On the basis of the physical properties and analysis, it is assumed that the product is 1,2-bis-(9-acridyl)-ethylene, $C_{28}H_{18}N_2$, and that it may result from the air oxidation of 9-methylacridine.[32]

Reduction of the Pyruvic Esters

All of the reductions were carried out in a steel reaction vessel under 200–300 atmospheres of hydrogen at a maximum temperature of 265°. Approximately 15 g. of copper chromite catalyst[33] and 100 ml. of dioxane were used per 0.1 mole of compound to be reduced. Catalyst prepared according to the directions of Riener[13] was found to decrease the reaction time 75% and to give better yields. In working up the reaction mixture, dioxane, water, and ethanol were removed by distillation through a ten-inch Fenske column at atmospheric pressure. With the exception of octahydropyrrocoline, b. p. 161° (760 mm.), the product was distilled at 0.5 to 2 mm. pressure. Picrate derivatives were prepared by the addition of the amine in ether to saturated picric acid in ether and were recrystallized from aqueous ethanol, from which all separated as bright yellow needles. Picrolonates were prepared in ether and recrystallized from aqueous ethanol. In Table II is recorded all pertinent information regarding the products of reductive cyclization and their derivatives.

Synthesis of 1-Ethyloctahydroindole (XIV).—Eight grams of 1-ethylindole (XV), prepared for us by Mr. Roy H. Bible according to the method of Fischer and Hess,[34] was hydrogenated over 8 g. of copper chromite catalyst[13] in 100 ml. of dioxane. Within one and one-half hours, the hydrogen pressure dropped from 3000 to 2400 lb. at 260°. The product was worked up in the usual way and the fraction boiling at 81–83° (20 mm.) was collected. A solution of 1 g. of the base in 150 ml. of petroleum ether (b. p. 40–60°) was chromatographed on a 15-g. column of activated alumina. One of the racemic modifications of 1-ethyloctahydroindole was not absorbed to an appreciable extent and was isolated as the picrate, m. p. 160–162°, from the first 150 ml. of petroleum ether which passed through the column. The other racemate was found in the first portion of the petroleum ether–benzene percolate and formed a picrate, m. p. 134–135°. Recrystallization of both picrates from aqueous ethanol gave yellow needles, one melting at 162–163°, the other at 134–135°. These derivatives were individually identical with the picrates, m. p. 162–163° and 134–135°, respectively, which were obtained by reductive cyclization of ethyl *o*-nitrophenylpyruvate followed by similar chromatography and picrate formation. All picrates had the correct analysis for $C_{10}H_{19}N{\cdot}C_6H_3N_3O_7$ (for representative values, see Table II), and no depression in melting point was observed on mixing the 162–163° picrates or on mixing the 134–135° picrates.

Summary

A general method has been devised for the synthesis of fully-saturated nitrogen-heterocyclics having fused five- and six-membered rings. The essential feature of the method is the reductive cyclization of amino α-keto esters. The ester intermediates are available from the condensation of ethyl oxalate with active methyl compounds in which the activating group is an imino or nitro function.

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[32] The reaction is reminiscent of the air oxidation in alkaline medium of compounds of the chlorophyll type (Conant, Kamerling and Steele, THIS JOURNAL, **53**, 1615 (1931); Steele, *ibid.*, **53**, 3171 (1931)), and the product is similar in type to that obtained by the more vigorous selenium dioxide oxidation of lepidine (Kwartler and Lindwall, *ibid.*, **59**, 524 (1937)). Further work on this conversion is contemplated.

[33] "Organic Syntheses," **26**, 83 (1946).

[34] Fischer and Hess, *Ber.*, **17**, 559 (1884).

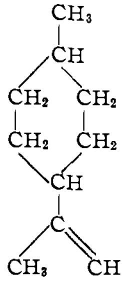
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

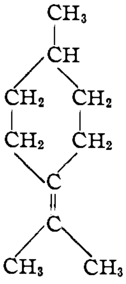
The Isomerization of 8(9)-*p*-Menthene[1,2]

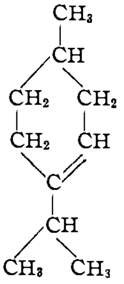
BY ROBERT L. FRANK AND ROBERT E. BERRY

Many terpenes contain either the isopropenyl or the isopropylidene group. Examination of presumably pure samples of such compounds, whether of natural or synthetic origin, has often shown them to be mixtures of the isopropenyl and isopropylidene forms. The interrelationship between these two forms has been one of the perplexing problems encountered by terpene chemists.[3,4,5]

A prime consideration in the successful synthesis of terpenes having the isopropenyl group is the stability of this group under the conditions used in such syntheses. Herein is reported a study of the ease of rearrangement of pure 8(9)-*p*-menthene (I) to 4(8)- and 3-*p*-menthenes (II and III, respectively).


