

35 ml. of 10% sodium hydroxide with vigorous stirring. The temperature of the mixture was then maintained at 50° and the mixture stirred until the dimethyl sulfate layer had disappeared. Then 10 ml. more of sodium hydroxide and 3.8 ml. of dimethyl sulfate were added and the mixture stirred until solution was complete. This step was repeated three more times. The solution was cooled and then acidified with hydrochloric acid. Filtration yielded a tan material. In order to saponify any ester that was formed, this was refluxed in 25 ml. of 20% sodium hydroxide for 45 minutes. Cooling, acidification, and filtration yielded 3.2 g. of tan product. Recrystallization from water accompanied by decolorization with carbon gave white crystals, m. p. 242–243°.

Alkaline oxidation of the methoxy compound with potassium permanganate gave the known 2,5-dimethoxyterephthalic acid. The identity of this compound was

verified by melting point, fluorescence, and also by conversion into the diethyl ester whose physical properties checked those given in the literature.

### Summary

Ethyl cyanoacetate, cyanoacetamide, and malonitrile react with *p*-benzoquinone in the presence of ammonium hydroxide to give highly colored, crystalline compounds.

Each of the colored compounds upon hydrolysis gave the colorless acid, 2,5-dihydroxy-*p*-benzene-diacetic acid. Several derivatives of this new acid are reported.

KNOXVILLE, TENNESSEE

RECEIVED FEBRUARY 9, 1944

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

## The Arylbutadiene–Maleic Anhydride Reaction

BY RICHARD T. ARNOLD AND EUGENE C. COYNER<sup>1</sup>

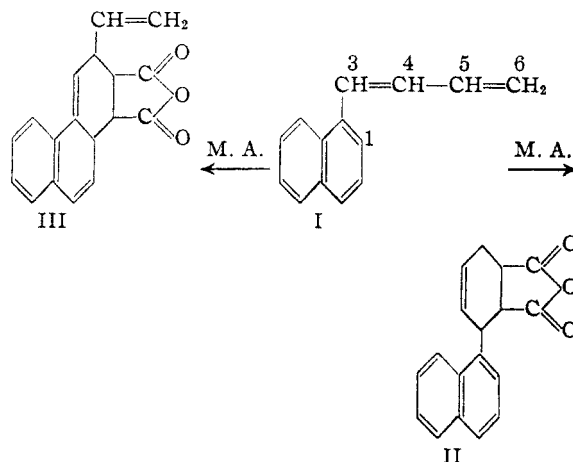
It has now been well established that certain aromatic double bonds will in conjunction with a vinyl group form a diene system which is reactive toward the common dienophiles (maleic anhydride, etc.). With one exception<sup>2</sup> (1,1-diphenylethylene), the examples thus far reported have the vinyl (or substituted vinyl) group attached to the  $\alpha$ -<sup>3</sup> or  $\beta$ -<sup>4</sup> positions in naphthalene, the 9-position<sup>5</sup> in phenanthrene, or the para position to one of the oxygen atoms in the veratrole or methylenedioxybenzene<sup>6</sup> systems.

That the success of this reaction must depend upon the importance of certain necessary resonance contributing structures has already been pointed out.<sup>6</sup>

If the vinyl group in the above-mentioned molecules is replaced by a butadienyl substituent, it becomes apparent that two competitive diene systems are present within a single molecule. Thus, for example, 1- $\alpha$ -naphthylbutadiene (I) can react with maleic anhydride (M. A.) to give two different isomeric adducts II and III depending upon whether the 3,6 or 1,4 diene system is involved.

A qualitative consideration of the relative importance of the resonance contributing structures in I leads to the supposition that II rather than III should be the predominant product formed. The experimental results reported in this paper show that adducts of the type II are produced perhaps exclusively.

Maleic anhydride has been allowed to react with three arylbutadienes each of which has two active diene groups. The aryl substituent con-



sisted of 1-naphthyl-3,4-dimethoxyphenyl, and 3,4-methylenedioxyphenyl. Structures of the adducts formed in the first two cases were established with certainty but all attempts to elucidate the carbon skeleton in the third case, although it is undoubtedly analogous to the other two, failed.

