quinoline, collected in the condenser and receiving flask. Thirty grams of the moist white solid was obtained. The liquid distillate was saturated with sodium sulfate and extracted with two 50-ml. portions of ether; these extracts were added to the white solid which dissolved. The solution was dried over sodium sulfate for two days. Distillation produced 17 g. of 3-fluoroquinoline (91.5% from the diazonium salt; 73.5% from the amine). Addition of water to the fluoroquinoline resulted in the formation of the solid hydrate.

Attempted Preparation of 4-Fluoroquinoline.—A solution of 3 g. of 4-aminoquinoline in 45 ml. of 40% fluoboric acid was cooled to 0° and diazotized with 1.5 g. of sodium nitrite in 2 ml. of water. The mixture was then cooled to −10° to ensure complete precipitation and filtered rapidly through a cold filter, washed thrice with cold dry ether, and transferred to a beaker of cold ether. The ether suspension was allowed to warm slowly; decomposition of the diazonium salt started at 10°, was moderate at 15°, and quite rapid at 22°. After decomposition was complete the solution was made alkaline with sodium hydroxide; the mixture was vigorously shaken and the ether layer separated and dried over sodium sulfate for twelve hours. Distillation produced a small amount of colorless liquid boiling at 119° (30 mm.), which was presumably 4-fluoroquinoline, with a considerable quantity of tarry material remaining in the distillation flask. The distillate solidified quite rapidly to a tan solid which shrivelled at 149°, softened at 165°, and melted at 180–195°. Analytical data suggest that this may be impure N-(4′-quinolyl)-4-fluoroquinolinium fluoride.

Anal. Calcd. for $C_{18}H_{12}N_2F_2$: N, 9.53; F, 12.91. Found: N, 7.54, 7.49; F, 11.58.

A picrate of this material was prepared; it contained no fluorine, but no other analysis was attempted because it could not be obtained pure; m. p. 180–195°. This may be the picrate of N-(4′-quinolyl)-4-quinolone if 4-fluoroquinoline is analogous to 4-fluoropyridine in its decomposition.[2]

5-Fluoroquinoline.—The treatment of 4.2 g. of 5-aminoquinoline by the method used for 3-aminoquinoline produced 9.5 g. (94%) of a brick-red diazonium fluoborate, m. p. 95° (dec.). Decomposition of this salt in toluene produced 2.6 g. of 5-fluoroquinoline (59% from the amine).

6-Fluoroquinoline.—A yield of 10.4 g. (95.5%) of 6-quinolinediazonium fluoborate was obtained from 5 g. of 6-aminoquinoline; the salt was precipitated from the fluoboric acid solution by addition of 50% ethanol–ether to the diazotized solution. Decomposition was carried out without solvent producing 3 g. of 6-fluoroquinoline (60% from the diazonium fluoborate).

7-Fluoroquinoline.—A 100% yield of 7-quinolinediazonium fluoborate, m. p. 123° (dec.), was prepared from 5.5 g. of the corresponding amine using the method described for 3-aminoquinoline. Decomposition of the salt in xylene gave 1.5 g. (26.7%) of 7-fluoroquinoline.

8-Fluoroquinoline.—A 74% yield of 8-quinolinediazonium fluoborate was obtained from 15 g. of the corresponding amine using the method described for 3-aminoquinoline. The salt was decomposed without solvent in 6-g. portions; the resulting tar was dissolved in dilute hydrochloric acid, the solution neutralized with sodium carbonate, extracted with ether, dried over sodium sulfate, and distilled. A yield of 4.9 g. (33.1% from the diazonium salt) was obtained.

Summary

The Schiemann reaction has been employed to prepare all the monofluoroquinolines with the possible exception of 4-fluoroquinoline; the latter compound is quite unstable, changing from a colorless liquid to a tan solid quite rapidly after distillation.