I


II


III

8(9)-*p*-Menthene (I) has previously been prepared by several means,[6,7,8] none of which, however, provided assurance that the product was not contaminated by the 4(8)-isomer. An unequivocal synthesis would appear to be the dehydration of 9-*p*-menthanol by some means which would not cause rearrangement of the double bond

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[1] This is the fourth communication on the chemistry of terpenes. For the third, see THIS JOURNAL, **72**, 1645 (1950).

[2] Presented before the Organic Division of the American Chemical Society, Philadelphia, Pa., April, 1950.

[3] Simonsen, "The Terpenes," Cambridge University Press, 2nd edition, 1947, Vol. I, p. 2; *Endeavour*, **8** [29], 26 (1949).

[4] Thompson and Whiffen, *J. Chem. Soc.*, 1412 (1948).

[5] Escourrou, *Bull. soc. chim.*, **43**, 1204 (1928).

[6] Semmler and Rimpel, *Ber.*, **39**, 2584 (1906).

[7] Perkin and Pickles, *J. Chem. Soc.*, **87**, 650 (1905).

[8] Bogert, Hasseltrom and Firmenich, *Am. Perfumer*, **26**, 377 (1931).

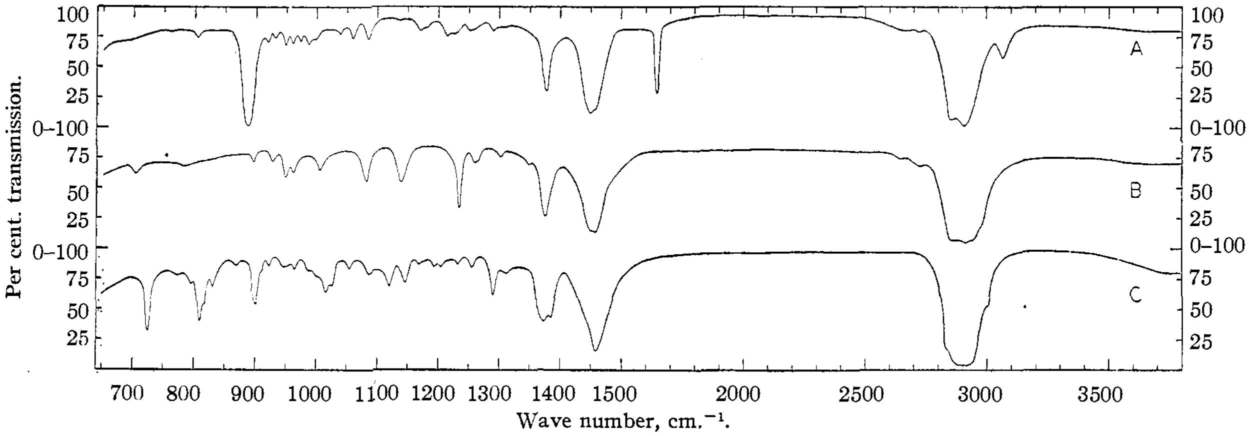

Fig. 1.—Infrared absorption spectra: A is 8(9)-*p*-menthene (I); B is 4(8)-*p*-menthene (II); C is 3-*p*-menthene (III).

initially formed in the 8(9)-position. Pyrolysis of the acetate is reported[9] to be such a method, and has indeed been successful in this instance. 9-*p*-Menthanol was prepared by the following steps: The Reformatsky reaction of 4-methylcyclohexanone with ethyl α-bromopropionate gave a 70% yield of ethyl α-(4-methyl-1-hydroxycyclohexyl)-propionate.[10a] Dehydration by means of phosphorus pentoxide gave ethyl α-(4-methyl-1-cyclohexenyl)-propionate in 80% yield, and this was hydrogenated in 72% yield over copper chromite catalyst to 9-*p*-menthanol. An attempt to reduce ethyl α-(4-methyl-1-hydroxycyclohexyl)-propionate directly to 9-*p*-menthanol resulted in carbon-to-carbon hydrogenolysis, the main product being 4-methylcyclohexanol.[11]

The 9-*p*-menthanol, probably a mixture of its four stereoisomers, was converted to its acetate in 90% yield by use of acetic anhydride–acetyl chloride. The acetate yielded 49% of structurally pure (although probably a mixture of *cis–trans* isomers) 8(9)-*p*-menthene (I) when pyrolyzed at 550°. The purity of this product was confirmed by the infrared measurements described below and also by ozonolysis. Formic acid was found in the distillate from ozonolysis, but no acetone could be detected. The semicarbazone of 4-methylhexahydroacetophenone was also prepared from the distillate.

