[Contribution from the Department of Chemistry, the University of Texas]

THE INTERACTION OF CERTAIN α-(4-MORPHOLINYL)ALKYL ARYL KETONES WITH POTASSIUM CYANIDE AND AMMONIUM CARBONATE[1]

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During recent years considerable attention has been devoted in this Laboratory to conversion of carbonyl compounds (1), especially ketones, into hydantoins (2). In general, the method of Bucherer (3), which employs interaction of the carbonyl compound with potassium cyanide and ammonium carbonate in diluted alcohol solution, has been employed successfully, and especially in the preparation of 5-phenyl- (or 5-substituted phenyl)-5-substituted hydantoins. Therefore, it occasioned considerable surprise when Rubin and Day (4), although reporting conversion of α-(4-morpholinyl)acetophenone (I) into 5-(4-morpholinyl) methyl-5-phenylhydantoin (II), recorded failure in attempts to prepare hydantoins from the next higher homolog of I, and from the 4-hydroxy and 3,4-dihydroxy derivatives of I.[3]

In the present study, reaction between potassium cyanide, ammonium carbonate, and these three ketones has been found to occur under conditions typical of the Bucherer method; 4-hydroxy-α-(morpholinyl)acetophenone (III) was converted into 5-(4-hydroxyphenyl)-5-(4-morpholinyl)methylhydantoin (IV) and 3,4-dihydroxyphenyl-α-(4-morpholinyl)acetophenone (V) into 5-(3,4-dihydroxyphenyl)-5-(4-morpholinyl)methylhydantoin (VI). In order to obtain a satisfactory yield of these two hydantoins it is desirable to employ a concentration of cyanide somewhat higher than that most typical of the Bucherer method, that is, 2.5 moles in the formation of IV and 3.5 moles in preparation of VI. This larger requirement of cyanide is associated with the tendency of the phenolic groups to react with an equivalent amount of potassium cyanide, since in each case solution of the phenolic ketone in the diluted alcohol occurred only upon addition of the cyanide. Compound VI is quite hygroscopic; it could be obtained, also, in the form of a stable monohydrate.

From interaction of α-(4-morpholinyl)propiophenone (VII) with potassium cyanide and ammonium carbonate the anticipated 5-[1-(4-morpholinyl)ethyl]-5-phenylhydantoin (VIII) was not obtained; instead, 5-phenylhydantoin (IX) and "dihydantil"[4] (X) were obtained. X must be considered as a secondary

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[1] From the Ph. D. dissertation of W. C. Craig, June, 1944.

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[3] Rubin and Day, *J. Org. Chem.*, **5**, 60 (1940), merely stated that: "Attempts to prepare the hydantoins of α-morpholinopropiophenone, ω-morpholino-*p*-hydroxyacetophenone, and ω-morpholino-3,4-dihydroxyacetophenone using the method of Bucherer failed." Thus no information was given to indicate whether failure to obtain the desired hydantoins was due to unreactivity of these ketones, inability to isolate the hydantoins, or to formation of other, non-hydantoin products.

[4] Gabriel (5) so named a product which is better termed 5-phenyl-5-[1-(5-phenylhydantyl)] hydantoin.

product formed from IX, for IX, when allowed to stand in alkaline solution exposed to air, is slowly converted into X. Since the initial attempts to convert VII into VIII involved heating the acidified reaction mixture, a preliminary assumption was made that IX represented a degradation product of VIII. However, in subsequent attempts to isolate the reaction product of VII in such a manner as to prevent the postulated decomposition, there was no change in the products obtained. In all such attempts, some unreacted VII was recovered, and no evidence of the existence of VIII was observed.