Unfortunately, the pure dienes polymerized so rapidly that they could not be isolated as such; consequently, the diene in each case was formed during the course of the reaction by dehydration (with maleic anhydride) of the appropriate alcohol.

The formula for compound IV follows from its conversion into dimethyl 3- $\alpha$ -naphthylphthalate (V) which was synthesized independently by means of an Ullmann reaction. Hydrogenation and cyclization of IV to give the hydrobenzanthronecarboxylic acid VI strongly indicates (as shown by models) the *cis* configuration for the  $\alpha$ -naphthyl group in IV with respect to the adjacent carbonyl linkage.

(1) Abstracted from the Ph.D. thesis of Eugene C. Coyner submitted to the Graduate Faculty of the University of Minnesota, April, 1944.

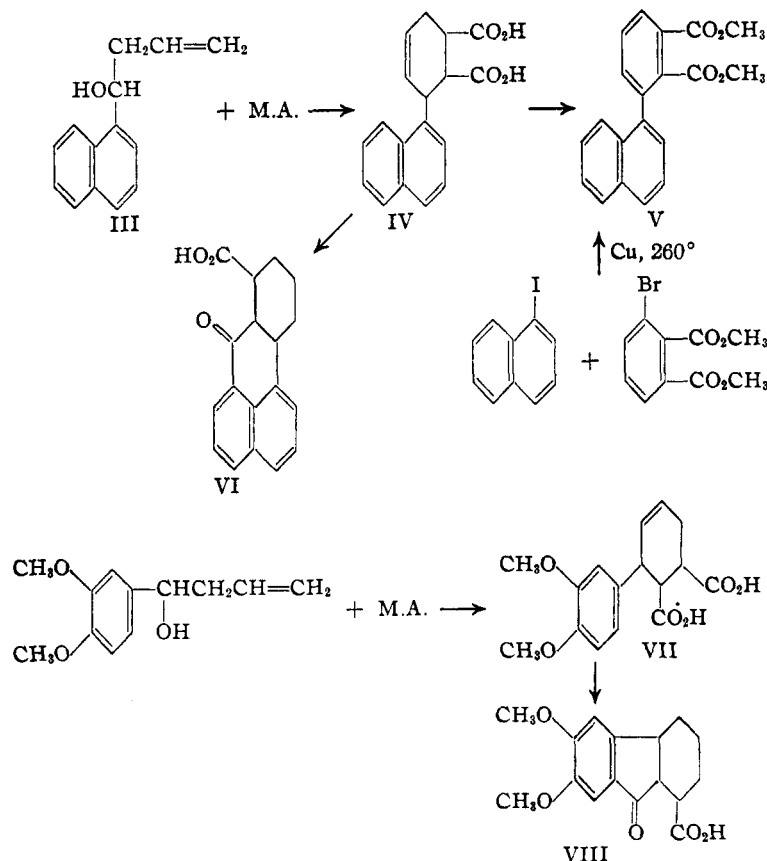
(2) Wagner-Jauregg, *Ann.*, **491**, 1 (1931).

(3) Cohen, *Nature*, **136**, 869 (1935).

(4) Cohen and Warren, *J. Chem. Soc.*, 1315 (1937).

(5) Bergmann and Bergmann, *This Journal*, **59**, 1443 (1937).

(6) Hudson and Robinson, *J. Chem. Soc.*, 715 (1941).



(M. A. = maleic anhydride)

Similarly, the reduction and cyclization of VII to produce compound VIII proves not only the carbon skeleton in VII but establishes without doubt the *cis* configuration for the 3,4-dimethoxyphenyl radical in this molecule.

### Experimental

**$\alpha$ -Naphthylallylcarbinol.**—Into a 500-cc. three-necked flask equipped with a condenser, stirrer and separatory funnel were placed 150 cc. of dry ether and 6.05 g. of magnesium. The reaction was started with 3 cc. of allyl chloride and this was followed by the slow addition (twenty-five minutes) of a solution containing allyl chloride (24.4 cc.),  $\alpha$ -naphthaldehyde (28.9 g.), and ether (75 cc.). The reaction was strongly exothermic and the mixture was stirred during the initial six hours. On the following day the Grignard solution was decomposed with ice and hydrochloric acid. There was obtained 31.3 g. (94%) of the desired carbinol; b. p.  $150$ – $151^\circ$  (5 mm.). Some dehydration occurred during the isolation.

