Pyrolysis of 2-(2-Azidobenzoyl)pyridine and 3-(2-Pyridyl)-2,1-benzisoxazoles. Preparation and Chemistry of Some Pyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salts (1)

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The pyrolysis of 3-(2-pyridyl)-2,1-benzisoxazoles **5A**, **5B**, and **5C** (**A**: unsubstituted; **B**: 5-bromo; **C**: 5,7-dibromo) at about 215° afforded 5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium hydroxide inner salt **6A**, the 2-bromo (**6B**) and the 2,4-dibromo (**6C**) compounds respectively in high yields. X-ray crystallographic analysis of **6B** unambiguously confirmed the structure. The benzisoxazoles **5A-5C** were obtained from the pyrolysis of the corresponding 2-(2-azidobenzoyl)pyridines **2A-2C** at about 112°. While **2A** and **2B** afforded the corresponding benzisoxazoles **5a** and **5B** in 82% and 51% yields respectively, 2-(2-azido-3,5-dibromobenzoyl)pyridine (**2C**) afforded a mixture of the benzisoxazole **5C** and the tricyclic compound **6C**, isolated in 43% and 41% yields respectively.

The properties of the novel mesoionic compounds of type **6**, their oxidative and reductive ring cleavage products together with alkylation and catalytic hydrogenation products are described. Electrophilic substitutions, substitutions in position 11 *via* the 11-thiones **11** and other miscellaneous transformations of **6** are also presented.

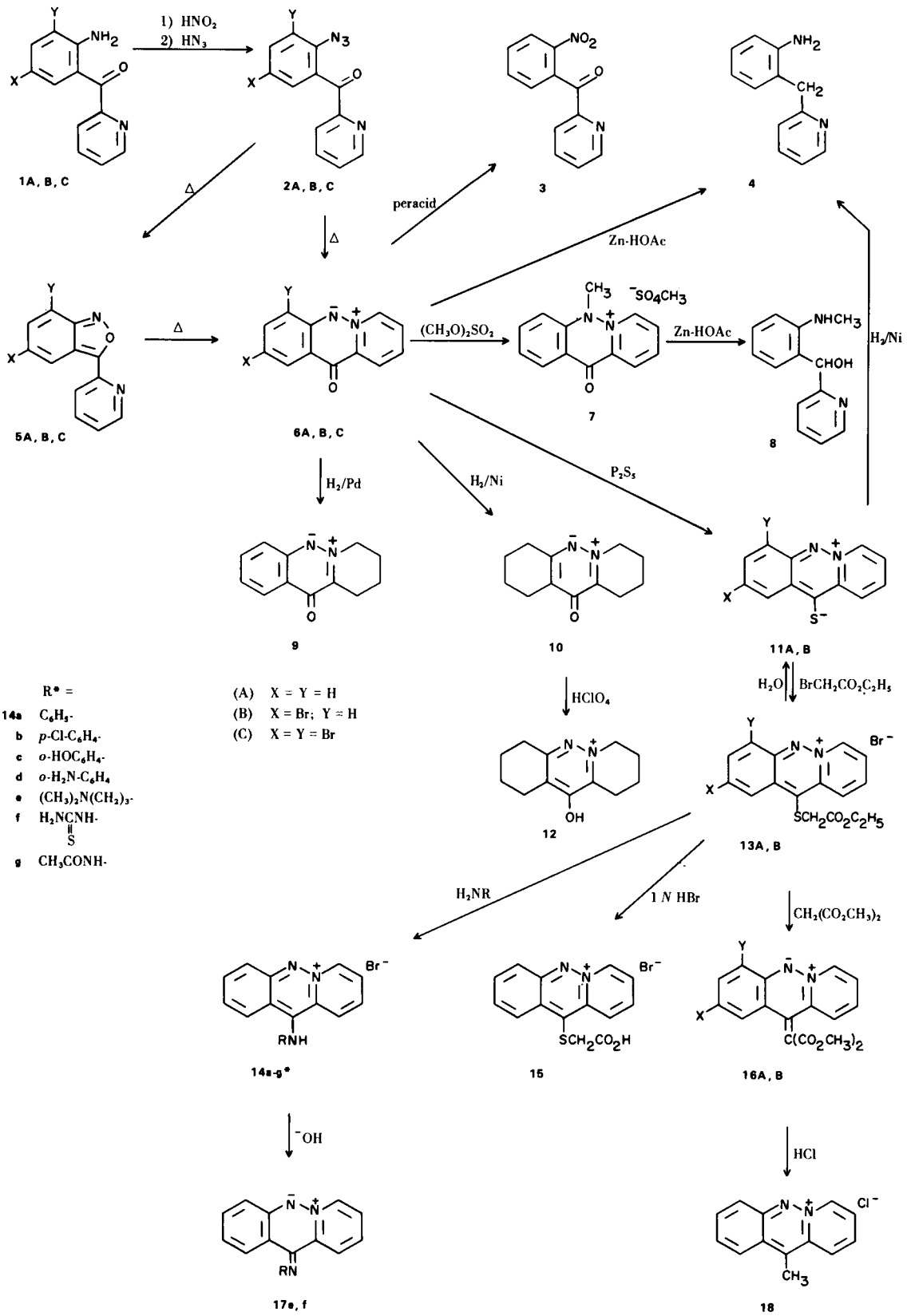
We wish to report an efficient preparation of 5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium hydroxide inner salts (2) **6** and some chemical transformations of this novel (3) mesoionic system.

