for D-fructose. While the estimated deuterium content per molecule for the D-mannose is the least accurate of our experimental results, due to uncertainty in the dilution factor occasioned by the low concentration of D-mannose produced in the isomerization reaction, nevertheless, our results indicate that the D-fructose contains a *higher* concentration of carbon-bound deuterium than does the D-mannose. Thus some D-mannose must arise directly from the enediol initially formed from D-glucose.

Possible Applications of Deuterated D-Fructose.—In addition to providing substantiative evidence for the classical enediol mechanism, the isomerization of D-glucose in alkaline heavy water comprises an easy and inexpensive route to isotopically labeled D-fructose. Assuming that labeling at other than carbon-1 and carbon-3 is negligible, the distribution of deuterium in the labeled D-fructose also is known. The isotopic content is such that considerable dilution is possible for studies, conducted in the absence of alkalinity, where it may be used for isotopic dilution analysis or as an auxiliary label for carbon-1 and carbon-3.

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ST. LOUIS, MISSOURI RECEIVED JULY 13, 1951

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY]

Bicyclo[1,2,3]octanol-2

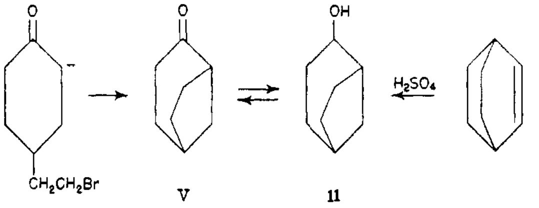
BY MELVIN S. NEWMAN AND YUEHLING TIEN YU[1,2]

The internal condensation of 4-(β-bromoethyl)-cyclohexanone brought about by lithium leads to bicyclo[1,2,3]octanol-2 instead of the expected bicyclo[2,2,2]octanol-1. The proof of structure and synthesis of intermediates is described. Bicyclo[1,2,3]octanol-2 is also formed by the sulfuric acid hydration of bicyclo[2,2,2]octene.

In an effort to prepare bicyclo[2,2,2]octanol-1 desired for studies on the behavior of bridgehead alcohols,[3] we attempted the intramolecular condensation of 4-(β-bromoethyl)-cyclohexanone (I). No reaction took place with magnesium but with lithium an alcohol, II, $C_8H_{14}O$, was isolated in very small yield along with a small amount of a ketone, V, $C_8H_{12}O$, and a large resinous fraction.

The alcohol was saturated and was exceedingly volatile. These properties suggested a bicyclic structure. On treatment with thionyl chloride and pyridine, II yielded a chloride, III, which gave an immediate precipitate when treated with aqueous alcoholic silver nitrate. Reduction of III with sodium in alcohol yielded a hydrocarbon, IV, C_8H_{14}, m.p. 136.8–137.2°. This hydrocarbon was undoubtedly bicyclo[1,2,3]octane.[4] The same hydrocarbon was obtained by oxidizing II to the ketone, V, followed by reducing to IV by the thioacetal hydrogenolysis method.[5] The lower melting points recorded are undoubtedly due to only small amounts of impurity since this type of hydrocarbon has a large cryoscopic constant.

The alcohol, II, was shown to be bicyclo[1,2,3]octanol-2 by comparison of its phenylurethan[6] with that prepared from an authentic sample.[7] In addition, we found that II resulted in good yield from the hydration of bicyclo[2,2,2]octene[8] with 80% sulfuric acid. It is interesting to note that rearrangement from the bicyclo[2,2,2]octyl to the bicyclo[1,2,3]octyl structure occurred in this hydration whereas hydrogen bromide adds to bicyclo[2,2,2]octene without rearrangement.[4d,9] However, 2-bromobicyclo[2,2,2]octane has been shown to rearrange to 2-bromobicyclo[1,2,3] octane on treatment with silver bromide.[4d]



The formation of the alcohol, II, from I may be explained as follows: either an organolithium derivative or lithium itself converts I into an enolate which then undergoes an intramolecular cyclization to yield the ketone, V; the ketone is then reduced to II, again either by an organolithium intermediate

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(1) Taken from the Ph.D. thesis of Mrs. Yu, O.S.U., 1950.

(2) This research was supported by the Office of Naval Research.

(3) P. D. Bartlett and L. H. Knox, THIS JOURNAL, **61**, 3184 (1939).

