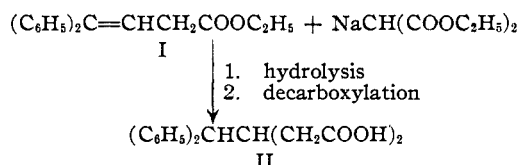


[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

 $\beta$ -Benzohydrilglutaric AcidBY MELVIN S. NEWMAN,<sup>1</sup> LLOYD M. JOSHEL<sup>2</sup> AND PAUL H. WISE

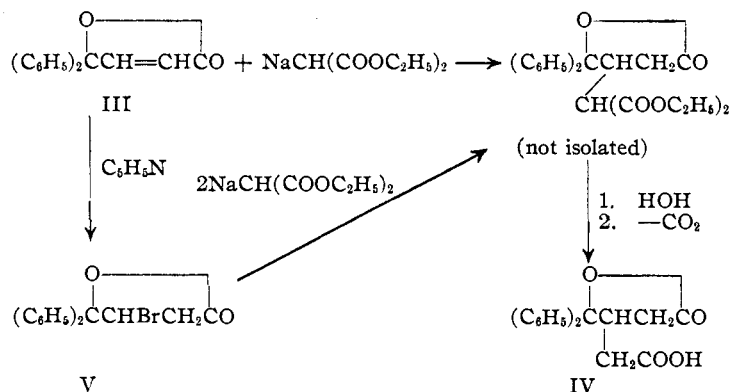
Inasmuch as  $\beta$ -benzohydrilglutaric acid, V, has been shown to be a desirable intermediate for the synthesis of various derivatives of 3,4-benzphenanthrene<sup>3,4</sup> an improved method for its preparation was sought. Although quite a number of new methods have been investigated, the method originally employed<sup>3</sup> remains the most satisfactory. The other procedures, however, are of sufficient interest to warrant brief descriptions.

We have shown that although ethyl 4,4-diphenyl-3-butenolate, I, is not an  $\alpha,\beta$ -unsaturated ester, it reacted with sodiomalonic ester<sup>5</sup> to give (after hydrolysis and decarboxylation) the desired  $\beta$ -benzohydrilglutaric acid, I.

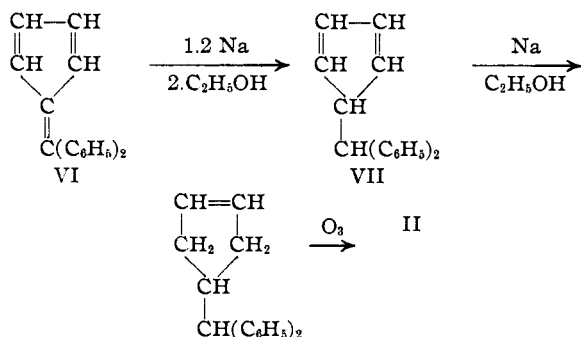


Since this experiment indicated that the double bond in I would not readily shift to the  $\alpha,\beta$ -position, it seemed advisable to employ as starting material a compound in which the double bond was fixed in the desired position. Accordingly sodiomalonic ester was condensed with the lactone of  $\gamma$ -hydroxy- $\gamma,\gamma$ -diphenylcrotonic acid III,<sup>6</sup> to yield the lactone of  $\beta$ -( $\alpha$ -hydroxybenzohydril)glutaric acid, IV. The same end-product was obtained if  $\beta$ -bromo- $\gamma,\gamma$ -diphenylbutyrolactone, V,<sup>6</sup> were substituted for III in the Michael reaction. However, in the reaction with V two molar proportions of sodiomalonic ester were desirable, the first evidently being used to remove the elements of hydrogen bromide from V to produce III. Although fair yields of the lactone, IV, were obtained by both methods, we were unable

to reduce IV to the desired  $\beta$ -benzohydrilglutaric acid, II.



Another approach investigated is illustrated by the following chart:



Schlenk and Bergmann<sup>7</sup> described a hydrocarbon,  $\text{C}_{18}\text{H}_{16}$ , m. p.  $36.5^\circ$ , obtained by the addition of two atoms of sodium to 6,6-diphenylfulvene, VI, followed by treatment with alcohol, to which they ascribed formula VII. We were unable to isolate any pure compound in satisfactory yield by repeating these experiments. However, by the condensation of benzohydril bromide with cyclopentadienylmagnesium bromide<sup>8</sup> we obtained a product which melted at  $25-30^\circ$ . Since our product yielded about 79% of benzophenone on ozonization, it was obvious that a rearrangement of double bonds had occurred.

