mination of the concentration of the respective hydrocarbons was achieved when the infrared spectra of the synthetic mixture matched that of the sample obtained from the reaction of *d*-limonene.

The composition of the product obtained from the reaction of *d*-limonene is given in Table II.

Determination of the Structure of III.—(±)-3-*p*-Menthyl nitrosyl chloride (VIII) was prepared from a pure sample of 3-*p*-menthene which was separated by chromatography from the product of reaction of *d*-limonene. The nitrosyl chloride which was obtained by the method described previously[12] melted at 135–136° after crystallization from ethanol. The following melting points have been reported for this compound: 129°,[13a] 128,[13b] 143.5° and 113°.[13c]

Anal. Calcd. for $C_{10}H_{18}ONCl$: C, 59.01; H, 8.85. Found: C, 59.28; H, 8.55.

***dl*-3-*p*-Menthene-5-oxime (IX).**—The oxime was prepared by refluxing 0.5 g. of VIII in 1 ml. of pyridine for five minutes. After the addition of 5 ml. of water, extraction with ether and evaporation, the residue was triturated with 50% ethanol, filtered and recrystallized from 50% ethanol. The oxime was obtained in the form of needles which melted at 66–67°.

Anal. Calcd. for $C_{10}H_{17}ON$: C, 71.85; H, 10.18. Found: C, 71.62; H, 10.15.

***dl*-3-*p*-Menthen-5-one (X)** was obtained in 90% yield from IX by hydrolysis and steam distillation from a 5% oxalic acid solution. The ketone distilled at 88–90° at 30 mm., $n^{20}D$ 1.4730.

Semicarbazone melted at 145–146° after crystallization from 40% ethanol and after solidification it remelted at 160–161°. The m.p. has been reported as 142–143°.[13b]

Anal. Calcd. for $C_{11}H_{19}ON_3$: C, 63.16; H, 9.09. Found: C, 63.60; H, 9.27.

The 2,4-dinitrophenylhydrazone after crystallization from ethanol melted at 145–146°.

Anal. Calcd. for $C_{16}H_{20}O_4N_4$: C, 57.83; H, 6.02. Found: C, 57.70; H, 5.94.

III. Reaction with (+)-*trans*-2-*p*-Menthene.—Twenty-one ml. of II and 0.5 g. of platinum hydroxide–barium sulfate catalyst were heated in a 50-ml. flask provided with a reflux condenser. When the reaction mixture reached its boiling point the heating was stopped. After cooling the colorless liquid was optically inactive and had $n^{20}D$ 1.4558. It was decanted from the catalyst and distilled on a spinning band column of 50 theoretical plates. The various fractions were analyzed by the procedure described for the reaction with *d*-limonene. The concentration of *p*-cymene present in the various fractions was determined by means of ultraviolet spectroscopy. The amount of *p*-menthenes found was estimated by means of bromine number while *p*-menthane was calculated by difference. The infrared spectrum showed that 3-*p*-menthene was the major component of the *p*-menthene fraction. The experimental results are summarized in Table III.

TABLE III

COMPOSITION OF THE PRODUCTS FROM THE REACTION OF *trans*-2-*p*-MENTHENE

Fraction B.p., °C.	$n^{20}D$	Vol., %	Menthane, %	Menthenes, %	*p*-Cymene %
173–174	1.4448	70	76	7.5	16.5
174–176.5	1.4635	15	46	7	47
176.5–178	1.4847	15	12.5	16.5	71
Total composition			61.2	8.8[a]	30.0

[a] Major component 3-*p*-menthene.

Acknowledgment.—The authors wish to thank Miss H. Beck for the elementary analyses.

EVANSTON, ILLINOIS

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[12] H. Pines and H. E. Eschinazi, THIS JOURNAL, **77**, 6314 (1955).

[13] (a) A. N. Kishner, *Chem. Zentr.*, **82**, **II**, 1925 (1911); (b) C. O. Wallach, *Ber.*, **39**, 1504 (1906); (c) C. A. Kötz and G. Busch, *J. prakt. Chem.*, **119**, 1 (1928).

[CONTRIBUTION FROM THE IPATIEFF HIGH PRESSURE AND CATALYTIC LABORATORY, DEPARTMENT OF CHEMISTRY, NORTHWESTERN UNIVERSITY]

Study in the Terpene Series. XXVII.[1] Isomerization of *p*-Menthenes in the Presence of Sodium–Organosodium Catalyst[2]

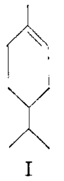
BY HERMAN PINES AND H. E. ESCHINAZI[3]

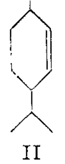
RECEIVED SEPTEMBER 15, 1955

p-Menthene isomers undergo isomerization when refluxed in the presence of a catalyst prepared by treating an excess of sodium with *o*-chlorotoluene in toluene. The composition of the product obtained from either 1- or 2-*p*-menthene after 20–22 hours of refluxing is 32% 1-*p*-menthene, 63% 3-*p*-menthene and 5% 8(9)-*p*-menthene. It is believed that this corresponds to the equilibrium mixture at about 170°. The mechanism of isomerization is discussed.

