

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 $C_{22}H_{28}N_2O_2 \cdot 2HCl$; 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.

PITTSBURGH 13, PA.

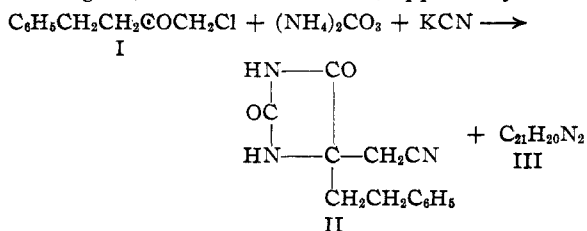
RECEIVED FEBRUARY 12, 1947

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

Pyrrole Formation During Attempted Hydantoin Synthesis¹

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 hydantoin.³ In such instances, reaction has led solely to formation of a hydantoin in good yield. Attempts⁴ have been made also to extend this study to include preparation of hydantoin 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

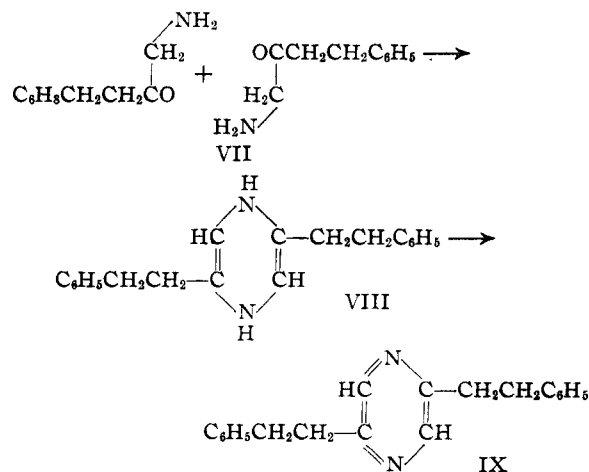
(1) From the Ph.D. dissertation of John Hampton Shown, Jr., June, 1944.

(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).

by stepwise procedure. Thus, hydrocinnamoyl-acetonitrile (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 hydrochloride⁵ 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)

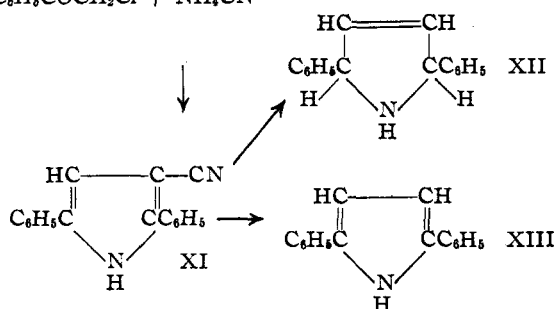
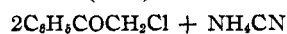


At this point in the study, the utilization of a lower homolog of I, namely, phenacyl chloride (X), was decided upon. Interaction of X with potassium cyanide and ammonium carbonate produced, seemingly in an analogous manner, a compound $C_{17}H_{12}N_2$ (XI). The latter reacted with boiling hydriodic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

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

and another substance $C_{16}H_{15}N$ (XII). Attempts to hydrolyze the nitrile (XI) without reduction, by boiling with concentrated hydrochloric acid or with a saturated ethanolic solution of sodium hydroxide, proved its resistance, like that of III, against hydrolytic cleavage. However, boiling XI with a solution of potassium hydroxide in propylene glycol likewise produced ammonia and carbon dioxide; from the reaction solution could also be isolated XIII ($C_{16}H_{13}N$) melting at 143.8° , the latter corresponding to the melting point of 2,5-diphenylpyrrole.⁶ Subsequent synthesis of the latter, by ring closure of the appropriate γ -diketone with ammonia, confirmed the structure of the degradation product XIII.