CHAPEL HILL, NORTH CAROLINA

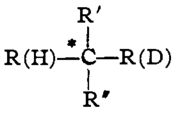
RECEIVED APRIL 12, 1948

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Optical Activity in Compounds Containing Deuterium. I. 2,3-Dideutero-*trans*-Menthane

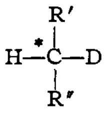
BY ELLIOT R. ALEXANDER AND A. G. PINKUS

An interesting aspect of stereochemistry is the question of whether or not a molecule can be optically active when the sole cause of asymmetry is the replacement of a hydrogen by a deuterium atom. Such molecules can be divided into the two general types, I and II



$$\mathrm{R(H)}-\overset{\mathrm{R'}}{\underset{\mathrm{R''}}{\overset{*}{\mathrm{C}}}}-\mathrm{R(D)}$$

I



$$\mathrm{H}-\overset{\mathrm{R'}}{\underset{\mathrm{R''}}{\overset{*}{\mathrm{C}}}}-\mathrm{D}$$

II

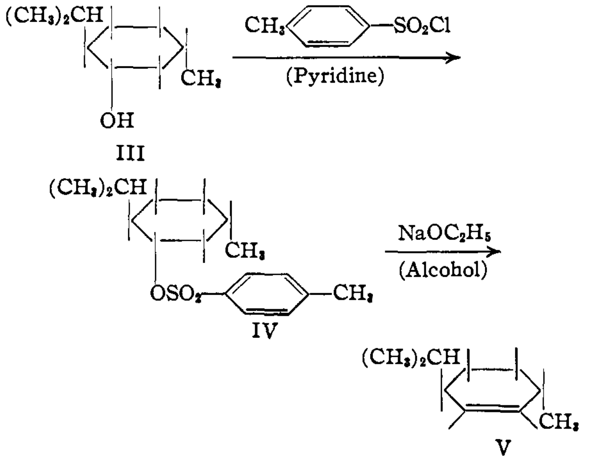
With the first of these, asymmetry results from a difference between two groups which are the same except that one contains hydrogen and the other contains deuterium. In the other (II), deuterium and hydrogen are compared directly at an asymmetric center. Many attempts have been made to demonstrate optical activity in compounds of type I[1-7] and type II,[8-14] but none of these investigations has shown conclusively that activity is present.

It is interesting, however, that when hydrogen is replaced by deuterium in an optically active molecule other than a hydrocarbon, there is often

(1) Clemo, Raper and Robson, *J. Chem. Soc.*, 431 (1939).
(2) Clemo and McQuillan, *ibid.*, 808 (1936).
(3) Clemo and Swan, *ibid.*, 1960 (1939); 370 (1942).
(4) Adams and Tarbell, THIS JOURNAL, **60**, 1260 (1938).
(5) McGrew and Adams, *ibid.*, **59**, 1497 (1937).
(6) Burwell, Hummel and Wallis, *J. Org. Chem.*, **1**, 332 (1936).
(7) Erlenmeyer and Schenkel, *Helv. Chim. Acta*, **19**, 1169 (1936).
(8) Erlenmeyer and Gärtner, *ibid.*, **19**, 145, 331 (1936).
(9) Erlenmeyer, Fischer and Baer, *ibid.*, **20**, 1012 (1937).
(10) Biilman, Jensen and Knuth, *Ber.*, **69**, 1031 (1936).
(11) Biilman, Jensen and Bak, *ibid.*, **69**, 1947 (1936).
(12) Leffler and Adams, THIS JOURNAL, **58**, 1551 (1936).
(13) Leffler and Adams, *ibid.*, **58**, 1555 (1936).
(14) Porter, *ibid.*, **57**, 1436 (1935).

a slight change in the rotatory power,[15–18] although there are a few cases where no such difference has been observed.[19,20] Consequently, one is led to suspect that molecules of type II should be capable of optical activity, although the rotation might be very small.[21]

Accordingly, it was the object of this work to prepare a compound of type II by the asymmetric reduction of an optically active olefin with deuterium gas. This paper describes the reduction of *trans*-2-menthene, prepared through the sequence of reactions III–V.



Experimental[22]

l-Menthol (III).—U. S. P., natural, m. p. 42–43°, $[\alpha]^{28}\text{D}$ −49.3° (c = 0.5, l = 2, 95% ethanol).

