

On cooling the mixture was poured into 250 cc. of water and treated with calcium oxide (27 g.). After filtering, the filtrate was treated with sodium carbonate to remove the excess calcium ion. Evaporation of the aqueous filtrate gave a semicrystalline mass. This was steam distilled at 145–150° in the presence of dilute sulfuric acid. One gram of starting hydrocarbon and one gram of benz[*f*]indane (m. p. 92–93°) were recovered. The latter formed its well known picrate, m. p. and mixed m. p. 116–118°.

(C) **6,7-Diethyltetralin**.—Eighteen grams of the hydrocarbon in sulfuric acid (80 cc.) was heated gradually while being stirred. At 60° complete solution was effected. The mixture was then heated at 95° for fifteen minutes and allowed to cool. Steam distillation at 150° gave 4.9 g. of liquid hydrocarbon. Oxidation of a portion of this material with nitric acid gave only mellophanic acid (methyl ester—m. p. and mixed m. p. 129–131°). Dehydrogenation of the hydrocarbon with palladium-charcoal gave 1,2-diethylnaphthalene a liquid hydrocarbon whose picrate melted at 105.5–107°.

(D) **5-Ethyl-6-methylhydrindene**.—Ten grams of the hydrocarbon was heated with 40 cc. of sulfuric acid at 90° for thirty minutes. Steam distillation as described above gave 1.4 g. of volatile hydrocarbon. Nitric acid oxidation gave only mellophanic acid (methyl ester—m. p. and mixed m. p. 129–131°).

(E) **s-Hydrindacene**.—Three grams of the hydrocarbon and 20 g. of sulfuric acid were heated at 70° for three minutes. More drastic conditions (*i. e.*, higher temperatures, etc.) gave only unidentifiable tarry materials. The solution was cooled and a solid sulfonic acid separated. To the total contents of the flask acetic acid (2 cc.) and sulfuric acid (5 cc.) were added and the temperature was raised to 98° and held there for one hour. Steam distillation gave the starting hydrocarbon (m. p. 52–53°) as the sole product. Considerable tarry residue remained in the distilling flask.

Action of Aluminum Chloride on the Hydrocarbons

(A) **6,7-Diethyltetralin**.—Thirteen grams of hydrocarbon and aluminum chloride (1 g.) was heated on the steam-bath for two and one-half hours and then allowed to

stand several days at room temperature. After decomposition with water followed by ether extraction there was obtained on fractionation at 11 mm. three cuts boiling at 124–140°, 142–152°, and 155–168°. The first cut on oxidation with nitric acid gave impure prehnitic acid (identified as its methyl ester—m. p. and mixed m. p. 109–110°). Fraction II (b. p. 142–152°) gave fairly pure prehnitic acid. Dehydrogenation of this fraction with palladium-charcoal gave a naphthalenic hydrocarbon whose picrate melted at 100–101°. This hydrocarbon must be 1,3-diethylnaphthalene.

(B) **5-Ethyl-6-methylhydrindene**.—Treatment of 20 g. of hydrocarbon with aluminum chloride (2.0 g.) as described above gave on fractionation at 15 mm. the following cuts: I, 86–100° (1 g.), II, 100–120° (7 g.), III, 120–140° (10 g.), IV, 140–180° (0.5 g.) and V, 215–230° (0.8 g.). Fraction III gave prehnitic acid on nitric acid oxidation (identified as its methyl ester) and fraction V gave benzenepentacarboxylic acid (pentamethyl ester—m. p. and mixed m. p. 146–148°).

(C) **s-Hydrindacene**.—The hydrocarbon (1.5 g.) was treated with aluminum chloride (0.5 g.) as described above. The reaction product was oxidized with nitric acid and the resulting carboxylic acid mixture was esterified with diazomethane. Penta- and hexacarbomethoxybenzenes were isolated; m. p. 146–148° and 184–186°, respectively.

