ate ester to stand with an equal volume of methyl iodide in a closed vessel in the absence of light until crystals formed. Washing with dry ether and crystallization from absolute ethanol gave pure salts. It was necessary to store these compounds in a dark area to reduce decomposition.

Acknowledgment. This research was performed on grant B-652 from the National Institutes of Health, Public Health Service, to which organization our sincere thanks are due. We also wish to thank the Union Carbide Chemicals Co. for supplying gratis the *N*,*N*-dimethyl- and *N*,*N*-diethylethanolamines used as intermediates.

KNOXVILLE, TENN.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AND MICROBIOLOGY, UNIVERSITY OF PENNSYLVANIA]

Some Derivatives of Glycineamidine[1]

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Phthalimidoacetonitrile has been converted through an imidoester to some derivatives of glycineamidine. The reactions of phthalimidoacetonitrile and ethyl phthalimidoacetate with ammonia under different conditions have been studied.

The discovery that formylglycineamidine ribotide is an intermediate in the biosynthesis of purines[2] prompted us to attempt the preparation of glycineamidine and derivatives which might serve as replacements or antagonists in biological systems. After our work was initiated, the preparation of glycineamidine dihydrobromide was reported by Mengelberg.[3]

The starting point of our synthesis was phthalimidoacetonitrile (I), which has been prepared in the past by the reaction of potassium phthalimide and chloroacetonitrile,[4] by the dehydration of phathalimidoacetamide,[5] and by the interaction of sodium cyanide and phthalimidomethyl-trimethyl ammonium iodide.[6] We found it convenient to prepare I by the phthaloylation[7] of the readily available aminoacetonitrile bisulfate[8] in pyridine or toluene. A shorter route involves the reaction of methyleneaminoacetonitrile[9] with phthalic anhydrate in refluxing *N*,*N*-dimethylformamide leading to a 64.5% yield of I.

Although earlier efforts have been reported unsuccessful,[4] we were able to convert phthalimidoacetonitrile (I) in 89% yield to the imidoester hydrochloride II using dioxane as the reaction medium. Since then the preparation of phthalimidoacetimido methyl ester hydrochloride has been reported[10] using benzene as the solvent.

When II was dissolved in cold water, a clear solution was obtained which almost immediately started to deposit a crystalline solid which was identified as *N*-phthaloylglycine ethyl ester (VIII). When II was maintained in the molten condition for a few minutes, it was converted into phthalimidoacetamide (IX), which was directly obtained from I by reaction with either concentrated sulfuric acid or with a basic solution of hydrogen peroxide. These observations are in accord with the imidoester structure for II.

When II was treated with an alcoholic solution of ammonia, a compound was obtained which, on the basis of its analysis and infrared spectrum, has been assigned the phthalamidoamidine structure III. Phthalimido compounds are known to give phthalamido compounds on reaction with ammonia.[10] This structure is supported by the observation that on treatment with a mixture of acetic and hydrobromic acids, III affords a compound to which the phthalimidoamidine structure IV has been assigned on the basis of its analysis and infrared spectrum.

When the amido amidine III is added to water a clear solution is first obtained which in the course of a few minutes starts to deposit a compound V which is insoluble in water and the usual organic solvents, but is soluble in dilute acid and alkali. The infrared spectrum of V indicates the lack of the phthalimido grouping and the presence of a salt like structure. The analysis corresponds to the formula $C_{10}H_{11}O_3H_3 \cdot H_2O$. One mole of water could be removed only after very intensive drying. Two plausible structures, V and XI, can be written to correspond to $C_{10}H_{11}N_3O_3$. A comparison with an authentic sample of (*o*-carboxamido)benzamidoacetamide

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(1) Supported in part by U.S.P.H.S. Grant CY-2714 and CY-2790.

(2) B. Levenberg and J. M. Buchanan, *J. Am. Chem. Soc.*, **78**, 504 (1956).

(3) M. Mengelberg, *Ber.*, **89**, 1185 (1956).

