Ring Closure Reactions with Nitriles. I. Formation of Pyrrolo[2,1-*c*][1,2,4]benzothiadiazines and Pyrrolo[1,2-*a*]quinazolines

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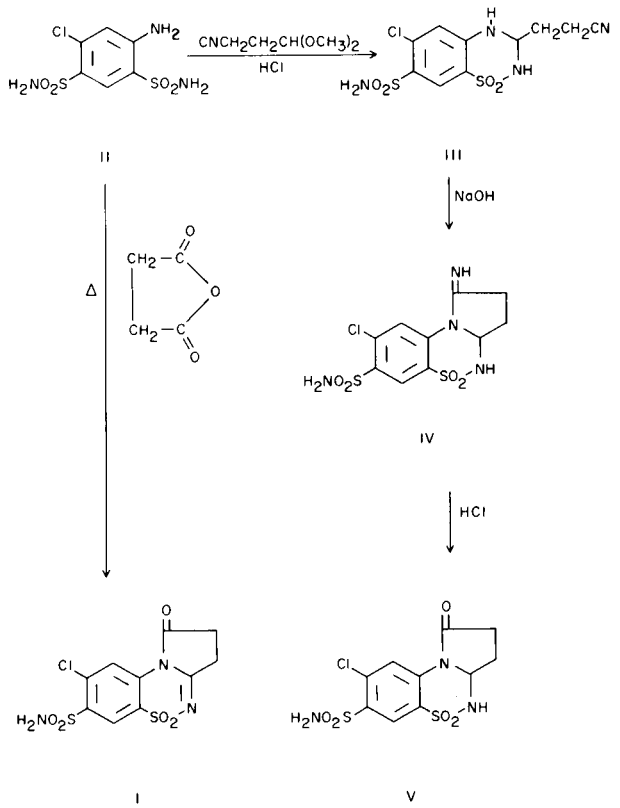
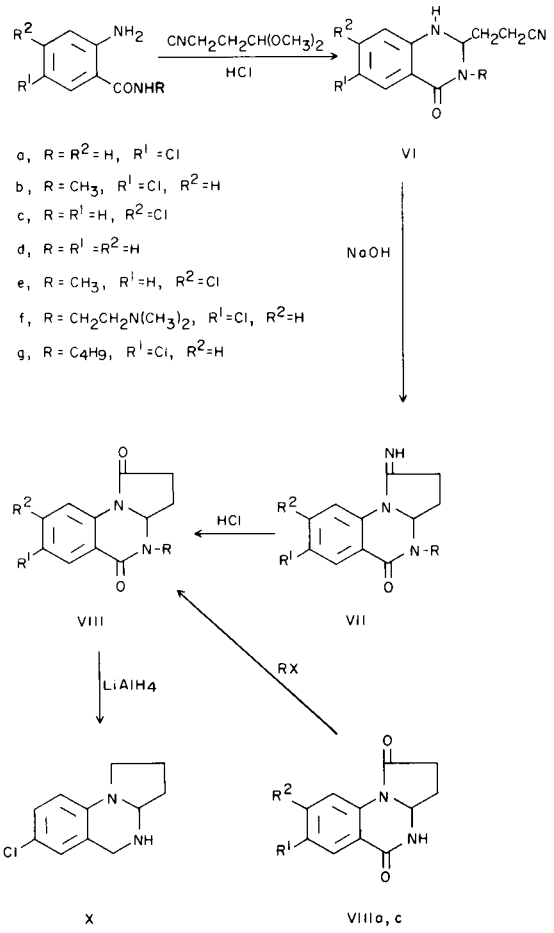
Pyrrolo[2,1-*c*][1,2,4]benzothiadiazines have been prepared from the reactions of *o*-aminobenzenesulfonamides with γ-cyanopropionaldehydes. Pyrrolo[1,2-*a*]quinazolines have been prepared from the reaction of anthranilamides with either γ-cyanopropionaldehyde or succinic anhydride. The cyclization of a 4-oxo-2-quinazolinepropionic acid has produced a pyrrolo[1,2-*a*]quinazoline and the isomeric pyrrolo[2,1-*b*]quinazoline.