Upon being heated with dilute hydrochloric acid, both II and 5-(4-morpholinyl)methyl-5-phenethylhydantoin (6) (XI) were decomposed with evolution of formaldehyde and formation of IX and 5-phenethylhydantoin (7) (XII), respectively. II was also decomposed when heated in very dilute hydrochloric acid solution, being converted into 5-hydroxymethyl-5-phenylhydantoin (XIII).[5]

5-Hydroxymethyl-5-phenylhydantoin (XIII), prepared for the first time in this investigation, was obtained also through cleavage of certain 5-alkoxymethyl-5-phenylhydantoins (8) by concentrated hydriodic acid. An attempt to synthesize XIII through interaction of benzoylcarbinol acetate (XIV), potassium cyanide, and ammonium carbonate, did not yield the anticipated hydantoin. Instead, there was obtained another crystalline substance (XV), analysis of which indicated the formula $C_{10}H_{10}N_2O_3$, identical with that of XIII. Unlike the latter compound, XV was decomposed readily both in 20% potassium hydroxide solution at room temperature and in hot 6 *N* hydrochloric acid.

Hydrolyzed by acid, XV was converted into ammonia and an acidic substance, $C_{10}H_9NO_4$ (XVI); the latter, by treatment with thionyl chloride followed by ammonia, could be reconverted into XV. Decomposition of the amide (XV) by excess sodium hydroxide solution yielded $C_9H_{11}NO_3$ (XVII), subsequently shown to be α-amino-β-hydroxy-α-phenylpropionic acid. Decomposition of the acid (XVI), by means of 9 *N* hydrochloric acid, also yielded XVII. These facts lead to the formulation of XV as 4-phenyl-2-oxazolidone-4-carboxamide, and XVI as the corresponding 4-carboxylic acid.

EXPERIMENTAL

α-(4-Morpholinyl)acetophenone hydrochloride. This compound was prepared according to Rubin and Day (4); one recrystallization produced a 61% yield of white, crystalline material melting at 222–223° (dec.).

5-(4-Morpholinyl)methyl-5-phenylhydantoin (II). Fifteen grams (0.062 mole) of α-(4-morpholinyl)acetophenone hydrochloride, 6 g. (0.092 mole) of potassium cyanide, 24 g. (0.25 mole) of ammonium carbonate, and 120 cc. of 50% alcohol were warmed at 55° for eleven hours; a crystalline solid began to separate after about three hours. After purification by recrystallization from hot ethyl alcohol, there was obtained 15.5 g. (72% yield) of II, m.p. 204–205° (corr.) (4).

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[5] At first it seemed probable that after hydrolysis of II to XIII, the latter, in turn, was decomposed to IX. However, only a very small percentage of XIII was found to decompose under conditions analogous to, although not quite identical with, those employed for cleavage of II. Hence, it is indicated that II, when heated in dilute hydrochloric acid solution, is converted into IX and, presumably, 4-morpholinylmethanol, the latter being subsequently decomposed into formaldehyde and morpholine.

5-(4-Hydroxyphenyl)-5-(4-morpholinyl)methylhydantoin (IV). The addition of a solution of 2.21 g. (0.034 mole) of potassium cyanide in 20 cc. of water to a suspension of 3 g. (0.0136 mole) of 4-hydroxy-α-(4-morpholinyl)acetophenone (4) in 95 cc. of 75% alcohol caused solution of the hydroxy ketone. After the addition of 5.4 g. (0.056 mole) of ammonium carbonate cubes, the reaction mixture was warmed at 58° for fourteen hours. Concentration of the solution, through evaporation under a stream of air, to one-fourth of the initial volume caused the precipitation of a tan colored, crystalline solid. The 2.85 g. of crude product, obtained by filtration and drying, was separated into two fractions by reason of differential solubility in boiling acetone. The acetone-soluble portion yielded 0.85 g. of unreacted ketone.

