involved some substances that are abundantly soluble in liquid ammonia alone.

The reduction of 1-naphthylamine with sodium does not proceed beyond the dihydro compound probably for the same reasons advanced to explain the limited extent of reduction of quinolines.[9] The reduction of naphthalene to tetrahydronaphthalene in liquid ammonia has been reported but the reactions were allowed to proceed over a much longer period of time[14] or were conducted at higher temperatures.[15] Under such conditions, sodium amide formed by the ammonolysis of the primary reduction product would cause the double bond in the 6,7-position to migrate to the 7,8-position.[16] Thus, conjugation with the unsaturation in the benzenoid ring would render the double bond susceptible to reduction by sodium.[17]

Although the reduction of 1-nitronaphthalene by sodium undoubtedly led to the formation of a dihydro-1-naphthylamine, the product bore no resemblance to the 5,8-dihydro-1-naphthylamine formed by the action of sodium upon 1-naphthylamine. It seems probable that hydrogenation of the ring to which the nitrogen was attached must have occurred and that the hydrogen probably entered the 1,4-positions.[9]

(14) Wooster and Smith, THIS JOURNAL, **53**, 179 (1931).
(15) Lebeau and Picon, *Compt. rend.*, **158**, 1514 (1914).
(16) Hückel and Bretschneider, *Ann.*, **540**, 157 (1939).
(17) Campbell and Campbell, *Chem. Rev.*, **31**, 82 (1942).

The reduction of 2-nitrofluorene to a tetrahydro-2-aminofluorene by means of sodium is a result analogous to that reported by Lebeau and Picon[18] for the reduction of dimethylfluorene.

## Summary

1. Nitrobenzene has been reduced to aniline in liquid ammonia solution by sodium and ammonium bromide and by sodium and methanol.

2. 1-Naphthylamine has been reduced to 5,8-dihydro-1-naphthylamine by sodium but reduced to apparently the same product only to a very limited extent by sodium and ammonium bromide.

3. 1-Nitronaphthalene has been reduced by sodium to a dihydro-1-naphthylamine that is different from the 5,8-dihydro compound and is probably the 1,4-dihydro derivative. Sodium and ammonium bromide gave incomplete reduction to 1-naphthylamine, while sodium and methanol yielded a mixture of the di and tetrahydro-1-naphthylamines.

4. 2-Nitrofluorene has been reduced to a tetrahydro-2-aminofluorene by sodium, and has been shown to be unaffected by sodium and ammonium bromide, but reduced to a mixture of tetra- and hexahydro-2-aminofluorenes by sodium and methanol.

(18) Lebeau and Picon, *Compt. rend.*, **173**, 84 (1921).

AUSTIN, TEXAS RECEIVED AUGUST 26, 1946

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[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE]

# Studies in the Quinoline Series. VIII. Some 6-β-Hydroxyethoxy-4-aminoquinolines

BY VIRGINIA G. RAMSEY AND LEONARD H. CRETCHER

Previous work in this Laboratory[1] had shown that in some 6-methoxy-8-alkylaminoalkylamino-quinolines and 6-methoxy-8-dialkylaminoalkylaminoquinolines the replacement of the methoxy group at position 6 by a β-hydroxyethoxy group lessened the toxicity to mice, but also lessened the activity of the compounds against avian malarial infection. It was considered desirable to determine if, by introduction of a β-hydroxyethoxy group in the 6-position of 4-aminoquinolines, detoxification without serious diminution of antimalarial activity could be obtained. For this purpose some derivatives of 6-β-hydroxyethoxy-4-aminoquinoline were prepared.