Our interest in fused ring systems containing 1,2,4-benzothiadiazine 1,1-dioxides (1,2) has been extended to fused ring systems containing quinazolin-4-ones. We now describe some additional syntheses of pyrrolo[2,1-*c*]-[1,2,4]benzothiadiazines as well as the extension of these reactions to the formation of pyrrolo[1,2-*a*]quinazolines. To the already reported synthesis (1) of 8-chloro-2,3-dihydro-1-oxo-1*H*-pyrrolo[2,1-*c*][1,2,4]benzothiadiazine-7-sulfonamide 5,5-dioxide (I) by the fusion of 4-amino-6-chloro-*m*-benzenedisulfonamide (II) with succinic anhydride, we add an alternative synthesis of a dihydro derivative of I.



The reaction of II with γ-cyanopropionaldehyde dimethyl acetal at room temperature in the presence of acid formed the 3-cyanoethyl-3,4-dihydro-1,2,4-benzothiadiazine (III). When treated *in situ* with base, III underwent ring closure to form the acid-soluble compound 8-chloro-2,3,3a,4-tetrahydro-1-imino-1*H*-pyrrolo[2,1-*c*][1,2,4]-benzothiadiazine-7-sulfonamide 5,5-dioxide (IV). The conversion of the nitrile (III) to the cyclized compound IV was indicated by absence of absorption of the -C≡N group in the infrared and formation of a peak at 6.08 μ indicative of a -C=N- group. The hydrolysis of compound IV in acid produced 8-chloro-2,3,3a,4-tetrahydro-1-oxo-1*H*-pyrrolo[2,1-*c*][1,2,4]benzothiadiazine-7-sulfonamide 5,5-dioxide (V).

Analogous reactions were found to take place with anthranilamides, forming the corresponding 2-(2-cyanoethyl)-4(3*H*)-quinazolinones (VI), 1-iminopyrrolo-[1,2-*a*]-quinazolin-5(4*H*)-ones (VII), and pyrrolo[1,2-*a*]quinazoline-1,5-diones (VIII). For example, the reaction of 5-chloroanthranilamide and γ-cyanopropionaldehyde dimethyl acetal in the presence of acid produced 6-chloro-2-(2-cyanoethyl)-1,2-dihydro-4(3*H*)-quinazolinone (VIa). Compound VIa subsequently underwent ring closure in base to 7-chloro-1,2,3,3a-tetrahydro-1-iminopyrrolo[1,2-*a*]quinazolin-5(4*H*)-one (VIIa), and VIIa was hydrolized in acid to 7-chloro-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (VIIIa). As with the reactions of the analogous 1,2,4-benzothiadiazine, the conversions of VI to the imines (VII) were indicated by the absence of -C≡N absorption in the infrared. Compound VIIa was soluble in dilute hydrochloric acid and reacted with chloroacetic anhydride to form a 1-acetylimino derivative (IX).



Several pyrrolo[1,2-*a*]quinazoline-1,5-diones (VIIIb,e,f) were also prepared by alkylation of the pyrrolo[1,2-*a*]-quinazoline-1,5-diones (VIIIa,c) in which the 4-nitrogen was unsubstituted.