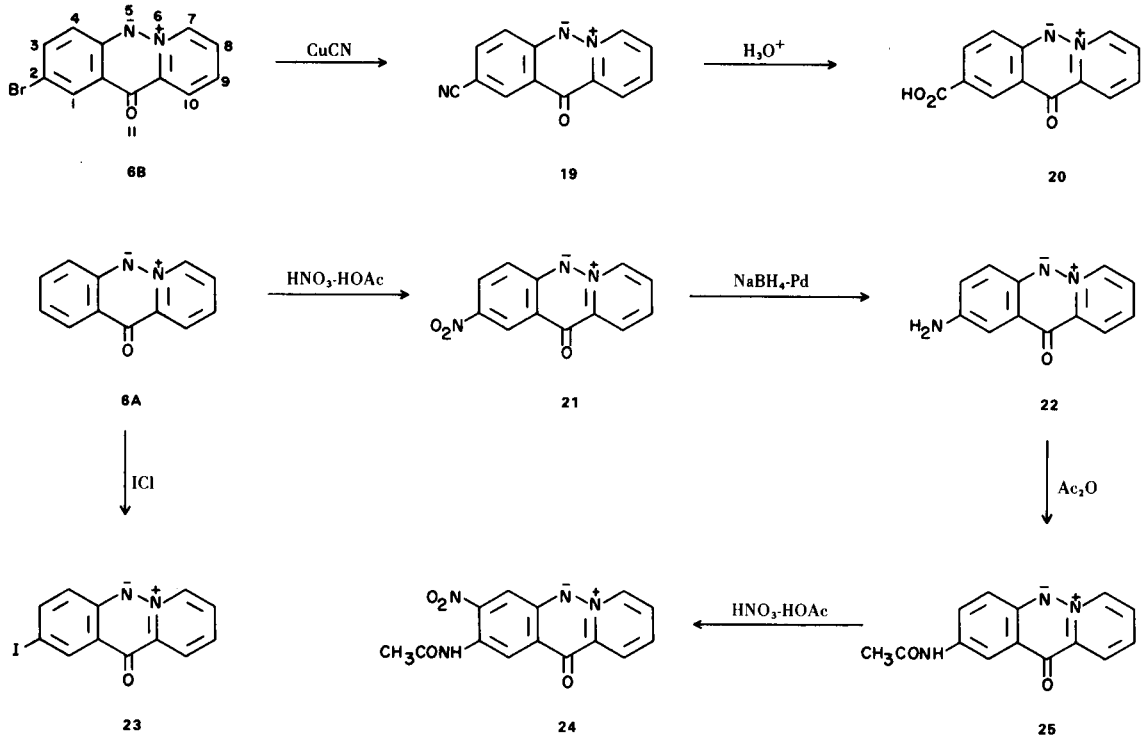
It is known that the pyrolysis of 2-azidobenzophenones gives 3-phenylanthranils (4), and that at higher temperatures, 3-phenylanthranils rearrange in moderate yields to give acridones (5-7). Since 2-(2-aminobenzoyl)pyridines **1** are readily available (8-11), we prepared the 2-(2-azidobenzoyl)pyridines **2**. Due to the tendency toward the formation of nitrogen-nitrogen bonds in nitrenoid reactions (12), we were interested in testing the extent to which processes leading to N-N bond formation might compete with N-O bond formation in the pyrolysis of **2**, and with the N-C bond formation in the pyrolysis of 3-(2-pyridyl)-2,1-benzisoxazoles **5** (13) (also known as anthranils) (14).