In attempting to prepare 1,1-diphenyl-2,2-dichloroethane desired as an intermediate in another projected synthesis of II, a new molecular rearrangement was found to occur. On treating di-

(1) The Elizabeth Clay Howald Scholar at The Ohio State University, 1939-1940.

(2) Part of the material herein presented formed part of the dissertation presented by Lloyd M. Joshel to The Ohio State University in partial fulfillment of the requirements for the Ph.D. degree, June, 1938.

(3) Newman and Joshel, *THIS JOURNAL*, **60**, 485 (1938).

(4) Newman and Joshel, *ibid.*, **62**, 972 (1940).

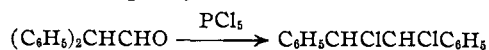
(5) Compare Vorländer and Strunk, *Ann.*, **345**, 237 (1906).

(6) Borsche, *ibid.*, **526**, 18 (1936).

(7) Schlenk and Bergmann, *ibid.*, **463**, 58 (1928).

(8) Courtot, *Ann. chim.*, [9], **4**, 69 (1915).

phenylacetaldehyde with phosphorus pentachloride, there was obtained a mixture of the stereoisomeric stilbene dichlorides instead of the expected 1,1-diphenyl-2,2-dichloroethane.



### Experimental<sup>9</sup>

**$\beta$ -Benzohydroxyglutaric Acid, II.**—In the best of several experiments in which the solvent, temperature, and reaction time were varied, 5.2 g. of ethyl 4,4-diphenyl-3-butenolate, b. p. 175° at 4 mm., (prepared by esterification of the acid<sup>6</sup>) was added to a solution of sodiomalonic ester (0.5 g. of sodium and 3.4 cc. of diethyl malonate) in 25 cc. of absolute ethanol. After refluxing for thirty hours and treatment with dilute acid, the neutral fraction was distilled under reduced pressure. A forerun of 3.7 g. (71%) of starting ester was collected. The yellow viscous oil, b. p. about 215° at 4 mm., was hydrolyzed and the crude acids decarboxylated by heating at 200° for ten minutes. On crystallization from benzene 0.52 g. (8.9%) of  $\beta$ -benzohydroxyglutaric acid, m. p. and mixed m. p. 176–177°, was isolated.

**$\beta$ -Bromo- $\gamma,\gamma$ -diphenylbutyrolactone, V.**—To a suspension of 33.2 g. of finely ground 4,4-diphenyl-3-butenic acid<sup>6</sup> in 65 cc. of water in a porcelain mortar was added dropwise 10 cc. of bromine while constantly grinding with a pestle. After a total of three hours with occasional grinding the yellow solid was collected, washed with water, and dissolved in benzene. Extraction with sodium carbonate yielded 8.7 g. of unchanged starting acid. From the benzene solution a total of 25.7 g. (79% allowing for recovered acid) of colorless prisms of V, m. p. 128–130.6°, was obtained. A sample recrystallized from benzene melted at 130.6–131.2°. This compound was prepared more easily but in poorer yield (50%) by treating a methyl alcoholic solution of 4,4-diphenyl-3-butenic acid with bromine. Borsche<sup>6</sup> prepared this compound in unstated yield by treating an acetic acid solution of the ethyl ester with bromine.

**Lactone of  $\gamma$ -Hydroxy- $\gamma,\gamma$ -diphenylcrotonic Acid, III.**—Borsche<sup>6</sup> prepared this compound by refluxing the above bromolactone in pyridine but gave no details or yield. By heating 10 g. of V with 50 cc. of pyridine for six hours and diluting with water, an almost theoretical yield of colorless plates, m. p. 131.6–132.2°, was obtained. No depression of the melting point was observed when mixed with a sample of II prepared according to Stobbe.<sup>10</sup>

**Lactone of  $\beta$ -( $\alpha$ -Hydroxybenzohydroxy)-glutaric Acid, IV.**—A suspension of 0.8 g. of sodium powder in dry ether was refluxed with 8 cc. of diethyl malonate until all of the metal had reacted. A solution of 5.0 g. of V in dry sulfur-free benzene was added and, after forty hours of refluxing, the mixture was treated with dilute sulfuric acid. The neutral fraction of the products was refluxed with a solution of 10 cc. each of water, acetic acid, and concentrated sulfuric acid for twenty-three hours. The acid fraction thus produced was heated to 250° to effect decarboxylation. On crystallization from acetone-benzene there was isolated 2.1 g. (44%) of colorless needles of IV, m. p.