Hydrolysis of a nitrile to yield a carboxylic acid is well established; hence, it may seem surprising that hydrolysis of XI requires such drastic conditions. But adequate evidence exists for the decarboxylation of a pyrrolecarboxylic acid by action of hot mineral acid.⁷ Also, the tendency of pyrroles to undergo 1,4-addition during reduction is fairly well known.⁸ And Fischer⁹ states that the pyrrolines, obtained by reduction of pyrrole and derivatives in acid solution, must be regarded as being Δ^3 -pyrrolines; the isomeric Δ^2 -pyrrolines are synthesized only by other methods. Therefore, it appears that interaction of phenacyl chloride (X) with potassium cyanide and ammonium carbonate produces 2,5-diphenyl-3-pyrrolenenitrile (XI). The latter in boiling alkaline propylene glycol solution yields 2,5-diphenyl-pyrrole (XIII), but is converted by action of boiling concentrated hydriodic acid into 2,5-diphenyl- Δ^3 -pyrroline-(XII).



The knowledge and experience gained through study of the synthesis and hydrolysis of XI was now applied to the material melting at 96° . When III was heated in propylene glycol solution with potassium hydroxide, again, ammonia and carbon dioxide were formed and a new product (XIV), $C_{20}H_{21}N_2$ was obtained. The latter gave a positive

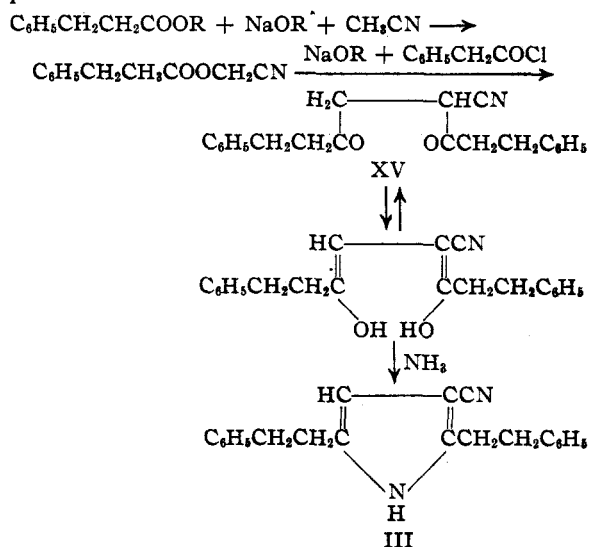
(6) Auger [Bull. soc. chim., **49**, 346 (1888)] prepared this compound from succinyl chloride and benzene in the presence of aluminum chloride and reported a m. p. of 134° ; Kapf and Paal [Ber., **21**, 3056 (1888)] listed $144\text{--}145^\circ$ as m. p.

(7) Knorr [Ber., **18**, 1565 (1885)] noted the decarboxylation thus of 2,5-dimethyl-3-pyrrololecarboxylic acid.

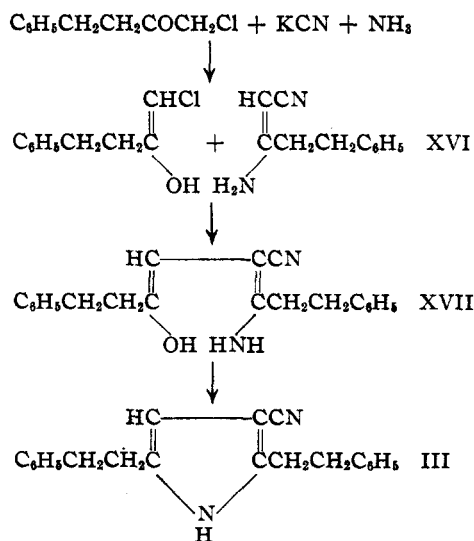
(8) Sonn, Ber., **69**, 148 (1935).

(9) Fischer-Orth, "Die Chemie Des Pyrrols," Adademische Verlagsgesellschaft m. b. H., Leipzig, Vol. I, 1934, p. 319.

test in the pyrrole pine-splinter test. Subsequently, synthesis of an authentic sample of 2,5-diphenethyl-3-pyrrolenenitrile, from α,β -dihydrocinnamoylpropionitrile (XV) and ammonia,¹⁰ permitted confirmation of the structure of III.