In a previous paper of this series it was reported[2] that *p*-menthadienes in the presence of sodium–organosodium catalyst undergo double bond migration and dehydrogenation to *p*-cymene. The purpose of the present investigation was to study the action of the same catalyst upon *p*-menthenes. The migration of a double bond in monoölefins catalyzed by sodium and an organosodium compound had been reported previously.[4] More recently the isomerization of olefins containing a terminal double bond to *trans*-2-olefins in the presence of organosodium compound was described.[5]

It has been found that in the presence of a catalyst composed of sodium-benzylsodium *p*-menthenes undergo reversible isomerization at their reflux temperatures, 165–175°. However unlike *p*-menthadienes they do not undergo dehydrogenation to *p*-cymene. Furthermore it has been determined that when 1-(I), 2-(II) and 3-*p*-menthene (III) react for a sufficient length of time an equilibrium is reached and the product of the reaction consists of 32% of I, 63% of III and 5% of 8(9)-*p*-menthene (IV). None of the other isomeric *p*-menthenes


I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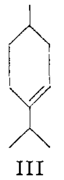
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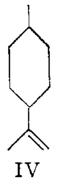
IV

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[1] For paper XXVI of this series see H. E. Eschinazi and H. Pines, THIS JOURNAL, **78**, 1176 (1956).

[2] Paper IV of the series of Sodium-catalyzed Reactions. For III see H. Pines and H. E. Eschinazi, THIS JOURNAL, **77**, 6314 (1955).

[3] Vladimir Ipatieff Postdoctoral Fellow 1953–1955.

[4] H. Pines, J. A. Vesely and V. N. Ipatieff, THIS JOURNAL, **77**, 347 (1955).

[5] A. A. Morton and E. J. Lanpher, *J. Org. Chem.*, **20**, 839 (1955).

have been found to be present in the equilibrium mixture in amounts over 1%, sufficient to be detected by means of infrared spectroscopy.

The study of the reaction using optically active (+)-1-*p*-menthene (I) has revealed that the rate of racemization is faster than that of isomerization. This is in agreement with the results obtained with *d*-limonene.[1]

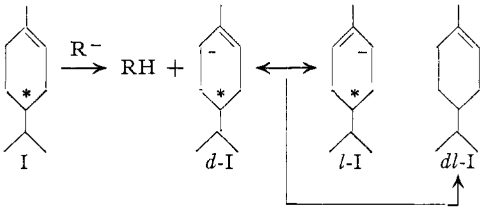
The investigation of the isomerization of (+)-*trans*-2-*p*-menthene (II) had as its main purpose determination of the relative concentration of the various *p*-menthenes produced prior to the establishment of equilibrium. For that reason samples of the reaction products were withdrawn at various intervals. It was found that the composition of the product at the point when (+)-2-*p*-menthene (II) had reacted completely and the optical rotation had fallen to zero was 65% of I, 33% of II and 1-2% of IV. On further refluxing, however, the concentration of 1-*p*-menthene (I) steadily diminished while that of III and IV increased until the equilibrium mixture was reached.

Whereas sodium-benzylsodium catalysts which were sluggish toward the conversion of 1-*p*-menthene showed high activity toward the conversion of *d*-limonene, the catalysts recovered from the latter reaction were much more active in the isomerization of 1-*p*-menthene.

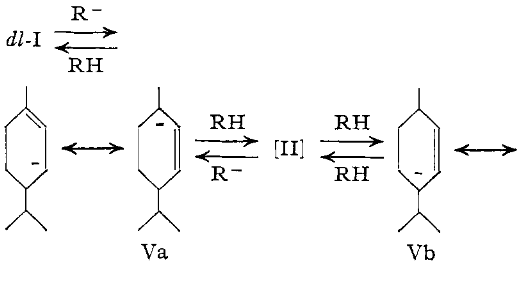
Discussion of Results

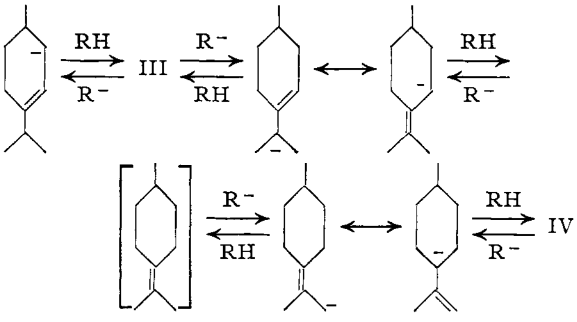
The racemization and isomerization of *p*-menthenes by means of sodium-organosodium catalyst can be explained by a mechanism similar to the one applied for the isomerization of *d*-limonene.[2]