The method chosen for the syntheses of the compounds involved, as a first step, the preparation of 6-methoxy-4-hydroxyquinoline (I) from ethoxymethylenemalonic ester and *p*-anisidine by the method of Price and Roberts.[2] With a mixture of phosphorus penta- and oxy- chlorides, in an application of the procedure recommended for the preparation of 4-chloroquinaldine,[3] I was converted to 6-methoxy-4-chloroquinoline (II) in better yield than with phosphorus oxychloride alone. By hydrolysis with strong sulfuric acid 6-hydroxy-4-chloroquinoline (III) was obtained from II. This compound (III) had been prepared by other workers[4] by diazotization of 6-hydroxy-4-aminoquinoline. Alkylation of III with ethylene carbonate proceeded smoothly to give 6-β-hydroxyethoxy-4-chloroquinoline (IV) which was then converted to 6-β-hydroxyethoxy-4-aminoquinoline (V) by refluxing in phenol in the presence of ammonia, a general method for the preparation of 4-aminoquinolines.[5]

6-β-Hydroxyethoxy-4-(1′-methyl-4′-diethylaminobutylamino)-quinoline (VI) was prepared by heating IV and Noval diamine in phenol. 6-β-Hydroxyethoxy-4-(3′-*i*-propylaminopropylam-

(1) (a) Morgan and Cretcher, THIS JOURNAL, **68**, 781 (1946); (b) Morgan and Tipson, *ibid.*, **68**, 1569 (1946).
(2) Price and Roberts, *ibid.*, **68**, 1204 (1946).
(3) Fisher, Diepolder and Wölfel, *J. prakt. Chem.*, **109**, 59 (1925).
(4) John and Andraschko, *ibid.*, **128**, 211 (1930).
(5) Eisleb, German Patent, 540,699 (1931); *Chem. Zentr.*, **103**, I, 1804 (1932).

ino)-quinoline (VII) was made by reaction of V with *i*-propylaminopropyl chloride hydrochloride[6] in an aqueous alcoholic sodium acetate solution as in the preparation of the 8-aminoquinoline analog (1b). Since compounds VI and VII decomposed on distillation they were isolated by fractional precipitation, VII as an oxalate, VI as the free base. A water-soluble, non-hygroscopic phthalate was prepared from VI. *p*-Diethylaminobenzaldehyde and V were condensed to give 6-β-hydroxyethoxy-4-(*p*-diethylaminobenzylideneamino)-quinoline (VIII) which was, in turn, hydrogenated to 6-β-hydroxyethoxy-4-(*p*-diethylaminobenzylamino)-quinoline (IX).

## Experimental[7]

**α-Carbethoxy-β-(*p*-anisidino)-acrylate** was prepared from *p*-anisidine and ethoxymethylenemalonic ester[8] as described by Price and Roberts[2] except that an inner temperature of 60° was maintained for three hours and a vacuum was applied to one neck of the container, thus drawing a current of air over the surface of the mixture and hastening the removal of the alcohol evolved. The theoretical amount of alcohol was lost. The oil remaining was used in the next step without purification.

**6-Methoxy-4-hydroxy-3-carbethoxyquinoline.**—The method of cyclization was essentially that described by the above workers.[2] Diphenyl ether (10 parts) was heated to reflux temperature with stirring and α-carbethoxy-β-(*p*-anisidino)-acrylate (1 part) added at such a rate that the inner temperature did not fall below 248°. Refluxing was continued until evolution of alcohol ceased (fifty minutes for 140 g. of acrylate). As the mixture cooled the quinoline ester precipitated. It was collected on a filter, washed well with ethyl ether, and dried at 100°. A 65% yield of 6-methoxy-4-hydroxy-3-carbethoxyquinoline (m. p. 275–277°) was obtained.

**6-Methoxy-4-hydroxyquinoline-3-carboxylic acid** was prepared from the ester (1 part) by refluxing for nine hours with a 10% aqueous solution of sodium hydroxide (4 parts). The hot solution was filtered and neutralized with hydrochloric acid. The precipitated acid (m. p. 265–266°) was collected; yield, 96%.