Diethylcarbitol.—Commercial grade diethylcarbitol was purified by a modification of the method used by Brewster.[23] One liter of technical grade diethylcarbitol was distilled *in vacuo* (30 mm.), discarding a first fraction of 50 ml. and leaving a similar quantity of residue. The main body of distillate was heated with 5 g. of sodium at 100–110° for sixteen hours and the brown residue was removed by filtration. Sodium (2 g.) was added to the filtrate, the mixture was heated two hours longer at the same temperature, and then distilled *in vacuo*, b. p. 92–92.5° (28 mm.).

***p*-Toluenesulfonyl Chloride.**—Technical grade *p*-toluenesulfonyl chloride was purified by the method of Knoop and Landsman[24] and dried to constant weight *in vacuo* over sulfuric acid, m. p. 66.5–67.5°.

Deuterium Gas.—Deuterium gas of 95% minimum purity was obtained from the Stuart Oxygen Co., San Francisco, Cal.

Pyridine.—Medicinal grade pyridine was dried over potassium hydroxide pellets and filtered immediately before use.

Absolute Alcohol.—Commercial absolute ethanol was purified by the method of Lund and Bjerrum,[25] b. p. 77.5° (747 mm.).

Petroleum Ether.—Commercial grade petroleum ether was washed in turn with four portions of sulfuric acid, water, three portions of 5% sodium carbonate and finally again with water. It was then dried over calcium chloride and distilled from sodium. The fraction boiling in the range of 37–40° (742 mm.) was collected.

1-Menthyl *p*-Toluenesulfonate (IV).—The tosyl ester was prepared by a modification of the method of Phillips,[26] but it was not recrystallized from alcohol. From 40 g. (0.256 mole) of 1-menthol, pyridine (50 ml.), and *p*-toluenesulfonyl chloride (60.0 g., 0.315 mole), was obtained 73 g. (96.7%) of 1-menthyl *p*-toluenesulfonate, m. p. 93–94.0°. It was dried to constant weight *in vacuo* over concentrated sulfuric acid, $[\alpha]^{28}\text{D}$ −67.8 ± 2.8° (c = 0.7, l = 2, chloroform).

***trans*-2-Menthene (V).**—This material was prepared by the method of Hückel and co-workers, which consists in treating l-menthyl *p*-toluenesulfonate with an alcoholic solution of sodium ethylate.[27,28] After two distillations from sodium through a seven inch column packed with glass helices, there was obtained from 73 g. (0.248 mole) of the tosyl ester: fraction 1 (0.27 g., $n^{20}\text{D}$ 1.4502), fraction 2 (0.53 g., $n^{20}\text{D}$ 1.4500) and fractions 3 (8.39 g.) and 4 (4.38 g.) both $n^{20}\text{D}$ 1.4499, all boiling at 58.0° (15 mm.). All of the fractions totaled 13.57 g. representing a 40% yield based on the ester. The infrared absorption curves of fractions 3 and 4 were identical (Fig. 1) and showed no absorption in the characteristic alcohol (3300–3700 cm.$^{-1}$) region. The observed rotation ($\alpha^{25}\text{D}$) of fraction 3, was +106.92°. Based upon a density of 0.8102 (20/4)[27] the specific rotation ($[\alpha]^{25}\text{D}$)[33] was calculated to be +132.0.[29]

***trans*-Menthane.**—*trans*-2-Menthene (fractions 3 and 4 above, 12.77 g., 0.0923 mole) was dissolved in purified diethylcarbitol (100 ml.) and the resulting solution [α_D + 31.09 (l = 2)] was divided into two equal parts. One of these was reduced with hydrogen at two atmospheres pressure[30] using a Raney nickel catalyst. The catalyst was washed several times by decantation with diethylcarbitol before adding the solution of olefin. In two hours and twelve minutes, 0.0441 mole (96%) of hydrogen was absorbed and no further pressure drop was observed on continued shaking. The solution was filtered and the observed rotation of the filtrate (α_D) was found to be +1.35° (l = 2), corresponding to about 95.6% reduction.[31] The filtrate was then added to 400 ml. of water in a separatory funnel, shaken, and extracted several times with petroleum ether. The petroleum ether extracts were combined and washed in turn with five 30-ml. portions of water, nine 20-ml. portions of cold, concentrated sulfuric acid, three 30-ml. portions of 5% sodium carbonate and finally with five 30-ml. portions of distilled water. The solution was then dried over sodium sulfate, filtered into a modified Claisen flask and the petroleum ether removed *in vacuo*. Distillation of the residue gave fractions 1 (0.71 g.) and 2 (1.55 g.) both $n^{20}\text{D}$ 1.4366[32] and

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(15) Erlenmeyer and Bitterlin, *Helv. Chim. Acta*, **23**, 207 (1940).