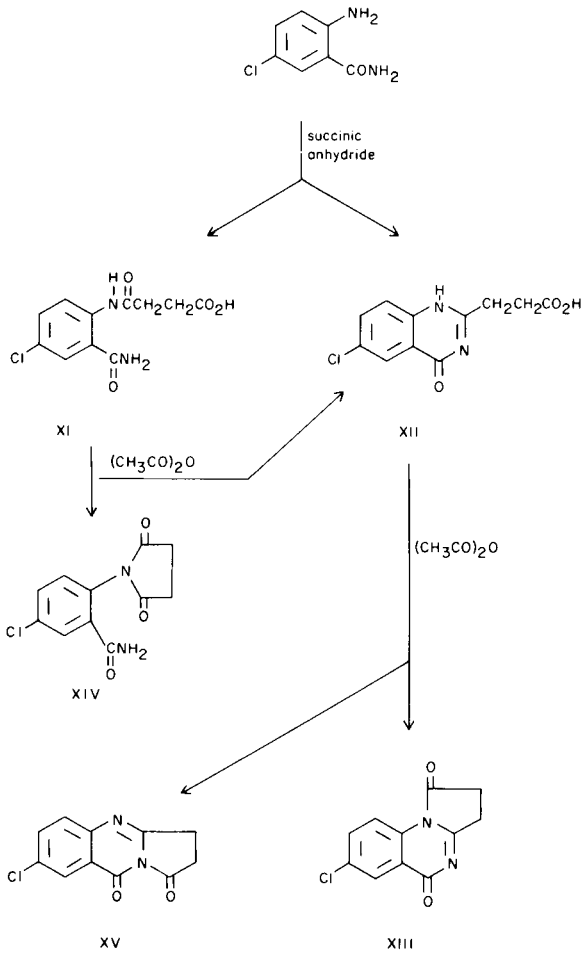
The possibility that VII had a linear rather than an angular structure was ruled out when VIIIb, formed by methylation of VIIIa, was shown to be identical with a sample prepared unambiguously by cyclization of 5-chloro-*N*-methylanthranilamide with γ-cyanopropionaldehyde dimethyl acetal.

The reduction of compound VIIIa with lithium aluminum hydride gave the tricyclic diamine (7-chloro-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinazoline, X).

The reactions of succinic anhydride with the anthranilamides did not proceed as readily as with the 4-amino-*m*-benzenedisulfonamides. From the reaction of 5-chloroanthranilamide with succinic anhydride in dimethylformamide at 150° only 2′-carbamoyl-4′-chlorosuccinanilic acid (XI) was isolated, and a fusion reaction at 200° produced 6-chloro-1,4-dihydro-4-oxo-2-quinazolinepropionic acid (XII) instead of the tricyclic pyrrolo[1,2-*a*]-quinazoline. An attempt to prepare 7-chloro-2,3-dihydropyrrolo[1,2-*a*]quinazoline-1,5-dione (XIII) by the reaction of XI with acetic anhydride produced XII together with a non-acidic isomer, 5-chloro-2-succinamidobenzamide (XIV). However, when XII was treated with acetic anhydride, ring closure was effected, but two isomeric compounds were obtained, XIII and the linear tricyclic compound 7-chloro-2,3-dihydropyrrolo[2,1-*b*]quinazoline-1,9-dione (XV). Only the angular tricyclic compound had been isolated from the analogous reactions previously reported (1).

The correct structures of the isomers were ascertained from the infrared and nmr spectra. Compound XIII had carbonyl absorption peaks at 5.64 and 5.99 μ, whereas XV had carbonyl peaks at 5.61 and 5.86 μ, the shift to lower wavelength being attributed to the CO-N-CO grouping.

A comparison of the nmr spectra of XIII and XV revealed a considerable difference in the aromatic region. In XV the aromatic proton adjacent to the 5-nitrogen had a normal value of δ 7.65, whereas in XIII the corresponding *ortho* proton was shifted downfield to δ 8.90. The analogous pyrrolo[2,1-*c*][1,2,4]benzothiadiazine (I) (1)



also had a large downfield shift (δ 8.95) for the corresponding *ortho* proton. Such a downfield shift of an *ortho* proton due to the orientation of the carbonyl group toward the phenyl ring has recently been discussed (3,4). Thus, the large downfield shift in XIII, produced by the deshielding from the adjacent carbonyl group, verified the fact that XIII is the angular isomer.

EXPERIMENTAL (5)

6-Chloro-3-(2-cyanoethyl)-3,4-dihydro-2*H*-1,2,4-benzothiadiazine-7-sulfonamide 1,1-Dioxide (III).