(4) (a) G. Komppa, *et al.*, *Ann.*, **521**, 242 (1936), reported the m.p. as 133° as did (b) J. W. Barrett and R. P. Linstead, *J. Chem. Soc.*, 611 (1936); (c) K. Alder and E. Windemuth, *Ber.*, **71**, 2404 (1938), reported 141°; (d) W. von E. Doering and M. Farber, THIS JOURNAL, **71**, 1515 (1949), reported 139.5–141°.

(5) M. L. Wolfrom and J. V. Karabinos, *ibid.*, **66**, 909 (1944).

(6) We are indebted to Dr. Doering for a sample of his authentic phenylurethan, m.p. 128–129.5°. We also prepared an authentic sample of phenylurethan from alcohol synthesized as in ref. 7.

(7) K. Alder and E. Windemuth, *Ber.*, **71**, 1939 (1938), and Doering and Farber, ref. 4d, report a melting point of 183–184° for this alcohol. The sample we obtained melted at 173.6–174.8° in a sealed tube. Again the impurity present (a small ketonic impurity as indicated by the infrared absorption spectrum) was surely not large as judged by the fact that compounds in this bicyclic series have large cryoscopic constants.

(8) We are indebted to Dr. H. Walborsky for a sample of bicyclo[2,2,2]octene.

(9) H. Meerwein and K. von Emster, *Ber.*, **55** 2500 (1922).

or by lithium. The isolation of ketone V from the reaction mixture is consistent with this reaction path.

The bromoketone, I, was made by the following sequence of reactions: reduction of *p*-hydroxyphenylhydrocinnamic acid to 4-hydroxycyclohexylpropionic acid; acetylation to 4-acetoxycyclohexylpropionic acid; silver salt–bromine degradation to β-(4-acetoxycyclohexyl)-ethyl bromide; hydrolysis and oxidation to I.

Experimental[10]

_p_-Hydroxycinnamic Acid.—This compound was prepared by heating a stirred mixture of 122 g. of *p*-hydroxybenzaldehyde, 104 g. of malonic acid, 12 cc. of dry pyridine and 400 cc. of benzene until water was no longer being formed.[11] On crystallization from methanol 120 g. (73%) of *p*-hydroxycinnamic acid, m.p. 210-212° dec., was obtained. The ethyl ester, b.p. 175–184° at 0.07 to 0.09 mm., was obtained in 90% yield using benzene and azeotropic distillation. After esterification, it is important not to remove too much solvent at atmospheric pressure because the residue on distillation becomes larger. Preferably, the solvent should be partly removed under reduced pressure.

β-(4-Hydroxycyclohexyl)-propionic Acid.—To a solution of 0.5 g. of sodium in 200 cc. of ethanol was added 117 g. of ethyl *p*-hydroxycinnamate and 10 g. of W-6 nickel.[12] This mixture was hydrogenated at 800 p.s.i. when one mole of hydrogen was absorbed in 5 minutes. The pressure was raised to 1800 p.s.i. and by the time the temperature had risen to 190° the theoretical pressure drop for three moles of hydrogen had been observed.[13] On cooling the catalyst was collected and the alcohol removed from the filtrate under reduced pressure. A wash with 5% sodium hydroxide removed phenolic material (small amount) and the remainder was rectified to yield 80% of an oil, b.p. 147–149° at 9 mm., $n^{20}\text{D}$ 1.4622, which was assumed to be the desired ester. This was saponified and the crude acids yielded 52 g. of solid acid, m.p. 116–125°, on crystallization from acetone. The filtrate contained viscous non-crystalline acid.[14]

This hydrogenation was more successful than others involving: an aqueous alkaline solution of sodium *p*-hydroxycinnamate, and ethyl β-(*p*-hydroxyphenyl)-propionate.

β-(4-Acetoxycyclohexyl)-propionic Acid.—To a solution of 99.5 g. of solid β-(4-hydroxycyclohexyl)-propionic acid in 200 cc. of pyridine was added 180 cc. of acetic anhydride. After standing at 25° for two hours and heating to 95° for one hour, the volatile reagents were removed under reduced pressure and the residue was rectified to yield 78.3 g. (67%) of acetoxy compound, b.p. 160–180° at 0.08 mm., m.p. 80–82°. An analytical sample, m.p. 82.0–82.6°, was prepared by crystallization from benzene–petroleum ether.