182.0–183.5°. By following an entirely analogous procedure starting from 0.3 g. of sodium, 5 cc. of diethyl malonate, and 3.0 g. of III, there was obtained a 54% yield of the same lactone-acid. For analysis a sample, crystallized from acetone-benzene, melted at 182.8–183.8°.

*Anal.* Calcd. for  $\text{C}_{19}\text{H}_{16}\text{O}_4$ : C, 72.96; H, 5.44. Found: C, 73.07; H, 5.41.

The reduction of this lactone-acid as attempted using the modified Clemmensen procedure,<sup>11</sup> zinc dust and alkali, and hydriodic acid in acetic acid failed to give any homogeneous acid.

**Reaction of Cyclopentadienylmagnesium Bromide with Benzohydroxy Bromide.**—A benzene solution of 24 g. of freshly distilled cyclopentadiene was added slowly to 200 cc. of an ether-benzene solution of the equivalent amount of ethylmagnesium bromide and the mixture refluxed for four hours under nitrogen. This solution of cyclopentadienylmagnesium bromide<sup>8</sup> was cooled in an ice-bath and a solution of 86 g. of benzohydroxy bromide in 200 cc. of benzene was added slowly keeping the temperature about 25°. After the addition was complete (three hours) the mixture was allowed to stand for two hours and then treated with 20% ammonium chloride solution. The organic layer was separated, washed with water, and dried over anhydrous calcium chloride, a small amount of hydroquinone being added to retard polymerization. The solvent was removed under reduced pressure and the product distilled. There was obtained 35 g. (41%) of a yellow viscous oil, b. p. 163–165° at 4 mm., which solidified in the icebox and melted at 25–30°. Attempts to crystallize this material from alcohol were abandoned because of the continuous separation of polymeric products. A solution of 2.50 g. of this substance in 125 cc. of acetic acid was ozonized and the ozonide (insoluble in cold acetic acid) was decomposed by adding to water at 80° and treating with hydrogen peroxide. The neutral portion of the ozonization products consisted of an oil (1.47 g. or 79%) which yielded the 2,4-dinitrophenylhydrazone of benzophenone, m. p. and mixed m. p. 241–243°.

**Stilbene Dichlorides.**—A solution of 4.9 g. of diphenylacetaldehyde, purified through the bisulfite compound and by distillation, in 75 cc. of dry benzene was added to 11 g. of phosphorus pentachloride and the mixture refluxed for two hours. After decomposing with iced water the benzene layer was washed with water and sodium carbonate solution. The benzene was distilled and replaced with petroleum ether. On concentrating judiciously 0.33 g. of the *meso* stilbene dichloride, m. p. 192.4–193.4°, and, from the mother liquors on standing in the icebox, 2.22 g. (41% in all) of racemic stilbene dichloride, m. p. 91.0–92.4°, was obtained.<sup>12</sup> The higher melting form gave no depression when mixed with the stilbene dichloride prepared from hydrobenzoin and thionyl chloride.<sup>13</sup>

### Summary

$\beta$ -Benzohydroxyglutaric acid has been prepared by a new method involving a Michael condensa-

(11) Martin, *THIS JOURNAL*, **58**, 1438 (1936).

(12) Zincke, *Ber.*, **10**, 999 (1877); Weissberger and Bach, *ibid.*, **64**, 1095 (1931).

(13) Kitasato and Sone, *ibid.*, **64**, 1142 (1931); Carre and Mauclere, *Compt. rend.*, **192**, 1567 (1931).

(9) All melting points corrected. Analyses by Mr. H. S. Clark.

(10) Stobbe, *Ann.*, **308**, 104 (1899).

tion between sodiomalonic ester and ethyl 4,4-diphenyl-3-butenolate.

The preparation of the lactone of  $\beta$ -( $\alpha$ -hydroxy-benzohydril)-glutaric acid is described.