4(8)-*p*-Menthene (II) was synthesized by the method of Wallach,[10b] the decarboxylation accompanied by rearrangement of α-(4-methyl-1-cyclohexenyl)-isobutyric acid. Rearrangement of the double bond appears to occur quantitatively in this reaction, since no trace of 3-*p*-menthene (III) (nor of 8(9)-*p*-menthene (I)) could be detected by infrared analysis (see Fig. 1).

3-*p*-Menthene was prepared by pyrolysis of *l*-menthyl acetate.[9b] Its infrared spectrum showed no significant absorption at 965 cm.$^{-1}$, the wave number expected to be characteristic of 2-*p*-menthene (of type $R_1CH{=}CHR_2$[4]). 2-*p*-Menthene is the impurity most likely to be present.

Infrared analysis has provided both a qualitative and a quantitative means of measuring the rearrangement of 8(9)-*p*-menthene (I) to its isomers II and III. Thompson and Whiffen[4] have reported that olefins of type $R_1R_2C{=}CH_2$ have a characteristic absorption band at 890 cm.$^{-1}$ and those of type $R_1R_2C{=}CHR_3$ have a band in the region 810–840 cm.$^{-1}$. 8(9)-*p*-Menthene (I) and 3-*p*-menthene (III) have strong bands at 888 cm.$^{-1}$ and 809 cm.$^{-1}$, respectively (Fig. 1). No such strong band has been described for olefins of the type represented by 4(8)-*p*-menthene (II).[4,12]

The lack of a strong band for the detection of 4(8)-*p*-menthene (II) has not been a disadvantage, however, because of the easy rearrangement of 4(8)-*p*-menthene (II) to 3-*p*-menthene (III), a fact first observed by Wallach.[10b] Treatment of 4(8)-*p*-menthene (II) with ethanolic sulfuric acid[13] gave a mixture having a strong band at 809 cm.$^{-1}$ and a weak band at 888 cm.$^{-1}$, indicating that most of the compound had rearranged to 3-*p*-menthene (III) and some of it to 8(9)-*p*-menthene (I). It was therefore possible to detect any rearrangement of 8(9)-*p*-menthene (I) by the appearance of an absorption band at 809 cm.$^{-1}$, on the assumption that a portion of any 4(8)-*p*-menthene (II) formed would rearrange in turn to 3-*p*-menthene (III).

An approximate quantitative measure of the rearrangement of 8(9)-*p*-menthene (I) was achieved by use of the strong absorption at 888 cm.$^{-1}$. The method of Barnes, Liddel and Williams,[14] by which the logarithms of the per cent. transmissions of known and unknown mixtures of the three isomers I, II and III were com-

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[9] (a) Schniepp and Geller, THIS JOURNAL, **67**, 54 (1945); (b) Van Pelt and Wibaut, *Rec. trav. chim.*, **60**, 55 (1941).

[10] (a) Wallach, *Ann.*, **360**, 52 (1908); (b) **360**, 70 (1908).

[11] Connor and Adkins, THIS JOURNAL, **54**, 4678 (1932).

[12] The band at 1234 cm.$^{-1}$ in the spectrum of 4(8)-*p*-menthene might have been used in its analysis, but this seemed inadvisable in view of the less strong interfering band of 3-*p*-menthene at 1233 cm.$^{-1}$.

[13] Wallach, *Ann.*, **365**, 255 (1909).

[14] Barnes, Liddel and Williams, *Ind. Eng. Chem., Anal. Ed.*, **15**, 659 (1943).