An alternate sequence for the formation of 2,5-diphenethyl-3-pyrrolenenitrile (III) may be based upon Hantzsch's¹¹ pyrrole synthesis (which involves interaction of a chloromethyl ketone, ammonia and a β -keto ester). Korschun,¹² who studied this method, showed that γ -diketo esters reacted only slowly with ammonia, whereas the β -keto ester reacted rapidly with ammonia at low temperature; cyclization to form the pyrrole occurred only after heating. Application of this information suggests that chloromethyl phenethyl ketone (I) in part is converted into γ -benzyl- β -



(10) Ring closure of the γ -diketo nitrile (XV) with ammonia is typical of the well known Paal-Knorr synthesis [Ber., **18**, 302, 367, 2251 (1885); Ann., **286**, 290 (1886)].

(11) Hantzsch, Ber., **23**, 1474 (1890).

(12) Korschun, *ibid.*, **38**, 1125 (1905).

aminocrotononitrile (XVI) which reacts subsequently with unchanged I to yield an imino derivative of α,β -dihydrocinnamoylpropionitrile (XVI). The latter, in turn, should undergo cyclization to produce 2,5-diphenethyl-3-pyrrolenitrile (III).

Experimental

Preparation of Hydrocinnamoylcarbinol Acetate.¹²—

Twenty and one-tenth grams (0.109 mole) of chloromethyl phenethyl ketone (I) was added to a mixture of 18 g. of anhydrous sodium acetate and 52.5 g. of glacial acetic acid in a round bottom flask, fitted with a reflux condenser; the flask was placed in an oil-bath at 170° for four hours. When cooled, the reaction mixture partially solidified; upon dilution with a large volume of water much more solid material separated. After filtration, the product was washed copiously with water; after drying in a vacuum desiccator the crude material weighed 24.3 g. After two recrystallizations from dilute alcohol, the acetate was obtained as fine white crystals; m. p. 45–46°; weight 15.2 g. (67.5% yield).

Anal. Calcd. for C₁₂H₁₄O₂: C, 69.88; H, 6.84. Found: C, 69.70; H, 6.95.

Preparation of Hydrocinnamoylcarbinol (V).—Fifteen and two-tenths grams (0.093 mole) of hydrocinnamoylcarbinol acetate was mixed with 180 g. of 5% sulfuric acid and heated under a reflux condenser in an oil-bath at 160° for four hours. The mixture was subjected to steam distillation for two hours, when the distillate no longer was acidic, and allowed to cool. After extraction of the contents of the flask with ether, the extract was washed with sodium bicarbonate solution and with water before being dried over anhydrous sodium sulfate. After evaporation of the ether, there remained an oil which later solidified. The solid was recrystallized from petroleum ether to yield white platelets melting at 45.3–46.4°; 9.9 g. (75% yield) was obtained. A mixture of crystals of this carbinol with those of the acetate liquified at room temperature.

Anal. Calcd. for C₁₀H₁₂O₂: C, 73.14; H, 7.37. Found: C, 72.85; H, 7.35.

Preparation of 5-Hydroxymethyl-5-phenethylhydantoin (VI).—To 3.6 g. (0.022 mole) of V dissolved in 40 ml. of 65% alcohol was added 1.8 g. (0.027 mole) of potassium cyanide in saturated aqueous solution and 7.5 g. of lump ammonium carbonate, and the mixture was heated in a flask equipped with an air condenser at 60° for nine hours. Upon cooling the solution practically solidified through separation of white crystalline material. The latter was filtered off and dried to weight 5 g.; m. p. 169–172°. Successive recrystallizations from dilute alcohol, water and 95% alcohol raised the m. p. to 199.8–201.2°.

Anal. Calcd. for C₁₂H₁₄N₂O₃: C, 61.50; H, 6.02; N, 12.09. Found: C, 61.35; H, 6.12; N, 11.95.

Preparation of Hydrocinnamoylacetonitrile (IV).—Methyl hydrocinnamate was obtained by hydrogenation of methyl cinnamate over Raney nickel at 100° and boiled at 238° (uncor.). It was dried over phosphorus pentoxide and redistilled before use.