Summary

1. The Jacobsen rearrangement has been studied with cyclic hydrocarbons related to hydrindene and tetralin.
2. The action of aluminum chloride on 6,7-diethyltetralin, 5-ethyl-6-methylhydrindene, and s-hydrindacene is reported.
3. A new and convenient synthesis of pure 1,4-diethylnaphthalene is described.
4. A mechanism for the Jacobsen rearrangement is proposed and discussed.

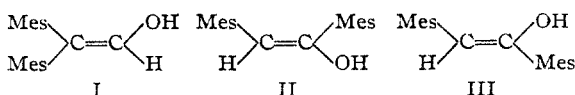
MINNEAPOLIS, MINNESOTA RECEIVED FEBRUARY 14, 1944

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

Vinyl Alcohols. IX.¹ Esters of 1,2-Dimesitylvinyl Alcohols

BY REYNOLD C. FUSON, L. J. ARMSTRONG² AND W. J. SHENK, JR.

For the dimesitylvinyl alcohol produced by the dehydration of hydromesitoin or isohydromesitoin¹ three structures are possible—1,1-dimesitylvinyl alcohol (I) and the *cis* (II) and *trans* (III) forms of 1,2-dimesitylvinyl alcohol. The present paper is concerned with the last two of these. Although it has not been possible to prepare these enols, evidence has been accumulated which shows both to be unstable and thus entirely different from the dehydration product. The structure, 1,1-dimesitylvinyl alcohol, (I), previously assigned to this product is thereby confirmed.



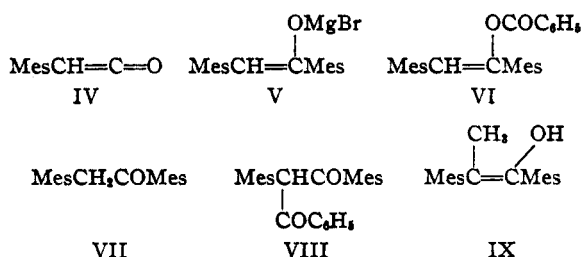
(1) For the preceding communication in this series see Fuson and Rowland, *THIS JOURNAL*, **65**, 992 (1943).

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One of the methods employed in attempts to make enols II and III consisted in the condensation of mesitylmagnesium bromide with mesitylketene (IV). The possibility of preparing enols from ketenes was suggested by the work of Gilman and Heckert,³ who found that the enolate formed by the addition of the Grignard reagent to diphenylketene was converted by the action of benzoyl chloride to the corresponding enol benzoate. Hydrolysis of this ester produced the enol, which immediately ketonized. It seemed possible that a more stable enol could be made by the condensation of a Grignard reagent with mesitylketene. Although this ketene could not be isolated it was prepared in solution and to the solution was added mesitylmagnesium bromide. The enolate (V) reacted with benzoyl chloride to yield a benzoate (VI) of desoxymesitoin (VII). The structure of the benzoate was established by

(3) Gilman and Heckert, *THIS JOURNAL*, **42**, 1010 (1920).

hydrolysis, which generated desoxymesitoin. That the benzylation product was not the 1,3-diketone (VIII) was shown by its failure to



generate methane in the Kohler-Richtmyer apparatus.⁴

An attempt to synthesize the new benzoate from desoxymesitoin led to an interesting result. Desoxymesitoin was treated with ethylmagnesium bromide, and benzoyl chloride was added to the solution of the resulting enolate. The benzoate formed in this way was not identical with that from the ketene. It had similar chemical properties, however. It likewise gave no gas in the Grignard machine⁴ and yielded desoxymesitoin when hydrolyzed. Evidently the two benzoates are *cis-trans* isomers. It also becomes certain that neither the *cis* (II) nor the *trans* (III) 1,2-dimesitylviny alcohol is stable with respect to the keto form. This result stands in marked contrast to the stability of the propenol, IX,⁵ and that of 1,1-dimesitylviny alcohol (I).