TABLE I

ISOMERIZATION OF 8(9)-*p*-MENTHENE

Expt.	Isomerization mixtures, ml. of	Time, hr.	Temp., °C.	% Isomn.
1	3 I + 10 10% aq. NaOH	10	Reflux	0
2	2 I + 30 2.0 *M* ethanolic NaOEt	3	Reflux	0
3	1 I + 50 2% ethanolic $LiAlH_4$	$^3/_4$	25	0
4	Pure I, distilled at 760 mm.	1	163	0
5	2 I + 0.5 g. Al_2O_3 in 100-ml. sealed tube	1	400	>90
6	1 I + 20 10% aq. H_2SO_4	3	Reflux	0
7	3 I + 6 30% aq. H_2SO_4	3	Reflux	30
8	3 I + 6 50% aq. H_2SO_4	3	Reflux	>90
9	2 I + 20 75% aq. H_2SO_4	10	100	No recov.
10	5 I + 10 12 *N* H_2SO_4 in 78% aq. ethanol	3	Reflux	100
11	1 I + 10 0.073 *N* ethereal HCl	3	Reflux	0
12	1 I + 10 saturated ethereal HBr	3	Reflux	0
13	1 I + 2.5 satd. soln. HCl in glacial acetic acid	2	Reflux	91
14	1 I + 3 acetic anhydride	1	Reflux	0
15	1 I + 3 acetic anhydride + 5 drops acetyl chloride	1	Reflux	0
16	1 I + 5.6 12% ethereal $SOCl_2$	3	Reflux	0
17	1 I + 2 5% iodine in $CHCl_3$	3	Reflux	0
18	2 I + 20 $SOCl_2$	3	Reflux	No recov.
19	3 I + 6 saturated $AlCl_3$ in CS_2	4	Reflux	No recov.

pared, was used in estimating 8(9)-*p*-menthene in concentrations of 0–70%. Above 70% the per cent. transmission varied too little with concentration to be of value.

The weak absorptions of 4(8)-*p*-menthene (II) and 3-*p*-menthene (III) at 888 cm.$^{-1}$ are fortunately approximately equal, so that the relative amounts of these isomers had no effect on the total transmission at this wave number.

Table I summarizes the isomerization experiments with 8(9)-*p*-menthene (I). The hydrocarbon is surprisingly stable under alkaline conditions (Expts. 1, 2 and 3) and also to heat in the absence of catalysts (Expt. 4). More striking than Expt. 4 is the fact that no isomerization occurs during its preparation, in which it is subjected to temperatures as high as 600°. Heating its vapors at 400° for one hour in the presence of alumina, on the other hand, resulted in greater than 90% rearrangement (Expt. 5).

Acidic conditions bring about isomerization, the amount depending on the acid medium and the concentration of acid (Expts. 6–13). Expts. 14–19 describe the effects of other reagents known to be catalysts for molecular rearrangements.

Experimental

Ethyl α-(4-Methyl-1-hydroxycyclohexyl)-propionate.—The procedure of Shriner[15] for ethyl 1-hydroxycyclohexylacetate was employed with 150 g. (1.43 moles) of 4-methylcyclohexanone, 250 g. (1.43 moles) of ethyl α-bromopropionate, 570 ml. of benzene, 500 ml. of toluene and 93 g. (1.43 gram atoms) of granulated zinc. The product, b. p. 80–83° (0.7 mm.) (lit.,[10a] 134–136° (13 mm.)), $n^{20}\text{D}$ 1.4564, weighed 214 g. (70%).

Catalytic Reduction of Ethyl α-(4-Methyl-1-hydroxycyclohexyl)-propionate.—A solution of 130 g. (0.610 mole) of the hydroxy ester in 220 ml. of dry dioxane (the solution previously purified by refluxing over Raney nickel) was hydrogenated in two portions over 15-g. amounts of copper chromite catalyst in a 250-ml. steel autoclave at 270° (initial pressure at 25° 3400 pounds per square inch). Distillation of the products gave 42–60 g. (60–70%) of 4-methylcyclohexanol, b. p. 72–76° (14 mm.); $n^{20}\text{D}$ 1.4570, m. p. of phenylurethan 124–125° (mixed m. p. with an authentic sample was not depressed).

Ethyl α-(4-Methyl-1-cyclohexenyl)-propionate.—A mixture of 163 g. (0.763 mole) of ethyl α-(4-methyl-1-hydroxycyclohexyl)-propionate, 137 g. (0.965 mole) of phosphorus pentoxide and 500 ml. of benzene was refluxed for three hours. The cooled mixture was then washed with water to bring the total volume to three liters. The water layer was extracted with three 200-ml. portions of benzene, and the extracts combined with the original organic layer. These were washed with two 200-ml. portions of 5% aqueous sodium hydroxide, once with 200 ml. of water, and dried over magnesium sulfate. Fractional distillation in a ten-inch helix-packed column yielded 120 g. (81%) of product, b. p. 62–70° (0.6 mm.) (lit.,[10a] 114–116° (13 mm.)); $n^{20}\text{D}$ 1.4587; sp. gr.$^{20}_{20}$ 0.945; *MR* calcd., 56.58; *MR* found, 56.72.