In an excess of absolute methanol was dissolved 8.67 g. (0.377 gram atom) of freshly cut sodium. Most of the excess alcohol was removed under diminished pressure before placing the flask, with applied vacuum, in an oil-bath at 110° for thirty minutes. The sodium methoxide, obtained as a white cake, was broken up with a stirring rod and powdered by shaking the stoppered flask.

The flask was equipped with a mercury sealed stirrer, a reflux condenser protected against moisture, and a dropping funnel with stem bent to direct liquid directly onto the stirrer. Nineteen and three-tenths grams (0.471 mole) of acetonitrile was introduced onto the methoxide and the temperature of the bath was raised to 140° for

fifteen minutes. The bath was allowed to cool to 100° before adding 40 ml. of dry dioxane.¹⁴ During a period of fifteen minutes 61.9 g. (0.377 mole) of methyl hydrocinnamate was added. The temperature was raised to 125° and maintained there for two hours. A downward sloping condenser was attached to the flask and 30 ml. of liquid boiling at 65–70° was distilled from the flask. The previous, protected reflux condenser was refitted to the flask and 10 ml. of acetonitrile was added to the reaction mixture. Heating and stirring were continued for three hours when the contents of the flask had become a creamy paste. Enough dry dioxane was added to cover the mass and the heating and the stirring continued for a total of eleven hours.

The flask was placed in a vacuum desiccator and evacuated overnight. The dried cake was broken up and dissolved in water. Upon acidification of the solution with dilute sulfuric acid; a creamy precipitate formed and was filtered off and dried to weigh 58.6 g. (87% yield) of hydrocinnamoylacetonitrile (IV). One recrystallization from benzene yielded 35 g. (54% yield) of white crystals melting at 71°.

Anal. Calcd. for C₁₁H₁₁NO: C, 76.27; H, 6.39; N, 8.08. Found: C, 76.00; H, 6.31; N, 7.82.

A preparation of IV from ethyl hydrocinnamate [prepared by hydrogenation of ethyl cinnamate over Raney nickel at 100°; b. p. 145–150° (45 mm.)], dried sodium ethoxide and acetonitrile gave only 37% yield of recrystallized product melting at 70.2–71.2°.

Interaction of Hydrocinnamoylacetonitrile (IV), Potassium Cyanide and Ammonium Carbonate.—To 3.0 g. (0.173 mole) of IV dissolved in 40 ml. of 65% alcohol was added 1.13 g. (0.173 mole) of potassium cyanide and 5.92 g. (0.519 mole) of ammonium carbonate. The mixture was heated in a water-bath at 60° for six hours. When the solvent had been partially removed, solid material separated. One gram (29.5% yield) of a light tan powder (II) was obtained; after one crystallization from ethyl acetate the m. p. was 186–187°.

Holder⁴ prepared 5-phenethyl-5-hydantoinacetonitrile (II) in an average yield of 32% by treatment of chloromethyl phenethyl ketone (I) with two equivalents of potassium cyanide and excess ammonium carbonate in 65% alcohol and reported m. p. 188–189°. A mixture of this material prepared from I and that produced from IV melted unchanged at 188°.

Preparation of the Hydrochloride of Hydrocinnamoylmethylamine. A. Synthesis of N-Hydrocinnamoylmethylphthalimide.—To 14.2 g. (0.078 mole) of I dissolved in 125 ml. of 95% alcohol was added 14.4 g. (0.078 mole) of potassium phthalimide. The solution was refluxed for three hours, then was chilled; the solution practically solidified with separating material. After addition, with stirring, of 45 ml. of water, the mixture was filtered. The residue on the filter was washed twice with small portions of alcohol and then twice with water. After drying over concentrated sulfuric acid, the residue weighed 15 g. (66% yield) and melted at 105°. One recrystallization from petroleum ether yielded feathery white crystals melting at 106–107°.

Anal. Calcd. for C₁₁H₁₃NO₃: C, 73.72; H, 5.15; N, 4.77. Found: C, 73.24; H, 5.16; N, 5.01.