Two acetates have also been prepared from desoxymesitoin. One of these had been made earlier by Barnes, Cooper, Tulane and Delaney⁶ by heating desoxymesitoin with acetic anhydride and potassium acetate. It melted at 106° and, presumably, has the *trans* configuration. A low-melting acetate (67–68°), presumably the *cis* modification, was prepared by the action of acetyl chloride on the enolate formed by treating desoxymesitoin with ethylmagnesium bromide.

As might be expected, the synthesis of highly hindered ketenes offered difficulty. Mesitylketene was obtained in solution by the action of zinc on α -bromomesitylacetyl bromide. However, attempts to isolate it yielded only the dimer.

An attempt to prepare 2,4,6-triethylphenylketene by the same method led to similar results. The ketene could not be isolated. However, when water was added to the solution the hydration product of the ketene, 2,4,6-triethylphenylacetic acid, was formed.

An attempt to prepare mesitylketene from mesityldiazomethane likewise gave only the hydration product, mesitylacetic acid. Similar results were obtained in attempts to prepare 2,4,6-triisopropylphenylketene.

(4) Kohler and Richtmyer, *THIS JOURNAL*, **52**, 3736 (1930).

(5) Fuson, Corse and McKeever, *ibid.*, **62**, 3250 (1940); Fuson, Byers and Rabjohn, *ibid.*, **63**, 2639 (1941).

(6) Barnes, Cooper, Tulane and Delaney, *J. Org. Chem.*, **8**, 153 (1943).

Experimental

α -Bromomesitylacetyl Bromide.—A mixture of 50 g. of mesitylglycolic acid⁷ and 30 cc. of phosphorus tribromide was heated on the steam-bath for six hours. The lower layer was removed and distilled *in vacuo*; b. p. 138–139° (9 mm.); yield 65%.

Mesitylketene Dimer.—A solution of 26 g. of α -bromomesitylacetyl bromide in 50 cc. of absolute ether was added rapidly, with stirring, to a suspension of 15 g. of granulated zinc in 150 cc. of boiling absolute ether. The mixture was boiled for thirty minutes. The zinc bromide was precipitated from the yellow solution by the addition of 700 cc. of low-boiling petroleum ether. The solution was filtered and the solvent evaporated rapidly. The ketene dimer was purified by recrystallization first from a chloroform-petroleum ether mixture and then from methanol. It formed colorless crystals, melting at 197–200°, which were insoluble in 5% sodium hydroxide solution and in 5% hydrochloric acid.

*Anal.*⁸ Calcd. for $\text{C}_{22}\text{H}_{24}\text{O}_2$: C, 82.48; H, 7.56; mol. wt., 320. Found: C, 82.36; H, 7.85; mol. wt. (ebullioscopic in chloroform), 325.

***trans*-1,2-Dimesitylviny Benzoate.**—A solution of mesitylketene was prepared according to the foregoing directions from 55 g. of α -bromomesitylacetyl bromide and 25 g. of zinc in 200 cc. of dry ether. After the reaction mixture had been heated under reflux for ten minutes, 800 cc. of low-boiling petroleum ether was added to precipitate the zinc bromide formed during the reaction. To the resulting solution was added a solution of mesitylmagnesium bromide prepared from 20 g. of bromomesitylene and 2.4 g. of magnesium in 50 cc. of dry ether. The reaction mixture was stirred for twenty minutes at room temperature. Twenty cubic centimeters of benzoyl chloride was then added, and stirring was continued for an hour at room temperature. The solution was filtered and shaken with 200 cc. of 5% sodium hydroxide solution and 20 cc. of alcohol to remove the excess benzoyl chloride. The ether-petroleum ether layer was washed successively with water, 10% potassium bicarbonate solution and water. It was dried over calcium chloride, and most of the solvent was removed by evaporation. When allowed to stand overnight the solution deposited the benzoate in clusters of white needles. These were collected on a filter, washed with low-boiling petroleum ether and recrystallized from methanol; m. p. 147–148°; yield, 5 g.