The acetone-insoluble fraction was purified by solution in dilute hydrochloric acid, treatment with Norit, filtration, and neutralization with sodium hydroxide solution. After drying over sulfuric acid, the hydantoin was in the form of a white powder, and weighed 1.55 g. (55% yield based on unrecovered ketone); m.p. 253–254° (dec. with frothing). IV is insoluble in water, acetone, and ethyl acetate, is sparingly soluble in hot methanol and ethanol, and dissolves readily both in dilute acidic and in dilute basic solutions. It gives a positive test (9) with Millon's reagent, but does not give a color in very dilute hydrochloric acid solution with ferric chloride solution.

Anal. Calc'd for $C_{14}H_{17}N_3O_4$: C, 57.72; H, 5.88; N, 14.43.
Found: C, 57.61; H, 5.80; N, 14.35.

Employing a ratio of only 1.5 mole of potassium cyanide to one mole of ketone gave IV in much smaller yield.

5-(3,4-Dihydroxyphenyl)-5-(4-morpholinyl)methylhydantoin (VI). A reaction mixture consisting of 5.9 g. (0.025 mole) of 3,4-dihydroxy-α-(4-morpholinyl)acetophenone [m.p. 204° (dec. with frothing)] (4), 5.7 g. (0.087 mole) of potassium cyanide,[6] 10 g. (0.105 mole) of ammonium carbonate cubes, and 90 cc. of 50% alcohol was warmed at 58–60° for seventeen hours. The cooled reaction mixture was concentrated[7] through evaporation under a stream of air to one-third of its original volume, and was then filtered to obtain a tan-colored, crystalline solid. After purification by solution in acid, treatment with Norit, filtration, and neutralization with alkali, there was obtained 4.35 g. (56% yield) of white, crystalline material. The latter was recrystallized from hot alcohol to yield a hydrate which decomposed with frothing at 211–212°.

Anal. Calc'd for $C_{14}H_{17}N_3O_5 \cdot H_2O$: C, 51.68; H, 5.88; N, 12.92.
Found: C, 51.66; H, 6.01; N, 12.86.

When this hydrate was dissolved in dilute hydrochloric acid and allowed to stand at room temperature for three days, a solid gradually separated in the form of cubic crystals, which enlarged to flat, transparent, rectangular plates. Dried in a desiccator over concentrated sulfuric acid, the crystals disintegrated to an opaque powder which melted with frothing and decomposition at 202–204°.

Anal. Calc'd for $C_{14}H_{17}N_3O_5 \cdot HCl$: Cl, 10.32; N, 12.22.
Found: Cl, 10.39; N, 12.11.

A solution of the hydrochloride in warm water, containing a few drops of concentrated hydrochloric acid to facilitate solution, was neutralized with morpholine; the white, crystalline solid that separated was filtered off, recrystallized from hot alcohol, and dried in a vacuum desiccator over concentrated sulfuric acid for two days to yield VI, which melted with frothing and decomposition at 215–216°.

Anal. Calc'd for $C_{14}H_{17}N_3O_5$: N, 13.67. Found: N, 13.50.

When allowed to stand in contact with the atmosphere for a short time and then dried over sulfuric acid, the hydantoin had reverted to the monohydrate. The latter is insoluble in water, but is soluble in alcohol. It dissolves in 5% sodium hydroxide solution with

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[6] Addition of the cyanide caused solution of the hydroxy ketone in the diluted alcohol.

[7] The mixture became black as evaporation progressed.

gradual formation of a red-violet color. The hydrate dissolves also in dilute hydrochloric acid; such a solution treated with a very dilute solution of ferric chloride develops a blue color.

Employing a ratio of only 2.5 moles of potassium cyanide to 1 mole of ketone gave a much smaller yield of the hydantoin monohydrate.