B. Conversion into N-(Hydrocinnamoylmethyl)-phthalamic Acid.—Twenty-three grams of N-hydrocinnamoylmethylphthalimide was added to about 25 ml. of 95% alcohol in which 4.4 g. (one equivalent) of potassium hydroxide had been dissolved. The solution was heated ten minutes on the steam cone and diluted with water; a small amount of solid material separated and was removed by filtration. The filtrate was extracted twice with small portions of ether and the aqueous layer was made acidic with dilute hydrochloric acid. Upon standing, solid material separated from the solution, and was redissolved in dilute alkali solution and again precipitated with dilute acid. The precipitate was removed by filtra-

(13) Patterned after Evan's (*Am. Chem. J.*, **28**, 119 (1906)) conversion of phenacyl bromide into benzoylcarbinol acetate.

(14) Eigenberger, *J. prakt. Chem.*, **130**, 75 (1931).

tion, and washed with ether. After drying, 18 g. (74% yield) was obtained.

This material, obtained initially as white crystals, appeared to be contaminated by a purple colored impurity on storage overnight in a desiccator. Further purification was obtained by resolution in alkali and reprecipitation in acid, recrystallization from dilute alcohol and then from benzene. Thus obtained, the white crystalline material, melting at 124.6–125.5°, could be stored for several days in a desiccator filled with natural gas without much discoloration occurring.

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.45; H, 5.50; N, 4.50. Found: C, 69.23; H, 5.56; N, 4.69.

C. Conversion into VII.—To 310 ml. of concentrated hydrochloric acid was added 31 g. of N-(hydrocinnamoylmethyl)-phthalamic acid and the mixture was refluxed overnight. Upon cooling, phthalic acid separated and was filtered off; the filtrate was extracted twice with small portions of ether. The aqueous layer was concentrated to a volume of about 75 ml. by heating, and to dryness in a vacuum desiccator. The residue was allowed to stand over solid sodium hydroxide and was recrystallized from *n*-amyl alcohol. Eight grams (40% yield) of white needles melting at 139–141° was obtained.¹⁵

Anal. Calcd. for $C_{10}H_{14}ClNO$: Cl, 17.76. Found: Cl, 17.85.

Preparation of 1,4-Dihydro-2,5-diphenethylpyrazine (VIII).—To 15 ml. of water, previously boiled to expel dissolved oxygen, was added 2.6 g. of hydrocinnamoylmethylamine hydrochloride. A solution of sodium carbonate was cautiously added with stirring, causing immediate precipitation of solid material. That separating first was colored yellow and was filtered off. Upon further addition of carbonate solution to the filtrate, more material, but much lighter in color, precipitated. This was collected quickly by filtration and dried in a desiccator filled with natural gas; 1.7 g. (87% yield) of solid was obtained.

This material was recrystallized from diluted alcohol, care being taken not to heat the solution above 80°. Upon being chilled, the solution deposited crystals which were only faintly yellow. After being dried as before, these melted at 98–100°. The pyrazine derivative formed a silver mirror when warmed on the steam cone with ammoniacal silver nitrate solution. It is sensitive to air and its melting point is lowered by extensive contact with air.

Anal. Calcd. for $C_{20}H_{22}N_2$: C, 82.72; H, 7.63; N, 9.65. Found: C, 82.75; H, 7.66; N, 9.76.

Preparation of 2,5-Diphenethylpyrazine (IX).—Eight grams of hydrocinnamoyl methylamine hydrochloride was dissolved in water and neutralized with sodium carbonate solution. The dihydropyrazine, which precipitated, was dissolved in acetone and about 10 ml. of 30% hydrogen peroxide was added to the solution. The solution was boiled ten minutes after which it was cooled and diluted with water. White crystal separated which, after being filtered off and dried, weighed 4 g. and melted at 103–105°. After one recrystallization from alcohol and two recrystallizations from benzene the melting point was unchanged.

Anal. Calcd. for $C_{20}H_{20}N_2$: C, 83.30; H, 7.00; N, 9.72. Found: C, 82.80; H, 7.12; N, 10.04.