Anal. Calcd. for $\text{C}_{27}\text{H}_{28}\text{O}_2$: C, 84.34; H, 7.34. Found: C, 84.09; H, 8.00.

The benzoate was insoluble in 5% sodium hydroxide solution and 5% hydrochloric acid. Analysis in the Grignard machine⁴ showed the absence of active hydrogen. When treated with copper acetate in ether the benzoate failed to yield a copper derivative.

Hydrolysis of the Benzoate.—One gram of the benzoate was dissolved in a solution made from 40 cc. of ethanol, 2 g. of sodium and 2 cc. of water. This solution was heated under reflux for two and one-half hours, cooled, diluted with an equal volume of water and extracted twice with ether. The ether solution was washed with water and dried over calcium chloride. Evaporation of the solvent left a solid residue. It was recrystallized from a mixture of methanol and water; m. p. 91–92°; yield 0.5 g. A mixture with an authentic specimen of desoxymesitoin showed no lowering of the melting point.

Enolization of Desoxymesitoin.⁹—Desoxymesitoin yielded 0.96 mole of methane in the Grignard machine,⁴ but when the reaction mixture was treated with water the original ketene was recovered. Enolizing agents such as alcoholic alkali, sodium ethoxide and sodium amide likewise failed to produce a stable enol.

***cis*-1,2-Dimesitylviny Benzoate.**⁹—To the Grignard reagent, prepared from 0.7 g. of magnesium, 1.9 g. of ethyl

(7) Fuson, Emerson and Gray, *THIS JOURNAL*, **61**, 481 (1939).

(8) The microanalyses reported in this paper were carried out by Miss Theta Spoor and Miss Dorothy Schneider.

(9) This experiment was performed by Dr. Stanley P. Rowland.

bromide and 20 cc. of dry ether, was added a solution of 2.3 g. of desoxymesitoin in 25 cc. of dry ether. The mixture was heated under reflux for one hour. An ether solution of 2 cc. of benzoyl chloride was added, and the refluxing continued for three hours. The decomposition of the mixture and the isolation of the product were conducted in the usual way. The benzoate was purified by recrystallization from methanol. It formed fine, white platelets melting at 104–105.5°.

Anal. Calcd. for $C_{27}H_{28}O_2$: C, 84.34; H, 7.34. Found: C, 84.31; H, 7.34.

cis-1,2-Dimesitylvinyl Acetate.⁹—The preceding synthesis was repeated, acetyl chloride being used in place of benzoyl chloride. The vinyl acetate boiled at 188–193° (4 mm.) and melted at 68–69°. It was purified by recrystallization from methanol.

Anal. Calcd. for $C_{22}H_{26}O_2$: C, 81.94; H, 8.12. Found: C, 81.91; H, 8.26.

Mesitylgyoxal Monohydrazone.—This compound was prepared by the procedure used by Nenitzescu and Solomonica¹⁰ for the synthesis of the monohydrazone of benzil. A solution of hydrazine acetate, prepared from 54 g. of hydrazine sulfate and 77 g. of anhydrous sodium acetate in 250 cc. of water, was boiled for five minutes. The sodium sulfate was precipitated by the addition of 250 cc. of ethanol and removed by filtration. The hydrazine acetate solution was added rapidly from a dropping funnel to a warm solution of 58 g. of mesitylgyoxal in 100 cc. of ethanol. The mixture was heated for ten minutes under reflux. When cold it deposited the hydrazone in white crystals. The yield of crude product was 90%. The monohydrazone was purified by recrystallization from a mixture of ether and low-boiling petroleum ether; m. p. 129–131°.

Anal. Calcd. for $C_{11}H_{14}N_2O$: C, 69.44; H, 7.42. Found: C, 69.40; H, 7.60.