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{14}\text{O}$ : C, 84.81; H, 7.12. Found: C, 85.57; H, 7.55.

***cis*- $\alpha$ -Naphthyl-1,2,3,6-*cis*-tetrahydrophthalic Acid.**—Maleic anhydride (4.9 g.) and  $\alpha$ -naphthylallylcarbinol (9.9 g.) were placed in a flask equipped with an air condenser and heated to a temperature of  $150^\circ$ . A violent exothermic reaction took place which was moderated by cooling the flask with water. After one minute the flask was replaced in the metal bath and heated at  $145$ – $155^\circ$  for forty-five minutes. A brittle, tan solid remained which upon cooling and treatment with ether deposited 7.4 g. of white crystalline solid; decomposition of this substance begins at  $165^\circ$ .

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{16}\text{O}_4$ : C, 72.96; H, 5.44; neut. equiv., 148. Found: C, 72.80; H, 5.24; neut. equiv., 147.

Lower yields resulted when excesses of maleic anhydride were employed.

**3- $\alpha$ -Naphthyl-1,2,3,6-tetrahydrophthalic Anhydride.**—A solution containing  $\alpha$ -naphthylallylcarbinol (4.0 g.), maleic anhydride (3.0 g.), and xylene (50 cc.) was heated at its boiling point under partial reflux for six hours. The resulting solution after being cooled in a refrigerator overnight deposited 2.1 g. of a white solid (m. p.  $159$ – $160^\circ$ ). This substance after recrystallization from benzene-petroleum ether melted at  $160$ – $161^\circ$ .

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{14}\text{O}_3$ : C, 77.68; H, 5.07. Found: C, 78.16; H, 5.18.

***cis*-3- $\alpha$ -Naphthyl-*cis*-hexahydrophthalic Acid.**—Catalytic hydrogenation of 3.0 g. of 3- $\alpha$ -naphthyl-1,2,3,6-tetrahydrophthalic acid dissolved in alcohol with 50 mg. of platinum and hydrogen (30 pounds pressure) resulted in the theoretical uptake of hydrogen in forty-five minutes. There was isolated 2.7 g. of the hexahydro acid which showed no thermal decomposition below  $180^\circ$ .

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{18}\text{O}_4$ : C, 72.46; H, 6.08. Found: C, 72.33; H, 6.38.

**Dimethyl *cis*-3- $\alpha$ -naphthyl-1,2,3,6-*cis*-tetrahydrophthalate.**—When the corresponding acid was dissolved in ether and treated with a slight excess of ethereal diazomethane for twenty-four hours, there was obtained, after removal of the solvent, a quantitative yield of the ester; m. p.  $79$ – $81^\circ$  after recrystallization from benzene-petroleum ether.

*Anal.* Calcd. for  $\text{C}_{20}\text{H}_{18}\text{O}_4$ : C, 74.05; H, 6.21. Found: C, 74.02; H, 6.58.

**Dimethyl *cis*-3- $\alpha$ -Naphthyl-*cis*-hexahydrophthalate.**—This ester was prepared in quantitative yield by allowing the dibasic acid to react with an excess of ethereal diazomethane; m. p.  $88$ – $89.5^\circ$  after recrystallization from benzene-petroleum ether.

*Anal.* Calcd. for  $\text{C}_{20}\text{H}_{22}\text{O}_4$ : C, 73.60; H, 6.79. Found: C, 73.46; H, 6.61.

