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

STUDIES IN THE TERPENE SERIES. XXV.¹ ADDITION OF 3,8(9)-p-MENTHADIENE TO MALEIC ANHYDRIDE

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Hultzsch (2) reported that when limonene was reacted with maleic anhydride an anhydride was formed which melted at 42° . The latter on hydrolysis gave a diacid melting at 147° . The diacid had a slight optical rotation, contained two double bonds, and the dimethyl ester of the acid did not undergo isomerization when treated with sodium methoxide. On the basis of the above observations Hultzsch suggested that his compound was a limonenyl succinic anhydride to which he assigned the structure I.



Alder and Schmitz (3) repeated Hultzsch's experiment and likewise observed that when limonene was reacted with maleic anhydride under relatively mild conditions there was formed an anhydride melting at 53° and a diacid melting at 147°. Unlike the dimethyl ester of the diacid reported by Hultzsch the dimethyl ester of this diacid was converted, under the action of sodium methoxide to a diacid which melted at 200°. On the basis of this and of the isolation of 4,7-dimethylnaphthalene-1,2-dicarboxylic acid anhydride (III) in 10% yield as the result of dehydrogenation with bromine, Alder and Schmitz concluded that their product was the dienic adduct (II) derived from the conjugated terpene 3, 8(9)-p-menthadiene (IV) which was evidently produced from limonene as a result of isomerization due to maleic anhydride. This however would scarcely be expected if d-limonene was isomerized to p-menthadiene by maleic anhydride since such an isomerization would have been accompanied by racemization. Thus if the Hultzsch adduct actually has the structure of (II) it must have been formed from active p-menthadiene present in d-limonene. Recently Alder and Schumacher (4) left the question open by stating that the p-menthadiene (IV) might have been originally present in *d*-limonene.

Inasmuch as 3,8(9)-p-menthadiene obtained from the base isomerization of *d*-limonene (1) yielded an adduct and an acid having different melting points

¹ For the previous paper in this series see Reference (1).

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from those reported by the previous workers, it was decided to reinvestigate Alder's and Schmitz's reaction. The present study shows that *d*-limonene⁴ does not react with maleic anhydride under conditions specified by Alder and Schmitz. Furthermore the melting points of the anhydride and of the *cis* dicarboxylic acid reported by these investigators failed to agree with the melting points of the adduct 68–69° and of the *cis* diacid (V), 203–204°, obtained from the reaction of synthetically prepared *dl*-3,8(9)-*p*-menthadiene with maleic anhydride.



The results obtained with the synthetic *p*-menthadiene are in agreement with the results obtained previously by us (1). The presently obtained *cis* diacid melting at $203-204^{\circ}$ was converted to the dimethyl ester and the latter by treatment with sodium methoxide then was converted to the *trans* diacid (VI) which also melted at $202-203^{\circ}$. The melting point of the mixture of the two acids was depressed. Both the *cis* and the *trans* diacid yielded on dehydrogenation with either selenium or bromine the corresponding 4,7-dimethylnaphthalene-



1,2-dicarboxylic acid (VII) melting at 236-237° and a partially aromatized acid melting at 225-226°. The latter corresponds to a tetrahydro-4,7-dimethyl-naphthalene-1,2-dicarboxylic acid having either the structure VIII or VIIIa. Both acids seemed to melt with apparent dehydration.

Compound VII was further characterized by its dimethyl ester which melted

⁴ Kindly furnished by Minute Maid Corp., Plymouth, Florida. The crude limonene obtained from orange oil was steam-distilled and the distillate after drying was flash-distilled under reduced pressure at 110-120° over sodium, $[\alpha]_{2}^{25}$ 120°, n_{μ}^{20} 1.4728. The purified limonene did not contain any conjugated dienes as evidenced by the absence of absorption bands in the region of 235-262 m μ .

at 125°. Both compound VII and its ester had the same melting points as those reported by Alder and Schmitz.



On the basis of the present study it can be concluded that d-limonene does not react with maleic anhydride under the conditions specified by Alder and Schmitz. The adduct obtained by these investigators is not identical with the adduct obtained presently from the racemic 3,8(9)-p-menthadiene; this is based on the melting points of the adduct of the *cis* diacid derived thereof and of the dimethyl ester of the *cis* diacid.

The apparent similarity of the products formed by the dehydrogenation of the presently obtained adduct and of that reported by Alder and Schmitz cannot be explained.

Perkins and Wallach (5) first synthesized 3,8(9)-*p*-menthadiene by a rather laborious procedure. Presently compound IV was prepared by the following reactions:



EXPERIMENTAL PART

SYNTHESIS OF 3,8(9)-p-MENTHADIENE (IV)

4,9-p-Menthanediol (X). This diol was prepared in 82% yield by the lithium aluminum hydride reduction (6) of ethyl α -(4-methyl-1-hydroxycyclohexyl)propionate (IX) (7). Compound X distilled at 120-121° at 4 mm., n_2^{20} 1.4818.

Anal. Calc'd for C₁₀H₂₀O₂: C, 69.76; H, 11.62.