(4) A. Sonn and S. Falkenheim., *Ber.* **55**, 2975 (1922); Y. Chi and S. Tshien, *J. Am. Chem. Soc.*, **64**, 90 (1942).

(5) E. Radde, *Ber.*, **55**, 3174 (1922).

(6) R. O. Atkinson, *J. Chem. Soc.*, 1329 (1954).

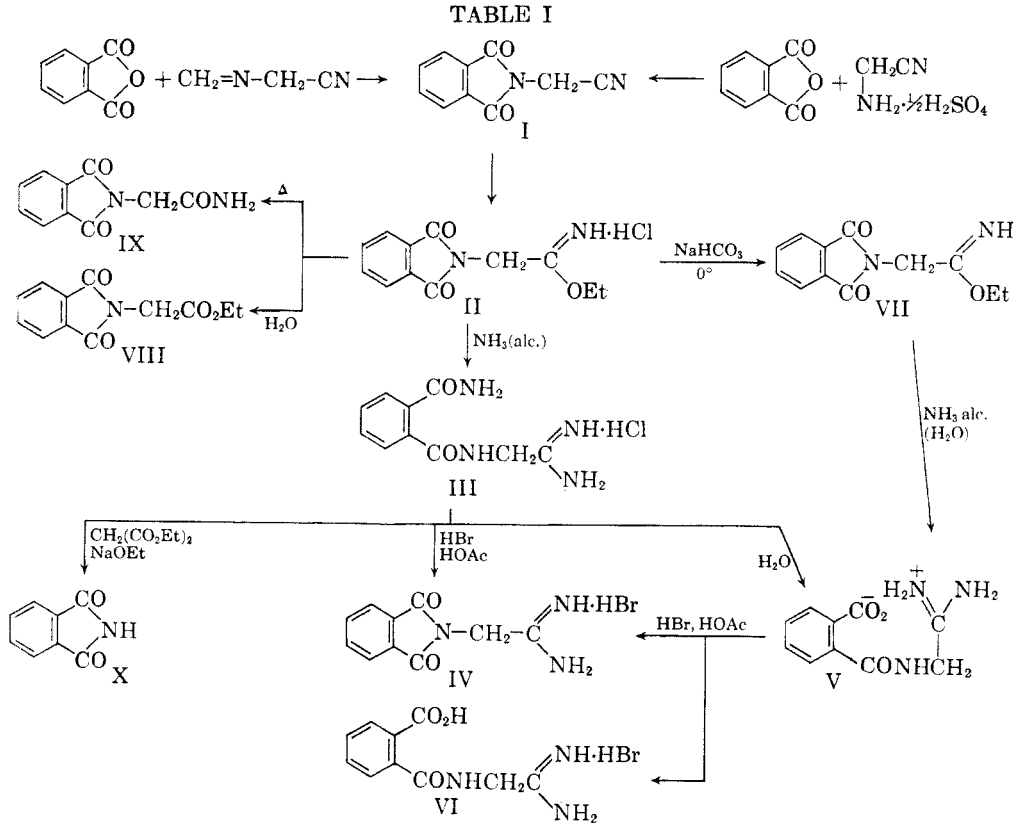
(7) A. K. Bose, F. Greer and C. C. Price, *J. Org. Chem.*, **23**, 1335 (1958).

(8) W. K. Auslow and H. King, *Org. Syntheses*, **Coll. Vol. I**, 298 (1943).

(9) R. Adams and W. D. Langley, *Org. Syntheses*, **Coll. Vol. I**, 355 (1943).

(10) P. E. Peterson and C. Niemann, *J. Am. Chem. Soc.*, **79**, 1389 (1957).