**Dehydrogenation of Dimethyl *cis*-3- $\alpha$ -Naphthyl-1,2,3,6-*cis*-tetrahydrophthalate.**—A mixture of 2.23 g. of the tetrahydro ester and 0.23 g. of palladium-charcoal (30%) was heated in the presence of carbon dioxide at  $245^\circ$  for thirty-six hours. The product was taken up in benzene, filtered, and the benzene was then removed *in vacuo*. Treatment of the residual oil with a mixture of petroleum ether and diethyl ether yielded a tan solid (0.49 g.). This was partially dissolved in hot petroleum ether (b. p.  $90$ – $100^\circ$ ) and filtered. The filtrate after standing overnight at  $0^\circ$  gave 0.2 g. of white pellets; m. p.  $118$ – $130^\circ$ . Two recrystallizations from methanol resulted in pure dimethyl 3- $\alpha$ -naphthylphthalate; m. p.  $133$ – $134^\circ$ .

*Anal.* Calcd. for  $\text{C}_{20}\text{H}_{16}\text{O}_4$ : C, 74.99; H, 5.03. Found: C, 74.60; H, 5.12.

**Dimethyl 3- $\alpha$ -Naphthylphthalate.**—Attempts to prepare this compound by Gomberg's method failed. The Ullmann procedure proved satisfactory.

To a mixture of dimethyl 3-bromophthalate (5.5 g.) and  $\alpha$ -iodonaphthalene (20.3 g.) heated to  $255$ – $260^\circ$  was added activated copper powder (25 g.). Heating and occasional stirring were continued for two hours. Then more copper (5.5 g.) was added and the heating continued for an additional thirty minutes. The reaction mass was cooled and extracted with five 30-cc. portions of hot chloroform. Removal of the solvent left a sirup from which no crystalline material could be isolated. This residue was saponified by heating with potassium hydroxide (3.4 g.) in metha-

nol (100 cc.) for twenty hours. Removal of a portion of the solvent caused the precipitation of 3.2 g. of impure  $\alpha$ -binaphthyl; m. p. 147–152°. This solid after being leached with water and recrystallized from petroleum ether melted at 152–154°. Ullmann and Bielecki<sup>7</sup> reported 155°. Acidification of the basic solution gave 2.2 g. of crude 3- $\alpha$ -naphthylphthalic acid; decomposition point 180–190°. This acid on methylation with ethereal diazomethane gave the pure dimethyl 3- $\alpha$ -naphthylphthalate (1.4 g.); m. p. 134–136° after one recrystallization from methanol. A mixed melting point determination with the sample obtained from the above described dehydrogenation showed no depression.

**Dimethyl 3-Bromophthalate.**—Several attempts to prepare this ester were unsatisfactory because of the rapid formation of tetramethyl 2,3,2',3'-diphenyltetracarboxylate. The procedure finally adopted is as follows. Dimethyl 3-nitrophthalate (89.7 g.) was reduced catalytically with hydrogen and Raney nickel. One-third of the amino ester so formed was added to constant boiling hydrobromic acid (126 cc.) and to this solution held at 0° was added sodium nitrite (9.5 g.) in water (16 cc.) over a period of thirty minutes. Stirring was continued for fifteen minutes and the solution was filtered. The filtrate was treated at 0° with cuprous bromide (19.7 g.) in hydrobromic acid (50 cc., 48%) over a period of twenty minutes. The temperature of the mixture was slowly raised to 80° to complete the reaction. The cooled solution was extracted with two 100-cc. portions of ether. Distillation in a sausage flask gave 22.6 g. (66.2% based on nitrophthalate used); b. p. 141–145° (5 mm.); m. p. 81–82° from aqueous methanol.

*Anal.* Calcd. for  $C_{10}H_8O_4Br$ : C, 43.98; H, 3.32. Found: C, 44.52; H, 3.69.

The microanalyst (Mr. Stanley Rolfson) reported that all the carbon-hydrogen determinations were higher than the calculated values when the sample was burned.

**1,9-(5a,5,6,7,8,8a-Hexahydro)-benzanthrone-10-carboxylic-5 Acid.**—A solution of 3- $\alpha$ -naphthylhexahydrophthalic acid in anhydrous hydrogen fluoride (50 cc.) was allowed to stand overnight in a loosely covered cylindrical copper vessel. The last traces of hydrogen fluoride were removed in a stream of air. The dark residue was dissolved in sodium hydroxide (75 cc., 1.0 N), filtered and treated with norite. Acidification gave the crude keto acid, 0.8 g. Recrystallization from aqueous methanol and benzene-ligroin gave a pure product which decomposed at 208–215°.