(16) Erlenmeyer and Schenkel, *ibid.*, **19**, 1199 (1936).

(17) Young and Porter, THIS JOURNAL, **59**, 328, 1437 (1937).

(18) Schoenheimer and Rittenberg, *J. Biol. Chem.*, **111**, 183 (1935).

(19) Coppock and Partridge, *Nature*, **137**, 907 (1936).

(20) Coppock, Kenyon and Partridge, *J. Chem. Soc.*, 1069 (1938).

(21) See, however, Fréon, *J. phys. radium*, [8] **1**, 374 (1940).

(22) All melting points and boiling points are uncorrected.

(23) Brewster, Ph.D. thesis, University of Illinois, June, 1948.

(24) Knoop and Landsman, *Z. physiol. Chem.*, **89**, 159 (1914).

(25) Lund and Bjerrum, *Ber.*, **64**, 210 (1931).

(26) Phillips, *J. Chem. Soc.*, 2584 (1925).

(27) Hückel and Tappe, *Ann.*, **537**, 113 (1938).

(28) Hückel, Tappe and Legutke, *Ann.*, **543**, 191 (1940).

(29) Hückel and Tappe (ref. 27) report the value of +132.2° for the specific rotation ($[\alpha]^{20}\text{D}$).

(30) Adams and Voorhees, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 61.

(31) In previous runs, addition of fresh catalyst and repeated hydrogenation produced no significant change in the optical rotation, either when hydrogen or when deuterium was employed. However, in one experiment where hydrogenation was carried out at 105° under 2000 pounds per square inch pressure, complete reduction was obtained as evidenced by the inactivity of the resulting solution. We suspect that incomplete reduction is due to the presence of small amounts (about 4%) of 3-menthene, which is apparently more difficult to reduce than 2-menthene. Adams and Leffler, for example, were unable to effect reduction of 3-menthene with Raney nickel or platinum oxide at moderate pressures under a variety of conditions (Leffler, Ph.D. thesis, University of Illinois, 1936).

(32) Keats (*J. Chem. Soc.*, 2003 (1937)) obtained 1.4366 for the refractive index of pure *trans* menthane which he prepared from 1-menthone, and also from *trans*-8-hydroxy *p*-menthane.

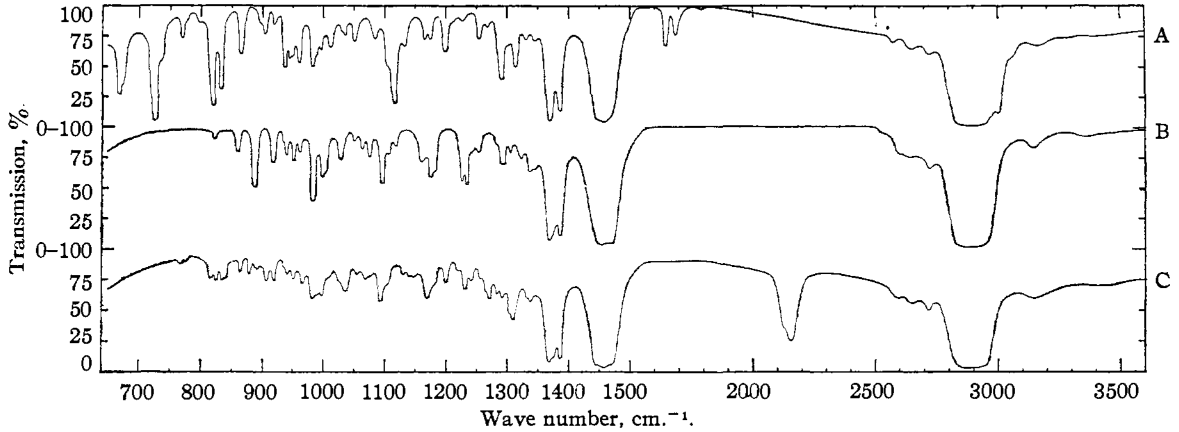


Fig. 1.—Infrared absorption curves (A) *trans*-2-menthene; (B) *trans*-menthane; (C) *trans*-2,3-dideuteromenthane.