The relatively rapid racemization of (+)-1-*p*-menthene can be explained by a chain mechanism involving the intermediate formation of the allylic carbanions Id and Il. Reaction of Id and Il with another molecule of (+)-1-*p*-menthene produces an optically inactive *dl*-1-*p*-menthene. The chain is thus propagated through this proton transfer in a process which can be represented as



The isomerization of I to III and IV can be explained by a sequence of reactions in which the first step consists of the removal of a proton from C-3 of 1-*p*-menthene, as indicated by the following scheme





RH = *p*-menthene; R$^-$ = *p*-menthenyl carbanion

The study of the reaction of optically active *trans*-(+)-2-*p*-menthene (II) has revealed that this compound isomerizes to 1-*p*-menthene (I) more rapidly than to 3-*p*-menthene (III). When the reaction was interrupted before the equilibrium was reached, the ratio of isomers I to III was 2 to 1. The ratio of these two isomers in the equilibrium mixture of *p*-menthenes was 1 to 2. The formation of isomers I and III can best be explained by the formation of intermediates Va and Vb by abstraction of a proton from C-1 or C-4 of II. The early predominance of I over III requires that the proton at C-1 be abstracted more readily than that at C-4 where an isopropyl group is attached. The greatest ease of the removal of the proton from C-1 may be due to the greater stability of the carbanion Va over Vb.

It is not excluded, however, that steric considerations may be responsible for the greater ease of the formation of the carbanion Va.

It is interesting to note that although the starting *trans*-2-*p*-menthene (II) was optically active, the 1-*p*-menthene (I) produced therefrom was optically inactive. This is not entirely unexpected since the rate of racemization of optically active I had been observed to be relatively more rapid than its rate of isomerization.

Experimental Part

Materials. (+)-1-*p*-**Menthene (carvomenthene) (I)** was prepared by hydrogenation of *d*-limonene.[6] The hydrogenated product was chromatographed[7] to remove small amounts of *p*-menthane produced during the hydrogenation. The 1-*p*-menthene had an optical rotation $\alpha^{25}\text{D}$ +96° and $n^{20}\text{D}$ 1.4569.

(+)-*trans*-2-*p*-**Menthene (II)** was synthesized from 1-menthyl *p*-toluenesulfonate[8] according to the method of Hückel and co-workers.[9]

3-*p*-Menthene (III) was obtained from the disproportionation of limonene.[1]

Isomerizations. Apparatus and procedures were similar to those described previously.[2]

(+)-1-*p*-**Menthene** (I).—Forty ml. of I was refluxed in the presence of a catalyst which was prepared from 5 g. of sodium and 2.5 g. of *o*-chlorotoluene in 25 ml. of toluene, according to the method described previously.[2] After 32 hours of reflux the optical rotation decreased only to $\alpha^{25}\text{D}$ +48° and it remained constant after an additional ten hours at reflux. The liquid product was then removed by a flash distillation under reduced pressure. The liquid consisted,

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[6] V. N. Ipatieff, H. R. Appell and H. Pines, THIS JOURNAL, **72**, 4260 (1950).

[7] B. J. Mair and A. F. Forziatti, *J. Research Natl. Bur. Standards*, **32**, 151, 165 (1944).

[8] E. R. Alexander and A. G. Pinkus, THIS JOURNAL, **71**, 1786 (1949).

[9] W. Hückel and W. Tappe, *Ann.*, **537**, 113 (1938); W. Hückel, W. Tappe and G. Legutke, *Ann.*, **543**, 191 (1940).

according to infrared spectral analysis, of only 1-*p*-menthene, partly racemized.

Forty ml. of *d*-limonene was introduced into the flask in order to determine the activity of the recovered catalyst. After two hours at reflux the optical rotation decreased from α^{25}D +103° to α^{25}D +20°, which indicated that the catalyst was active. The limonene and its reaction product was then removed from the catalyst by flash distillation under reduced pressure and the previously recovered 1-*p*-menthene was reintroduced into the reaction flask. After 25 hours at reflux the optical rotation dropped to α^{25}D +10°. After 22 hours longer at reflux the liquid product was removed and analyzed according to the method described previously.[1] The composition of the product is given in Table I.