To 150 ml. of water containing 5 g. of sodium hydroxide was added 3.7 g. of 1,4-dihydro-2,5-diphenethylpyrazine (VIII). The mixture was heated on the steam cone with stirring while 14.8 g. of potassium permanganate in saturated solution was added slowly from a dropping funnel. The addition of the permanganate solution required about two hours; at the end of this time the purple color of permanganate was still evident. The contents of the flask was heated to boiling for four hours; a small amount of VIII had not reacted. Alcohol was added to destroy

the excess of permanganate and the solution was evaporated to a volume of about 200 ml. and filtered from the manganese dioxide and solid organic material. Extraction of the residue with acetone yielded 1 g. of 2,5-diphenethylpyrazine (IX).

The filtrate was acidified and the precipitate which formed was removed by filtration. This residue was stirred with ether to remove benzoic acid; the ether was removed and combined with an ether extract of the filtrate. Evaporation of the solvent yielded 1.6 g. (70% recovery) of benzoic acid. The ether-insoluble residue weighed 0.5 g. (32% yield based on weight of unrecovered material). The acidic residue was recrystallized from ethanol and was dried under vacuum for five hours at 100°. Thus obtained, the white powder melted at 269° with decomposition. Stolte¹⁶ reported that 2,5-pyrazinedicarboxylic acid decomposes at 272° while Stoehr¹⁷ noted that it tends to sublime at 270°.

Anal. Calcd. for $C_8H_4N_2O_4$: C, 42.86; H, 2.35; N, 16.65. Found: C, 42.59; H, 2.46; N, 17.67.

Interaction of Phenacyl Chloride (X) with Potassium Cyanide and Ammonium Carbonate.—To a solution of 50 g. (0.323 mole) of X in 660 ml. of 65% alcohol was added 21.2 g. (0.323 mole) of potassium cyanide and 110 g. (0.969 mole) of ammonium carbonate and the mixture was warmed in a water-bath at 60° for twelve hours. At this time the solution was of a light brown color and there was present a light yellow precipitate. This was filtered off and the filtrate concentrated to half its original volume by blowing a stream of air across the solution. A small amount of solid separated and was shown by melting point to be more of that initially obtained. The two portions were combined, washed with water and dried; weight 7 g. The light yellow solid was recrystallized from ethyl alcohol to yield fine white crystals melting at 218.5–219.6°.

Anal. Calcd. for $C_{17}H_{12}N_2$: mol. wt., 244.3; C, 83.58; H, 4.83; N, 11.46. Found: mol. wt., 263; C, 83.40; H, 4.98; N, 11.50.

These data indicate it to be 2,5-diphenyl-3-pyrroleanitrile (XI).

Further evaporation of the filtrate from XI caused separation of gummy material which failed to yield any crystalline material. The supernatant liquid was acidified, but no hydantoin derivative was found.

When two equivalents of potassium cyanide was used instead of one, a much darker colored solution was produced and the yield of crystalline material was lower.

Treatment of XI with Hydriodic Acid.—In a flask, connected to a reflux condenser by a ground glass connection, was mixed 2.3 g. of XIV and 50 ml. of 57% hydriodic acid. The gases issuing from the top of the condenser could be directed into barium hydroxide solution. The flask was slowly warmed in an oil-bath until the acid boiled gently almost immediately a white precipitate appeared in the alkaline solution. The nitrile gradually dissolved as heating was continued and was almost completely in solution after fifteen hours. After decolorizing iodine, the hot, pale yellow solution was filtered and cooled, when slowly neutralized with strong potassium hydroxide solution, a white amorphous precipitate appeared and the odor of ammonia was recognizable. Addition of the alkali was continued until the solution was basic. Upon being chilled for several hours the amorphous material became crystalline. It was filtered off and dried; the small white crystals weighed 0.5 g. and melted at 56–57°. Recrystallization from diluted alcohol raised the m. p. to 60–61°. The analytical data corresponds to those calculated for a dihydro-2,5-diphenylpyrrole (XII).

Anal. Calcd. for $C_{16}H_{18}N$: C, 87.04; H, 6.83; N, 6.33. Found: C, 87.17; H, 7.00; N, 6.38.

A picrate of this compound was formed and, after two recrystallizations from alcohol, melted with decomposi-

(15) Pascual and Rebollo [*Anales soc. españ. fis. quim.*, **32**, 381 (1934)] report m. p. of 170° for this compound and for the chlorine content 31.58 and 31.53%.