**6-Methoxy-4-hydroxyquinoline** was prepared by decarboxylation of the quinoline acid in a solvent rather than by heating the dry acid at its melting point. Diphenyl ether (10 parts) was heated to 210°, the acid (1 part) added in one portion, and the temperature slowly increased. Decarboxylation began when the temperature of the reaction mixture was 220° and continued vigorously for one half hour at 229–235°. After another hour at 245° little carbon dioxide was evolved and little suspensate remained. Crude 6-methoxy-4-hydroxyquinoline separated as the solution cooled and was collected on a filter and washed with ether. To remove any unreacted acid the product was twice suspended for one hour in a 10% aqueous solution of sodium carbonate with stirring. After drying at 100° the yield of 6-methoxy-4-hydroxyquinoline (m. p. 245–248°) was 85%.

**6-Methoxy-4-chloroquinoline** (II).—The directions of Fisher, Diepolder, and Wölfel[3] for the preparation of 4-chloroquinaldine were followed. 6-Methoxy-4-hydroxyquinoline (72 g.) was mixed in a 3-liter beaker with powdered phosphorus pentachloride (80 g.). Phosphorus oxychloride (30 cc.) was added and the mixture heated with frequent stirring for one hour at a bath temperature of 110–115°. The cooled reaction mixture was hydrolyzed with ice and water (500 cc.), made alkaline to congo red (but not to litmus) with a 30% aqueous solution of sodium hydroxide, and filtered. The *filtrate* gave a further small amount of product (2 g.) when made strongly alkaline with sodium hydroxide. The *precipitate* was twice dissolved in dilute hydrochloric acid and reprecipitated; discard of the small amount of oil which appeared each time neutrality was approached increased the purity. The total yield of II, after drying at 60°, was 71 g. (89%); m. p. 77–79°.

**6-Hydroxy-4-chloroquinoline (III).**—6-Methoxy-4-chloroquinoline (122.4 g.) was dissolved in 60% sulfuric acid (780 cc. concentrated acid plus 444 cc. water) and refluxed five hours. The cooled solution was poured over ice, made alkaline with ammonium hydroxide, and filtered. Neutralization of traces of sulfate and removal of certain impurities was obtained by suspending the precipitate in 2 liters of a 2% aqueous sodium carbonate solution, stirring mechanically overnight, and washing with water. On drying, material melting at 204–206° was obtained in a yield of 98% (112 g.) and was used for the next step without further purification. A small portion, on crystallization from 80% alcohol then from ether, melted at 208°. John and Andraschko,[4] preparing the compound from 6-hydroxy-4-aminoquinoline by diazotization, found a melting point of 210°.

*Anal.* Calcd. for $C_9H_6ClNO$: Cl, 19.73. Found: Cl, 19.95.

**6-β-Hydroxyethoxy-4-chloroquinoline (IV).**—A mixture of III (112 g.), ethylene carbonate[8a] (564 g.), and anhydrous potassium carbonate (56 g.), in a flask equipped with a condenser, thermometer and mechanical stirrer, was heated for two and three-quarters hours. Water (1 liter) was added to the cool solution, the mixture stirred for one hour, and the precipitated IV filtered off. The precipitate was freed of unreacted hydroxyquinoline (III) by stirring for three hours with a 3% aqueous solution of sodium hydroxide (650 cc.). The resulting product was further purified by treatment with absolute ether in a Soxhlet extraction apparatus; IV crystallized from the ether extract to give 107 g. (76% yield) of white powder; m. p. 117–118°. The material was soluble in chloroform, dioxane, acetone, alcohol, ether and hot benzene and slightly soluble in hot water.

*Anal.* Calcd. for $C_{11}H_{10}ClNO_2$: Cl, 15.81; N, 6.26. Found: Cl, 15.77; N, 6.08.

**6-β-Hydroxyethoxy-4-aminoquinoline Hydrochloride.**—For three and one-half hours dry ammonia was passed through a refluxing mixture of IV (50 g.) and phenol (150 g.). Addition of acetone (200 cc.) to the cooled reaction mixture precipitated the hydrochloride. The yield of 6-β-hydroxyethoxy-4-aminoquinoline hydrochloride (m. p. 280–282°) was 89% (52.5 g.). The compound crystallized from alcohol as a white powder.