α-(4-Morpholinyl)propiophenone hydrochloride. To a well-stirred solution of 70 g. (0.328 mole) of α-bromopropiophenone in 80 cc. of ethyl alcohol was added 60 g. (0.686 mole) of morpholine, the temperature of the mixture being maintained between 5° and 15°. After dilution with 270 cc. of ether, the precipitated morpholine hydrobromide was removed by filtration and the filtrate saturated with hydrogen chloride. The product was filtered off and dried; weight 94 g. This product was extracted with 200 cc. of alcohol to remove any morpholine hydrochloride present, then recrystallized by dissolving in 500 cc. of hot alcohol and chilling; 69 g. (82% yield) of purified material was thus obtained. The final product was a white, crystalline solid which darkened slightly at 224–226° and melted with decomposition at 239–240° (corr.).[8]

Anal. Calc'd for $C_{13}H_{18}ClNO$: Cl, 13.86; N, 5.48.
Found: Cl, 13.89; N, 5.58.

α-(4-Morpholinyl)propiophenone (VII). To a solution of 15 g. of α-(4-morpholinyl)propiophenone hydrochloride in 100 cc. of water was added a 10% aqueous solution of sodium hydroxide until the mixture was basic to litmus. A light yellow oil separated, was extracted with ether, and the extract fractionated under diminished pressure to give 12 g. (93% yield) of VII boiling at 210–211° (73 mm.); d_4^{25} 1.09880; n_D^{25} 1.5393; Σ*MR*[9] 62.56; MR found 62.56.

The *semicarbazone* of VII formed readily and melted at 206–207° after recrystallization from diluted alcohol.

Anal. Calc'd for $C_{14}H_{20}N_4O_2$: N, 20.28. Found: N, 20.37.

Attempted preparations of 5-[1-(4-morpholinyl)ethyl]-5-phenylhydantoin [VIII]. Nine and four-tenths grams (0.098 mole) of ammonium carbonate cubes was added to a solution of 6 g. (0.0244 mole) of α-(4-morpholinyl)propiophenone hydrochloride and 2.4 g. (0.037 mole) of potassium cyanide in 80 cc. of 80% alcohol, and the mixture was warmed at 58–60° for twenty-three hours. The mixture was evaporated on a steam-cone to one-third of its initial volume, acidified with hydrochloric acid and heated just below its boiling point for ten minutes. After cooling to room temperature, filtration removed white solid material; the latter was washed well with water and dried; weight 1.7 g. This material was extracted with warm alcohol; the alcohol-soluble portion was obtained as white, crystalline flakes melting at 180.5–181.5° (uncorr.), and after purification was identified as *5-phenylhydantoin* (IX).

Anal. Calc'd for $C_9H_8N_2O_2$: N, 15.90. Found: N, 15.80.

The alcohol-insoluble material was obtained as an alkali-soluble, white powder melting with decomposition at 325–327° (uncorr.), and proved to be *5-phenyl-5-[1-(5-phenylhydantyl)]hydantoin* (X) (4).

Anal. Calc'd for $C_{18}H_{14}N_4O_4$: N, 15.99. Found: N, 15.81.

Three grams of unreacted hydrochloride was recovered from the acidified reaction mixture filtrate by making it alkaline, extracting with ether, drying the extract over anhydrous sodium sulfate and then saturating with dry hydrogen chloride. On the basis of unrecovered material, 77% of the morpholinyl ketone can be accounted for in the form of IX and 5% in the form of X.

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[8] Rubin and Day (ref. 4, p. 57) reported for this substance the m.p. 224° (corr.) with decomposition. Our material could be made to melt gradually at 225–226° (corr.) by holding the melting point bath at this temperature for approximately ten minutes.

[9] The Σ*MR* was obtained by summation of the appropriate atomic refractions plus an increment of 0.64 for the exaltation effect of the benzoyl group in propiophenone observed by Auwers (10).

A second attempt differed from the initial effort in that 70% alcohol was used as the solvent; the reaction mixture was acidified and filtered from precipitated material before evaporation of the filtrate. However, the same products were obtained in essentially the same proportions.

Another trial involved addition of more ammonium carbonate (three molar equivalents) at eight-hour intervals during the course of a heating period of thirty hours; 'acidification was followed by evaporation under a stream of air at room temperature. The results again were the same as before.

