrous methanol and 5.0 g. (0.0403 mole) of bicyclo(3.2.1)octanone-2 dissolved in 40 ml. of anhydrous ether. To this solution over a period of one hour were added a total of 5.5 g. (0.793 mole) of lithium in small portions. The lithium methylate was neutralized with 42.0 g. (0.793) of ammonium chloride and the ammonia was allowed to evaporate. After the addition of 300 ml. of water, the solution was extracted 5 times with 100-ml. portions of ether. The combined extracts were concentrated *in vacuo*, the residue taken up in pentane, and dried over anhydrous sodium sulfate. The pentane was removed *in vacuo* to yield 4.6 g. (90%) of product.

A sample was sublimed, m.p. 177–180°, for infrared analysis. Strong absorption occurred at 1065 cm.$^{-1}$, but at 1015 cm.$^{-1}$ only a weak shoulder appeared.

Fractional crystallization of the crude alcohol yielded two crops, m.p. 182–183° and 180–181°, which were combined (2.3 g., 45.7%) and 1.3 g. (23.2%), m.p. 169–170°.

The *p*-nitrobenzoate was prepared in the usual manner from 2.3 g. of the higher melting crops to yield, after fractional crystallization from pentane, 1.6 g. (32.6%) of product, m.p. 83–84°.

Anal. Calcd. for $C_{15}H_{17}NO_4$: N, 5.09. Found: N, 5.29.

The ester was hydrolyzed to the alcohol in the same manner as described for the other isomer. From 1.5 g. of ester was obtained 0.2 g. (20%) of alcohol, m.p. 194–195° by crystallization from pentane. The infrared spectrum showed strong absorption at 1065, none at 1015 cm.$^{-1}$.

(c) **Sodium Borohydride in Methanol.**—A solution of 0.90 g. of bicyclo(3.2.1)octanone-2 (0.0077 mole) in 15 ml. of methanol was added to a solution of 0.3 g. of sodium borohydride in 20 ml. of 15% aqueous methanol at such a rate that a moderate reflux was obtained. After completion of the addition the mixture was refluxed for four hours, 10 ml. of 2 *N* sodium hydroxide added, and the heating continued for an additional two hours. The hydrolyzed solution was extracted continuously with ether for 24 hours. The ether was collected, washed and dried. Evaporation of the solvent *in vacuo* gave a solid (0.85 g., 94%) which was sublimed *in vacuo without fractionation* before infrared analysis. Absorption bands at 1065 and 1015 cm.$^{-1}$ were present.

(d) **Lithium Tri-*t*-butoxy Aluminum Hydride.**[25]—In a three-necked flask equipped with a sealed stirrer, reflux condenser and a dropping funnel was placed 10 ml. of approximately 1 *M* solution of lithium *t*-butoxy aluminum hydride in tetrahydrofuran. A solution of 0.90 g. of bicyclo(3.2.1)-octanone-2 dissolved in 25 ml. of anhydrous tetrahydrofuran was added and the mixture was stirred at room temperature for 24 hours. Careful decomposition with water followed by continuous ether extraction and evaporation of the solvent gave a solid which, from its infrared spectrum, appeared to be a mixture of the alcohol and the starting ketone. Accordingly, the reduction product was treated again with lithium *t*-butoxy aluminum hydride (10 ml. of approximately 1 *M* solution) and the mixture refluxed for 16 hours. Working up the reaction mixture as above led to the isolation of the alcohol in 93% yield, which was subjected to sublimation without fractionation prior to infrared analysis. Absorption bands at 1065 and at 1015 cm.$^{-1}$ were present.

(e) **Lithium Aluminum Hydride.**—Bicyclo(3.2.1)octanone-2 (1 g.) was reduced by lithium aluminum hydride in ether for four hours at room temperature according to the usual procedure. The resulting alcohol was sublimed without fractionation. Absorption bands at 1065 and at 1015 cm.$^{-1}$ were present.

Equilibration of Bicyclo(3.2.1)octanol-2.—The alcohol (2–3 g.) was heated under reflux with an equal amount of freshly prepared and distilled aluminum isopropoxide in 100 ml. of anhydrous isopropyl alcohol containing 1 ml. of acetone for 94 hours. The internal temperature was 88–89°. The solution was poured into 500 ml. of water containing 20 ml. of concentrated hydrochloric acid and extracted several times with ether. The ethereal layer was washed with water, saturated sodium bicarbonate solution, dried over anhydrous sodium sulfate and evaporated *in vacuo*. The equilibrated product was recovered in 95–96% yield and sublimed without fractionation prior to the infrared analysis.

The equilibrium was reached using both the 90% and the 46% *cis* isomer mixture.

Rearrangement of 2-Aminomethylbicyclo(2.2.1)heptane.—Alder's[3] method for nitrous acid rearrangement of the amine was modified in the following manner to give a 70% yield of bicyclo(3.2.1)octanol-2.

A solution of 35 g. (0.21 mole) of 2-aminomethylbicyclo-(2.2.1)heptane hydrochloride in 75 ml. of water and 25 ml. of acetic acid was cooled in an ice-salt-bath, and a solution of 28.7 g. (0.42 mole) of sodium nitrite dissolved in 50 ml. of water was added slowly to the cold solution with stirring. The mixture was stirred overnight at room temperature and then hydrolyzed by heating with aqueous potassium hydroxide for one hour. The alcohol was steam distilled and the distillate extracted thoroughly with ether, washed with water, sodium bicarbonate, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave the alcohol (19 g., 70%), which was sublimed without fractionation. The infrared spectrum showed the absorption bands at 1065 and 1015 cm.$^{-1}$ were present.