A mixture of 15 g. of 4-amino-6-chloro-*m*-benzenedisulfonamide, 11.0 g. of γ-cyanopropionaldehyde dimethyl acetal, 200 ml. of ethanol, and 100 ml. of 1*N* hydrochloric acid was heated under reflux for 2 hours. The reaction mixture was cooled and diluted with 300 ml. of water. There was filtered off 12.8 g. of product which on recrystallization from alcohol-water had a m.p. of 218-220°, λ max (potassium bromide), 4.47 μ.

Anal. Calcd. for $C_{10}H_{11}ClN_4O_4S_2$: C, 34.24; H, 3.16; N, 15.97; Cl, 10.11; S, 18.28. Found: C, 34.37; H, 2.79; N, 15.75; Cl, 10.10; S, 17.90.

8-Chloro-2,3,3a,4-tetrahydro-1-imino-1*H*-pyrrolo[2,1-*c*][1,2,4]-benzothiadiazine-7-sulfonamide 5,5-Dioxide (IV).

To a mixture of 11.0 g. of III in 400 ml. of water was added 40 ml. of 4 *N* sodium hydroxide. The resultant solution was stirred for 1 hour and acidified with acetic acid. The product (9.0 g.), m.p. 225-226°, was purified by dissolving in dilute hydrochloric acid, filtering from impurities, and reprecipitating with ammonium hydroxide. The pure compound had a m.p. of 230-231°, λ max (potassium bromide), 6.08 μ.

Anal. Calcd. for $C_{10}H_{11}ClN_4O_4S_2$: C, 34.24; H, 3.16; N, 15.97; Cl, 10.11; S, 18.28. Found: C, 34.31; H, 3.32; N, 15.47; Cl, 10.10; S, 17.80.

8-Chloro-2,3,3a,4-tetrahydro-1-oxo-1*H*-pyrrolo[2,1-*c*][1,2,4]-benzothiadiazine-7-sulfonamide 5,5-Dioxide (V).

A solution of 3.0 g. of IV in 100 ml. of 1 *N* hydrochloric acid was heated on the steam bath for 1 hour. The reaction mixture was cooled and the solid collected and washed with alcohol to give 2.4 g. of product, m.p. 287-288° dec., λ max (potassium bromide), 5.83 μ.

Anal. Calcd. for $C_{10}H_{10}ClN_3O_5S_2$: C, 34.14; H, 2.87; N, 11.94; Cl, 10.08; S, 18.23. Found: C, 34.30; H, 3.13; N, 12.49; Cl, 10.00; S, 17.70.

6-Chloro-2-(2-cyanoethyl)-1,2-dihydro-4(3*H*)-quinazoline (VIa).

To a mixture of 17.0 g. of 5-chloroanthranilamide, 15.0 g. of γ-cyanopropionaldehyde dimethyl acetal, 100 ml. of ethanol, and 50 ml. of water was added slowly 100 ml. of 2.4 *N* hydrochloric acid. The solution was stirred for several hours, during which time a solid separated out. There was obtained 22.0 g. of solid which after recrystallization from ethanol had a m.p. of 186-188°, λ max (potassium bromide), 4.49, 5.98 μ.

Anal. Calcd. for $C_{11}H_{10}ClN_3O$: C, 56.05; H, 4.27; N, 17.85; Cl, 15.05. Found: C, 56.00; H, 4.59; N, 18.05; Cl, 14.90.

6-Chloro-2-(2-cyanoethyl)-1,2-dihydro-3-methyl-4(3*H*)-quinazolinone (VIb).

This compound m.p. 142-144°, was prepared from 5-chloro-*N*-methylanthranilamide and γ-cyanopropionaldehyde dimethyl acetal according to the procedure for VIa.

Anal. Calcd. for $C_{12}H_{12}ClN_3O$: C, 57.70; H, 4.85; N, 16.82; Cl, 14.20. Found: C, 57.45; H, 4.48; N, 16.30; Cl, 13.73.

7-Chloro-2-(2-cyanoethyl)-1,2-dihydro-4(3*H*)-quinazolinone (VIc).