In order to study the possible effect of enhanced buffering, two and one-half molar proportions of ammonium acetate was included with the reactants and an additional molar equivalent of ammonium carbonate was provided after the third hour of a fourteen-hour heating period. Again, the results were as before.

Another attempt utilized VII, instead of its hydrochloride, and employed a shorter heating period. The same products as usual were obtained although in lesser quantities.

Hydrolysis of II. A. *With water.* Two grams of II was suspended in 50 cc. of water and heated under a reflux condenser for four hours; all of the suspended solid had gone into solution after ninety minutes. Upon cooling, solid material separated and was removed by filtration. The filtrate was basic towards litmus, and gave a positive blue ring test for formaldehyde (9) with gallic acid. The dried solid, weighing 1.5 g., was fractionated by extraction with warm alcohol. The alcohol-soluble material was recovered II. The alcohol-insoluble portion was identified as *5-phenyl-5-[1-(5-phenylhydantyl)]hydantoin* (5) by comparison with an authentic sample.

B. *With very dilute hydrochloric acid.* One gram of II was boiled for eight hours with 30 cc. of water containing five drops of concentrated hydrochloric acid. After three hours a white solid began to separate and the odor of formaldehyde was evident. After cooling, the reaction mixture was filtered to obtain the solid material; the latter was recrystallized with difficulty from boiling alcohol and was dried at 105°. The material thus obtained was in the form of white needles which melted with frothing at 230.5–231.5°. It was identified as *5-hydroxymethyl-5-phenylhydantoin* (XIII) by comparison with a sample of that substance subsequently synthesized.

One and one-half gram of II was dissolved in 25 cc. of water containing just enough hydrochloric acid to dissolve the hydantoin at room temperature, and the solution was heated to boiling for twelve hours; the odor of formaldehyde could be noted. After cooling, the mixture was concentrated to half volume under a stream of air. Filtration yielded solid material, melting at 180.5–181.5° (uncorr.), which was purified and identified as *5-phenylhydantoin* (IX); m.p. 185°.

Hydrolysis of 5-[4-morpholinyl]methyl-5-phenethylhydantoin (5) [XI] with dilute hydrochloric acid. A suspension of 1.7 g. of XI in 40 cc. of water containing ten drops of concentrated hydrochloric acid was heated to boiling for sixteen hours; formaldehyde was evolved during this period. When cooled, a white crystalline solid separated from the solution and was filtered off, washed, and dried. The material thus obtained was essentially pure, melted at 167° and was identified as *5-phenethylhydantoin* [XII] by comparison with an authentic sample.[10]

Anal. Calc'd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72.
Found: C, 64.52; H, 6.08; N, 13.72.

5-Hydroxymethyl-5-phenylhydantoin (XIII). Four grams of 5-(*n*-butoxymethyl)-5-phenylhydantoin (8) was suspended in 20 cc. of 57% hydriodic acid (sp. gr. 1.7) and heated to boiling under a reflux condenser for ten minutes; all of the solid dissolved within three minutes, and after eight minutes a white solid began to separate from the boiling solution. The hot mixture was diluted with 30 cc. of boiling water and then allowed to cool. The filtered reaction product was washed with water, and was recrystallized from boiling alco-

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[10] Henze and Speer (7) noted the melting point 165° (uncorr.) for XIII prepared by interaction of hydrocinnamaldehyde, potassium cyanide, and ammonium carbonate.

hol, in which it is difficultly soluble, to give 2.95 g. (93.5% yield) of white, crystalline XIII; m.p. 230.5–231.5° (frothing and dec.).

Anal. Calc'd for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.59.
Found: C, 58.28; H, 5.05; N, 13.52.

The same product (XIII) was obtained in the same manner and in equally good yield by cleavage of the methoxymethyl and *s*-butoxymethyl analogs (8). XIII is but sparingly soluble in hot water, is slightly soluble in hot dioxane but dissolves more readily upon addition of a small amount of water to the solvent. The odor of formaldehyde is readily noted when a dry sample of XIII is heated above its melting point.