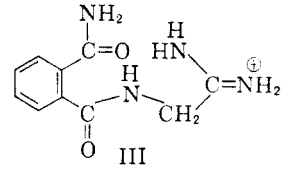
TABLE I



(XI) and the amphoteric nature of the compound ruled out the amide structure XI. Further confirmation for the structure V was obtained when it was found that the reaction with a mixture of hydrobromic acid and acetic acid afforded the amidine VI. The zwitter ion structure is written for V because it failed to react with diazomethane. It is remarkable that the amide group in III is hydrolyzed in water with such rapidity to give the carboxylate ion in V.

Bender, Chow, and Chloupek[11] have recently reported that at *p*H 3 the hydrolysis of phthalamic acid is about 10^5 faster than the hydrolysis of benzamide. This remarkable enhancement of the rate of hydrolysis has been ascribed to intramolecular catalysis involving the participation of the carboxy group. The high rate of hydrolysis of acetyl salicylate[12] and certain imidazole derivatives[13] has also been explained on the basis of intramolecular catalysis.

When a model of III was made, it was found that the nitrogen of the secondary amide group and the nitrogen of the amidine can both come in close proximity of the carbonyl of the primary amide without any strain in the molecule. The extremely high rate of hydrolysis of III is no doubt due to intramolecular catalysis—most probably involving the participation of the amidine group.



When finely powdered II was shaken for 2 min. with a saturated sodium bicarbonate solution and methylene chloride at room temperature, the organic layer afforded ethyl phthalimidoacetate (VIII). However, on lowering the reaction temperature to 0–5°, the product was mainly the free imidoester VII with some VIII as impurity. Pure VII could be obtained easily by repeated crystallization or by chromatography over Florisil.

When the imidoester VII was stirred with alcoholic ammonia a clear solution was obtained in a short time. On evaporating this solution after 2 or 3 days at room temperature, a product was obtained which from its analysis and infrared seemed to be identical with V ($C_{10}H_{11}N_3O_3 \cdot H_2O$). During storage the reaction mixture must have picked up enough moisture from the atmosphere for the conversion of VII to V. Treatment with a mixture of acetic acid and hydrobromic acid converted this intermediate into the known amidine hydrobromide IV with the reformation of the phthalimido ring.

(11) M. L. Bender, Y. L. Chow, and F. Chloupek, *J. Am. Chem. Soc.*, **80**, 5380 (1958).

(12) E. R. Garrett, *J. Am. Chem. Soc.*, **80**, 4049 (1958) and references cited therein.

(13) G. L. Schmir and T. C. Bruice, *J. Am. Chem. Soc.*, **80**, 1173 (1958) and references cited therein.

An attempt was made to check the structures III and V by an alternate synthesis. When phthalimidoacetonitrile (I) was treated with ammonium hydroxide for a short time or with alcoholic ammonia, (*o*-carboxamido)benzamidoacetonitrile (XIII) was obtained. In the hope of obtaining the amide XI, the compound XIII was treated with sulfuric acid and with alkaline hydrogen peroxide solution. The first reaction afforded phthalimidoacetamide (IX) and the second reaction, phthalimide (X). With the aim of obtaining an imidoester, the compound XIII was treated with alcohol and hydrogen chloride, but this resulted only in the regeneration of the phthalimido ring to give I.

An authentic sample of the amide XI was obtained following the method of Brigl and Klenk[14] involving the reaction of ammonium hydroxide with I. It was then found that the same compound was also produced on treatment of I with alcoholic ammonia. The reaction of I and VIII with ammonia under different conditions are summarized in Tables II and III.

