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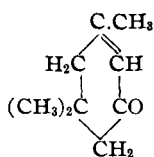
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A Chemical Study of Isophorone and Some of Its Derivatives*

By Austin A. Dodge† and Edward Kremers‡

Isophorone, known also as isoacetophorone, is 1,1,3-trimethylcyclohexen-3-one-5; its structure may be represented as follows:



It appears to have been first prepared in 1859 by Fittig (1), who condensed acetone in the presence of caustic lime. It has since been prepared by other investigators (2, 3, 4, 5, 6, 7, 8, 9) from the same source through the use of other condensation agents.

It seemed desirable to attempt the preparation of an alcohol by the catalytic hydrogenation of the ketone, with the view of obtaining, by dehydration of the former, an unsaturated hydrocarbon. Such a hydrocarbon might be regarded, at least empirically, as a 9-carbon lower homologue of the 10-carbon *meta* terpenes.

EXPERIMENTAL

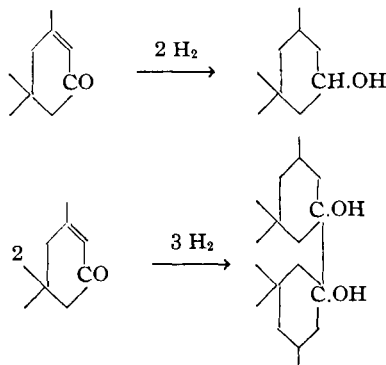
The isophorone used in this investigation was supplied through the kindness of the Carbide and Carbon Chemicals Corporation. The product had the following constants: $d^{24}_4 = 0.9204$, $n^{20}_D = 1.4778$. From it were prepared the oxime, m. p. 77-78° C., and the semicarbazone, m. p. 190-191°

C. Numerous investigators have made varying reports of the respective melting points:

Oxime, M. P., °C.	Semicarbazone, M. P., °C.	Author
102	...	Tissier (2)
75-76; 99-100	...	Bredt and Rübel (3)
79-80	...	Kerp (4)
74-75	186	Knoevenagel and Fischer (10)
79-80	...	Wolf (7)
...	186	Knoevenagel and Blach (11)
78	190-191; 193	Crossley and Gilling (12)
78; 105-106	187; 191	Delacre (13)
74	186	Hess and Munderloh (9)

Hydrogenation Product of Isophorone.—Isophorone was hydrogenated over platinum black at room temperature in an apparatus manufactured by the Parr Instrument Company. The initial pressure used was about 38 lb./sq. in. The ratio of catalyst to isophorone was 2:35. The absorption of hydrogen corresponded to 2 moles. Usually the reduction product began to crystallize before the absorption of hydrogen was complete. The white crystalline product had a decidedly minty odor, was volatile, and tended to sublime in a stoppered container. After recrystallization from petroleum ether, the compound melted at 58.5-59° C. It was saturated toward bromine.

It is conceivable that the addition of hydrogen to isophorone might result either in the formation of the corresponding saturated alcohol or of the pinacol:



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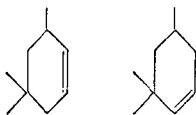
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Molecular weight determinations by the cryoscopic method with benzene as solvent indicated that the compound was the secondary alcohol: calculated for $C_9H_{17}OH$, 142.2; found, 148.6.

The 3,5-dinitrobenzoate of the compound melted at 98.5–99° C. after several recrystallizations from alcohol. The acetate was obtained as an oily liquid, $d^{31}_D = 0.9170$, $n^{26}_D = 1.4385$.

The crystalline hydrogenation product was dehydrated according to the method described by Richtmann and Kremers (14). The oily reaction product was steam distilled and separated from the aqueous portion of the distillate. It possessed the following constants: $d^{24}_D = 0.7933$, $n^{26}_D = 1.4385$. Five cubic centimeters of the reaction product were fractionated; 2.2 cc. distilled below 131° C. and 2.3 cc. distilled at 131–135° C. The product was unsaturated toward bromine. It is possible that it may be identical with the 1,3,3-trimethylcyclohexene, b. p. 139–141° C./759 mm., $d^{23}_D = 0.7981$, $n^{23}_D = 1.4453$, prepared from trimethylcyclohexanol by Knoevenagel and Fischer (10). These authors advanced for their compound the following possibilities of structure:



They further pointed out that their compound might be identical with the "isogeraniolene" of Tiemann and Semmler (15), which had b. p. 138–140° C., $d^{22}_D = 0.7978$, $n_D = 1.4434$, and to which the following structure was assigned by the latter authors:



Attempts to prepare the nitrosochloride and the nitrosite of the unsaturated hydrocarbon were unsuccessful. Further work will be necessary in order to characterize the compound.

Isophoronyl Alcohol.—Samples of a liquid substance labeled "isophoronyl alcohol" and of crystals bearing the same designation were supplied by the Carbide and Carbon Chemicals Corporation. Both products possessed a minty odor, and both appeared to be saturated toward bromine. The liquid product had $d^{25}_D = 0.8908$, $n^{20}_D = 1.4542$, and $[\alpha]_D = \pm 0^\circ$. Upon fractionation of a 10-cc. sample, 4.4 cc. distilled below 194° C./739 mm., and 5.1 cc. at 194–194.5° C./739 mm. The crystalline product melted at 38° C.