This compound, m.p. 173-175°, was prepared from 4-chloroanthranilamide and γ-cyanopropionaldehyde dimethyl acetal according to the procedure for VIa.

Anal. Calcd. for $C_{11}H_{10}ClN_3O$: C, 56.06; H, 4.28; N, 17.83. Found: C, 55.92; H, 4.14; N, 18.00.

7-Chloro-1,2,3,3a-tetrahydro-1-iminopyrrolo[1,2-*a*]quinazolin-5-(4*H*)-one (VIIa).

To a mixture of 16.0 g. of VIa in 210 ml. of ethanol was added 21 ml. of 4 *N* sodium hydroxide. The solution was stirred for several hours, then diluted with water. The resultant precipitate was filtered and washed with water and with ethanol, giving 9.7 g. of VIIa. Recrystallization from acetonitrile gave a pure compound, m.p. 226-227°, λ max (potassium bromide), 5.91, 6.09 μ.

Anal. Calcd. for $C_{11}H_{10}ClN_3O$: C, 56.05; H, 4.27; N, 17.85; Cl, 15.05. Found: C, 56.09; H, 4.13; N, 18.05; Cl, 15.0.

7-Chloro-1-imino-1,2,3,3a-tetrahydro-4-methylpyrrolo[1,2-*a*]quinazolin-5(4*H*)-one (VIIb).

This compound, m.p. 133-135°, was prepared from VIb and sodium hydroxide according to the procedure for VIIa.

Anal. Calcd. for $C_{12}H_{12}ClN_3O$: C, 57.70; H, 4.85; N, 16.82; Cl, 14.20. Found: C, 57.79; H, 4.51; N, 16.56; Cl, 14.20.

8-Chloro-1,2,3,3a-tetrahydro-1-iminopyrrolo[1,2-*a*]quinazolin-5(4*H*)-one (VIIc).

This compound, m.p. 230-232°, was prepared from VIc and sodium hydroxide according to the procedure for VIIa.

Anal. Calcd. for $C_{11}H_{10}ClN_3O$: C, 56.06; H, 4.28; N, 17.82; Cl, 15.05. Found: C, 55.93; H, 4.05; N, 18.06; Cl, 14.80.

1,2,3,3a-Tetrahydro-1-iminopyrrolo[1,2-*a*]quinazolin-5(4*H*)-one (VIId).

A mixture of 12.0 g. of anthranilamide, 12.0 g. of γ-cyanopropionaldehyde dimethyl acetal 0.5 ml. of 6 *N* hydrochloric acid, and 100 ml. of dimethoxyethane was refluxed for 18 hours. The solvent was removed *in vacuo* and the residue dissolved in a mixture of 100 ml. of ethanol and 30 ml. of 4 *N* sodium hydroxide. Upon dilution with 100 ml. of water and chilling, 11.0 g. of solid, m.p. 173-175°, precipitated out. Two recrystallizations from acetonitrile raised the m.p. of VIId to 194-196°,

Anal. Calcd. for $C_{11}H_{11}N_3O$: C, 65.67; H, 5.51; N, 20.88. Found: C, 65.68; H, 5.56; N, 21.08.

7-Chloro-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (VIIIa).

A solution of 7.0 g. of VIIa in 150 ml. of 1 *N* hydrochloric acid was heated on the steam bath for 4 hours and then chilled. There was collected 4.0 g. of product, m.p. 223-225°, which after recrystallization from acetonitrile had a m.p. of 226-227°, λ max (potassium bromide), 5.79, 5.96 μ.

Anal. Calcd. for $C_{11}H_9ClN_2O_2$: C, 55.83; H, 3.83; N, 11.84; Cl, 14.95. Found: C, 56.04; H, 3.96; N, 11.83; Cl, 14.90.

7-chloro-2,3,3a,4-tetrahydro-4-methylpyrrolo[1,2-*a*]quinazoline-1,5-dione (VIIIb).

Method A.

Compound VIIIb, m.p. 142-144°, was prepared from VIIb and hydrochloric acid according to the procedure for VIIIa.