fraction 3 (0.18 g., n^{20}D 1.4367) all boiling at 58.5° (15 mm.). All of the fractions totaled 2.44 g. representing a 37.7% yield. Fraction 2 was optically inactive, α^{25}D 0.00 ± 0.01° (l = 2, no solvent), d^{20}_{20} 0.7894, d^{20}_{4} 0.7880. Its infrared absorption curve (Fig. 1) showed no absorption in the characteristic alcohol (3300–3700 cm.$^{-1}$) or olefin (1650 cm.$^{-1}$) regions (see also the region 725 cm.$^{-1}$).

2,3-Dideutero-*trans*-menthane (VI).—The remaining half of the diethylcarbitol solution of menthene was reduced with deuterium gas in the same way. After two hours, 0.0444 mole (96%) of deuterium was absorbed. The filtered solution had an observed rotation of +1.25°, (l = 2), corresponding to about 96.0% reduction. By exactly the same procedure described above for *trans* menthane, the 2,3-dideutero-*trans*-menthane was isolated. Distillation gave fractions 1 (0.21 g.) and 2 (2.04 g.) both n^{20}D 1.4359 and fraction 3 (0.11 g., n^{20}D 1.4360) all boiling at 58.0° (15 mm.). All of the fractions totaled 2.36 g. representing a 35.9% yield. Fraction 2 had the following additional physical properties: d^{20}_{20} 0.8003, d^{20}_{4} 0.7989,[33] α^{25}D −0.07° ± 0.01° (l = 1, no solvent), α^{25}D −0.14° ± 0.01° (l = 2, no solvent), $[\alpha]^{25}$D[34] −0.09° (l = 2, no solvent). Its infrared absorption curve is shown in Fig. 1. Absorption in the region 2130–2160 cm.$^{-1}$ is characteristic of the C–D stretching frequency.

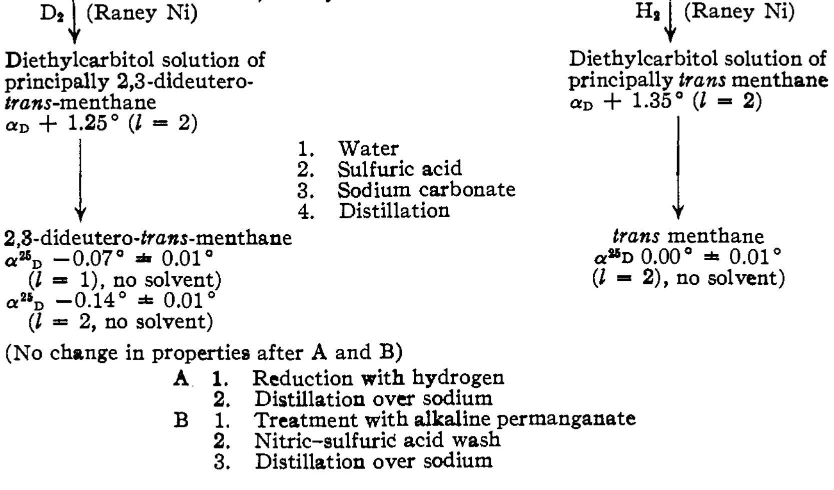
Attempted Hydrogenation of 2,3-Dideutero-*trans*-menthane.[11,13]—Fractions 1, 2 and 3 (2.36 g., 0.00166 mole) of 2,3-dideutero-*trans*-menthane were combined and dissolved in petroleum ether (50 ml.). Raney nickel (washed by decantation with several portions of diethylcarbitol and petroleum ether) was added and the mixture was hydrogenated at two atmospheres pressure for three hours. The solution was filtered, the petroleum ether was removed *in vacuo*, and the residue was heated for two hours at 60–70° over a pellet of sodium. Distillation from a modified Claisen flask gave fractions 1 (1.08 g.) and 2 (0.38 g.) both n^{20}D 1.4360 boiling at 58.0° (15 mm.). Fractions 1 and 2 totaled 1.46 g. representing a recovery of 61.8%. The optical rotation of fraction 1 had not changed: α^{25}D −0.07 ± 0.01° (l = 1, no solvent).