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.7; H, 8.4. Found: C, 62.0; H, 8.2.

The silver salt was prepared by adding a hot water slurry of the silver oxide (freshly prepared from 65 g. of silver nitrate and an equivalent of potassium hydroxide) to a melt of 78.3 g. of the acetoxyacid. Heating and stirring were maintained for 4 hours. The silver salt was collected, washed with hot methanol, well powdered, and dried in a vacuum oven at 70° to constant weight. The yield was 117.3 g. (90%).

4-(β-Bromoethyl)-cyclohexanone (I).—The entire amount of the above silver salt was added in portions during 1.5 hours to a stirred solution held near 0° of 20 cc. of *dry* bromine in 200 cc. of *dry* carbon tetrachloride. The mixture was slowly warmed to reflux for one half hour when gas evolution was ended. The bright yellow silver bromide was collected and washed well with dry ether. The filtrate and washings were washed with sodium bisulfite solution and then with sodium carbonate. Acidification of the carbonate wash yielded 3.5 g. of acetoxyacid. The ether and carbon tetrachloride were removed under reduced pressure (nitrogen atmosphere) and the residue heated with 200 cc. of methanol containing 3 drops of sulfuric acid under a column until the temperature at the head was 64° (b.p. of methanol), considerable methyl acetate being formed. The excess methanol was removed *in vacuo* and the residue was taken up in 300 cc. of benzene. This benzene solution was added dropwise to a well-stirred solution of 183.6 g. of sodium dichromate, 243 cc. of sulfuric acid and 135 cc. of acetic acid in 810 cc. of water, the temperature being maintained below 20° during the addition. The temperature was then held at 20–25° for one day. The oxidation product was then taken into benzene which was washed well with dilute bicarbonate solution and water. The solvent was removed *in vacuo* (nitrogen atmosphere) and the residue distilled at 0.1 mm. On redistillation, there was obtained 33 g. (45%) of colorless I, b.p. 94–96° at 0.1 mm., $n^{25}\text{D}$ 1.5032.

Anal. Calcd. for $C_8H_{13}OBr$: C, 46.8; H, 6.3; Br, 39.0. Found: C, 47.2; H, 6.3; Br, 39.0.

The 2,4-dinitrophenylhydrazone on recrystallization from alcohol and ethyl acetate melted at 142.6–144.6°.

Anal. Calcd. for $C_{14}H_{17}O_4N_4Br$: C, 43.6; H, 4.4. Found: C, 44.0; H, 4.1.

Bicyclo[1,2,3]octanol-2 (II) (a) From I.—To a well-stirred suspension of 0.8 g. of finely cut lithium wire in 50 cc. of dry ether was added 5 g. of I. No appreciable reaction was noticed but after stirring for 12 hours at room temperature the surface of the remaining lithium was bright. Another 3 g. of I in 100 cc. of ether was added whereupon the surface of the lithium became dull. After stirring for 12 hours, it was bright again. After refluxing for one hour the mixture was treated with saturated ammonium chloride solution. The washed and dried ether solution was distilled through a column to remove ether and the residue was steam distilled. The organic portion of the steam distillate was crystallized from a small amount of petroleum ether (b.p. 35–40°, Skellysolve F) at about −80°. The solid obtained was purified by three sublimations to yield 0.5 g. (10%) of II as colorless crystals,[7] m.p. 173.6–174.8° in a sealed tube. The molecular weight determined cryoscopically in benzene was 115 (theory 126). The *i* factor determined as described recently[15] varied with time as follows: 27 min., i = 3.28; 78, 3.54; 110, 3.68; 156, 3.93; 190, 4.06; 224, 4.10; 258, 4.31; 24 hours, 5.54. On extrapolation to zero time, the *i* factor was 3.1. This experiment indicates that I probably forms an acid sulfate in sulfuric acid as secondary alcohols do.

$$C_8H_{13}OH + 2H_2SO_4 \rightleftharpoons C_8H_{13}OSO_2OH^+ + H_3O^+ + HSO_4$$

This sulfate is then further acted upon by the sulfuric acid to produce oxidation products which cause the increase of *i* factor with time.