TABLE I

COMPOSITION OF PRODUCTS FROM THE ISOMERIZATION OF *p*-MENTHENES

Starting *x*-*p*-Menthene x =	Reaction time, hr.	Composition of reaction product *p*-Menthene, % 1-(I)	2-(II)	3-(III)	8(9)-(IV)
1-(I)	22	32	0	63	5
2-(II)	5	64	3	32	1
2-(II)	20	32	0	63	5
3-(III)	40	24	0	68	6

(+)-*trans*-2-*p*-Menthene (II).—Twenty ml. of II was refluxed in the presence of a catalyst prepared from 3 g. of sodium, 1.5 ml. of *o*-chlorotoluene and 15 ml. of toluene. After 5 hours the reflux temperature increased from 169 to 175° while the optical rotation dropped to α^{25}D +2°. A sample was withdrawn for infrared spectral analysis, while the remainder of the product was continued at reflux for an additional 15 hours. The compositions of the two reaction products are given in Table I.

3-*p*-Menthene (III).—The catalyst was prepared from 5 g. of sodium and 3 ml. of chlorotoluene in 30 ml. of toluene. Forty ml. of III was refluxed for 40 hours in the presence of the catalyst. During the reaction the temperature rose from 166 to 168.5°. The composition of the product is given in Table I.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

On the Geometrical Configuration of the Olefinic Components of Poison Ivy Urushiol. The Synthesis of a Model Compound

BY BERNARD LOEV[1] AND CHARLES R. DAWSON

RECEIVED JULY 11, 1955

A new synthesis of 3-alkenyl veratroles has been developed and used for the synthesis of 3-(*cis*-nonadecenyl-10′)-veratrole, a homolog of dimethylurushenol, the dimethyl ether of the monoölefinic component of the toxic principle of poison ivy. On the basis of a comparison of the infrared spectra and the melting points of the diastereoisomeric glycols of the above homolog with those of dimethyl urushenol obtained from poison ivy, the latter compound has been assigned the *cis* configuration. Inspection of the infrared spectra of the ethers of urushadienol and urushatrienol obtained from poison ivy indicates that the olefinic bonds of the di- and triolefinic components are also in the *cis* configuration.

The allergenic principle of poison ivy is a mixture of four compounds, each of which has the skeletal structure of 3-pentadecylcatechol (hydrourushiol), the minor component. The other three components contain one, two and three olefinic bonds, respectively, in the 15-carbon side chain. Recently the natural mixture has been methylated, separated by chromatography on alumina, and the positions of unsaturation of the olefinic components established.[2]

In the dimethyl ether form, the components of poison ivy "urushiol" are relatively inactive as allergens.[3] The removal of the methyl ether groups to restore the activity is not feasible because of the marked sensitivity of such alkenyl phenols to polymerization under the acid conditions required for demethylation. Consequently, the individual olefinic components of poison ivy "urushiol" cannot be made available for clinical study until either a method is developed for separating them in their free phenolic form or a method is developed for their synthesis. The latter route has already proven convenient for the saturated component, hydrourushiol (3-pentadecylcatechol),[4] and a method for the synthesis of the monoölefinic component, urushenol,[5] recently has been completed.[6]

It has been demonstrated previously[3] that the position and length of the side chain of alkyl catechols has important bearing on the degree and incidence of allergenic response observed after such catechols are applied to the skin of persons sensitive to poison ivy. The role of the double bond in the side chain, however, has received very little attention. The pure alkenyl phenols of varying degree of unsaturation have not been available for clinical study. That the double bond does have an important role is suggested by the fact that hydrourushiol is less active than urushiol as judged by the patch test. Nothing is known as yet in respect to the relationship between the olefinic structure of an alkenyl catechol and its ability to *induce* sensitization in persons not previously sensitized. This type of activity is of great interest because of its possible relationship to desensitization. If sensitization involves a specific reaction between the alkenyl catechol and certain proteins in the skin, then structural details such as the geometrical configuration of the olefinic bonds in the side chain

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[1] Pennsylvania Salt Mfg. Co., Philadelphia, Pa. This paper is based on a portion of the thesis submitted by Bernard Loev in 1952 to Columbia University in partial fulfillment of the requirements for the Ph.D. degree in chemistry.

[2] W. F. Symes and C. R. Dawson, THIS JOURNAL, **76**, 2959 (1954).

[3] H. Keil, D. Wasserman and C. R. Dawson, *J. Exptl. Med.*, **80**, 275 (1954).

[4] D. Wasserman and C. R. Dawson, THIS JOURNAL, **68**, 534 (1946).

[5] For simplicity in differentiating the olefinic components, it seems advisable to modify the name urushiol as originally used by Majima (*Ber.*, **55**, 172 (1922)). The term urushiol will hereafter be used to refer to the natural mixture, and the terms hydrourushiol (or 3-pentadecylcatechol), urushenol, urushadienol and urushatrienol, will be used to refer to the saturated, mono-, di- and triolefinic components.

[6] B. Loev and C. R. Dawson, to be published.