Analytical Procedures for Infrared Analysis.—The infrared analyses were made on a Perkin-Elmer model 21 spectrophotometer, using sodium chloride optics. Direct absorbance measurement was used, the base lines being reasonably identical. A large number of solutions were made up and interpolations made to the desired concentrations so as to obtain a precise matching of intensities between the band at 1065 cm.$^{-1}$ in the unknowns and the pure *cis*-bicyclo(3.2.1)octanol-2 as a reference compound. The estimated error in these measurements is 3–4%.

***cis*-Bicyclo(3.2.1)octyl-2 Acetate.**—Pure *cis*-bicyclo(3.2.1)-octanol-2 (2.4 g.) was heated with anhydrous sodium acetate (1.2 g.) and 12 ml. of distilled acetic anhydride for 2 hours on a steam-bath. The mixture was poured on ice, extracted thoroughly with ether, washed with water, and allowed to stand for two hours over anhydrous sodium carbonate and then dried over anhydrous sodium sulfate. The solvent was removed *in vacuo*, and the residue distilled to give a colorless

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[25] H. C. Brown and F. McFarlin, This Journal, **78**, 252 (1956).

liquid with a characteristic odor (2.8 g., 87%), b.p. 52–54° (2.5 mm.), $n^{23}D$ 1.4708.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.37; H, 9.59. Found: C, 70.78; H, 9.55.

***trans*-Bicyclo(3.2.1)octyl-2 Acetate.**—Pure *trans*-bicyclo-(3.2.1)octanol-2 was heated with 1 g. of anhydrous sodium acetate and 10 ml. of acetic anhydride for two hours; working up the reaction mixture as above and distilling the residue gave a colorless liquid (2.3 g., 83%), b.p. 56–57° (2 mm.), $n^{23}D$ 1.4711.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.37; H, 9.59. Found: C, 71.21; H, 9.60.

Bicyclo(2.2.2)octyl-2 Acetate.—Bicyclo(2.2.2)octanol-2 (2.8 g.) was heated with 2 g. of anhydrous sodium acetate and 15 ml. of acetic anhydride for two hours. The reaction mixture was worked up as above and the residue distilled to give a colorless liquid (3.2 g., 86%), b.p. 61–62° (2 mm.), $n^{23}D$ 1.4715.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.37; H, 9.59. Found: C, 71.10; H, 9.52.

Kinetic Measurements on Saponification of the Acetates.—The measurements were carried out with doubly distilled samples of high purity. Standard aqueous hydrochloric acid solution was prepared from constant boiling hydrochloric acid. Standard aqueous sodium hydroxide, carbonate free, was prepared using boiled distilled water, and it was stored in well stoppered polyethylene bottles. An exactly known weight of the acetate was dissolved in freshly distilled absolute alcohol and then weighed again, thus knowing the molarity of the solution. The exact amount required was run from a calibrated burette into a 50-ml. volumetric flask to which was added an equimolar quantity of aqueous sodium hydroxide solution and the flask filled to the mark with absolute alcohol, closed tightly, and kept in a constant temperature bath at 25 ± 0.05°. After suitable time intervals aliquots were drawn, the reaction was stopped immediately with a known excess of standard hydrochloric acid, and the excess was back-titrated against standardized sodium hydroxide solution.

The rate constants were calculated using the integrated form of the equation for a second-order reaction

$$\frac{1}{d-x} - \frac{1}{d} = kt$$

In typical runs the following results were obtained.

A plot of $1/d-x$ *vs.* time gave a good straight line in all the three esters saponified.

Product Analysis.—The alcohol obtained from the saponification of each ester was unrearranged as shown by identity of its infrared spectrum with that of the authentic alcohol.

cis-BICYCLO(3.2.1)OCTYL-2 ACETATE

$N_{HCl} = 0.009893\ N$ $N_{NaOH} = 0.01126\ N$

$T = 25 \pm 0.05°$ mmoles ester = mmoles NaOH = 0.5367

t, sec.	$d - x$	$k \times 10^3$ l. mole^{-1} sec.$^{-1}$
0	0.009875	..
64,000	.004463	1.96
71,520	.003871	2.19
81,000	.003618	2.16
90,000	.003280	2.26
106,500	.003008	2.16
147,600	.002327	2.22
173,100	.002029	2.26
	Average	2.17

trans-BICYCLO(3.2.1)OCTYL-2 ACETATE

$N_{HCl} = 0.01018\ N$ $N_{NaOH} = 0.01237\ N$

$T = 25 \pm 0.05°$ mmoles ester = mmoles NaOH = 0.5922

t, sec.	$d - x$	$k \times 10^3$ l. mole^{-1} sec.$^{-1}$
0	0.01107	..
34,980	.00829	0.87
74,400	.00606	1.00
117,480	.00466	1.01
162,660	.00390	1.03
197,100	.00345	1.01
241,950	.00300	1.00
291,300	.00257	1.03
	Average	1.02

BICYCLO(2.2.2)OCTYL-2 ACETATE

$N_{HCl} = 0.01018\ N$ $N_{NaOH} = 0.01230\ N$

mmoles ester = mmoles NaOH = 0.5922

t, sec.	$d - x$	$k \times 10^3$ *l.* mole^{-1} sec.$^{-1}$
0	0.01091	..
18,240	.00923	0.97
65,280	.00634	1.01
91,200	.00534	1.05
151,320	.00407	1.02
180,000	.00359	1.04
243,000	.00281	1.08
267,600	.00264	1.07
	Average	1.03

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