Found: 70.2; H, 11.4.

4,9-p-Menthanyl diacetate (XI). A solution consisting of 30 g. of compound X, 120 ml. of acetic anhydride, and 40 ml. of pyridine was refluxed for 2 hours. The reaction product then was distilled at atmospheric pressure till the temperature reached 160° and then distillation was continued under reduced pressure. The diacetate (XI), which was obtained in 82% yield, distilled at 125-127° at 5 mm., n_2^{20} 1.4590.

Anal. Calc'd for $C_{14}H_{24}O_4$: C, 65.61; H, 9.37.

Found: C, 65.68; H, 9.10.

3,8(9)-p-Menthadiene (IV). Compound XI, 30 g., was pyrolyzed at 550° by passing it through a tube packed with Pyrex beads (8 hours). The crude p-menthadiene (IV) thus produced in 85% yield was first washed with a sodium carbonate solution, then flash-distilled over sodium at 110° under reduced pressure, and fractionated at 30 mm., n_p^{20} 1.4932; ϵ 19,100 at 233.5 m μ , b.p. 183° at 760 mm. The infrared spectrum did not show any absorption in the 13-14 μ region which indicated the absence of 2,4(8)-p-menthadiene as a possible contaminant.

Anal. Calc'd for C₁₀H₁₆: C, 88.15; H, 11.85.

Found: C, 88.63; H, 11.63.

ATTEMPTED REACTION OF d-LIMONENE WITH MALEIC ANHYDRIDE

(a) In ether. A solution consisting of 100 g. of d-limonene,⁴ 15 g. of maleic anhydride, 1 g. of hydroquinone, and 200 ml. of diethyl ether was refluxed for 3 hours. The ether then was distilled off and the product was steam-distilled. The liquid hydrocarbon which was recovered in almost quantitative yield was composed of unchanged d-limonene having the same optical rotation and infrared spectra as the original product. There was no residue in the flask, indicating that there was no adduct formed.

(b) In benzene. A solution of 100 g. of d-limonene, 25 g. of maleic anhydride, 0.2 g. of hydroquinone, and 80 ml. of benzene was refluxed for 3 hours. The product then was distilled under reduced pressure. The pressure was so adjusted as to maintain the vapor temperature below 50° ; the liquid temperature did not exceed $120-125^{\circ}$. One gram of residue remained in the flask of which about 0.5 g. distilled below 150° under 2 mm. of pressure. The distillate was treated with 12% aqueous potassium hydroxide and was extracted with ether. About 0.2 g. of neutral product remained corresponding to a dimer of limonene.

The potassium hydroxide layer was acidified with hydrochloric acid, extracted with ether. About 0.2 g. of acidic material was obtained which failed to crystallize.

The *d*-limonene recovered remained unchanged according to its optical rotation and its infrared spectrum.

REACTION OF COMPOUND IV WITH MALEIC ANHYDRIDE

(a) In ether. A solution consisting of 13.6 g. of IV, 12 g. of maleic anhydride, 0.1 g. of hydroquinone, and 25 ml. of ether was refluxed for 3 hours. The ether solution then was decanted from some insoluble polymeric material, washed with water in order to remove the excess of maleic anhydride, and dried over sodium sulfate. After evaporation of the ether the product, 25 g., distilled at $171-174^{\circ}$ at 5 mm. The viscous distillate solidified on standing. After trituration with *n*-pentane it was filtered and crystallized from pentane. The adduct (IIa) melted at $68-69^{\circ}$.

Anal. Calc'd for C₁₄H₁₈O₃: C, 71.6; H, 7.7.

Found: C, 71.81; H, 7.69.

(b) In benzene. The reaction was carried out in benzene instead of ether. The yield of the adduct obtained after 3 hours reflux was identical with that from the ether experiment.

(c) In d-limonene and benzene. A solution composed of 10 g. of compound IV, 90 g. of freshly distilled d-limonene,⁴ 25 g. of maleic anhydride, 0.25 g. of hydroquinone, and 80 ml. of benzene was refluxed for 3 hours. The experimental procedure used by Alder and Schmitz was very closely followed. The adduct (IIa) which was formed, 14 g., melted at $68-69^{\circ}$ and was identical, according to its melting point and its infrared spectrum, with the adduct obtained by us previously (1).

A similar experiment made in the absence of hydroquinone gave identical results.

CHARACTERIZATION OF THE ADDUCT IIA

(a) cis-[4,7-Dimethyl-1,2,3,5,6,7,8,9-octahydronaphthalene]-1,2-dicarboxylic acid (V). The crude anhydride (II) (5 g.) obtained from experiment c was dissolved in a 12% potas-

sium hydroxide solution by heating. The solution then was extracted with ether and the aqueous layer was acidified with hydrochloric acid. The precipitate was extracted with ether. The residue, after evaporation of the ether, was triturated with 25 ml. of 40% acetic acid and was filtered. After recrystallization from 40% aqueous acetic acid about 4 g. of large crystals were obtained in the form of blocks which melted at 203-204°. The crystals were identical with those obtained previously (1).