*Anal.* Calcd. for  $C_{18}H_{16}O_3$ : C, 77.12; H, 5.75. Found: C, 77.25; H, 5.97.

**3,4-Dimethoxyphenylallylcarbinol.**—Into a 1-liter, 3-necked flask equipped with efficient condenser, stirrer and separatory funnel were placed dry ether (200 cc.) and magnesium (17 g.). Five cubic centimeters of allyl chloride was added to start the reaction and this was followed by a solution containing allyl chloride (60.1 g.), veratric aldehyde (66.4 g.) and dry ether (300 cc.) which was added during the course of forty-five minutes. The mixture was decomposed with ice and hydrochloric acid after twenty-three hours. Evaporation of the ether yielded 72.7 g. (87%) of the solid carbinol; m. p. 74–78°. Recrystallization from benzene-petroleum ether raised the melting point to 79–80°.

*Anal.* Calcd. for  $C_{15}H_{16}O_3$ : C, 69.21; H, 7.75. Found: C, 69.22; H, 7.38.

**cis-3-(3,4-Dimethoxyphenyl)-1,2,3,6-cis-tetrahydrophthalic Acid.**—A solution of 3,4-dimethoxyphenylallylcarbinol (10.4 g.), maleic anhydride (7.4 g.) and xylene (75 cc.) was heated under reflux for seven and one-half hours. The solution was concentrated to a volume of 25 cc. cooled and filtered. The tan solid so collected was dissolved in hot sodium hydroxide, treated with norite, filtered, and acidified. A crystalline solid separated which weighed 8.5 g. This material had no definite melting point but began to decompose when heated above 160°.

*Anal.* Calcd. for  $C_{18}H_{18}O_6$ : C, 62.74; H, 5.92; neut. equiv., 153. Found: C, 62.94; H, 5.92; neut. equiv., 155.

(7) Ullmann and Bielecki, *Ber.*, **34**, 2184 (1901).

When the concentrated xylene solution described above was allowed to stand at 0°, a 58.5% yield of cis-3-(3,4-dimethoxyphenyl)-1,2,3,6-cis-tetrahydrophthalic anhydride was obtained; m. p. 127–129°.

*Anal.* Calcd. for  $C_{18}H_{18}O_5$ : C, 66.67; H, 5.59; neut. equiv., 144. Found: C, 66.97; H, 5.39; neut. equiv., 143.

**Dimethyl cis-3-(3,4-Dimethoxyphenyl)-1,2,3,6-cis-tetrahydrophthalate.**—The corresponding dibasic acid was dissolved in ether and allowed to stand overnight in the presence of an excess of ethereal diazomethane. A quantitative yield of methyl ester was obtained; m. p. 70–71°.

*Anal.* Calcd. for  $C_{18}H_{20}O_6$ : C, 64.65; H, 6.63. Found: C, 64.95; H, 6.78.

**cis-3-(3,4-Dimethoxyphenyl)-cis-hexahydrophthalic Acid.**—A solution of cis-3-(3,4-dimethoxyphenyl)-1,2,3,6-tetrahydrophthalic acid (3.1 g.) in absolute alcohol (60 cc.) was reduced with hydrogen (35 pounds pressure) and platinum oxide (50 mg.). Two and nine-tenths grams of the hexahydro acid was isolated; decomposition range 170–200°.

*Anal.* Calcd. for  $C_{18}H_{20}O_6$ : C, 62.32; H, 6.54. Found: C, 62.63; H, 6.80.

**Dimethyl cis-3-(3,4-Dimethoxyphenyl)-cis-hexahydrophthalate.**—Prepared from the corresponding acid in quantitative yield by treatment with ethereal diazomethane; m. p. 76.5–77.5°.

*Anal.* Calcd. for  $C_{18}H_{24}O_6$ : C, 64.27; H, 7.19. Found: C, 64.62; H, 7.29.