*Anal.* Calcd. for $C_{11}H_{12}N_2O_2 \cdot HCl$: Cl, 14.73; N, 11.64. Found: Cl, 14.94; N, 11.85.

**6-β-Hydroxyethoxy-4-aminoquinoline (V).**—On addition of sodium hydroxide to a suspension of 6-β-hydroxyethoxy-4-aminoquinoline hydrochloride in 10 volumes of water, the free base was precipitated in a yield of 93%. (To insure complete precipitation a large excess of alkali was used and the mixture allowed to stand overnight before filtering.) The compound (V) melted at 167–168° and was soluble in alcohol, hot acetone, or hot water; very slightly soluble in ether, dioxane, chloroform and toluene. A sample for analysis crystallized from acetone as a white, granular powder.

*Anal.* Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.70; H, 5.93; N, 13.73. Found: C, 64.78; H, 6.20; N, 13.76.

**6-β-Hydroxyethoxy-4-(1′-methyl-4′-diethylaminobutylamino)-quinoline (VI).**—A mixture of IV (22.3 g.), Noval diamine (15.8 g.), phenol (45 g.) and a few crystals of potassium iodide was heated for forty-three hours at an inner temperature of 145–160°. The reaction mixture was cooled, transferred to a separatory funnel with 25% sodium hydroxide (100 cc.), and extracted with chloroform. To remove unreacted Noval diamine, material

(6) From a sample presented by Dr. R. C. Elderfield of Columbia University to Dr. Marcus Morgan of this Laboratory.

(7) All melting points are uncorrected. Microanalyses were carried out by Mr. G. L. Stragand of the University of Pittsburgh.

(8) Kindly presented by Parke, Davis and Company.

recovered from the chloroform was heated in a bath at 195–200° and 1–2 mm. pressure; final weight of residue, 29 g. This material (29 g.) was dissolved in concentrated hydrochloric acid (20 cc.) and then diluted with water (40 cc.). The solution was made just alkaline (*p*H 8) with a saturated solution of potassium carbonate and extracted with chloroform thus removing 9 g. of dark resin containing unreacted IV. On saturation of the *aqueous layer* with potassium carbonate, extraction with chloroform and evaporation of the dried chloroform extracts, a residue weighing 20 g. and containing the desired condensation product was obtained. This 20-g. fraction was dissolved in chloroform (80 cc.) under reflux and hexane (140 cc.) was added to the refluxing solution. After cooling to room temperature the clear supernatant liquid was decanted and the adhering solvent removed from the residue under reduced pressure to leave 15.7 g. of brittle resin. The supernatant liquid, on evaporation, gave 4 g. of oil from which no product could be isolated.

To the brittle resin (15.7 g.), dissolved in absolute alcohol (25 cc.), anhydrous ether (850 cc.) was added in portions. The turbid mixture was shaken with 0.5 g. of diatomaceous earth (Celite) to hasten separation of the precipitated, dark oil and filtered. The clear filtrate was evaporated to a volume of 500 cc. and hexane (200 cc.) was added with refluxing. After refrigerating overnight the solvent was decanted, leaving 7 g. of light brown resin (fraction A).

The liquid decanted from fraction A was evaporated to a volume of 200–300 cc. and refrigerated until crystallization occurred (two–three weeks). The white, granular precipitate (fraction B) was filtered off, washed on the filter with anhydrous ether, and dried at 60° giving 3 g. of VI melting at 79–80°.

*Anal.* Calcd. for $C_{20}H_{31}N_3O_2$: C, 69.53; H, 9.04; N, 12.17. Found: C, 69.28; H, 8.88; N, 12.17.

Fraction A was again subjected to purification in solvent mixtures. Five grams of A was dissolved in 10 cc. of absolute alcohol and anhydrous ether added until further addition of ether produced no turbidity (500 cc.). Filtration and addition of hexane (110 cc.) to the filtrate produced an oily precipitate (0.4 g.) which was discarded. The clear, supernatant liquid decanted was treated with hexane (350 cc.) and the mixture reduced to a volume of 200–300 cc. by evaporation. When the concentrate was seeded with crystals from fraction B and cooled in the refrigerator for three weeks partial crystallization occurred. After decanting the solvent there remained a yellow, semi-crystalline oil weighing 3.5 g. which was converted to a phthalate in the manner described below.