(b) Dimethyl-cis-[4,7-dimethyl-1,2,3,5,6,7,8,9-octrahydronaphthalene]-1,2-dicarboxylic acid (XII) was prepared by reacting V with diazomethane. The ester distilled at 150° at 2 mm. On recrystallization from methanol it formed lustrous needles which melted at 62-63°.

Anal. Cale'd for C₁₆H₂₄O₄; C, 68.54; H, 8.57.

Found: C, 68.49; H, 8.52.

The dimethyl ester obtained by Alder and Schmitz from their *cis* diacid melted at 79-80°.

(c) trans-[4,7-Dimethyl-1,2,3,5,6,7,8,9-octahydronaphthalene]-1,2-dicarboxylic acid (VI). The dimethyl ester (XII), 2.6 g., was refluxed for 3 hours in a methanol solution of sodium methoxide (40 ml. of methanol and 3 g. of sodium); after cooling 40 ml. of water was added and the solution was refluxed for another 1.5 hours. From the solution upon applying the conventional methods, the trans acid (VI) was obtained, which after recrystallization from 20% methanol melted at 202-203°, yield 1.7 g.

Anal. Cale'd for C₁₄H₂₀O₄: C, 66.66; H, 7.94.

Found: C, 67.31; H, 8.13.

A mixture of this acid with the cis isomer (V) melted at 172-180°.

(d) Dehydrogenation of cis diacid (V) with bromine. To a boiling solution of 3.7 g. of V in acetic acid was added dropwise 9.2 g. of bromine in 12 ml. of acetic acid. The refluxing was continued for 6 hours until no more hydrogen bromide evolved. After evaporation of the acetic acid the solid residue was extracted with hot toluene and filtered. Upon cooling yellow crystals were obtained which melted at 200-210°. The crystals were submitted to a distillation under 10 mm. of pressure in order to decompose any bromides present. The distillate after crystallization from toluene formed yellow microcrystals (compound III) which melted at 236-237°. Yield 1.1 g.

Anal. Calc'd for C14H10O3: C, 74.33; H, 4.42.

Found: C, 74.72; H, 4.30.

(e) Dehydrogenation of adduct IIa with selenium. Six g. of IIa, m.p. 69°, and 12 g. of selenium powder were heated gradually in a flask to 350° and were maintained at this temperature for 1.5 hours. The reaction mixture then was distilled; yield 4.3 g. of a solid. Upon triturating with toluene 1.2 g. of crystals were obtained melting at 232°. Recrystallization from toluene gave yellow microcrystals (III), which melted at 235-236° and which were identical with those obtained from the bromine dehydrogenation.

The material remaining in the toluene mother liquors was distilled at 30 mm. to yield 1.7 g. of a solid. This was hydrolyzed with a 12% solution of potassium hydroxide and the aqueous solution, after extraction with ether, was acidified; then the precipitate was extracted with ether leaving 0.3 g. of the aromatic dicarboxylic acid adduct. The ether solution then was evaporated and the residue after two recrystallizations from a 50% ethanol yielded white crystals, m.p. 225-226° which corresponded to compound VIII or VIIIa.

Anal. Calc'd for C14H16O4: C, 67.74; H, 6.45.

Found: C, 67.40; H, 6.12.

(f) Dehydrogenation of trans-diacid (VI) with selenium. One g. of crude trans diacid (VI) m.p. 194-195° and 2 g. of powdered selenium were treated as described in e. The reaction product 0.6-0.7 g. which was obtained by distillation, was treated once more with selenium at 340° and then was extracted with toluene. Upon recrystallization from toluene it melted at 233-234° and was identical with III obtained from either procedure d or e.

(g) 4,7-Dimethylnaphthalene-1,2-dicarboxylic acid (VII). Compound III, 0.3 g., m.p. 232-234° was dissolved in 10% potassium hydroxide with boiling and then after filtration,

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was acidified. After recrystallization from 50% ethanol white crystals were obtained, which turned yellow upon standing. The observed melting point was $236-237^{\circ.5}$

Anal. Calc'd for C₁₄H₁₂O₄: C, 68.85; H, 4.92.

Found: C, 68.50; H, 4.70.

(h) Dimethyl-4,7-dimethylnaphthalene-1,2-dicarboxylic acid. The ester was prepared from 0.2 g. of VII by reaction with diazomethane. After recrystallization from methanol the ester melted at 125°.

Anal. Calc'd for C₁₆H₁₆O₄: C, 70.59; H, 5.88. Found: C, 70.40; H, 5.58.

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SUMMARY

It was found that purified limonene does not give a dienic adduct with maleic anhydride as claimed by previous investigators.

dl-3,8(9)-*p*-Menthadiene was synthesized by a novel procedure, and its reaction with maleic anhydride was investigated. It was found that the adduct formed by this reaction had properties different from those that had been assigned to it by previous investigations.

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⁵ Since no depression in melting point was noticed with the starting material it is reasonable to assume that the real melting point was higher and that dehydration occurred during the determination of the melting point.