This product may contain some isomeric ethyl α-(4-methylcyclohexylidene)-propionate, but according to Wallach[16] and some of our own results the above dehydration gives essentially the β,γ-unsaturated ester.

9-*p*-Menthanol.—A solution of 51.9 g. (0.265 mole) of ethyl α-(4-methyl-1-cyclohexenyl)-propionate in 130 ml. of dioxane (the solution previously purified by refluxing over Raney nickel) was hydrogenated in a 250-ml. steel autoclave over 15 g. of copper chromite catalyst at 265° (initial pressure 3000 pounds per square inch at 20°). The solution was rehydrogenated with fresh catalyst, after which it was fractionally distilled in a ten-inch helix-packed column to yield 29.9 g. (72%) of 9-*p*-menthanol, b. p. 64–66° (0.3 mm.); $n^{20}\text{D}$ 1.4683; sp. gr.$^{20}_{20}$ 0.918; *MR* calcd., 47.7; *MR* found, 47.3.

Anal.[17] Calcd. for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.61; H, 13.09.

The only previous reference to this compound is that of Kinney and co-workers[18] who obtained it by reducing artemisol. No solid derivatives have been reported; attempts to obtain a phenylurethan, α-naphthylurethan, 3,5-dinitrobenzoate or 3-nitrophthalate were unsuccessful.

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(15) Shriner, "Organic Reactions," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 17.

(16) Wallach, *Ann.*, **365**, 255 (1909).

(17) Microanalyses were carried out by Misses Emily Davis and Rachel Kopel.

(18) Kinney, Jackson, DeMytt and Harris, *J. Org. Chem.*, **6**, 612 (1941).

9-*p*-Menthanyl Acetate.—A solution of 26.2 g. (0.168 mole) of 9-*p*-menthanol, 34.3 g. (0.336 mole) of acetic anhydride and 3 ml. of acetyl chloride was refluxed for one hour, then fractionally distilled in a ten-inch helix-packed column to yield 29.9 g. (90%) of ester, b. p. 70–72° (0.6 mm.); n^{20}D 1.4516; sp. gr.$^{20}_{20}$ 0.938; *MR* calcd., 57.0; *MR* found, 57.0.

Anal. Calcd. for $C_{12}H_{22}O_3$: C, 72.68; H, 11.18. Found: C, 72.79; H, 11.13.

8(9)-*p*-Menthene (I).—Into a 0.5 × 10-inch vertical Pyrex tube packed with glass beads and heated to 550° was dropped (twenty drops per minute) 120 g. (0.606 mole) of 9-*p*-menthanyl acetate. The products were collected in an ice-cold aqueous sodium carbonate solution at the bottom of the tube. This solution was then shaken thoroughly, extracted with ether, and the ether solution dried over magnesium sulfate and fractionally distilled. The product was 16.1 g. (49% after accounting for recovered starting material) of 8(9)-*p*-menthene, b. p. 60° (18 mm.); n^{20}D 1.4554; sp. gr.$^{20}_{20}$ 0.819 (lit.,[6] 1.4566 and 0.810, respectively); *MR* calcd., 45.73; *MR* found, 45.77, and 72.8 g. of the starting material.

Anal. Calcd. for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 86.93; H, 13.19.

Ozonolysis of 8(9)-*p*-Menthene.—A stream of 33 × 10^{-5} mole of ozone per minute was passed for thirty-seven minutes through a solution of 1.34 g. (0.0097 mole) of 8(9)-*p*-menthene in 15 ml. of methylene chloride cooled in a Dry Ice–acetone-bath. The ozonide was decomposed by the addition of 2 ml. of 30% hydrogen peroxide, 50 ml. of water and 0.2 ml. of concentrated sulfuric acid, followed by refluxing for one hour. Approximately 30 ml. was then distilled. The distillate formed a gray precipitate on heating with mercuric oxide, a test for formic acid,[19a] but showed no trace of acetone in the Legal reaction,[19b] although control solutions showed this to be a sensitive test. A semicarbazone prepared from the distillate formed microcrystals from ethanol, m. p. 157–158°. Darzens[20] reported m. p. 158–159° for the semicarbazone of 4-methylhexahydroacetophenone.

