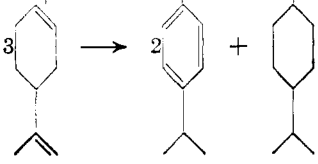
[CONTRIBUTION FROM THE CENTRAL CITRUS PRODUCTS RESEARCH LABORATORY AND THE WEIZMANN INSTITUTE OF SCIENCE, REHOVOTH, ISRAEL]

The Mechanism of Disproportionation of *d*-Limonene

BY H. EMILE ESCHINAZI AND ERNST D. BERGMANN

Limonene (I) is dehydrogenated at 300° to *p*-cymene (II) in the presence of palladium black.[1] At 185°, palladized asbestos causes limonene vapors to disproportionate to *p*-cymene and *p*-menthane (III) according to the equation[2]



I II III

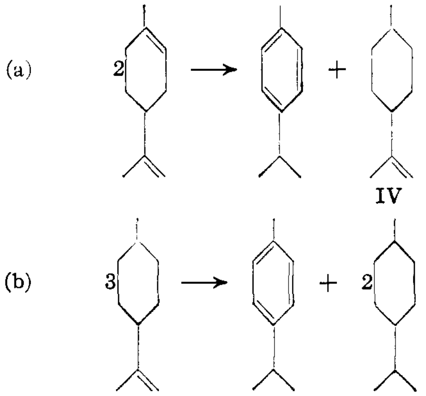
The mechanism of this seemingly trimolecular reaction was investigated using liquid limonene at its boiling point (178°) and palladium hydroxide on barium sulfate as catalyst.[3] The reaction is strongly exothermic. If large quantities are involved, it has proven useful to employ the final mixture of cymene and menthane as diluent and to add, in portions, the new limonene to be disproportionated.

Palladium appears to be specific in its catalytic action. Platinum hydroxide and platinum black did not show any significant activity.[4] Raney nickel produced only a negligible effect, and copper–nickel formate suggested by Palmer and Bibb[5] proved inactive when tried at 178°. The above-mentioned palladium hydroxide, on the other hand, causes complete dismutation in about one hour, if 0.1 g. or more of palladium is applied per kg. of limonene.

There are two easily determinable criteria for following the process: the optical rotation (α_D + 100°, 1-dm. tube) and the bromine absorption (theoretical value, 2.35 mg./mg.)[6] of limonene, which both disappear in the course of the reaction. As a corollary, the intensity of the ultraviolet absorption of *p*-cymene can be measured.[6a]

Whilst the bromine absorption of limonene, reacting at 178° in the presence of the catalyst, decreases to approximately zero within one hour, its optical rotation disappears within ten minutes ("*zero rotation time*"). The bromine absorption, after this latter period, has fallen to approximately 25% of its initial value, showing logically the presence of either 25% of a diene, isomeric with limonene (I),[7] or 50% of a monoölefin (both calculated on the starting material) in the reaction mixture after this period of time.

Spectrographic analysis has shown that at "zero rotation time," 50% of the limonene had been converted into *p*-cymene. Therefore, the bromine value observed refers to a monoölefin and not to a diene, and the following scheme is suggested for the dismutation reaction



In the first step, two molecules of limonene give one each of *p*-cymene and 1-methyl-4-isopropenylcyclohexane ($\Delta^{8,9}$-menthene) (IV). In the second step, three molecules of the latter yield one molecule of *p*-cymene and two of *p*-menthane. Step (a) has been postulated by Ipatieff, Pines and Olberg[8] for the "hydrogen disproportionation of limonene" in presence of iodine or organic halogen compounds, however, without any indication as to the nature of the cyclic monoölefin formed. In analogy to step (b), *p*-menthene has been known to undergo dismutation to (II) and (III) in presence of copper (290–300°)[9] or palladized asbestos (175–180°).[10]

It is noteworthy that in step (a), the endocyclic double bond is the hydrogen acceptor; otherwise the reaction product would have formula (V)

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(1) Zelinsky, *Ber.*, **56**, 787 (1923).

(2) Zelinsky, *ibid.*, **57**, 2058 (1924). Compare Moroe, *C.A.* **44**, 1458 (1950).

(3) The catalyst of Kuhn and Stroebele (*Ber.*, **70**, 785 (1937)) was slightly modified (see Experimental Part).

(4) Platinized asbestos was inactive even at 245° (vapor phase), while palladized asbestos is active at 185° (see ref. 2). Linstead and co-workers (*J. Chem. Soc.*, 1139 (1940)), however, achieved dismutation by means of platinized charcoal.

(5) Palmer and Bibb, U. S. Patent 2,211,432 (*C. A.*, **35**, 467 (1941)).