TABLE II

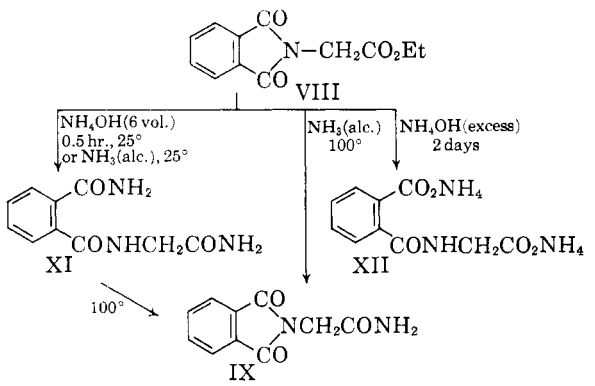
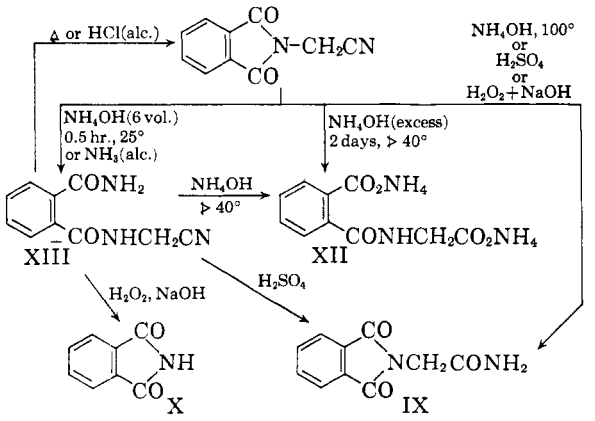


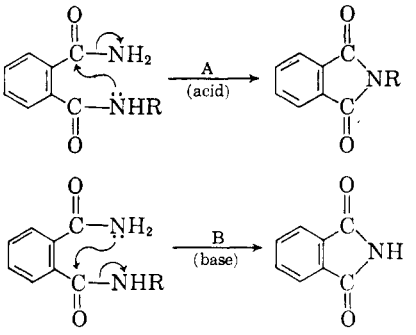
TABLE III



With the intention of preparing a pyrimidine derivative, the compound III was treated with diethyl malonate and sodium ethoxide, but the only product isolated was phthalimide (X).

(14) P. Brigl and E. Klenk, *H. Seyler's Z. Physiol. Chem.*, **131**, 66 (1923).

An *N*-alkylphthalamido compound such as XIV can undergo ring closure in two ways depending on which nitrogen function is eliminated. From the above experiments it appears that an acidic medium favors the path A and a basic medium, the path B.



Compound II showed greater than 50% inhibition of growth of E. coli B at 100γ/ml., while V showed less than 50% inhibition at 1000γ/ml. (Dwight B. McNair Scott and Mary Lou Rogers). These and further biological results of the compounds described herein will be reported elsewhere.

EXPERIMENTAL

Phthalimidoacetonitrile (I). The reaction of aminoacetonitrile bisulfate[8] with phthalic anhydride in pyridine[7] at 80–90° for 1.5 hr. resulted in 85.5% yield of a material that could be used for the next step without further purification.

When 1.7 g. of methyleneaminoacetonitrile[9] and 3.7 g. of phthalic anhydride were heated together at 145–150° for 0.5 hr. and cooled, a dark brown material was obtained from which 1.6 g. (34.5%) of I could be extracted with ether.

A suspension of 1.7 g. of methyleneaminoacetonitrile and 3.7 g. of phthalic anhydride in 25 ml. of *N,N'*-dimethylformamide was heated under reflux for 1.5 hr. when a dark solution was formed which was poured into excess water and the solid that separated was crystallized from ether to give 3 g. (64.5) of I, m.p. 127–129.5°.

On heating together for 1 hr. on a steam bath, a mixture of 1.7 g. of methyleneaminoacetonitrile, 3.7 g. of phthalic anhydride, and 20 ml. of pyridine, a pale yellow solution was obtained which was poured on 150 g. of cracked ice. The nearly colorless crystalline material that separated was collected by filtration, washed with water, and dried when 1.2 g. (25.5%) of I, m.p. 129.5–130.5°, was obtained. The filtrate from above was acidified with hydrochloric acid and set aside. On filtering the next day, 1.08 g. of phthalic acid was obtained.