**3,4-Dimethoxy-5a,5,6,7,8,8a-hexahydrofluorenone-9-carboxylic-8 Acid.**—A solution of cis-3-(3,4-dimethoxyphenyl)-cis-hexahydrophthalic acid (0.8 g.) in sulfuric acid (4.3 cc.; 86%) was maintained at a temperature of 43–45° for ten minutes and poured onto about 15 g. of ice. The keto acid (500 mg.) melted with decomposition at 280–288° after recrystallization from aqueous acetic acid.

*Anal.* Calcd. for  $C_{18}H_{18}O_5$ : C, 66.19; H, 6.25; neut. equiv., 290. Found: C, 66.10; H, 6.01; neut. equiv., 286.

The methyl ester of this acid was prepared in quantitative yield by the use of diazomethane as described above for analogous cases; m. p. 112–113.5°.

*Anal.* Calcd. for  $C_{17}H_{20}O_5$ : C, 67.08; H, 6.62. Found: C, 66.81; H, 6.41.

**Piperonylallylcarbinol.**—This compound was prepared from piperonal (60 g.), allyl chloride (65 g.) and magnesium (17 g.) with ether (500 cc.) as solvent; yield 54.4 g.; b. p. 139–140° (6 mm.).

*Anal.* Calcd. for  $C_{11}H_{12}O_3$ : C, 68.73; H, 6.29. Found: C, 68.35; H, 5.58.

**3-Piperonyl-1,2,3,6-cis-tetrahydrophthalic Acid.**—This acid was prepared in almost quantitative yield by allowing piperonylallylcarbinol (2.1 g.) to react with maleic anhydride (2.2 g.) in xylene (30 cc.) at its boiling point for three hours. The acid decomposed when heated above 195°.

*Anal.* Calcd. for  $C_{15}H_{14}O_6$ : C, 62.06; H, 4.86; neut. equiv., 145. Found: C, 62.01; H, 4.58; neut. equiv., 143.

The anhydride of this acid melts at 156–157° when recrystallized from benzene.

*Anal.* Calcd. for  $C_{15}H_{12}O_5$ : C, 66.17; H, 4.44. Found: C, 66.20; H, 4.41.

**3-Piperonyl-cis-hexahydrophthalic Acid.**—Catalytic hydrogenation of the tetrahydro acid (5.8 g.) in absolute alcohol (150 cc.) with platinum oxide (75 mg.) gave an 89% yield of the hexahydro acid. The compound decomposed at 197–218°.

*Anal.* Calcd. for  $C_{16}H_{16}O_6$ : C, 61.64; H, 5.52; neut. equiv., 146. Found: C, 61.88; H, 5.32; neut. equiv., 146.

## Summary

OH

1. Compounds of the type  $R-CHCH_2CH=CH_2$ , in which R— is  $\alpha$ -naphthyl, 3,4-dimethoxy-

phenyl, and 3,4-methylenedioxyphenyl, have been treated with maleic anhydride.

2. Structure determinations carried out on the adducts formed in the first two cases prove that maleic anhydride reacts preferentially with the aliphatic side chain. In these two examples the

aryl group occupies the *cis* position with regard to the adjacent carbonyl group.