The reaction of cyclopentadienylmagnesium bromide with benzohydril bromide has been shown to form a product in which one of the

double bonds has migrated to a position of conjugation with the phenyl groups.

Diphenylacetaldehyde has been shown to yield a mixture of the stereoisomeric stilbene dichlorides upon treatment with phosphorus pentachloride.

COLUMBUS, OHIO

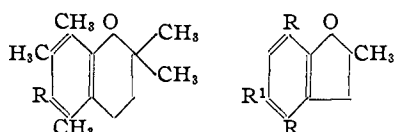
RECEIVED APRIL 25, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

## The Chemistry of Vitamin E. XXIII. A New Synthesis of 2,4,6,7-Tetramethyl-5-hydroxycoumaran and of 2-Methyl-5-hydroxycoumaran. Oxidation Products of the Tetramethylcoumaran<sup>1</sup>

BY LEE IRVIN SMITH, HARVEY H. HOEHN AND AMBROSE G. WHITNEY

Two reports have been published which describe experiments leading to preparation of *p*-hydroxy-chromans and -coumarans in which the introduction of the hydroxyl group para to the bridge oxygen atom constitutes the final step in the series of reactions. One of these reports<sup>2</sup> dealt with the conversion of chroman I into II by bromination, followed by oxidation of the Grignard reagent prepared from the bromo compound. The other report<sup>3</sup> dealt with the conversion of coumarans III into IV by coupling III with diazotized 2,4-dinitroaniline, reductively cleaving the azo compound to the aminocoumaran, and replacing the amino group by the hydroxyl group in the usual way via the diazonium salt. In both



I, R = H

II, R = OH

III, R = H or CH<sub>3</sub>; R' = H

IV, R = H or CH<sub>3</sub>; R' = OH

series of reactions, the over-all yields left much to be desired. Oxidation of the Grignard reagent from I gave a poor yield of II, while the aminocoumaran from III gave only poor yields of IV via the diazonium salt. Moreover, apparently only the most active diazonium salts will couple with chromans and coumarans; diazotized sulfanilic acid gave a very poor yield of azo compound from I<sup>2</sup> and while diazotized 2,4-dinitroaniline coupled well with III, reductive cleavage of the resulting azo compound gave a mixture of two water insoluble amines which had to be separated.<sup>3</sup> In

the specific examples cited, this separation was successful, but for higher members of the chroman and coumaran series, in which steam distillation would probably be of little use, the separation of two basic amines might offer some difficulties.

Since diazotized sulfanilic acid couples well with phenols, a new approach to the synthesis of compounds such as II and IV has been studied in which an allylic phenol was coupled with the diazonium salt and the latter was converted into the aminophenol before the ring was closed. In the model experiments an allyl halide was used; consequently cyclization led to a coumaran. In order to be more certain that the various products would be solids (IV, R = H was reported to be a liquid<sup>3</sup>), 2,3,5-trimethylphenol V was used.

To avoid any para allylation, the phenol V was converted into the allylic phenol VI by rearrangement of the phenyl allyl ether.<sup>4,5</sup> It was found that allyl chloride could be used in preparing the phenyl allyl ether, but the reaction was more rapid, and better yields were obtained when finely powdered potassium iodide was added to the reaction mixture.<sup>6</sup> The allylic phenol VI coupled well with diazotized sulfanilic acid, and the azo compound, when reductively cleaved by sodium hydrosulfite, gave a good yield of the aminophenol VII. In a similar way, 4-amino-2,3,5-trimethylphenol was prepared in good yield from V. The aminophenol VII was converted to the aminocoumaran XIII by action of hydro-

(4) Hurd, *THIS JOURNAL*, **52**, 1702 (1930).

(5) Smith, Ungnade, Hoehn and Wawzonek, *J. Org. Chem.*, **4**, 309 (1939). In this paper, bottom of p. 309 and top of p. 310, there is an error. The directions calling for extraction by ether and subsequent washing of the ether extracts with Claisen's alkali should read *petroleum ether* instead of ether.

(6) Mauthner, *J. prakt. Chem.*, **148**, 95 (1937).

(1) Paper XXII, *THIS JOURNAL*, **62**, 145 (1940).

(2) Smith, Hoehn and Ungnade, *J. Org. Chem.*, **4**, 351 (1939).

(3) Karrer and Fritzsche, *Helv. Chim. Acta*, **22**, 657 (1939).