Anal. Calcd. for $C_{12}H_{11}ClN_2O_2$: C, 57.49; H, 4.42; N, 11.13;

Cl, 14.15. Found: C, 57.18; H, 4.26; N, 10.70; Cl, 14.00.

Method B.

To 0.55 g. of 55% sodium hydride in 25 ml. of dimethylformamide was added 3.0 g. of VIIIa in 30 ml. of dimethylformamide. The mixture was warmed at 70° for 45 minutes, then cooled, and 2.0 g. of methyl iodide was added. Stirring was maintained for 30 minutes, little water was added, and the mixture was concentrated to dryness. The residue was washed with water and recrystallized twice from ethanol to give 1.2 g. of VIIIb, m.p. 143-145°.

8-Chloro-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (VIIIc).

This compound, m.p. 271-273°, was prepared from VIIc and hydrochloric acid according to the procedure for VIIIa.

Anal. Calcd. for $C_{11}H_9ClN_2O_2$: C, 55.83; H, 3.83; N, 11.84; Cl, 14.99. Found: C, 55.83; H, 3.83; N, 11.65; Cl, 14.90.

8-Chloro-2,3,3a,4-tetrahydro-4-methylpyrrolo[1,2-*a*]quinazoline-1,5-dione (VIIIe).

This compound m.p. 170-172°, was prepared from VIIIc and methyl iodide according to the procedure for VIIIb, Method B.

Anal. Calcd. for $C_{12}H_{11}ClN_2O_2$: C, 57.49; H, 4.42; N, 11.18; Cl, 14.10. Found: C, 57.21; H, 4.20; N, 10.99; Cl, 14.10.

7-Chloro-4-(2-dimethylaminoethyl)-2,3,3a,4-tetrahydropyrrolo-[1,2-*a*]quinazoline-1,5-dione (VIIIf).

This compound, m.p. 99-102°, was prepared from VIIIa and dimethylaminoethyl chloride according to the procedure for VIIIb, Method B.

Anal. Calcd. for $C_{15}H_{18}ClN_3O_2$: C, 58.54; H, 5.89; N, 13.65; Cl, 11.52. Found: C, 59.00; H, 5.64; N, 13.69; Cl, 11.40.

4-Butyl-7-chloro-2,3,3a,4-tetrahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (VIIIg).

N-Butyl-5-chloroanthranilamide, m.p. 116-118° was prepared from the reaction of *n*-butylamine with 5-chloroisotoic anhydride. A solution of 18 g. of γ-cyanopropionaldehyde (prepared by refluxing 2,4,6-tris(2-cyanoethyl)trioxane in water in the presence of Dowex 50W-X8) and 150 ml. of water was added to a solution of 33 g. of *N*-butyl-5-chloroanthranilamide, 30 ml. of concentrated hydrochloric acid, and 300 ml. of water. The mixture was stirred at room temperature for 1 hour, the solvent was removed *in vacuo*, and the residue was dissolved in alcohol. The solution was made alkaline with excess sodium hydroxide and the solvent was decanted from the resultant oily residue, which was then extracted with ether. The ether was removed and the residue was extracted with 1 *N* hydrochloric acid. The acid solution was heated on the steam bath for 4 hours and extracted with ether. After removal of the ether the residue was recrystallized from cyclohexane, giving 2.0 g. of product, m.p. 79-81°.

Anal. Calcd. for $C_{15}H_{17}ClN_2O_2$: C, 61.54; H, 5.85; N, 9.57; Cl, 12.11. Found: C, 61.54; H, 5.58; N, 10.03; Cl, 12.10.

7-Chloro-1-chloroacetylamino-1,2,3,3a-tetrahydropyrrolo[1,2-*a*]-quinazolin-5(4*H*)-one (IX).

A mixture of 2.0 g. of VIIa and 5.0 g. of chloroacetic anhydride was heated on the steam bath for 5 minutes. To the melt was added 30 ml. of dioxane and the reaction mixture was heated under reflux for 15 minutes. On cooling there was collected 1.2 g. of IX, m.p. 192-194°, which melted at 194-196° after recrystallization from ethanol.