Anal. Calcd. for $C_8H_{14}O$: C, 76.1; H, 11.2. Found: C, 76.4; H, 11.2.

The *p*-nitrobenzoate melted at 78.4–79.4°.

Anal. Calcd. for $C_{15}H_{17}NO_4$: C, 65.5; H, 6.2; N, 5.1. Found: C, 65.4; H, 6.2; N, 5.0.

The phenylurethan melted at 129.0–129.8° alone and mixed with an authentic sample[6] of the phenylurethan of bicyclo[1,2,3]octanol-2.

The material remaining in the mother liquors of the recrystallization of II from Skellysolve F was partly crystalline (mainly more II). On treatment with Girard's reagent P a crystalline ketone fraction was obtained but it proved difficult to purify (hence no analysis) because of its extreme volatility. The 2,4-dinitrophenylhydrazone prepared therefrom was light orange and melted at 137.8–138.6° after three recrystallizations from methanol and ethyl acetate and did not depress the melting point of the same derivative made from a sample of ketone, V, which had been prepared by oxidation of II.

Anal. Calcd. for $C_{14}H_{16}O_4N_4$: C, 55.3; H, 5.3; N, 18.4. Found: C, 55.4; H, 5.4; N, 18.5.

No accurate yield can be reported for the ketone, V, formed in the lithium cyclization of I, but it was present in

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[10] All melting points corrected. Microanalyses by H. S. Clarke Laboratory, Urbana, Illinois.

[11] Compare K. C. Pandya and T. A. Vahidy, *Proc. Indian Acad. Sci.*, **4A**, 140 (1936).

[12] H. Adkins and H. R. Billica, THIS JOURNAL, **70**, 695 (1948).

[13] Compare H. E. Ungnade and F. V. Morriss, *ibid.*, **70**, 1898 (1948).

[14] P. Mastagli and M. Metayer, *Compt. rend.*, **224**, 1779 (1947), report a m.p. of 127° for the high melting isomer, the other being liquid.

[15] M. S. Newman and N. C. Deno, THIS JOURNAL, **73**, 3644 (1951).

at least as large an amount as the alcohol, II (10% minimum).

(b) **From Bicyclo[2,2,2]octene.**—Three grams of bicyclo[2,2,2]octene[3] was added to a solution of 3 cc. of water and 6 cc. of concentrated sulfuric acid. The mixture was shaken at 20–25° until homogeneous, diluted with water and steamed. Purification of the distillate by sublimation yielded an alcohol, m.p. 173.4–176.2°, which was identical to that obtained by the above cyclization experiment. The yield of purified alcohol, II, was 73%.

Bicyclo[1,2,3]octane, IV. (a) **Via Chloride, III.**—A mixture of 0.8 g. of II, 0.6 cc. of dry pyridine, and 3 cc. of pure thionyl chloride was mixed at −80° and sealed into a small tube. After maintaining at 80° for 20 hours, the mixture was poured into ice-water and steamed. The distillate was extracted with ether and this extract washed with bicarbonate, water, and saturated salt solution. The ether was removed by distilling through a column, the last traces under reduced pressure. The residue was sublimed to yield 0.61 g. (66%) of crude solid chloride, III. After three partial sublimations under reduced pressure at 50°, the chloride obtained formed a colorless solid, m.p. 66.6–67.6° in a sealed tube. The chloride is extremely volatile and all operations must be carried out with precautions to avoid loss. It proved difficult to get correct analytical figures as the chloride was always accompanied by oxygenated impurities.

Anal. Calcd. for $C_8H_{13}Cl$: C, 66.4; H, 9.0; Cl, 24.6. Found: C, 65.3; H, 8.9; Cl, 23.2.

In a small flask 0.2 g. of III was dissolved in 8 cc. of absolute alcohol and 0.8 g. of sodium in small pieces was added. The mixture was then refluxed for one hour. It was then diluted with water and steamed into a wide tube within a sublimation tube cooled by a bath held at −80°. The hydrocarbon formed steam distils very rapidly with the first portions of alcohol. The frozen distillate was wiped from the wide tube with cotton and some calcium chloride was added, the whole being pushed down into the sublimation tube. The hydrocarbon was then sublimed onto a cold finger condenser at room temperature. This hydrocarbon is extremely volatile and much was lost in other experiments before adequate precautions were taken. After another sublimation from phosphorus pentoxide a sample of the hydrocarbon, IV, melted at 136.8–137.2° in a sealed tube.[4]

Anal. Calcd. for C_8H_{14}: C, 87.3; H, 12.7. Found: C, 87.0; H, 12.8.