**6-β-Hydroxyethoxy-4-(1′-methyl-4′-diethylaminobutylamino)-quinoline Phthalate.**—Solutions of phthalic acid (2 g.) and VI (3.5 g.) in 25 cc. and 10 cc. of anhydrous isopropyl alcohol, respectively, were refluxed together for one and one-half hours. After refrigeration the reaction mixture was filtered. The precipitate was washed on the filter with anhydrous isopropyl alcohol, then with absolute ether and dried in a vacuum oven at 100°, giving 3.6 g. of a white, water-soluble powder; m. p. 156–158°.

A phthalate prepared in this manner from 0.5 g. of the crystalline, analyzed VI (fraction B) was a white, water-soluble powder melting at 156–158°.

*Anal.* Calcd. for $C_{20}H_{31}N_3O_2 \cdot C_8H_6O_4$: C, 65.73; H, 7.29. Found: C, 65.17; H, 6.93.

A *small* excess of acid over that calculated on the basis of a strict stoichiometric relationship was found to be necessary to obtain the 1:1 mole ratio of acid to base desired.

**6-β-Hydroxyethoxy-4-(3′-isopropylaminopropylamino)-quinoline Oxalate (VII).**—Isopropylaminopropyl chloride hydrochloride (10.8 g.), V (12.9 g.), sodium acetate (2 equivalents), and a 50% aqueous solution of alcohol (32 cc.) were refluxed for one hundred and eighteen hours at a bath temperature of 100–110°. The cool reaction mixture was filtered, the crystals of sodium chloride and sodium acetate washed with a little alcohol, and the filtrates evaporated to dryness under reduced pressure. The residue was taken up in water (60 cc.) and filtered to remove some hydrochloride of V (3.1 g.). To the filtrate a 70% aqueous solution of potassium carbonate (54 cc.) was added and the mixture extracted thoroughly with chloroform. The quinoline base (V, 4.5 g.) precipitated was insoluble in both solvents and removed by filtration. The chloroform extracts, after drying with sodium sulfate, were evaporated to leave isopropylaminopropyl chloride (5.75 g.). Saturation of the aqueous layer with potassium carbonate and thorough extraction with ether and chloroform removed a further amount of oil (1.5 g.). The saturated, aqueous solution was finally extracted with isopropyl alcohol (3 × 100 cc.), the extracts dried over sodium sulfate, and the alcohol evaporated leaving 5.5 g. of residue containing the desired product.

The residue (5.5 g.) was dissolved in a mixture of chloroform (60 cc.), acetone (25 cc.) and *n*-butyl alcohol (5 cc.) with refluxing and the solution filtered hot to remove a small amount of inorganic salt. On adding hexane (100 cc.) to the filtrate, refluxing, cooling and decanting the clear supernatant liquid, there remained a viscous oil (4.5 g.) which contained the desired condensation product. The oil was soluble in methyl, ethyl, isopropyl and *n*-butyl alcohols; insoluble in ether or chloroform.

A portion of the oil (2.6 g.) was dissolved in *n*-butyl alcohol (175 cc.). To the stirred, refluxing solution oxalic acid (0.33 g.) in *n*-butyl alcohol (50 cc.) was added dropwise over a period of fifteen minutes. After twenty-five minutes the hot suspension was filtered and the precipitated oxalate washed with methanol and dried at 100° giving 1.7 g. of VII. For purification the material was dissolved in 30 cc. of water, isopropyl alcohol added until the boiling solution was turbid, and the hot mixture filtered. On cooling the filtrate, a tan powder separated which, after drying in a vacuum oven at 100° for two days, melted at 239–240°. The compound contained one half mole of water.