Pyrolysis for 3-4 hours of **2A** and the monobromo derivative **2B** in refluxing toluene afforded, in 82% and 51% yields respectively, the corresponding anthranils **5**. Pyrolysis of the dibromo derivative **2C** in toluene, however, resulted in a mixture of the anthranil **5C** (43%) and the mesoionic compound **6C** (41%). Under the pyrolytic conditions used, **5C** was found to be quite stable, hence it is not an intermediate in the formation of **6C** from **2C**. This interesting difference in the pyrolysis of **2A** and **2B** as compared with that of dibromo derivative **2C** is being further investigated.

While the anthranils **5** are stable at about 112° (refluxing toluene), they rearrange at about 215° (refluxing trichlorobenzene) in high yields (75-93%) to 5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium hydroxide inner salts **6**. We failed to isolate any of the isomeric pyrido[3,2-*b*]-quinolin-10(5*H*)ones (15) which could have resulted in analogy to the formation of acridones from 3-phenylanthranils mentioned earlier.

The 5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium hydroxide inner salts **6** are stable, yellow crystalline materials melting between 220-250°. They show carbonyl bands of weak to moderate intensities at about 1640 cm^{-1}. Using ultraviolet spectroscopic measurements in sulfuric acids, a pK_a value of -0.25 was found for **6A**. Since the spectrum of **6A** in 9 *M* sulfuric acid was found to be nearly identical to that of the *N*-methyl salt **7**, the site of protonation is on the 5-nitrogen and not the oxygen. The structures of compounds of type **6** have been unambiguously established by an X-ray crystallographic analysis of **6B** (16). The stereoscopic picture, bond-lengths and bond-angles obtained from this analysis are shown in Figure 1.


1) HNO2
2) HN3
1A, B, C
2A, B, C
3
4
peracid
Δ
Zn-HOAc
5A, B, C
6A, B, C
(CH3O)2SO2
7
8
H2/Ni
H2/Pd
H2/Ni
P2S5
9
10
11A, B
H2O
BrCH2CO2C2H5
HClO4
12
13A, B
H2NR
1 N HBr
CH2(CO2CH3)2
14a-g*
15
16A, B
-OH
HCl
17e, f
18
R* =
14a C6H5-
b p-Cl-C6H4-
c o-HOC6H4-
d o-H2N-C6H4
e (CH3)2N(CH2)3-
f H2NCNH-
S
g CH3CONH-
(A) X = Y = H
(B) X = Br; Y = H
(C) X = Y = Br



When compound **6A** was oxidized with *m*-chloroperbenzoic acid or reduced with zinc in acetic acid, cleavage of the N-N bond occured, resulting in the known compounds **3** (18) and **4** (19). Heating of **6A** with dimethyl sulfate afforded the *N*-methyl methylsulfate **7** (strong carbonyl band at 1655 cm^{-1}) which on reduction with zinc in acetic acid yielded the methylaminocarbinol **8**.

In contrast to the N-N bond cleavage by zinc in acetic acid, catalytic hydrogenations of **6A** appear to result mainly in tetrahydro and octahydro derivatives in which the central, mesoionic ring remained intact. When hydrogenated over palladium-on-carbon, **6A** yielded a mixture of the tetrahydro derivative **9** (37%) and the octahydro derivative **10** (13%). When Raney nickel was used as catalyst, the octahydro derivative **10** was the major product (68%). Both **9** and **10** showed a strong infrared band at 1570 cm^{-1}. Ultraviolet, mass and nmr spectra together, as presented in the experimentals, support the assigned structures. It is interesting to note that in 0.1 *N* hydrochloric acid, **10** is almost completely protonated. In further contrast to the protonation of **6A**, the site of protonation appears to be on the oxygen. The prechlorate salt of **10**, compound **12**, lacks the strong infrared absorption in the 1500 to 1700 cm^{-1} range.