(16) Stolte, *Beitr. Chem. Physiol. Path.*, **11**, 22 (1907); through *Chem. Zentr.*, **79**, I, 224 (1908).

(17) Stoehr, *J. prakt. Chem.*, [2] **47**, 488 (1893).

tion at 186–189°. Satisfactory analysis for nitrogen for the picrate were not obtained, all values being low.

Anal. Calcd. for $C_{22}H_{18}N_4O_7$: C, 58.66; H, 4.03. Found: C, 58.78; H, 4.11.

That the nitrile group is very resistant to hydrolysis was shown by boiling 4 g. of XI with 150 ml. of concentrated hydrochloric acid for five hours; 90% of the nitrile was recovered with unchanged melting point. Refluxing with a saturated solution of potassium hydroxide in ethyl alcohol also failed to alter the compound.

Three grams of XI was added to 100 ml. of propylene glycol containing 12 g. of potassium hydroxide. The mixture was boiled under reflux for sixty hours. Liberation of ammonia began almost as soon as the solution reached the boiling temperature.

The solution was transferred to a distilling flask and about 20 ml. of propylene glycol was distilled off under reduced pressure. The viscous solution was diluted with water, causing separation of solid material. After being filtered off, washed with water and dried, the residue weighed 2 g. and melted at 136–139°. One recrystallization from ethyl alcohol raised the m. p. of XIII to 143.8°. ¹⁸

Three and one-half grams of diphenacyl was heated in a metal bomb with 200 ml. of a saturated solution of ammonia in alcohol for nine hours at 140°. The solution was concentrated to one-half volume and largely diluted with water; solid separated and was filtered off, washed and dried to yield 2.7 g. (80% yield). After one recrystallization from ethyl alcohol, the product (XIII) melted at 142–143°. A mixture of these crystals with those obtained on decarboxylation of XI showed no depression in melting point.

Hydrolysis and Decarboxylation of III.—One gram of III was added to 50 ml. of propylene glycol containing 6 g. of potassium hydroxide and the mixture was heated to reflux for eighteen hours while ammonia was being liberated. The solution was reduced in volume by evaporation and diluted with 250 ml. of water; solid material separated and crystallized. It was removed by filtration and dried over sulfuric acid. About 0.5 g. was obtained and was crystallized twice from dilute alcohol to yield white needles melting at 83–84°. A pine splinter moistened with concentrated hydrochloric acid turned red when held in the vapor of this substance. The data derived from analysis of this product, substantiate the view that it is the previously unreported 2,5-diphenethylpyrrole (XIV).

Anal. Calcd. for $C_{20}H_{18}N$: C, 87.28; N, 7.75; N, 5.08. Found: C, 86.58 and 86.99; H, 7.71 and 8.06; N, 5.23.

Additional Synthesis of 2,5-Diphenethyl-3-pyrrolenitrile.—**A. Preparation of α,β -Dihydrocinnamoylpropionitrile (XV).**—In 50 ml. of methanol was dissolved 0.63 g. (0.274 gram atom) of freshly cut sodium. Subsequently, 4.5 g. (0.260 mole) of hydrocinnamoylacetonitrile was added with rapid stirring and the solution was heated to boiling for fifteen minutes. The mixture was allowed to cool before rapid addition of 5 g. (0.274 mole) of chloromethyl phenethyl ketone dissolved in 50 ml. of methanol. Stirring was continued and the solution was refluxed for two hours. The homogeneous solution was rather dark in color, hence, was treated with Norite and filtered before being concentrated under reduced pressure in a vacuum desiccator. The product, which crystallized from solution, was filtered off and recrystallized from dilute alcohol. Four grams, melting at 78°, was obtained; further crystallization from petroleum ether did not alter the melting point.

Anal. Calcd. for $C_{21}H_{21}NO_2$: C, 78.96; H, 6.63; N, 4.38. Found: C, 78.75; H, 6.5; N, 4.42.

(18) Kapf and Paal [*Ber.*, **21**, 3061 (1888)] reported m. p. of 143° for 2,5-diphenethylpyrrole synthesized by interaction of diphenacyl¹⁹ and ammonia.