Ethyl phthalimidoacetimidate hydrochloride (II). A solution of 25 g. of I in 75 ml. of dry dioxane and 6.5 g. of ethanol was cooled in an ice bath and dry hydrogen chloride was bubbled through it for 20 min. The weight of hydrogen chloride absorbed was 15 g. (large excess). After storing overnight at 0–5°, the reaction mixture was filtered and the colorless crystalline product was washed with ether and dried; the yield was 32 g. (89%). An analytical sample, m.p. 258–260° (dec.), was prepared by dissolving this material in the minimum of absolute ethanol, filtering and precipitating with ether.

Anal. Calcd. for $C_{12}H_{13}ClN_2O_3$; C, 53.64; H, 4.88; N, 10.43. Found: C, 53.16; H, 4.79; N, 10.67.

Reactions of ethyl phthalimidoacetimidate hydrochloride (II). (a) *With ammonia.* To a suspension of 15 g. of II in 50 ml. of

ethanol was added 40 ml. of ethanol containing 3 g. of dissolved ammonia. After two days in an ice box the mixture was filtered, yielding 14.5 g. (95.5%) of a colorless solid (III), m.p. 177–178° (dec.).

Anal. Calcd. for $C_{10}H_{13}ClN_4O_2$: C, 46.78; H, 5.09; N, 21.82. Found: C, 46.70; H, 5.01; N, 21.66.

(b) *Hydrolysis.* When the imidoester was added to water, a clear solution was first obtained which started depositing a colorless solid, m.p. 109–111°, within 1 min. In another experiment the imidoester was heated with water and, on cooling, phthaloylglycine ethyl ester, m.p. 111–112°, crystallized in 85% yield.

(c) *Thermal decomposition.* A sample of II was kept in the molten condition for a few minutes. On crystallizing the melt from ethanol, phthalimidoacetamide was obtained.

Principal infrared bands: 2.82, 2.92 and 3.03μ (N—H); 5.62 and 5.82μ (imide carbonyls): 5.95μ (amide CO), 6.20μ (NH_2, primary amide).

Reactions of (o-carboxamido)benzamidoacetamidine hydrochloride (III). (a) When 2 g. of III was shaken with water, a clear solution was formed which, on standing for a few minutes, started to deposit a solid. This solid (1.4 g.) was collected by filtration, washed with ethanol, and dried for 3.5 hr. at 110° under vaccum. The sample so obtained melted at 218–219°, with decomposition and evolution of gas. The infrared spectrum seemed to indicate the presence of water of crystallization.

Anal. Calcd. for $C_{10}H_{11}N_3O_3 \cdot H_2O$: C, 50.20; H, 5.48; N, 17.57. Found: C, 50.26, 50.55; H, 5.63, 5.66; N, 16.92, 17.00.

Another sample showed the following analysis:

Anal. Calcd. for $C_{10}H_{11}N_3O_3 \cdot {}^1/_2H_2O$: C, 52.17; H, 5.25; N, 18.24. Found: C, 52.76; H, 5.28; N, 18.93.

(b) To a solution of 1.8 g. of sodium in 100 ml. of ethanol was added 5.5 g. of III with stirring. Diethyl malonate (3.2 g.) was next added and the stirring continued overnight at room temperature. After removing the solvent from the reaction mixture, a brown solid was obtained which was dissolved in water. On acidifying this solution with hydrochloric acid, 0.5 g. of a colored solid was obtained which gave yellow needles on crystallization from alcohol. This product, m.p. 224–225°, was identified as phthalimide.

Anal. Calcd. for $C_8H_5NO_2$: C, 65.30; H, 3.43; N, 9.52. Found: C, 64.70; H, 3.42; N, 9.39.

(c) A suspension of 2 g. of III in 10 ml. of acetic acid and 5 ml. of hydrobromic acid (48%) was shaken from time to time for 1 hr. and then allowed to stand overnight. The reaction mixture was then filtered to give 0.7 g. of a white crystalline solid, IV, m.p. 262–264° (dec.). This solid was purified by washing with ether.