(6) For the determination of the "bromine number," a slight modification of Francis' method (*Ind. Eng. Chem.*, **18**, 821 (1926)) was used, which was shown to give reproducible figures and is, therefore, free of the general objections raised by Joshel, Hall and Palkin (*Anal. Ed.*, **13**, 447 (1941)) against the reliability of halogenation methods in the terpene series. Compare also Wilson, *J. Inst. Petr.*, **36**, 25 (1950).

(6a) See Elliott and Cook, *Anal. Ed.*, **16**, 20 (1944).

(7) Racemization of the limonene is unlikely; it is generally assumed that no hydrocarbon racemizes "in its resting state." See, *e. g.*, the isomerization of pinene: Smith, THIS JOURNAL, **49**, 43 (1921); Conant and Carlson, *ibid.*, **51**, 3464 (1929); Kassel, *ibid.*, **52**, 1935 (1930).

(8) Ipatieff, Pines and Olberg, *ibid.*, **67**, 694 (1945).

(9) Komatsu and Kurata, *Chem. Zentr.*, **99**, II, 1326 (1928).

(10) Zelinsky and Pawlow, *Ber.*, **57**, 1066 (1924).

and should be optically active. Of (IV), two isomerides (*cis* and *trans*), are possible, neither of them resolvable into optical antipodes. According to preliminary observations, (V) reacts vigorously, (IV) only very sluggishly with N-bromosuccinimide. The hydrocarbon from the "zero rotation dismutate" showed a very slow response to the reagent.

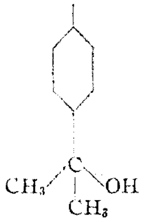
Both hydrocarbons ($\Delta^{8,9}$-menthene (IV) and $\Delta^{1,2}$-menthene (V)) are known[11,12]; their constants, as recorded in the literature, compare as follows with those of the cycloölefin isolated from a "zero rotation dismutate" by fractional distillation.

Table I

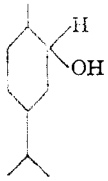
Constants of Dihydrolimonenes

	IV	V	Cycloölefin, isolated from "zero rotation dismutate"
B. p.	168-169°	175-177°	168-168.5°
n_D	1.45602, 1.4567	1.4563 (18°), 1.463, 1.4580 (30°)	1.44655 (25°)
d	0.8104 (20°)	0.8246 (18°), 0.829 (20°), 0.8257 (30°)	0.8095 (25°)
Rotation	0	$[\alpha]_{436}$ +234° α_D +40°, +78.2°, +90.3°	0


V



VI



VII

It is noteworthy that catalytic hydrogenation attacks the exocyclic and dismutation, the endocyclic double bond of *d*-limonene. As Vavon[12] has found, absorption of one mole of catalytically activated hydrogen gives an optically active mono-olefin, *viz.*, (V).[12a]

The proposed scheme classifies the dismutation of limonene with the "hydrogen transfer" reactions, recently studied by Ipatieff, Pines and their co-workers.[13] One should, therefore, expect that the presence of other hydrogen acceptors may divert the dismutation reaction and give *p*-cymene as the only hydrocarbon in the end product. If this is to be achieved, the diversion should preferably be effected in the second step of the dismutation scheme, *i.e.*, in the decomposition of 1-methyl-4-isopropenylcyclohexane (IV). Also the high reaction rate of the first step will operate against participation of a foreign acceptor in that step of the dismutation process. As hydrogen acceptor, mesityl oxide was used; and the following observations were made: (1) No significant hydrogenation of mesityl oxide (to .methyl isobutyl ketone) takes place before the optical rotation has become zero (step (a) of the dismutation scheme). (2) The final dismutate, consisting of two moles of cymene (II) and one mole of menthane (III), does not transfer hydrogen to mesityl oxide, in presence of the palladium catalyst, at the boiling temperature of the reaction mixture. (3) In step (b) of the dismutation scheme, mesityl oxide is hydrogenated easily; *i.e.*, the hydrogen dissociated from 1-methyl-4-isopropenylcyclohexane (IV) prefers mesityl oxide to another molecule of (IV). Yields of 90% have been obtained, calculated on the basis of equation (c)

(c)

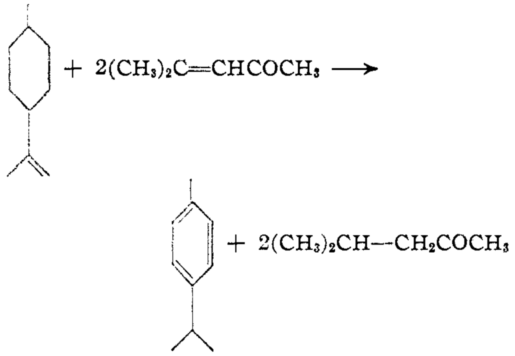


Table II summarizes such an experiment.