3. Attempts to prove the structure of the adduct from maleic anhydride and 3,4-methylenedioxyphenylallylcarbinol failed.

MINNEAPOLIS, MINNESOTA

RECEIVED JULY 3, 1944

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

## Synthesis of 5-(Substituted-methyl)-5-phenethylhydantoins<sup>1</sup>

BY HENRY R. HENZE AND CHARLES B. HOLDER<sup>2</sup>

Recently, we<sup>3</sup> reported the synthesis from 1-chloro-4-phenyl-2-butanone of certain derivatives of 5-phenethylhydantoin in which the basicity of the latter had been increased through utilization of a 5-dialkylaminomethyl-, 5-(4-morpholinyl)-methyl-, or 5-(N-ethyl-N-phenylaminomethyl)-grouping. Since, upon being tested,<sup>4</sup> these hydantoins of enhanced basicity were found not to possess useful pharmacological activity, it was decided to prepare related compounds in which the 5-methyl grouping had been altered through introduction of an acidic (carboxyl) radical, or of derivatives of such acidic grouping. Hydantoins of this type are homologs of certain 5-phenylhydantoins previously prepared in this Laboratory.<sup>5</sup> The latter were synthesized from keto esters and keto nitriles containing the benzoyl group, these intermediates being easily attainable by appropriate application of the Claisen condensation. However, when preparation of the desired keto ester or keto nitrile requires utilization of two compounds each capable of self-condensation, employment of the Claisen condensation is not wholly satisfactory. In the present instance, since preparation of ethyl hydrocinnamoylacetate or ethyl hydrocinnamoylacetoneitrile would involve use of such self-condensable intermediates, an alternate route was thought to be desirable. It was visualized that perhaps 1-chloro-4-phenyl-2-butanone could be converted into 5-phenethyl-5-hydantoinacetoneitrile by utilization of the Bucherer<sup>6</sup> method if additional potassium cyanide was used. Such conversion, involving reaction of

cyanide with both halogen and carbonyl groups in a chloro ketone, has not previously been reported. No difficulty was to be anticipated in subsequent conversion of the nitrile into other derivatives of 5-phenethyl-5-hydantoinacetic acid.

Interaction of 1-chloro-4-phenyl-2-butanone with a mixture of at least two equivalents of potassium cyanide and three of ammonium carbonate did yield some of the anticipated substituted hydantoinacetoneitrile. However, this conversion represented neither the only reaction in which the chloro ketone was involved, nor involved the major portion of that compound. There was produced in larger yield another substance, probably of composition  $C_{21}H_{20}N_2$ , the structure of which has not yet been established. With less than two equivalents of cyanide, the chloro ketone yielded little or no hydantoin, indicating that conversion of the carbonyl group into the hydantoin nucleus occurs subsequent to reaction of the halogen.

Ethyl 5-phenethyl-5-hydantoinacetate was synthesized also, although in poorer yield, from ethyl hydrocinnamoylacetate, since our samples of 1-chloro-4-phenyl-2-butanone had physical properties differing essentially from those reported elsewhere.<sup>7</sup> The properties of the hydantoinacetate, prepared by either method, were uniformly the same, hence the identity of the chloroketone, and of its chlorohydrin precursor, is confirmed.

A study of the material melting at 96° [ $C_{21}H_{20}N_2$ ] obtained as a by-product in the preparation of 5-phenethyl-5-hydantoinacetoneitrile, indicates that it is formed from interaction of two molecules of the chloro ketone with potassium cyanide and ammonium carbonate, but not from the action of either of the latter alone. The product must be heterocyclic, possess aromatic properties and but one active hydrogen atom. It is quite resistant, under usual conditions of treatment, toward hydrolysis, oxidation and reduction.

### Experimental

**Application of Bucherer Method to 1-Chloro-4-phenyl-2-butanone.**—To a flask equipped with a condenser were added 40 g. (0.22 mole) of the chloro ketone, 31.4 g. (0.48 mole) of potassium cyanide, 69.4 g. (0.35 mole) of ammonium carbonate, and 550 cc. of 65% alcohol. After

(1) From Part II of the Ph.D. dissertation of C. B. Holder, June, 1941.

(2) Present address: Texas Company, Beacon, N. Y.

(3) Henze and Holder, *THIS JOURNAL*, **63**, 1943 (1941).

(4) Through the courtesy of Parke, Davis and Company three of these compounds have received preliminary testing for possible pharmacological activity with results as follows

R-	Activity		Dose, (mg./kg.)	Anti-convulsic
	M. L. D. Anal- (mg./kg.)	Hyp- notic		
Diethylamino	100	a	50	None
Di-n-propylamino	350	a	95 <sup>b</sup>	None
4-Morpholinyl	400	a	250	None

<sup>a</sup> Little if any analgesic activity. <sup>b</sup> At the level of 110 mg./kg. the cat was dead at the end of two hours.

(5) Henze and Rogers, *THIS JOURNAL*, **63**, 2190 (1941).

(6) Bucherer and Lieb, *J. prakt. Chem.*, [2] **141**, 5 (1934).

(7) See ref. 3, pp. 1943-1944.