*Anal.* Calcd. for $C_{17}H_{25}N_3O_2 \cdot C_2H_2O_4 \cdot {}^1/_2H_2O$: C, 56.71; H, 7.01; N, 10.44; $H_2O$, 2.24. Found: C, 56.53; H, 6.83; N, 10.65; $H_2O$, 2.23.

**6-β-Hydroxyethoxy-4-(*p*-diethylaminobenzylideneamino)-quinoline (VIII).**—*p*-Diethylaminobenzaldehyde (10.6 g.) and V (8 g.) were mixed in a flask equipped with a stirrer, a thermometer, and a Stark and Dean trap and condenser. Piperidine (10 drops), as a catalyst, and enough xylene to fill the trap and to reflux were added. The mixture was heated at an inside temperature of 140–145° for two and one-half hours; the water evolved in the reaction collected in the trap. The xylene was removed under reduced pressure and the residue dissolved in ether (600 cc.). On refrigeration there separated from the ether a yellow precipitate which melted at 127–128° after crystallization from isopropyl alcohol; yield, 9.5 g. (65%). The compound was soluble in ethyl alcohol, isopropyl alcohol, chloroform and acetone; slightly soluble in benzene or ether.

*Anal.* Calcd. for $C_{22}H_{26}N_3O_2$: C, 72.51; H, 7.19. Found: C, 72.36; H, 6.90.

**6-β-Hydroxyethoxy-4-(*p*-diethylaminobenzylamino)-quinoline (IX).**—6-β-Hydroxyethoxy-4-(*p*-diethylaminobenzylideneamino)-quinoline (VIII, 5.3 g.), platinum oxide (0.2 g.) and methanol (150 cc.) were shaken together in the presence of hydrogen at 2–3 atmospheres pressure until the yellow color of the solution was discharged (seventeen hours). The mixture was filtered and the filtrate evaporated to dryness under reduced pressure. The residue was dissolved in a mixture of benzene (50 cc.). and isopropyl alcohol (20 cc.) and the hot solution filtered. From the filtrate, on cooling, white leaflets of IX (m. p. 158–159°) separated; yield, 75% (4 g.). The material was soluble in methyl, ethyl and isopropyl alcohols; very slightly soluble in ether or benzene.

*Anal.* Calcd. for $C_{22}H_{28}N_3O_2$: C, 72.10; H, 7.70; N, 11.47. Found: C, 72.04; H, 7.50; N, 11.34.

**6-β-Hydroxyethoxy-4-(*p*-diethylaminobenzylamino)-quinoline Dihydrochloride.**—The free base, IX, (6.4 g.)

was dissolved in anhydrous isopropyl alcohol (100 cc.) and 3 *N* isopropanolic hydrogen chloride (11.2 cc.) was added. The dihydrochloride precipitated on cooling and was collected on a filter, washed with anhydrous ether, and dried over phosphorus pentoxide. The yield of dihydrochloride (m. p. 139–144°) was practically quantitative.

*Anal.* Calcd. for $C_{22}H_{28}N_3O_2 \cdot 2HCl$: Cl, 16.13; N, 9.56. Found: Cl, 15.76; N, 9.34.

**Acknowledgment.**—The authors wish to thank Dr. Alice G. Renfrew for her advice and interest in this work.

## Summary

A method which afforded the preparation of 6-hydroxy-4-chloroquinoline from 6-methoxy-4-chloroquinoline was described.

6-β-Hydroxyethoxy-4-chloroquinoline and 6-β-hydroxyethoxy-4-aminoquinoline were synthesized and from these compounds four derivatives of 6-β-hydroxyethoxy-4-aminoquinoline were prepared.