Table II

Hydrogen Transfer from *d*-Limonene to Mesityl Oxide (Equimolar Quantities)

Reaction time, min.	Optical rotation α_D (1 dm tube)	(% of hydrocarbon fraction) Limonene	IV	*p*-Cymene	Mesityl oxide converted (% of initial)
0	+60°	100	0	0	0
20	+30°	50	25.0	25.0	0
40	+15°	25	37.5	37.5	0
60	+ 5°	8.4	45.8	45.8	0
75	0°	0	50.0	50.0	0
120	0°	0	37.5	62.5	25
240	0°	0	25.5	75.0	50
420	0°	0	12.5	87.5	75
1280	0°	0	6.0	94.0	88

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[11] (IV) has been obtained by decomposition of dihydrocarvone hydrazone (Semmler and Feldstein, *Ber.*, **47**, 384 (1914); Kishner, *Chem. Zentr.*, **82**, II, 1925 (1911)), reductive dehalogenation of isopulegyl chloride (Semmler and Rimpel, *Ber.*, **39**, 2584 (1906)) and dehydration of *p*-menthanol-(8) (VI), (Perkin and Pickles, *J. Chem. Soc.*, **87**, 650 (1905)).

[12] (V) has been prepared by catalytic hydrogenation of limonene (Vavon, *Bull. soc. chim. France*, [4] **15**, 283 (1914); *Compt. rend.*, **152**, 1675 (1911); Ipatieff, *Ber.*, **43**, 3547 (1910); Sabatier and Senderens, (*Compt. rend.*, **134**, 1130 (1902)), reductive dehalogenation of limonene monohydrochloride (Semmler, *Ber.*, **36**, 1036 (1903); Bacon, *Chem. Zentr.*, II, **79**, 795 (1908)), dehydration of carvomenthol (VII) (Wallach, *Ann.*, **277**, 132 (1893); Henderson and Schotz, *J. Chem. Soc.*, **101**, **2566** (1912)) and *p*-menthanol- (1) (Wallach, *Ann.*, **381**, 58 (1911)), and by dehydrohalogenation of carvomenthyl halides or 1-chloro-*p*-menthane (Kondakow and Lutschinin, *J. prakt. Chem.*, [2] **60**, 273 (1899); Maxwell, *Ann. chim.*, [9] **17**, 351 (1922)).

[12a] Compare also Smith, Fuzek and Meriwether, This Journal, **71**, 3765 (1949).

[13] Ipatieff, Pines and Olberg, *ibid.*, **70**, 2123 (1948); Pines, A. Weizmann and Ipatieff, *ibid.*, **70**, 3859 (1948).

Due to the dilution and the lowering of the boiling point of the mixture, the reaction is considerably slowed down, which permits a more accurate observation. In this experiment, the limonene was determined from the optical rotation. The bromine number of the (higher-boiling) hydrocarbon fraction gave the 1-methyl-4-isopropenylcyclohexane (IV), after deduction of the bromine corresponding to the quantity of limonene present, and the bromine number of the ketone fraction gave the unreacted mesityl oxide. The cymene content of the hydrocarbon fraction was calculated by difference. The table shows, in accordance with the proposed reaction scheme, that for every two per cent. of the olefin (IV) disappearing, four per cent. of mesityl oxide are hydrogenated.

(4) It is to be expected that simultaneously with the reaction resulting from equations (a) and (c), conversion of limonene into *p*-cymene and *p*-menthane according to the combination of steps (a) and (b) will take place, and that increase of the relative amount of limonene will cause a more complete reduction of the mesityl oxide employed. This has been verified experimentally. At the same time, it has been observed that the excess of limonene over and above the 1:1 molar ratio, is not converted into *p*-cymene and *p*-menthane in the ratio 2:1; the presence of mesityl oxide causes a larger proportion to be transformed into *p*-cymene and a smaller one into *p*-menthane. It may be mentioned that also in the normal dismutation the cymene yield is sometimes slightly higher than the theoretical value—it can be assumed that the catalyst also causes direct dehydrogenation of limonene to the aromatic hydrocarbon (II).

Experimental

***d*-Limonene.**—Limonene samples, isolated from Israeli sweet orange oil, were carefully fractionated and had the following constants: b. p. 175–177°, $\alpha^{22}\text{D}$ +100°; their bromine consumption indicated 99–100% diolefin, and they did not contain more than 0.5% of oxygenated compounds (aldehydes, calculated as citral). *d*-Limonene isolated from lemon oil had a lower optical rotation, but showed no difference in behavior.