Mesityldiazomethane.—A mixture of 5 g. of mesitylgyoxal monohydrazone and 6 g. of yellow mercuric oxide was added to a flask containing a mixture of 500 cc. of low-boiling petroleum ether, two drops of saturated alcoholic potassium hydroxide solution and 3 g. of finely ground calcium sulfate. The mixture was stirred for three hours at ice-bath temperatures. The solid material was removed by filtration and washed with a little ether. Evaporation of the solvent from the filtrate and washings left the diazomethane in yellow crystals. The yield of crude product was 75%. It crystallized from methanol in fine, yellow needles; m. p. 59–61°, with decomposition.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.21; H, 6.43. Found: C, 70.36; H, 6.19.

In an attempt to prepare mesitylketene a solution of 5 g. of mesityldiazomethane in 50 cc. of dry benzene was dropped slowly into a 10-cc. modified Claisen flask placed in a metal bath held at 100–110°. After the benzene had been distilled nitrogen was passed in and the residue distilled *in vacuo*. No sharp fraction could be obtained; the material in the receiver was a yellow, resinous mass.

Mesitylacetic Acid.—One gram of mesityldiazomethane was treated for thirty minutes with 100 cc. of boiling water. The solution was allowed to cool, 3 g. of potassium carbonate was added and the mixture extracted twice with ether. Acidification of the carbonate solution yielded 0.3 g. of mesitylacetic acid; m. p. 165–166°.

2,4,6-Triethylphenylacetic Acid.—Thirty-five grams of 2,4,6-triethylphenylglycolic acid⁸ was mixed with 15 cc. of phosphorus tribromide and the mixture allowed to stand overnight on the steam-bath. An additional 5 cc. of phosphorus tribromide was added and the heating continued for twelve hours. The organic layer was distilled *in vacuo*, yielding 27 g. of α -bromo-2,4,6-triethylphenylacetyl bromide; b. p. 140–142° (5 mm.).

A solution of 20 g. of α -bromo-2,4,6-triethylphenylacetyl bromide, 50 cc. of dry ethyl ether and 50 cc. of dry butyl

ether was added dropwise, with stirring, to a mixture of 5 g. of granulated zinc and 30 cc. of dry ethyl ether. The addition required five minutes, and the mixture was stirred and warmed for ten minutes longer. During this time nitrogen was passed through the container. The zinc bromide was precipitated by the addition of 350 cc. of low-boiling petroleum ether. A solution of 5 cc. of water and 50 cc. of ether was added, and the reaction mixture was stirred for ten minutes. The zinc bromide and a considerable amount of sticky material was removed by filtration, and the filtrate was extracted with 5% sodium hydroxide solution. Acidification yielded the 2,4,6-triethylphenylacetic acid as an oil, which could be crystallized from dilute ethanol; m. p. 98°; yield 0.5 g. A mixed melting point with an authentic sample showed no lowering.

2,4,6-Triisopropylphenylglycolic Acid.—A mixture of 84 g. of selenium dioxide and 700 cc. of 95% ethanol was heated at 50° until the solid had dissolved. Methyl 2,4,6-triisopropylphenyl ketone (153 g.)¹¹ was added and the mixture heated under reflux, with stirring, for seven hours. The selenium was removed by filtration, and the solvent was distilled. The 2,4,6-triisopropylphenylglyoxal distilled at 138–143° (7.5 mm.). The yield was 77% of the theoretical.

A mixture of 95 g. of the glyoxal and 1 l. of 10% potassium hydroxide solution was heated on a steam-bath for twenty-four hours and acidified with hydrochloric acid. The 2,4,6-triisopropylphenylglycolic acid dissolved with difficulty in dilute potassium hydroxide solution. The solution was washed repeatedly with ether and acidified with hydrochloric acid. The glycolic acid was recrystallized twice from 66% acetic acid; m. p. 163–164° (cor.); yield 73%.

Anal. Calcd. for $C_{17}H_{26}O_3$: C, 73.34; H, 9.42. Found: C, 73.60; H, 9.62.

Methyl 2,4,6-Triisopropylphenylglycolate.—This ester was obtained in 65% yield by heating the acid for three hours with methanol which had been saturated previously with hydrogen chloride. It was recrystallized from ligroin; m. p. 94–95°.