A suspension of XIII in 25 cc. of water containing 1 cc. of concentrated hydrochloric acid was heated to boiling under a reflux condenser for nineteen hours; approximately two-thirds of the hydantoin dissolved during that time. Upon cooling, 0.93 g. of unaltered XIII was recovered by filtration. Although the filtrate gave a positive test for formaldehyde (9), no 5-phenylhydantoin was recovered.

The tendency of XIII to decompose into formaldehyde and IX was demonstrated as follows: One gram of XIII was dissolved in 2 cc. of concentrated hydrochloric acid and 20 cc. of hot dioxane and the solution was boiled under a reflux condenser for eleven hours. Upon cooling, solid separated and was filtered off, washed with cold dioxane, dried, and identified as unaltered XIII. To 1 cc. of water was added 0.25 cc. of the dioxane filtrate; this solution gave a strongly positive test for formaldehyde (9). The remainder of the dioxane filtrate was evaporated to a small volume with a stream of air, was then diluted with water and filtered from additional XIII; the total recovery of the latter was 0.84 g. Evaporation of the aqueous filtrate yielded a small quantity of a white crystalline solid, melting at 181° (uncorr.), which, after purification, proved to be IX by comparison with the known material.

Benzoylcarbinol acetate[11] (XIV). This material was prepared in 82.5% yield from interaction of 61 g. (0.40 mole) of phenacyl chloride, 65 g. (0.79 mole) of anhydrous sodium acetate and 150 cc. of glacial acetic acid at 132° for four hours; m.p. 41°.[12] Recrystallized from a mixture of benzene and Skellysolve C, it melted at 48–49°.

4-Phenyl-2-oxazolidone-4-carboxamide (XV). In an attempt to synthesize 5-hydroxymethyl-5-phenylhydantoin (XII), 7.35 g. (0.113 mole) of potassium cyanide dissolved in 10 cc. of water, and 25.4 g. (0.264 mole) of ammonium carbonate cubes were added to a solution of 15 g. (0.084 mole) of XIV in 50 cc. of alcohol. The reaction mixture was warmed at 58–60° for four hours. Upon diluting this mixture to 500 cc. with water, a solid material gradually separated from solution and was filtered off, washed with water, dried, and recrystallized from hot alcohol to yield 10.3 g. (53%) of a white crystalline solid, which melted at 187–188° (corr.). This product (XV) is soluble in hot water, dilute sodium hydroxide solution, acetone, alcohol, and dioxane, but is not soluble in dilute hydrochloric acid, benzene, ether, ethyl acetate, or carbon tetrachloride. It is decomposed both in 20% potassium hydroxide solution at room temperature and in hot, concentrated hydrochloric acid. The odor of formaldehyde may be noted when XV is heated above its melting point.

Anal. Calc'd for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.59.
Found: C, 58.38; H, 4.95; N, 13.58.

In another preparation of XV, a 79% yield was obtained by warming at 58° for six hours a mixture of 20 g. (0.112 mole) of benzoylcarbinol acetate, 9.8 g. (0.151 mole) of potassium cyanide, 40 g. (0.416 mole) of ammonium carbonate cubes, and 75 cc. of 80% alcohol; 16.25 g. of product resulted.

When a suspension of 11.7 g. of XV in 60 cc. of 6 *N* hydrochloric acid was heated to boiling, within three minutes all of the material had dissolved and ten minutes later white crystals began to appear in the hot solution; the total period of heating was fourteen min-

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[11] Evans (10) employed phenacyl bromide to prepare this compound; purified by distillation under diminished pressure, XIV was obtained thus in 80% yield.