It appears likely that the crystalline "isophoronyl alcohol" is identical with *trans*-dihydroisophorol, m. p. 37° C., prepared by Kerp (4) through the reduction of isophorone with sodium and moist ether. By reducing isophorone with sodium and absolute alcohol, Knoevenagel and Fischer (10) secured *trans*-

dihydroisophorol, m. p. 34.5° C., and the *cis* form, b. p. 201–203° C./750 mm., $d^{20}_D = 0.8906$, $d^{16}_D = 0.9006$, $n^{16}_D = 1.4550$. The latter constants agree quite closely with those observed for the liquid sample examined.

A molecular weight determination by the cryoscopic method made on the liquid sample gave a value of 156.4. Since it had been observed that the liquid deposited crystals upon chilling, a similar determination was made on these; the value found was 161.0.

In like manner, the molecular weight of the crystalline "isophoronyl alcohol" was found to be 164.1. All of these values are at variance with that demanded for $C_9H_{17}OH$, *viz.*, 142.

The 3,5-dinitrobenzoates of the respective "isophoronyl alcohols" were prepared; the derivative of the liquid product melted at 61.5–63° C., and that of the crystalline product melted at 71.5–72.5° C.

A sample of the liquid "isophoronyl alcohol" was dehydrated by refluxing it over potassium acid sulfate for 12 hrs. at 170–190° C. The oily reaction product was steam distilled and separated; it was found to have $d^{26}_D = 0.8269$ and $n^{26}_D = 1.4427$. The product was unsaturated toward bromine. Further work will be carried out on this substance in the future.

SUMMARY

1. Isophorone and two forms of "isophoronyl alcohol" (liquid and crystalline) supplied by the Carbide and Carbon Chemicals Corporation were examined. The oxime and semicarbazone of the former possessed melting points in general agreement with those recorded by earlier investigators.

2. A saturated secondary alcohol in crystalline form was obtained by the hydrogenation of isophorone over platinum black at room temperature. Its melting point differed from that of any reduction product of isophorone reported in the literature.

3. Compounds believed to be unsaturated hydrocarbons were prepared by the dehydration of the isophorone reduction product and of the liquid form of "isophoronyl alcohol." These products differed in their physical constants.

4. Since the 3,5-dinitrobenzoates of the isophorone reduction product and the two "isophoronyl alcohols" differed in their respective melting points, it would appear that three distinct compounds are represented. It is likely that the two "isophoronyl alcohols" are the *cis* and *trans* forms of dihydroisophorol.

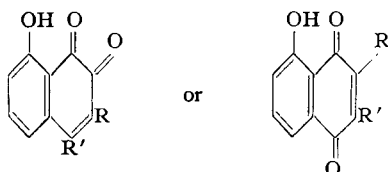
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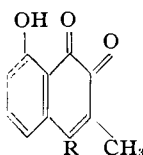
The Constitution of Celastrol, Part IV

By Ole Givold*

In previous publications (1) it was shown that celastrol, a pigment found in the outer bark of the root of *Celastrus scandens*, has the formula $C_{22}H_{30}O_3$. It was postulated to be either a mono- or dialkyl substituted β - or α -naphthoquinone with one of the following tentative formulas, in which the sum of R and R' equals $C_{12}H_{26}$.



Subsequent investigations on the constitution of this pigment indicate that it is a 3,4 - dialkyl - 8 - hydroxy - β - naphthoquinone. The alkyl group in position 3 appears to be a methyl group and the one in position 4, a homohydrogeranyl group ($-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$), or possibly a hydrogeranyl group ($-\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$), as shown in the following formula:



The evidence presented in this paper together with that of Fieser and Jones (2) clearly indicates that the pigment is definitely a substituted β -naphthoquinone. In a previous paper by the author (1), the solubility of celastrol in bisulfite was not carried out to the best advantage, as shown by Fieser. Also the very small amount of a derivative prepared by a reaction of methyl celastrol with *o*-phenylenediamine left room for doubt that it was an orthoquinone. The author has since tried to prepare a derivative with *o*-phenylenediamine and also with substituted hydrazines with negative results.

Previous oxidative studies yielded little if any satisfactory quantities of identifiable fragments. The most successful of this type of investigation was that carried out with cold permanganate.

Samples of celastrol were ozonized in glacial acetic acid and the ozonide decomposed in the presence of hydrogen peroxide. This type of oxidative study yielded about 60% of an identifiable fragment; however, difficulty was encountered in attempting to purify the degradation product. The main degradation product responded to tests for a keto acid, but it failed to give a color reaction with ferric chloride. A 2,4-dinitrophenylhydrazone was readily obtained in a pure form suitable for analysis, the results of which corresponded to the formula $C_{26}H_{32}O_7N_4$, m. p. 192°C .

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