(19) Auger [*Bull. soc. chim.*, **49**, 346 (1888)] prepared diphenacyl from succinyl chloride, benzene and aluminum chloride and recorded that the m. p. as 134°. Kapf and Paal¹⁸ reported m. p. 144–146°; our sample m. p. 146°.

B. Conversion into III.—Two and eight-tenths grams of α,β -dihydrocinnamoylpropionitrile (XV) was dissolved in 75 ml. of ethyl alcohol and heated with 15 g. of ammonium carbonate lumps in a metal bomb at 75° for five hours. The deeply colored solution was treated with Norite and concentrated by evaporation under an air jet. The residual dark brown, semi-solid material was extracted five times with boiling petroleum ether to obtain 0.7 g. (29% yield) of yellow crystalline material. Two recrystallizations from petroleum ether, with the aid of Norite, yield very faintly yellow crystals melting at 96–97°. A mixture of these crystals with those obtained from interaction of chloromethyl phenethyl ketone with potassium cyanide and ammonium carbonate showed no alteration of melting point.

Anal. Calcd. for $C_{21}H_{20}N_2$: C, 83.96; H, 6.71; N, 9.33. Found: C, 83.72; H, 6.94; N, 9.10.

Attempts to Form Azo Derivatives from Certain Pyrroles.—According to Fischer²⁰ pyrroles show a pronounced tendency to couple with diazotized aromatic amines. Hence, such coupling was attempted between diazotized *m*-nitraniline and 2,5-diphenylpyrrole (XIII), 2,5-diphenethylpyrrole (XIV), 2,5-diphenyl-3-pyrrolenitrile (XI) and 2,5-diphenethyl-3-pyrrolenitrile (III).

A. Reaction with XIII.—To a solution of 8 ml. of water and 1.17 ml. of concentrated hydrochloric acid (sp. gr. 1.178; 36% hydrogen chloride) was added 0.63 g. (0.0456 mole) of *m*-nitraniline. The mixture was stirred until the amine had dissolved, then was cooled in an ice-bath to below –10°. A solution of 0.48 g. (0.07 mole) of sodium nitrite in 6 ml. of water was added slowly with stirring and the solution of diazotized amine was poured into a cold solution of 1 g. (0.0456 mole) of XIII in 100 ml. of alcohol. Upon standing in an ice-bath, bright red crystals of 2,5-diphenyl-3-(3-nitrophenylazo)-pyrrole separated. About 1 g. of material was obtained subsequent to two recrystallizations; m. p. 207°.

Anal. Calcd. for $C_{22}H_{18}N_4O_2$: C, 71.72; H, 4.37. Found: C, 71.39; 4.36. Despite all attempts, values for nitrogen, lower than calculated, were obtained.

B. Reaction with XIV.—This preparation was attempted exactly as in the case of XIII. When the diazotized amine solution was added to the solution of XIV, a dark red color was observed and a brown gummy material separated but could not be caused to crystallize. None of the pyrrole could be recovered. The use of sodium acetate as a buffer led to no success.

C. Reactions with XI and III.—When the solution of the diazotized amine was added to those of the pyrroles, no color or sign of reaction was observed and most of the pyrroles was recovered unchanged.

Summary

1. The substance melting at 96°, resulting from interaction of chloromethyl phenethyl ketone, potassium cyanide and ammonium carbonate, has been identified as being 2,5-diphenethyl-3-pyrrolenitrile.
2. This method of synthesis has been extended to the preparation of a lower homolog.
3. Three additional 2,5-disubstituted pyrroles have been prepared; the tendency of these to form azo derivatives has been investigated.
4. In addition, a new pyrroline, in all probability 2,5-dihydro-2,5-diphenyl-pyrrole, has been obtained.
5. The first synthesis of a 5-hydroxyalkyl-5-substituted hydantoin has been accomplished.
6. A new pyrazine and a new dihydropyrazine have been prepared.

AUSTIN, TEXAS

RECEIVED MARCH 14, 1947

(20) See ref. 9, p. 116.