Anal. Calcd. for $C_{13}H_{11}Cl_2N_3O_2$: C, 50.02; H, 3.55; N, 13.46; Cl, 22.71. Found: C, 50.52; H, 3.57; N, 13.05; Cl, 22.50.

1-Acetylamino-1,2,3,3a-tetrahydropyrrolo[1,2-*a*]quinazolin-5(4*H*)-one.

A mixture of 3.0 g. of VIId and 80 ml. of acetic anhydride was heated under reflux for 2-3 minutes and concentrated to about one-third the original volume. On cooling there was obtained 1.6 g. of product, which upon recrystallization from acetonitrile had a m.p. of 204-206°.

Anal. Calcd. for $C_{13}H_{13}N_3O_2$: C, 64.18; H, 5.39; N, 17.28. Found: C, 64.00; H, 5.37; N, 16.90.

7-Chloro-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinazoline (X).

To a suspension of 3.0 g. of lithium aluminum hydride in 100 ml. of tetrahydrofuran was added 3.9 g. of VIIIa. The reaction mixture was refluxed for 2 hours and carefully treated with water. The mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was dissolved in dilute acetic acid, filtered from impurities, and the product (2.0 g.) precipitated with sodium carbonate. After recrystallization from hexane, X had a m.p. of 96-97°.

Anal. Calcd. for $C_{11}H_{13}ClN_2$: C, 63.31; H, 6.28; N, 13.43; Cl, 16.99. Found: C, 62.91; H, 6.18; N, 13.32; Cl, 16.99.

2′-Carbamoyl-4′-chlorosuccinanilic Acid (XI).

To a mixture of 25.0 g. of 5-chloroanthranilamide in 100 ml. of dimethylformamide was added 20 g. of succinic anhydride. The reaction mixture was gradually heated to 150° over 2 hours, cooled, and diluted with water. There was collected 35 g. of XI, m.p. 222-224°. Recrystallization from methoxyethanol gave pure XI, m.p. 225-227°.

Anal. Calcd. for $C_{11}H_{11}ClN_2O_4$: C, 48.81; H, 4.10; N, 10.35; Cl, 13.10. Found: C, 48.78; H, 4.20; N, 9.99; Cl, 13.00.

6-Chloro-1,4-dihydro-4-oxo-2-quinazolinepropionic Acid (XII).

Method A.

A mixture of 17.0 g. of 5-chloroanthranilamide and 12.0 g. of succinic anhydride was heated to 190-200°. The resultant melt bubbled for 15 minutes, then solidified. The reaction mixture was cooled, triturated with ethanol, and the solid recrystallized from dimethylformamide-water. There was obtained 7.8 g. of XII, m.p. 254-257°.

Anal. Calcd. for $C_{11}H_9ClN_2O_3$: C, 52.29; H, 3.59; N, 11.09; Cl, 14.03. Found: C, 52.51; H, 3.57; N, 11.38; Cl, 13.80.

Method B.

A mixture of 30.0 g. of XI in 150 ml. of dimethylformamide and 70 ml. of acetic anhydride was kept at room temperature for 2 weeks. The solution was diluted with 200 ml. of benzene and 200 ml. of cyclohexane and chilled. There was obtained 4.0 g. of crude XII, m.p. 245° dec. From the filtrate, on addition of more benzene and cyclohexane, there was obtained 7.9 g. of 5-chloro-2-succinamidobenzamide (XIV), m.p. 189-191°. Recrystallization from water and from ethanol gave pure XIV, m.p. 210-211°, λ max (potassium bromide), 6.00-6.10 (broad, $CONH_2$) and 5.67, 5.87 μ (CONCO).

Anal. Calcd. for $C_{11}H_9ClN_2O_3$: C, 52.29; H, 3.59; N, 11.09; Cl, 14.03. Found: C, 52.66; H, 3.44; N, 10.59; Cl, 14.00.

7-Chloro-2,3-dihydropyrrolo[1,2-*a*]quinazoline-1,5-dione (XIII).