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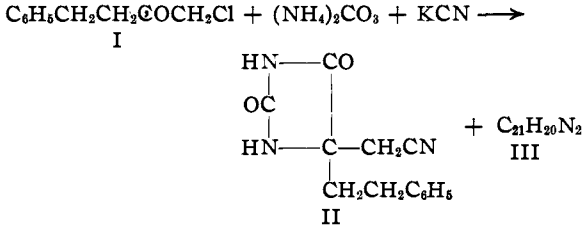
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

# Pyrrole Formation During Attempted Hydantoin Synthesis[1]

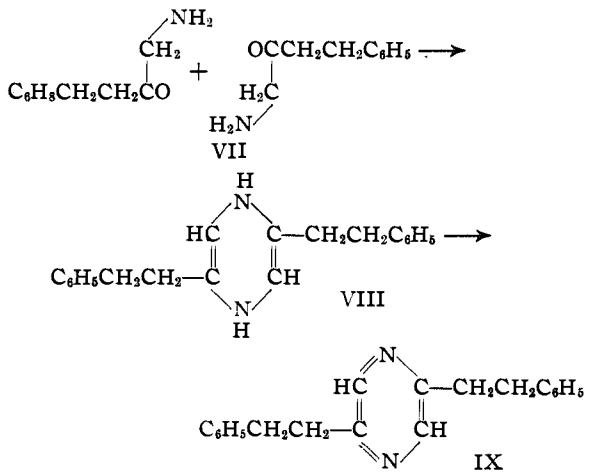
BY HENRY R. HENZE AND JOHN H. SHOWN, JR.[2]

For several years past there has been in progress in this Laboratory a detailed study of the conversion of ketones, by interaction with ammonium carbonate and potassium cyanide, into 5,5-disubstituted hydantoins.[3] In such instances, reaction has led solely to formation of a hydantoin in good yield. Attempts[4] have been made also to extend this study to include preparation of hydantoins from ketones possessing an additional functional group. Thus, chloromethyl phenethyl ketone (I) was subjected to the usual conditions for such conversion and yielded some 5-phenethyl-5-hydantoinacetonitrile (II) and in addition material (III) melting at 96°. This substance, apparently to be




formulated as $C_{21}H_{20}N_2$, was practically insoluble in water and in solutions of acids and bases, and was virtually unaffected by heating overnight with dilute or concentrated hydrochloric acid, or by heating for six days at the reflux temperature of a 10% aqueous solution of potassium hydroxide. Likewise, exposure of III to reduction, by action of tin and hydrochloric acid or catalyzed by platinum, produced no alteration. Attempted oxidation of III by potassium permanganate in acetone solution likewise produced little or no change, whereas alkaline permanganate solution yielded only benzoic acid. Bromination resulted in formation of a monobromo derivative.

In trying to elucidate the structure of III, attempts have now been made to convert I into III by stepwise procedure. Thus, hydrocinnamoylacetonitrile (IV) and hydrocinnamoylcarbinol (V), the nitrile and alcohol which might have resulted from I by replacement of chlorine by cyanide and hydroxyl, respectively, were subjected to the conditions under which III was formed. However, only II or 5-hydroxymethyl-5-phenethylhydantoin (VI) resulted. Again, should I react initially with ammonia, hydrocinnamoylmethylamine (VII) might result. Accordingly, the hydrochloride[5] of VII was synthesized; in alkaline solution the liberated amine (VII) underwent reaction typical of other α-amino ketones to form a pyrazine derivative (IX)




At this point in the study, the utilization of a lower homolog of I, namely, phenacyl chloride (X), was decided upon. Interaction of X with potassium cyanide and ammonium carbonate produced, seemingly in an analogous manner, a compound $C_{17}H_{12}N_2$ (XI). The latter reacted with boiling hydriodic acid to form ammonia and carbon dioxide, a behavior suggestive of initial hydrolysis of a nitrile with subsequent decarboxylation of an acid,

(1) From the Ph.D. dissertation of John Hampton Shown, Jr., June, 1944.

(2) Present address: General Aniline and Film Corporation, Grasselli, New Jersey.

(3) Henze and Spear, THIS JOURNAL, **64**, 522 (1942).

(4) Henze and Holder, *ibid.*, **63**, 1943 (1941); **66**, 1545 (1944).

(5) Pascual and Rebollo (*Anales soc. espan. fis. quim.*, **32**, 381 (1934)), reported a m. p. of 170° for this compound; our sample melted at 141°.