Palladium Hydroxide–Barium Sulfate Catalyst.—The catalyst was freshly prepared for every batch and, unless otherwise specified, used in moist form. A 1% solution of palladous chloride acidified with a few drops of hydrochloric acid was used as a stock solution. For a batch of 500–750 ml. of *d*-limonene, the following procedure of preparation was adopted: Solutions of 2 g. of barium chloride (dihydrate) and 2 g. of sodium sulfate, each in 50 ml. of boiling water, were mixed. The precipitate was separated by decantation, and washed with 100 ml. of hot water. Then, 10 ml. of the palladous chloride solution was added together with 50 ml. of water, the whole mixture was brought to boiling temperature, and a 10% sodium carbonate solution added until slightly alkaline reaction (*p*H 9). After three minutes boiling, the catalyst was left to settle, separated by decantation, washed with 100 ml. of water and filtered. The resulting moist cake was used as such in the dismutation reaction; it proved to be more active in this form than after drying over potassium hydroxide.

Determination of Bromine Number.—The following modification of the Francis method[6] has given reproducible values varying from each other by not more than 2%.

Reagents used, 0.5 *N* bromide–bromate solution, 0.2 *N* sodium thiosulfate solution, 10% sulfuric acid, and 10% potassium iodide solution.

In a glass-stoppered Erlenmeyer flask of 100–150 ml. capacity, one adds to 1 cc. of the analytical sample, 10% sulfuric acid in an amount of about 1.5 times the volume of the bromide–bromate solution required; the latter is determined approximately in a trial run. Bromide–bromate solution is added in 5-ml. portions at the beginning and in 0.5-ml. portions toward the end of the analysis (the reaction slows down gradually), and the mixture is shaken vigorously after the addition of each portion until the color of the bromide disappears. The reaction is complete when the color persists for more than thirty seconds. One adds 5 ml. of 10% potassium iodide solution and titrates with 0.2 *N* thiosulfate.

Normal Limonene Dismutate. Step (a).—To 100 ml. of *d*-limonene, contained in a 1000-ml. flask fitted with dropping funnel, reflux condenser, water trap and a thermometer, the freshly prepared catalyst is added and the reaction mixture heated to the boiling point (175–178°), in an inert atmosphere. As soon as the water has been removed, the catalyst turns black, and a violent exothermic reaction sets in. The heating is interrupted, and the reaction mixture maintained at the boiling point by slow addition of 500–600 ml. of limonene. This usually takes 35–50 minutes. The reaction is completed five to ten minutes later, when the optical rotation has fallen to zero ("zero rotation dismutate"). The boiling point of the reaction mixture is now 173–174° and the bromine absorption very nearly 25% that of the original value. The analysis of such a reaction mixture showed it to consist of 52–53% *p*-cymene, 40–42% 1-methyl-4-isopropenylcyclohexane (IV), and 4–6% *p*-menthane.

(IV) was separated from *p*-cymene by direct fractionation in a 60-plate column, and showed the following constants: b. p. 168–168.5, $n^{29}\text{D}$ 1.4452, $n^{25}\text{D}$ 1.44655, d_{25} 0.8095; bromine absorption, theoretical.

Step (b).—When the above reaction mixture was heated for a further hour until the bromine absorption approached zero, it boiled at 170–171° and consisted of approximately 66–67% *p*-cymene and 30–33% *p*-menthane.

The Hydrogen Transfer to Mesityl Oxide. Step (c).—To 100 ml. of a mixture of 150 ml. of *d*-limonene and 100 ml. of mesityl oxide, a quantity of catalyst corresponding to 5 ml. of 1% palladous chloride solution was added, and the mass was heated. After the water had been removed, the reaction started in much the same way as described above. Heating was interrupted, and the balance (150 ml.) of the mixture was added slowly. After one hour, the boiling temperature had fallen from 142 to 140°, and the optical rotation to 0°. The hydrogen transfer now began to take place. Refluxing was maintained for about ten hours, until the bromine number became constant (about 15% of the mesityl oxide unchanged, see Table II). The boiling point had then dropped to 137°. The ketonic fraction consisting of approximately 90% of methyl isobutyl ketone (b. p. 115°) and 10% mesityl oxide (b. p. 127°) was separated from the *p*-cymene and analyzed separately. The cymene showed a purity of a 95–98%.

