(IIA) has one-tenth the activity of the methylheptanol.[2] This tenfold difference in activity has also been observed in the series containing the piperidyl group.[2] The data on compounds IVA and VA show what has already been observed with respect to *p*-alkyl substituents on the phenyl group.[3] As has already been observed in these amino alcohols with the phenyl group in the 3-position,[2] the naphthylheptanol (IXA) is more active than the corresponding pentanol (VIIA). The fact that the 4-chloro-1-naphthyl derivatives (VIA, VIIIA and XA) are less active than their parent ketone[5] must be attributed, at least in part, to their low solubility in the test medium.

Table II lists seven piperidyl tertiary alcohols. It is interesting that the cyclopentyl propanol (IB) is only one-tenth as active as the corresponding cyclohexyl propanol.[2] In this series the 2-naphthylpentanol (IIIB) and heptanol (VB) have the same activity, and are more active than the 1-naphthylpentanol.[3] The activities of compounds IIB, IIIB and VB when compared with the corresponding members of the morpholinyl series (VIA, VIIA and IXA) illustrate the superiority of the piperidyl group for conferring antispasmodic activity. The unexpected decrease in activity shown by the higher homologs (IVB and VIB) of compound IIB is probably due partially to their lower solubility in the test medium.

Experimental

Procedures a and b are identical with the corresponding procedures described in paper II of this series.[3]

Procedure c.—The Grignard reagent was prepared as in procedure b. The appropriate amino ketone hydrochloride was then added as a finely divided solid at 50–70°. The ratio of Grignard reagent to ketone varied between 3:1 and 4:1. The remainder of the procedure is identical with procedure b.

Acknowledgments.—The authors greatly appreciate the coöperation in this work of Dr. R. W. Cunningham, Dr. B. K. Harned and their assistants of the Pharmacology Department of the Lederle Laboratories Division, who have determined the antispasmodic activity of these compounds. For their technical assistance in the synthesis of some of these compounds, we wish to thank Mr. Peter Drenchko, Miss Ellen G. Lee and Mr. Elmer K. Norton. The authors are indebted to Mr. O. E. Sundberg, Mrs. M. E. Nielsen and Miss I. H. Prokul for all microanalyses.

Summary

Seventeen new morpholinyl and piperidyl tertiary alcohols have been prepared by the addition of Grignard reagents to the corresponding β-aminoethyl aromatic ketones, and their antispasmodic activities have been reported.

Active amino alcohols show greater activity than the ketones from which they were derived.

Alcohols with complex aromatic substituents are, in general, less active than the corresponding alcohols with a simple phenyl substituent.

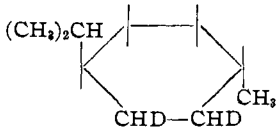
Bound Brook, New Jersey
Received November 30, 1949

NOTES

Optical Activity in Compounds Containing Deuterium. II. 3-Deutero-*trans*-*p*-menthane

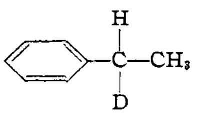
By Elliot R. Alexander

In an earlier communication[1] it was shown that the catalytic reduction of *trans*-2-*p*-menthene with deuterium gas gave an optically active 2,3-dideutero-*trans*-*p*-menthane (I). More recently it has been found[2] that the reduction of optically active α-phenylethyl chloride with a mixture of lithium aluminum deuteride and lithium deuteride produced an optically active deuterohydrocarbon (II). These appear to be the only two compounds reported in which optical activity depends solely upon the replacement of hydrogen atoms by deuterium atoms. The preparation of an optically active 3-deutero-*trans*-*p*-menthane (III) by the reaction of lithium aluminum deuteride with *l*-menthyl *p*-toluenesulfonate was particularly attractive since the same reaction with lithium



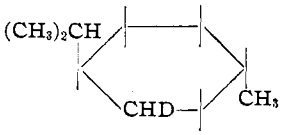
$[\alpha]^{25}_{D}$ −0.09 ± 0.01° (l = 2, no solvent)

I



$[\alpha]^{25}_{D}$ −0.30 ± 0.02° (l = 2, no solvent)

II



$[\alpha]^{25}_{D}$ −0.09 ± 0.02° (l = 2, no solvent)

III

---

[1] Alexander and Pinkus, This Journal, 71, 1786 (1949).