(b) **Via Ketone, V.**—A mixture of 0.2 g. of V, 3 cc. of ethyl mercaptan, 0.12 g. of sodium sulfate and 0.16 g. of freshly fused zinc chloride was held at 5–10° for one day and at 20–25° for 4 hours and then poured into water. The organic product was taken into ether, washed with 10% sodium hydroxide, water, and the ether extract was dried over sodium sulfate. The ether was distilled and the oily residue was refluxed for 15 hours with 20 g. of Raney nickel and 20 cc. of absolute alcohol.[5] The hydrocarbon, IV, was isolated as described above and had the same properties and melting point.

COLUMBUS 10, OHIO RECEIVED JULY 9, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MICHIGAN]

The Competitive Formation of Different Olefins from Quaternary Amines

BY PETER A. S. SMITH AND SIMON FRANK[1]

A series of mixed tetraalkylammonium hydroxides has been submitted to the Hofmann degradation. A quantitative comparison of the relative ease of olefin formation has been obtained by mass-spectrometric analysis of the mixtures of olefins produced. Increased branching at the γ-position of an alkyl group successively decreases its conversion to olefin, and in certain cases a statistical effect can be demonstrated.

The decomposition of quaternary ammonium hydroxides on heating to form olefins, water and tertiary amines was described by A. W. Hofmann[2] in 1851 and bears his name. His investigation gave rise to the familiar "Hofmann rule," that ethylene is preferentially formed whenever the quaternary base has an N-attached ethyl group. Since its original formulation, this rule has undergone certain revisions,[3] although it is still substantially valid.

As part of a program of investigation of elimination reactions, Hanhart and Ingold[4] determined the compositions of the mixtures of olefins obtained by the pyrolysis of some quaternary ammonium hydroxides of the type $RR'N(CH_3)_2{}^+OH^-$. Their determinations of the proportions of olefins were accomplished by fractional distillation of the olefin dibromides, and led to the generalization that the alkyl group having the most acidic β-hydrogen is preferentially eliminated as olefin. Because of the limitations of the method of analysis then available, the ratios of olefins obtained were only semiquantitative; in addition, certain not readily obtainable alkyl groups of theoretical interest are not represented in their work.

We have carried out similar experiments on a series of quaternary ammonium hydroxides of the type $(R—CH_2—CH_2)_2N^+(CH_2—CH_2—R')_2\ OH^-$, and some related types. We were able to determine the ratios of olefins produced with some accuracy, due to the availability of mass-spectrometric analysis, and thus to confirm the results of Hanhart and Ingold. In addition, we were able to extend Hanhart and Ingold's measurements to include the β-*t*-butylethyl group, and to demonstrate the operation of a statistical effect in compounds of the type $(R-CH_2CH_2)_{2+n}N^+(CH_2CH_2-R')_{2-n}OH^-$.

Discussion of Results

The quaternary bases examined and the composition of olefins obtained from them are given in Table I. The first three compounds allow a comparison to be made of the relative effect of the groups H–, CH_3–, CH_3CH_2– and $(CH_3)_2CH$–, inasmuch as these groups constitute R and R′ in $(R-CH_2-CH_2)_2N^+(CH_2-CH_2-R')_2$. It is apparent that the difference between H– and CH_3– in the β-position is very much greater than the differences among the alkyl groups themselves. Even when a statistical correction is made for the presence of three β-hydrogens in an ethyl group as compared with only two in groups of the type $R-CH_2-CH_2-$

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(1) From the doctoral dissertation of Simon Frank, 1950.

(2) A. W. Hofmann, *Phil. Trans.*, **II**, 357 (1851); *Ann.*, **78**, 253 (1851).

(3) For leading references, see E. R. Alexander, "Principles of Ionic Organic Reactions," John Wiley and Sons, New York, N. Y., 1950, Chapter 5; also R. B. Woodward and W. E. Doering, THIS JOURNAL, **66**, 849 (1949).

(4) W. Hanhart and C. K. Ingold, *J. Chem. Soc.*, 997 (1927).