Anal. Calcd. for $C_{10}H_{10}BrN_3O_2$: C, 42.26; H, 3.55; N, 14.79. Found: C, 42.59; H, 3.68; N, 15.50.

Principal infrared maxima: 2.9, 3.13, 5.65, 5.9, 6.0μ.

On the addition of excess ether to the filtrate from above, 0.55 g. more solid, m.p. 264° (dec.), separated, bringing the total yield of phthalimidoacetamidine hydrobromide (IV) to 56%.

(o-Carboxy)benzamidoacetamidine hydrobromide (VI). Finely powdered V (0.9 g.) was added to a mixture of 6 ml. of acetic acid and 4 ml. of hydrobromic acid (48%). At first a clear solution was obtained but, after a few minutes, a crystalline solid started to separate. After 3 hr. the crystalline product (0.5 g.) was collected by filtration, washed with ether, and dried at room temperature under vacuum. This melted with decomposition at 261°.

Anal. Calcd. for $C_{10}H_{12}BrN_3O_3$: C, 39.70; H, 3.97; N, 13.90. Found: C, 39.98; H, 4.27; N, 14.35.

The infrared spectrum showed an associated hydroxy (and/or N—H) band in the 3μ region and the following bands in the carbonyl region: 5.80, 5.92, 6.0–6.15μ.

Ethyl phthalimidoacetimidate (VII). Finely powdered II (1 g.) was shaken vigorously for 2 min. with a saturated solution of sodium bicarbonate and methylene chloride at room temperature. The organic layer was separated, dried over anhydrous magnesium sulfate, and evaporated. The product so obtained was 0.48 g. of ethyl phthalimidoacetate (VIII), m.p. 110–111°, identified from its infrared spectrum, and from comparison with an authentic sample of VIII. Principal infrared bands of VIII: 5.65, 5.75μ (imide CO); 5.82μ (ester CO).

When this experiment was repeated with 3 g. of II keeping the temperature of the reaction mixture at 0–5° and extending the time of shaking to 15 min., the product was a white solid (2.2 g.), m.p. 154–157°. On several recrystallizations from ether-chloroform or methanol, silky needles, m.p. 159–161°, were obtained.

Principal infrared maxima: 3.0μ (N—H): 5.65 and 5.85μ (imide carbonyls); 6.0μ (C=N).

Anal. Calcd. for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 5.21; N, 12.06. Found: C, 62.14; H, 5.12; N, 12.04.

The desired compound VII can be separated from VIII by chromatography over Florisil. The latter was eluted with petroleum ether (60–65°) acetone (3–6%) and the former (VII) with petroleum ether acetone (9%). Repeated crystallization from methanol is also effective.

Finely powdered VII (1 g.) was left with 50 ml. of alcoholic ammonia solution (about 8% in ammonia) at room temperature. After 1.5 hr. nearly all the solid had dissolved. The reaction mixture was filtered and the filtrate stored at room temperature for 3 days. On evaporating the solution under vacuum at a temperature not exceeding 40°, a gray solid (0.85 g.), m.p. 208–210° (dec.), was obtained. The infrared spectrum was almost identical with that for V. The product, m.p. 218–220°, obtained in a second experiment was washed with ethanol and ether and analyzed, after drying under vacuum at 50°. It was easily soluble in dilute acid and alkali, but insoluble in the usual organic solvents.

Anal. Calcd. for $C_{10}H_{11}N_3O_3 \cdot H_2O$: C, 50.20; H, 5.48; N, 17.57, Found: C, 49.45; H, 6.06; N, 17.11.

The product above (0.45 g.) was treated with 3 ml. of glacial acetic acid and 2 ml. of hydrobromic acid (48%). The clear solution formed was centrifuged and stored at room temperature. After 1 day, ether was added to the reaction mixture and the sides of the flask were scratched. A crystalline solid (0.33 g.) separated. This solid was washed thoroughly with ether and dried. It was identified as the amidine hydrobromide IV from its infrared spectrum.