A mixture of 24 g. of XII, 65 ml. of dimethylformamide, and 35 ml. of acetic anhydride was heated on the steam bath for 25 minutes. The reaction mixture was cooled and filtered and the solid was washed with ethanol to give 18 g. of product, m.p. 224-226°. Recrystallization from dimethylformamide gave XIII, m.p. 230-233°, λ max (potassium bromide), 5.64, 5.99 μ. In the

nmr the 1,2,4-aromatic protons had the following values: 1, δ 8.90 (doublet, J = 9.0 cps); 2, δ 7.80 (doublet of doublets, J = 9.0, 2.5 cps); 4, δ 8.02 (doublet, J = 2.5 cps).

Anal. Calcd. for $C_{11}H_7ClN_2O_2$: C, 56.30; H, 3.01; N, 11.94; Cl, 15.11. Found: C, 56.29; H, 2.80; N, 11.98; Cl, 14.90.

2,3-Dihydropyrrolo[1,2-*a*]quinazoline-1,5-dione.

A mixture of 9.2 g. of 1,4-dihydro-4-oxo-2-quinazolinepropionic acid, 50 ml. of dimethylformamide, and 20 ml. of acetic anhydride was stirred for 48 hours at room temperature. The reaction mixture was chilled and 5.0 g. of product, m.p. 202-203°, was collected.

Anal. Calcd. for $C_{11}H_8N_2O_2$: C, 65.99; H, 4.03; N, 14.00. Found: C, 65.69; H, 4.12; N, 13.66.

7-Chloro-2,3-dihydropyrrolo[2,1-*b*]quinazoline-1,9-dione (XV).

A mixture of 24.0 g. of XII, 70 ml. of dimethylformamide, and 35 ml. of acetic anhydride was heated on the steam bath for 45 minutes and cooled, affording 14.0 g. of a precipitate, m.p. 197-204°. The carbonyl absorption peaks in the infrared indicated a mixture of about two parts of XIII to one part of XV. Recrystallization from acetonitrile gave 4.7 g. of XV, m.p. 225-227°, λ max (potassium bromide), 5.61, 5.86 μ. In the nmr the 1,2,4-aromatic protons had the following values: 1, δ 7.65 (doublet, J = 9.0 cps); 2, δ 7.90 (doublet of doublets, J = 9.0, 2.0 cps); 4, δ 8.10 (doublet, J = 2.0).

Anal. Calcd. for $C_{11}H_7ClN_2O_2$: C, 56.30; H, 3.01; N, 11.94. Cl, 15.11. Found: C, 56.40; H, 2.83; N, 11.97; Cl, 15.00.

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(4) Although the shift in anilides, unlike that in unsubstituted anilines, is downfield 0.1-0.3 ppm to the δ 7.2-7.4 region (*Cf.* R. E. Carter, *Acta Chem. Scand.*, 21, 75-86 (1967)), we have found that acetanilides which have one *ortho* position substituted have an unusually large downfield shift for the remaining *ortho* proton. For example, the following are nmr values (in deuteriochloroform) for *ortho* protons: 2′-benzoyl-2,4′-dichloroacetanilide, δ = 8.3 (J = 9.5 cps), S. C. Bell, T. S. Sulkowski, C. Gochman, and S. J. Childress, *J. Org. Chem.*, 27, 562 (1962); 2′-(α-acetoxymethyliminobenzyl)-4′-chloroacetanilide, δ = 8.6 (J = 9.0 cps), S. C. Bell and P. H. L. Wei, *ibid.*, 30, 3576 (1965); 2-*N*-(acetoxyacetamido)-2′-benzoyl-4′-chloroacetanilide, δ = 8.45 (J = 9.0 cps), S. C. Bell, R. J. McCaully, and S. J. Childress, *Tetrahedron Letters*, 33, 2889 (1965).

(5) Melting points are uncorrected. Nmr spectra were run in DMSO-d_6 using tetramethylsilane as the internal reference. Infrared spectra were determined in potassium bromide pellets.

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