[2] Eliel, *ibid.*, 71, 3970 (1949).

aluminum hydride gave *trans-p*-menthane[3] and since we had found that *l*-menthyl chloride was inert to this reagent.

In Chart 1 are summarized the experiments which were carried out. It is evident that the reduction of *l*-menthyl *p*-toluenesulfonate with lithium aluminum deuteride gives a deutero-hydrocarbon whose optical rotation is far beyond the limits of experimental error. It is unlikely that optical activity is caused by the presence of impurities. In support of this conclusion it should be observed that: (1) Reduction of the same batch of *l*-menthyl *p*-toluenesulfonate with lithium aluminum hydride resulted in an optically inactive hydrocarbon. (2) Treatment of the 3-deutero-*trans-p*-menthane with such reagents as hydrogen and platinum, alkaline potassium permanganate, sulfuric acid, a mixture of nitric and sulfuric acids, and metallic sodium changed none of the physical properties of the material.

CHART I

l-Menthyl *p*-Toluenesulfonate
[$[\alpha]^{28}\mathrm{D}$ $-67.8 \pm 2.8°$ ($c = 0.7$, $l = 2$, chloroform)]

$\downarrow$ $LiAlH_4$ (in ether)	$\downarrow$ $LiAlD_4$ (in ether)
trans-p-menthane	3-deutero-*trans-p*-menthane
$\alpha^{25}\mathrm{D} = 0.00 \pm 0.02°$	$\alpha^{25}\mathrm{D} = -0.14 \pm 0.02°$
($l = 2$, no solvent)	($l = 2$, no solvent)

(No change in properties after A and B)

A. Catalytic hydrogenation over platinum
B. 1. Treatment with alkaline potassium permanganate
 2. Nitric–sulfuric acid wash
 3. Distillation over sodium

Experimental[4]

trans-p-Menthane.[3]—*l*-Menthyl *p*-toluenesulfonate[1] (14.0 g., 0.0452 mole) was added portionwise to a solution of 90 ml. of dry ether and 2.45 g. (0.0645 mole) of lithium aluminum hydride contained in a clean dry three necked flask fitted with a mechanical stirrer, a reflux condenser carrying a calcium chloride tube, and a glass stopper. After each addition some frothing occurred but the reaction did not appear to be exothermic. The transformation was completed by stirring and heating the reaction mixture overnight under gentle reflux. During this time a granular white solid separated.

Decomposition of the metal complexes was carried out by the cautious addition of a solution of 10 ml. of water and 40 ml. of dioxane followed in turn by 100 ml. of water and enough concentrated hydrochloric acid (about 75 ml.) to dissolve completely the flocculent aluminum salts which were formed. The layers were then separated. The aqueous layer was extracted twice with 10-ml. portions of ether and the combined ether extracts were dried over anhydrous magnesium sulfate. After removing as much ether as possible on a water-bath, 100 ml. of low boiling petroleum ether was added to the residue and the petroleum ether solution was washed successively with three 25-ml. portions of water, six 75-ml. portions of concd. sulfuric acid and four 50-ml. portions of water. The solution was then dried over anhydrous potassium carbonate, filtered into a modified Claisen flask and the petroleum ether was removed on a water-bath. Distillation of the residue gave fractions 1 (0.2 g., $n^{20}\mathrm{D}$ 1.4367) and 2 (3.5 g., $n^{20}\mathrm{D}$ 1.4374), both of which boiled at 57° (17 mm.). Fraction 2 was optically inactive, $\alpha^{25}\mathrm{D} = 0.00 \pm 0.02°$ ($l = 2$, no solvent), d^{20}_{20} 0.7920, d^{20}_{4} 0.7906 and represents a yield of 55% based upon *l*-menthyl *p*-toluenesulfonate. Its infrared absorption curve[5] was identical with that of the *trans-p*-menthane prepared by the catalytic hydrogenation of *trans*-2-*p*-menthene.[1]