Attempted Oxidation of 2,3-Dideutero-*trans*-menthane.—Fractions 1 and 2 from the attempted hydrogenation of 2,3-dideutero-*trans*-menthane (1.46 g., 0.00103 mole) were combined and heated for fourteen and one-half hours under reflux with a mixture of potassium permanganate (50 ml. of a 2% aqueous solution, 0.00623 mole) and sodium hydroxide (1 ml. of a 10% aqueous solution, 0.0025 mole). The mixture was cooled, petroleum ether (50 ml.) was added, and the two-phase system was filtered with suction. The ether layer was then washed successively with water, five 20-ml. portions of a mixture of two parts of concentrated nitric acid and five parts of concentrated sulfuric acid cooled to 0–5°, three 20-ml. portions of 5% aqueous sodium carbonate and four 30-ml. portions of water. After drying over sodium sulfate, the solution was filtered into a modified Claisen flask and the petroleum ether was removed *in vacuo*. The residue was then heated for two hours at 50–70° over a pellet of sodium and distilled under reduced pressure. After one or two drops of fore-run, 0.91 g. (62.3%) of 2,3-dideutero-*trans*-menthane was recovered, b. p. 58.0° (15 mm.), n^{20}D 1.4360, α^{25}D −0.07° ± 0.01° (l = 1, no solvent). The infrared absorption curve of this material was identical with the one which had been previously obtained (Fig. 1).

Results

In chart 1 are summarized the results of our experiments.

CHART 1


trans-2-Menthene, diethylcarbitol solution, α_D + 31.09°

D_2 (Raney Ni)

H_2 (Raney Ni)

Diethylcarbitol solution of principally 2,3-dideutero-*trans*-menthane α_D + 1.25° (l = 2)

Diethylcarbitol solution of principally *trans* menthane α_D + 1.35° (l = 2)

1. Water
2. Sulfuric acid
3. Sodium carbonate
4. Distillation

2,3-dideutero-*trans*-menthane
α^{25}_D −0.07° ± 0.01°
(l = 1), no solvent)
α^{25}_D −0.14° ± 0.01°
(l = 2, no solvent)

trans menthane
α^{25}D 0.00° ± 0.01°
(l = 2), no solvent)

(No change in properties after A and B)

A 1. Reduction with hydrogen
2. Distillation over sodium

B 1. Treatment with alkaline permanganate
2. Nitric–sulfuric acid wash
3. Distillation over sodium

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[33] This value is in agreement with the equation 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 0.7990.

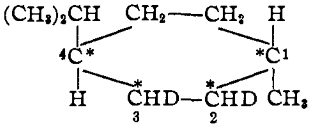
[34] Specific rotation: α^{25}D/(1) (Density).

It is evident that in these experiments (which were carried out twice from *l*-menthol), the reduction of *trans* 2-menthene with deuterium gas in the presence of Raney nickel led to optically active 2,3-dideutero-*trans*-menthane.

Discussion

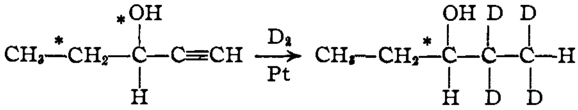
We believe that the optical activity of the 2,3-dideutero-*trans*-menthane, which has been prepared, is due to the asymmetric introduction of deuterium into the molecule and not to the presence of traces of impurities. In support of this conclusion, the following points seem particularly significant: (1) Hydrogenation of one-half of the *same solution* from which optically active 2,3-dideutero-*trans*-menthane was obtained, resulted in an optically inactive *trans*-menthane. (2) Rather drastic treatment of the 2,3-dideutero-*trans*-menthane with such reagents as hydrogen and nickel, alkaline potassium permanganate, sulfuric acid, a nitrating mixture, and metallic sodium, changed none of the physical properties of the material.