Anal. Calcd. for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found: C, 73.80; H, 9.73.

Saponification with aqueous alkali converted it to the original acid.

Dioxolone from 2,4,6-Triisopropylphenylglycolic Acid.—A mixture of 9 g. of the acid, 40 cc. of acetone and 2 cc. of concentrated sulfuric acid was stirred for thirty minutes at ice-bath temperatures. The dioxolone was obtained in beautiful, white crystals melting at 165–165.5°; yield 75%.

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.59; H, 9.82.

Treatment of the dioxolone with hydrazine hydrate converted it to the corresponding hydrazide. A solution of 1.5 g. of the dioxolone, 50 cc. of absolute ethanol and 2 g. of hydrazine hydrate was heated for four hours under reflux. The product was recrystallized from a ligroin–benzene solution (7:3). It formed white crystals melting at 156–157°.

Anal. Calcd. for $C_{17}H_{28}O_2N_2$: C, 69.82; H, 9.65; N, 9.58. Found: C, 70.22; H, 9.32; N, 9.85.

The Hydrazone of 2,4,6-Triisopropylphenylglyoxal.¹²—The procedure was similar to that given for the mesityl analog. From 62.4 g. of the glyoxal there was obtained 59 g. (90%) of the hydrazone, melting at 147–151°, with decomposition. It was recrystallized repeatedly from dilute ethanol. The hydrazone formed white cubes melting at 153–154°, with decomposition.

Anal. Calcd. for $C_{17}H_{26}N_2O$: C, 74.41; H, 9.55. Found: C, 74.38; H, 9.65.

2,4,6-Triisopropylphenylacetic Acid.—(a) A finely ground mixture of 7 g. of yellow mercuric oxide, 2.5 g. of

(10) Nenitzescu and Solomonica, "Org. Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 496.

(11) Fuson, Botteroff and Speck, *THIS JOURNAL*, **64**, 1450 (1942).

(12) This compound was prepared by Dr. Quentin F. Soper.

anhydrous calcium sulfate and 5 g. of the hydrazone of 2,4,6-triisopropylphenylglyoxal was covered with 75 cc. of dry ether and stirred for twelve hours at room temperature. The ether was decanted through a filter paper and the black residue washed by decantation with a total of 100 cc. of dry ether. Removal of the ether left the diazo compound as a yellow powder, which decomposed explosively at 125°. After recrystallization from methanol it was found to decompose at 104°; yield 4.5 g.

It was covered with water and a pinch of silver oxide was added. The mixture was boiled for thirty minutes. Eight grams of potassium hydroxide pellets was added and the boiling continued for fifteen minutes. A solid was removed by filtration and recrystallized from ether. It formed pale yellow crystals melting at 204–205°. This substance was not identified. When the filtrate was acidified the 2,4,6-triisopropylphenylacetic acid was precipitated. It was recrystallized from 75% acetic acid and then from ligroin; m. p. 146–146.5°. A mixture with an authentic specimen of the acid (see below) showed no depression in melting point.

(b)¹³ The hydrolysis of 2,4,6-triisopropylbenzyl cyanide could not be effected satisfactorily with 50–80% sulfuric acid. The method of Redemann and Lucas¹⁴ for the saponification of esters, however, was found to be suitable. A mixture of 87 g. of the pure nitrile, 500 cc. of diethylene glycol, 100 g. of potassium hydroxide and 20 cc. of water was heated under reflux for twelve hours and poured into water. The 2,4,6-triisopropylphenylacetic acid, precipitated by acidification of the mixture, was recrystallized from aqueous ethanol; m. p. 144–145°; yield 85%.

Anal. Calcd. for $C_{17}H_{26}O_2$: C, 77.80; H, 9.99. Found: C, 78.08; H, 9.67.

Hydrolysis of the nitrile with potassium hydroxide and

ethanol produced 2,4,6-triisopropylphenylacetamide. It was recrystallized from ethanol; m. p. 170–171°.