Reactions of ethyl phthalimidoacetate (VIII) *with ammonia.* (a) A suspension of 2.5 g. of powdered ethyl phthalimidoacetate in 15 ml. of ammonium hydroxide (58%) was stirred vigorously for 15 min. After storage at room temperature for 30 min., 100 ml. of water was added and the mixture was filtered. The solid so obtained was washed with two 50-ml. portions of methanol and one 50 ml. portion of ether. After drying, 1 g. of a white crystalline powder, m.p. 268–264°, dec., was obtained which was identified as (*o*-carboxamido)-benzamidoacetamide (XI) (lit.[11] m.p. 255°, dec.).

Anal. Calcd. for $C_{10}H_{11}N_3O_3$: C, 54.17; H, 5.01, N, 19.01. Found: C, 54.35; H, 4.78; N, 18.68.

Principal infrared bands: 2.94 (sh), 2.97, 3.00 (sh), 3.16μ (N—H/O—HO; 6.02μ (primary amide CO); 6.13μ (secondary amide CO); 6.20μ (NH_2 deformation, primary amide); 6.40μ (NH deformation, secondary amide).

(b) Powdered ethyl phthalimidoacetate (VIII) (2 g.) was dissolved in 50 ml. of ethanol almost saturated with ammonia at room temperature by occasional stirring. The clear solution slowly deposited a white solid (1.25 g.) which was collected by filtration at the end of three days and identified as XI from its infrared spectrum.

(c) A suspension of 5.8 g. of VIII in 100 ml. of ammonium hydroxide was shaken from time to time. After 4 days the clear solution was evaporated on a steam bath and the solid so obtained was crystallized from 95% ethanol. The first crop of 3.8 g. of needle-shaped crystals, m.p. 253–254°, was identified as phthalimidoacetamide (IX). The mother liquor gave a second crop, which appeared to contain some XI also.

When alcoholic ammonia was substituted for ammonium hydroxide the only product obtained was IX.

(d) On leaving 1 g. of VIII and 20 ml. of ammonium hydroxide together for 4 days, a clear solution was obtained which was concentrated under reduced pressure at 35–40°. The crystalline solid (0.3 g.) that separated was collected by filtration, washed with ethanol, and dried. The product, which has been assigned the structure XII, showed the following principal infrared bands: 2.89 (sh), 2.94, 3.08 (sh), 3.16–3.29μ, 5.94, 6.06, 6.23, 6.30 (sh), 6.38–6.48μ.

Anal. Calcd. for $C_{10}H_{15}N_3O_5$: C, 46.69; H, 5.88; N, 16.34. Found: C, 47.01; N, 6.08; N, 15.59.

Reactions of phthalimidoacetonitrile (I) *with ammonia.* (a) Powdered phthalimidoacetonitrile (1.5 g.) was stirred with 9 ml. of ammonium hydroxide (58%) for 20 min. and then filtered. The solid product was washed with small amounts of water and with methyl alcohol and dried. A white powder (0.6 g.), m.p. 160°, was obtained. Further purification by crystallization was not successful. From its analysis and infrared spectrum, this solid was identified as a slightly impure sample of (*o*-carboxamido)benzamidoacetonitrile (XIII).

Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.10; H, 4.46; N, 20.68. Found: C, 58.67; H, 4.38; N, 19.82.

Principal infrared maxima (in μ): 3.02, 3.20 (N—H); 5.97 (C=O, secondary amide); 6.03 (C=O, primary amide); 6.15 (N—H, primary amide); 6.47 (N—H, secondary amide). (b) Powdered phthalimidoacetonitrile (5 g.) was added to 25 ml. of ice cold ethanol saturated with ammonia. In a few minutes a clear solution was obtained which was immediately filtered. The filtrate deposited gradually a nearly colorless crystalline solid which was collected by filtration after 2 hr. washed with ether, and dried. The product, 2.3 g., m.p. 146–147°, dec., was found to be an impure sample of XIII from its infrared spectrum and analysis.

Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.10: H, 4.46; N, 20.68. Found C, 58.66;H, 4.43; N, 19.08.

(c) Powdered I (1 g.) was left overnight with 45 ml. of ammonium hydroxide. The undissolved solid was removed by filtration and the filtrate allowed to stand at room temperature for 2 days. On evaporating this solution under vacuum at 40°, a solid was obtained which, from its infrared spectrum, appeared to be identical with XII.

(d) Phthalimidoacetonitrile (2 g.) and ammonium hydroxide (50 ml.) were left together for 3 days and the resulting clear solution was evaporated on a steam bath. The residue was crystallized from ethanol to give 1 g. of a colorless solid, m.p. 240–242°, dec. The infrared spectrum and the analysis indicated it to be an impure specimen of phthalimidoacetamide.

Anal. Calcd. for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.95; N, 13.72. Found: C, 58.15; H, 4.44; N, 13.60.

(e) A solution of 0.5 g. of phthalimidoacetonitrile in 3 ml. of concentrated sulfuric acid was stored overnight at room temperature and then poured over cracked ice. The solid that separated in a nearly quantitative yield was identified as phthalimidoacetamide (IX) from its melting point and its mixture melting point with an authentic sample prepared from phthaloylglycine ethyl ester.

(f) A mixture of 0.3 g. of I, 30 ml. of ethanol, 10 ml. of 0.1*N* sodium hydroxide solution and 6 ml. of 30% hydrogen peroxide solution was kept at 50–60° for 3 hr. and then concentrated under reduced pressure. The first crop of crystal (0.14 g.) was identified as phthalimidoacetamide.

Reactions of (*o-carboxamido*)*benzamidoacetonitrile* (XIII). (a) On keeping 0.4 g. of XIII in the molten state ammonia was evolved. After 20 min. the melt was cooled, dissolved in ethanol, and the hot solution decolorized with charcoal. After cooling the solution there was obtained 0.3 g. (83%) of a lightly colored material, m.p. 126–128°. Admixture with an authentic sample of phthalimidoacetonitrile (I) did not depress the melting point.

(b) A solution of 0.5 g. of XIII in 3 ml. of concentrated sulfuric acid was stored overnight at room temperature and then poured on crushed ice. The solid that separated was collected by filtration, washed with water, and dried. From its melting point and infrared spectrum the product (0.15 g., 28%) was identified as phthalimidoacetamide (IX).

(c) A solution of 0.2 g. of XIII in 20 ml. of ethanol, 10 ml. of 0.1*N* sodium hydroxide solution and 3 ml. of 30% hydrogen peroxide were mixed together and stored overnight at room temperature. The clear solution was evaporated under vacuum at room temperature and the residue was crystallized from ethanol, when 0.05 g. of phthalimide, m.p. 232–234°, was obtained.

(d) A suspension of 2.5 g. of XIII in 100 ml. of dry benzene and 1 ml. of ethanol was cooled in an ice bath and hydrogen chloride passed through it for 10 min. After storing overnight at 0–5°, the reaction mixture was filtered and the solid so obtained was washed with ether and benzene. The infrared spectrum showed the presence of the phthalimido ring. This compound was impure phthalimidoacetonitrile since, on boiling with water, it gave an impure sample of phthalimidoacetamide and on treatment with alcoholic ammonia, it afforded impure XIII, for which the following analysis was obtained.

Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.10; H, 4.46; N, 20.68. Found: C, 58.78; H, 4.36; N, 19.30.

(e) A suspension of 0.5 g. of XIII in 50 ml. of concentrated ammonium hydroxide was left at room temperature for 3 days by which time a clear solution was obtained. This solution was evaporated under reduced pressure at 50° and the residue was washed with ethanol to give 0.15 g. of a light brown powder which, from its infrared spectrum, appeared to be identical with XII.

Acknowledgment. Thanks are due to the Upjohn Co. for the microanalysis and infrared spectrum of several compounds.

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