4-(8)-*p*-Menthene (II).—α-(4-Methyl-1-cyclohexenyl)-isobutyric acid, 33.3 g. (0.183 mole), prepared by the method of Wallach,[10b] was decarboxylated by distillation from a Claisen flask at atmospheric pressure. The partially solid distillate was extracted with two 15-ml. portions of 10% aqueous sodium hydroxide, washed with two 15-ml. portions of water, dried over magnesium sulfate, and distilled to yield 12 g. (42%) of liquid product, b. p. 176°; n^{20}D 1.4689 (lit.,[10b] b. p. 172–174°; n^{21}D 1.4647). Infrared analysis showed no absorption at 809 cm.$^{-1}$, nor at 888 cm.$^{-1}$ (Fig. 1).

3-*p*-Menthene (III).—This was obtained from *l*-menthyl acetate by the method of Van Pelt and Wibaut.[9b] The product boiled at 58° (16 mm.); n^{20}D 1.4519 (lit.,[9b] 1.4523). Its infrared spectrum (Fig. 1) showed no absorption band at 965 cm.$^{-1}$, which would have indicated the presence of 2-*p*-menthene.[4]

Isomerization of 4(8)-*p*-Menthene.—Five milliliters of 4(8)-*p*-menthene (II) was refluxed for three hours with 10 ml. of 30% ethanolic sulfuric acid. The reaction mixture was steam distilled, and the organic layer of the distillate separated, dried over magnesium sulfate, and distilled at 171–173°. Infrared analysis showed a strong band at 809 cm.$^{-1}$ and a weak one, indicating less than 5% 8(9)-*p*-menthene, at 888 cm.$^{-1}$.

Infrared Analyses.—Infrared measurements were kindly carried out by Miss Elizabeth Petersen using a Perkin–Elmer Model 12B infrared spectrometer with rock salt optics. Measurements were made on the undiluted liquids using a constant slit width and an amalgamated cell of 0.025 mm. thickness. The quantitative data were obtained by use of the 888 cm.$^{-1}$ band for 8(9)-*p*-menthene (I), the percentages of this compound being judged by comparison of the log I/I_0 values of an unknown mixture with the data from known mixtures shown below.[14] The first column lists the concentrations of 8(9)-*p*-menthene in mixtures of the three isomers I, II and III (it has already been pointed out that the relative amounts of the 4(8)- and 3-*p*-menthenes (II and III) are not important in this analysis):

% 8(9)-*p*-Menthene	I	I/I_0	log I/I_0
0 (empty cell)	16.1		
91	1.0	0.062	−1.21
70	1.4	.087	−1.06
58	1.9	.108	−0.97
27	4.8	.298	−0.53

Isomerizations of 8(9)-*p*-Menthene (I).—One- to five-ml. quantities of 8(9)-*p*-menthene (I) were treated as described in Table I. The hydrocarbon mixtures were recovered in various ways, depending on the experiment. In Expts. 1, 2 and 3 water was added, the solution acidified with dilute sulfuric acid, extracted with ether, and the ether extracts dried over magnesium sulfate and distilled, b. p. 60° (18 mm.); n^{20}D 1.4562. In Expts. 5–8 and 10–16 the mixtures were steam distilled and the organic layers of the distillates separated, dried over magnesium sulfate, and redistilled. The same technique was used in Expt. 17 except that aqueous sodium bisulfite was added before the steam distillation. Recoveries were nearly quantitative, except for Expt. 16, in which only a few drops of hydrocarbon, b. p. 56° (16 mm.), were obtained. No recovery was made in Expts. 9, 18 and 19 because the reaction mixtures resinified.

There was little possibility that distillation of the recovered hydrocarbons would result in fractionation and change the ratios of the isomers, since all three hydrocarbons have nearly identical boiling points.

Summary

1. Pure samples of 8(9)-*p*-menthene, 4(8)-*p*-menthene and 3-*p*-menthene have been synthesized.

2. Infrared analysis has been employed for detecting and measuring the isomerization of 8(9)-*p*-menthene into 4(8)- and 3-*p*-menthenes under the influence of various catalysts.

3. 8(9)-*p*-Menthene is stable in the presence of alkaline reagents and at temperatures up to 600° in the absence of catalysts. It rearranges under the influence of alumina at 400°. Refluxing with acidic reagents causes varying amounts of isomerization.

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(19) Huntress and Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1941, (a) p. 179; (b) p. 374.

(20) Darzens, *Compt. rend.*, **144**, 1124 (1907).