[12] Some melting points recorded for XIV are: 40° (11); 44° (12); 49° (13).

utes. After cooling to room temperature, the mixture was diluted by addition of 20 cc. of water and filtered. The filtrate yielded a positive test for ammonia with Nessler's reagent. The solid reaction product was washed twice with water and dried; this material, *4-phenyl-2-oxazolidone-4-carboxylic acid* (XVI), weighed 10.6 g. (90% yield) and melted at 188-189°. It is soluble in dilute sodium hydroxide solution, hot water, acetone, alcohol, dioxane, ethyl acetate, glacial acetic acid, and pyridine. It is insoluble in dilute hydrochloric acid, benzene, carbon tetrachloride, chloroform, and Skellysolve C.

Anal. Calc'd for $C_{10}H_9NO_4$: Neut. equiv. 207.2; C, 57.97; H, 4.37; N, 6.76.
Found: Neut. equiv. 207.5; C, 57.92; H, 4.41; N, 6.80.

Two and one-half grams of XVI was dissolved in 20 cc. of hot thionyl chloride, and heated for twenty minutes. The solution was cooled and added slowly to chilled, concentrated ammonium hydroxide solution. During the period of one hour solid material separated, was filtered off and recrystallized from hot alcohol to yield 1.0 g. of XV melting at 187-188°.

Preparation of α-amino-β-hydroxy-α-phenylpropionic acid. A. A solution of 10 g. of XVI in 60 cc. of hot hydrochloric acid was boiled for five and one-half hours, then was cooled, neutralized, concentrated, and filtered to obtain the solid material which had formed. The latter was recrystallized from hot glacial acetic acid, washed with alcohol, and dried at 105-110° for three hours. Two and eight-tenths grams of *α-amino-β-hydroxy-α-phenylpropionic acid* (XVII), melting with frothing and decomposition at 254-255°, was thus obtained.[13]

B. A solution of 4 g. of XV in 25 cc. of 20% potassium hydroxide solution (carbonate free) was allowed to stand at 27°; within ten minutes ammonia was detected in a stream of natural gas, previously bubbled through concentrated sulfuric acid and then through sodium hydroxide solution, passed through the reaction solution. After evolution of ammonia had ceased, the solution was warmed at 55-57° for thirty minutes, then was chilled. Upon acidification, carbon dioxide could be detected in the stream of natural gas, and a small amount of a white solid formed; the latter was separated by filtration and dried. The filtrate was concentrated by evaporation under an air-jet; a white solid formed, was filtered off, purified by solution in alkali with subsequent precipitation upon acidification, was digested with hot alcohol and dried. Both portions of the product (XVII) constituted fine white crystals melting with decomposition at 254-255°.[13]

However, the best method for preparing XVII from XV is first to hydrolyze the latter with dilute hydrochloric acid to obtain XVI, and subsequently to decompose XVI with dilute sodium hydroxide solution.

SUMMARY

1. Contrary to experience elsewhere, both 4-hydroxy-α-(4-morpholinyl)acetophenone and 3,4-dihydroxy-α-(4-morpholinyl)acetophenone have been converted into the corresponding hydantoins according to the Bucherer method.

2. Under these same conditions, α-(4-morpholinyl)propiophenone does not yield the corresponding hydantoin; instead, 5-phenylhydantoin and, subsequently, 5-phenyl-5-[1-(5-phenylhydantyl)]hydantoin are formed.

3. Both 5-(4-morpholinyl)methyl-5-phenylhydantoin and 5-(4-morpholinyl)-methyl-5-phenethylhydantoin are decomposed, when digested in dilute hydrochloric acid solution, to 5-phenylhydantoin and 5-phenethylhydantoin, respectively.

4. The initial synthesis of 5-hydroxymethyl-5-phenylhydantoin is reported.

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[13] The identity of XVII was confirmed by comparison with an authentic sample prepared for this purpose; details of this synthesis, and of the essential proof of the assigned structure, will be subsequently reported.

5. Interaction of benzoylcarbinol acetate, potassium cyanide and ammonium carbonate resulted not in the formation of an anticipated hydantoin, but in 4-phenyl-2-oxazolidonecarboxamide.

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