Alternatively, it is possible to add the mesityl oxide to a "zero rotation dismutate," *i. e.*, after completion of step (a). Care, however, must be taken to add the ketone before step (b) has set in, as otherwise hydrogen transfer does not take place or remains incomplete.

Acknowledgment.—This investigation was carried out under the auspices of the Scientific Department of the Israeli Ministry of Defence and is published with its permission.

Summary

The liquid phase dismutation of limonene at 175–178° and in presence of a palladium hydroxide–barium sulfate catalyst was investigated.

A two-step mechanism has been suggested for this reaction which is to be classified as a "hydrogen transfer reaction."

As an acceptor for the hydrogen transferred, foreign substances can be used. As an example, mesityl oxide was investigated as hydrogen acceptor.

The dismutation is accompanied by direct dehydrogenation of limonene to *p*-cymene. This reaction seems to be accelerated by the presence of mesityl oxide.

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Improvement of the Synthesis of Bisdehydrodoisynolic Acid[1]

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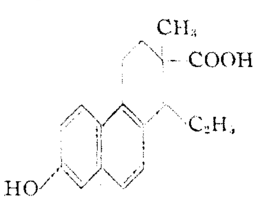
In our recent synthesis of the potent estrogen bisdehydrodoisynolic acid[4] (I) all of the steps were satisfactory except for the cyclization of the anhydride II which gave the desired phenanthrene ketone III (R = H) in at best 20% yield. The main product was the isomeric benzhydrindone IV (R = H) arising from five- instead of six-membered ring closure. These findings have been confirmed in essence by Heer and Miescher[5] who, using our earlier method,[4a] obtained III (R = H) in only about 8% yield.



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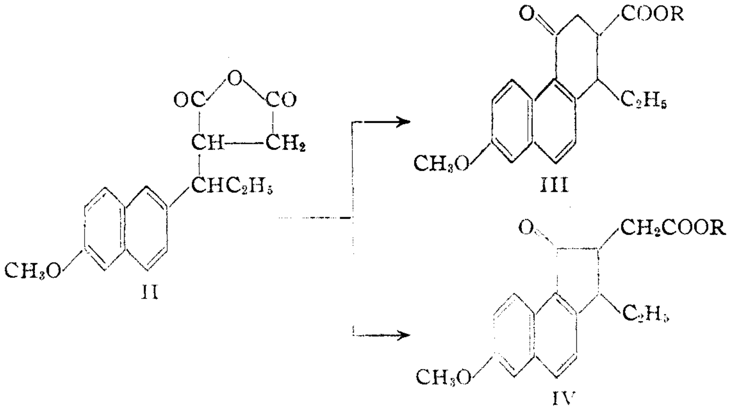

In the present communication we are describing a study which not only has led to a striking improvement in the cyclization step, but at the same time has reduced the total number of steps in the synthesis to seven starting from 2-methoxynaphthalene. These objectives were realized as the result of the discovery that the half-ester VI can be cyclized to give almost exclusively the desired keto ester III (R = CH_3). The total 7-step synthesis is depicted in the accompanying flow sheet.

The crystalline half-ester VI was prepared easily in 52% over-all yield by hydrogenation of the crude oily mixture of half-esters produced by the Stobbe condensation of 2-propionyl-6-methoxynaphthalene (V) with dimethyl succinate. This half-ester was identical with material produced by selective saponification of the dimethyl ester resulting from the action of diazomethane on the 165° dibasic acid (corresponding to formula VI) previously described.[4] When a benzene solution of VI was treated for 45 minutes in the cold with phosphorus pentachloride, then for 10 minutes at 0° with stannic chloride,[6] cyclization occurred giving the crystalline keto ester III (R = CH_3) of good purity in 67% yield. The identity was confirmed by mixed melting point comparison of the ester and the free acid (obtained on saponification) with authentic specimens described previously.[4] Since the keto ester III (R = CH_3) is known to be easily convertible by hydrogenolysis into the ester VII which upon methylation and hydrolysis yields bisdehydrodoisynolic acid I,[4] the synthesis is thus completed.

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[4] Johnson and Graber, This Journal, (a) **70**, 2612 (1948); (b) **72**, 925 (1950).

[5] Heer and Miescher, *Helv. Chim. Acta*, **33**, 178 (1950); "Auf jeden Fall ist die Tatsache festzuhalten, dass die elegante und relativ kurze Synthese von Johnson and Graber nur in untergeordneter Ausbeute wirksame α-Bisdehydro-doisynolsäure ergibt, zur Hauptsache aber zu unwirksamer Cyclopentano-naphtalin-essigsäure führt."

[6] *Cf.* Fieser and Novello, This Journal, **62**, 1855 (1940).