The origin of optical activity in 2,3-dideutero-*trans*-menthane has not yet been established. There are four asymmetric carbon atoms in the molecule (VI), and they are of two kinds: Carbon atoms 1 and 4 belong to that class indicated by the general formula (I).



VI

Carbon atoms 2 and 3 are asymmetric because of the direct comparison of hydrogen and deuterium atoms attached to the asymmetric center (II). It is probable, however, that the measurable optical activity is due to carbon atoms 2 and 3. McGrew and Adams,[5] for example, were able to resolve 1-pentyn-3-ol (VIII), but on reduction with deuterium, no optical activity could be detected. Consequently, we would expect the contribution of carbon atoms 1 and 4 toward optical activity to be very small.



$$CH_3-CH_2-\overset{*}{C}H(OH)-C\equiv CH \xrightarrow[Pt]{D_2} CH_3-CH_2-\overset{*}{C}H(OH)-CD_2-CD_2-H$$

VII (no detectable activity)

Acknowledgment.—The authors are indebted to Mrs. J. L. Johnson for the determination and interpretation of the infrared absorption curves which are shown in the paper.

Summary

The reduction of *trans* 2-menthene in diethylcarbitol solution with deuterium in the presence of Raney nickel produces optically active 2,3-dideutero-*trans*-menthane, $[\alpha]^{25}D$ $-0.09 \pm 0.01°$ ($l = 2$, no solvent). The sole cause of asymmetry in this molecule is the replacement of hydrogen atoms by deuterium atoms.

URBANA, ILLINOIS RECEIVED DECEMBER 6, 1948

[CONTRIBUTION NO. 706 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

Electric Moments and Structure of Substituted Thiophenes. II. Certain Thiotolene Derivatives[1,2]

BY RAM KESWANI AND HENRY FREISER

This work, dealing with the thiotolenes and some of the derivatives of 2-thiotolene, is part of an extensive program for the determination of the electric moments of substituted thiophenes. Since it was found helpful in the case of the halogenated thiophenes[1] to make comparisons with the corresponding halogenated benzenes, a similar procedure is used here to help explain the results of electric moment measurements of the methylthiophenes, 2-thenyl chloride, 2-thiophenealdehyde, 2-acetylthiophene, and 2-carbethoxythiophene.

Experimental

Purification of Materials.—All of the materials studied were liquids and were purified by careful fractionation[3] through a three-foot glass helices-packed column as described previously.[1] A summary of their physical properties is presented in Table I. The benzene used is Jones and Laughlin reagent-grade. The thiotolenes and 2-acetylthiophene were 99 mole % grade obtained from the Socony-Vacuum Company. The 2-carbethoxythiophene was obtained by the esterification of thiophenic acid formed by the action of alkali hypochlorite on 2-acetylthiophene. The 2-thiophene-aldehyde was prepared from 2-thenyl chloride according to the directions of Dunn, *et al.*,[4] while

TABLE I

PHYSICAL PROPERTIES OF COMPOUNDS

	B. p., °C.	P, mm.	d^{20}_4, g./ml.	$n^{20}D$	MR_D, cc./mole
2-Methylthiophene	112.1-.3	747.2	1.0095	1.5118_5	29.2
3-Methylthiophene	114.2	741.6	1.0109	1.5126_0	29.2
2-Thenyl chloride	84.5	30	1.1950	1.5552_5	35.6
2-Thiophene-aldehyde	89-90	20	1.2143	1.5838_0	30.9
2-Acetylthiophene	208.0	740	1.1606	1.5606_0	35.2
2-Carbethoxythiophene	81.7	6	1.1749	1.5174_5	40.3

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[1] For paper I, see THIS JOURNAL, **71**, 218 (1949).

[2] Part of this work is abstracted from a thesis submitted by Ram Keswani to the University of Pittsburgh in partial fulfillment of the requirements for the Master of Science degree, February, 1949.

[3] The acetylthiophene was purified first by fractional crystallization.

[4] Dunn, Waugh and Dittmer, THIS JOURNAL, **68**, 2118 (1946).