3-Deutero-*trans-p*-menthane.—Following exactly the same procedure as described above the reaction was carried out with 22.2 g. (0.0717 mole) of *l*-menthyl *p*-toluenesulfonate, 200 ml. of dry ether and 3.0 g. (0.0717 mole) of lithium aluminum deuteride.[6] Distillation gave fractions 1 (0.3 g., $n^{20}\mathrm{D}$ 1.4365) and 2 (4.6 g., $n^{20}\mathrm{D}$ 1.4372) both of which boiled at 55° (17 mm.). Fraction 2, which amounted to a yield of 46%, had the following additional physical properties: d^{20}_{20} 0.7971, d^{20}_{4} 0.7956,[7] $\alpha^{25}\mathrm{D} = -0.07 \pm 0.01°$ ($l = 1$, no solvent), $\alpha^{25}\mathrm{D} = -0.14 \pm 0.02°$ ($l = 2$, no solvent), $[\alpha]^{25}\mathrm{D}$ 0.09 ± 0.01° ($l = 2$, no solvent).[8] Its infrared absorption curve[5] showed no absorption in the alcohol (3300–3700 cm.$^{-1}$) or olefin (1650 cm.$^{-1}$) regions but there was strong absorption in the region 2133 cm.$^{-1}$ which is characteristic of the C-D stretching frequency.

Attempted Hydrogenation of 3-Deutero-*trans-p*-menthane.—To a solution of 2.0 ml. (1.6 g., 0.0113 mole) 3-deutero-*trans-p*-menthane in 50 ml. of ether was added 0.1 g. of Adams platinum oxide catalyst and the mixture was hydrogenated at 45 pounds per square in. pressure for four hours. No hydrogen appeared to be absorbed. The solution was filtered, the ether was removed on a water-bath and the residue was distilled under reduced pressure from a modified Claisen flask. Fractions 1 (0.1 g.) and 2 (1.3 g.) both boiled at 54° (17 mm.) and had the same refractive index, $n^{20}\mathrm{D}$ 1.4371. The optical rotation of fraction 2 had not changed, $\alpha^{25}\mathrm{D} = -0.07 \pm 0.01°$ ($l = 1$, no solvent) and no change was found in its infrared absorption curve. Fractions 1 and 2 weighed 1.4 g., which represents an 87% recovery.

Attempted Oxidation of 3-Deutero-*trans-p*-menthane.—Another 2.0-ml. sample was withdrawn from fraction 2 of 3-deutero-*trans-p*-menthane and oxidized with alkaline potassium permanganate by the procedure already described for 2,3-dideuteromenthane.[1] After two drops of fore-run, 1.2 g. (75%) of 3-deutero-*trans-p*-menthane was recovered, b. p. 57° (18 mm.), $n^{20}\mathrm{D}$ 1.4371, $\alpha^{25}\mathrm{D} = 0.07 \pm 0.01°$ ($l = 1$, no solvent). The infrared absorption curve of this material was the same as those which had been obtained previously.

---

[3] Schmid and Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949).

[4] All melting points and boiling points are uncorrected.

[5] We are indebted to Miss Elizabeth Petersen and Dr. H. S Gutowsky for the determination and interpretation of the infrared data mentioned in this paper.

[6] Obtained from Metal Hydrides, Inc., Beverly, Massachusetts, on allocation from the United States Atomic Energy Commission. The isotopic purity of this material was 96 atom per cent. deuterium.

[7] This value is in agreement with the formula of McLean and Adams [THIS JOURNAL, **58**, 804 (1936)] for calculating the density of a deuterium compound from the density of its hydrogen analog. The calculated value is 0.7958.

[8] $[\alpha]^{25}\mathrm{D} = \alpha^{25}\mathrm{D}/(l)$ (density).

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS
URBANA, ILLNOIS

RECEIVED FEBRUARY 27, 1950

The Preparation of 4,4'-Dihydroxyhydrobenzoin by Electrolytic Reduction at Constant Cathode Potential

BY MILTON J. ALLEN

Biedermann[1] and Hertzfeld[2] both prepared 4,4'-dihydroxyhydrobenzoin by reduction of *p*-hydroxybenzaldehyde with sodium amalgam. This method yielded both the alcohol and the

---

[1] Biedermann, *Ber.*, **19**, 2374 (1886).

[2] Hertzfeld, *ibid.*, **10**, 1267 (1877).