Anal. Calcd. for $C_{17}H_{27}NO$: C, 78.11; H, 10.41. Found: C, 78.15; H, 10.57.

2,4,6-Triisopropylbenzyl Cyanide.¹¹—2,4,6-Triisopropylbenzyl chloride, prepared by the chloromethylation of 1,3,5-triisopropylbenzene,¹⁸ was converted to the corresponding cyanide by treatment with cuprous cyanide. A mixture of 149 g. of the chloride, 57.8 g. of cuprous cyanide and 60 cc. of dry pyridine was heated at 210–220° for ninety minutes. When the mixture had cooled to 150° it was poured into a mixture of 500 g. of ice and 200 cc. of ammonium hydroxide. The mixture was allowed to stand overnight, and the crude nitrile was collected on a filter and distilled, b. p. 129–130° (4 mm.); m. p. 81–82°; yield 64%.

Anal. Calcd. for $C_{17}H_{26}N$: C, 83.89; H, 10.35. Found: C, 83.40; H, 10.26.

Summary

Methods of synthesis of hindered aldoketenes have been studied.

The *cis* and *trans* enol benzoates of desoxymesitoin have been prepared. Hydrolysis was found to convert them to desoxymesitoin, showing that the *cis* and *trans* enols of desoxymesitoin were unstable and ketonized rapidly. The corresponding *cis* and *trans* acetates were also prepared. These results confirm the conclusion reached earlier that the dehydration product of hydromesitoin or isohydromesitoin is 1,1-dimesitylvinyl alcohol.

(15) Fuson, Horning, Ward, Rowland and Marsh, *THIS JOURNAL*, **64**, 30 (1942).

URBANA, ILLINOIS

RECEIVED MARCH 13, 1944

The Relation of Estrogenic Activity to Structure in Some 4,4'-Dihydroxydiphenylmethanes¹

By E. EMMET REID AND EDITH WILSON²

Estrogenic activity has been noted by Dodds and Lawson³ in some 4,4'-dihydroxydiphenylmethanes, $(HOC_6H_4)_2CRR'$. It seemed worthwhile to prepare a number of these to see how the estrogenic activity varies with the size and character of the groups R and R'. Two series have now been made: one, in which R is methyl and R' varies from methyl to hexyl, and the other, in which R and R' are identical and vary from methyl to amyl. Besides these several compounds of different types, including the double one, $(HOC_6H_4)_2C(CH_3)CH_2CH_2C(CH_3)(C_6H_4OH)_2$, from acetonyl-acetone have been studied. In order to have comparable estrogenic data, the known compounds have been prepared and tested along with the new. For better chemical characterization the benzoates of all of them have been prepared. The results are in Table I. The activities of the members

of the second series are plotted in Fig. 1. When our work was nearly completed, an article by Campbell⁴ covering part of the same ground appeared.

The activity reaches a peak in the first series with the methyl-propyl and in the second series a much higher peak at the propyl-propyl, which is ten times as potent as any of the others. The activities for ethyl-propyl and for propyl-butyl are borrowed from Campbell. For comparison the data for the corresponding *trans*-4,4'-dihydroxy- α,β -dialkylstilbenes⁵ are plotted in Fig. 1, but they are in rat units per milligram while ours are in the same units per gram. The ethylene derivatives are around a thousand times as active as the methane derivatives, yet the shapes of the two curves are strikingly alike except that the maximum is at the ethyl-ethyl in the one and at the propyl-propyl in the other. The rise is gradual through the methyl-ethyl in the one and through the ethyl-propyl in the other. In both

(1) Original manuscript received October 20, 1942.

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(3) Dodds and Lawson, *Proc. Roy. Soc. (London)*, **B125**, 222 (1938).

(4) N. R. Campbell, *ibid.*, **B129**, 528 (1940).

(5) Dodds, Goldberg, Lawson and Robinson, *ibid.*, (London), **B127**, 140 (1939).