Many attempts at bringing about selective reactions at the carbonyl group of **6** failed. Thiation with phosphorous pentasulfide however was successful affording **11A** and **B** in 77% and 65% yields respectively. Alkylation of compound **11** with ethyl bromoacetate afforded in good yields the 11-ethoxycarbonylmethylthiopyrido[1,2-*b*]cinnolin-6-ium bromides **13A**, **B**. Compound **13A** can be hydrolyzed to the carboxylic acid **15** or back to the

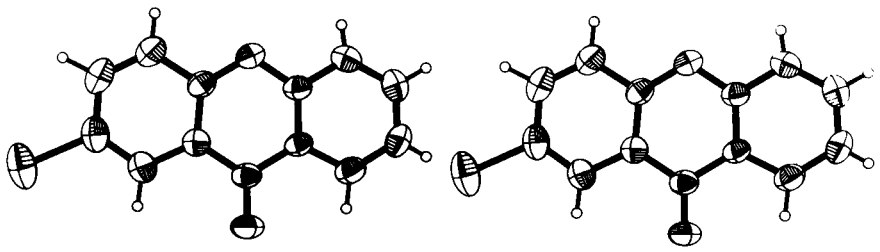
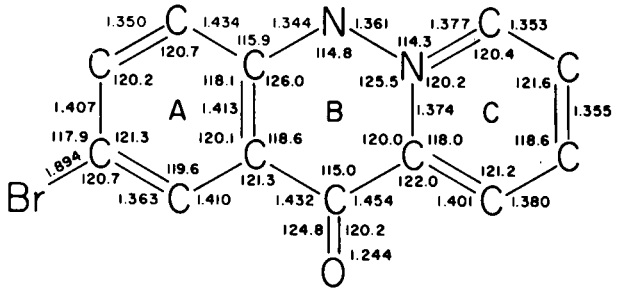


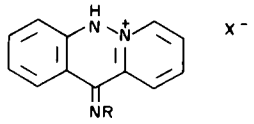
Figure 1. Stereoscopic picture and bond lengths and bond-angles of 2-bromo-5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium hydroxide inner salt (**6B**) obtained from X-ray crystallographic analysis.

BOND LENGTHS AND BOND ANGLES BY X-RAY CRYSTALLOGRAPHY



Estimated Standard Deviations:
Bond Lengths - 0.005 A
Bond Angles - 0.3°

thione **11A**. The ethoxycarbonylmethylthio sidechain of **13A** was readily substituted by a variety of amines and hydrazides. Reaction of **13A** with aniline, *p*-chloroaniline, *o*-aminophenol, *o*-phenylenediamine, 3-dimethylaminopropylamine, thiosemicarbazide and acetylhydrazine afforded, in this sequence, compounds **14a-g**. Treatment of **14e** and **14f** with dilute sodium hydroxide afforded the dehydrobrominated free bases **17**. Although we have assigned structures **14** to the bromide salts, based on the spectral data, however, the tautomeric structure **26** cannot be ruled out.



26

In the presence of sodium hydroxide, **13A** and **B** reacted with dimethyl malonate yielding purple colored 11-bis(methoxycarbonyl)methylene derivatives **16A** and **B**. When a solution of **16A** in 2*N* hydrochloric acid was heated to reflux for 4 hours, hydrolysis and decarboxylation of the ester groups occurred resulting in a 76% yield of the 11-methyl salt **18**. The uv spectrum of an aqueous solution of **18** showed no change when the *p*H of the solution was changed from 1 to 10. At *p*H above 11, an irreversible change in the uv spectrum occurred. The three protons of the methyl group appeared as a singlet at δ 3.66 ppm in the nmr spectrum.

The 2-bromo substituent of **6B** was exchanged with cuprous cyanide to give the 2-cyano derivative **19**. Hydrolysis of **19** afforded the carboxylic acid **20**. Nitration (HNO_3) and iodination (ICl) of **6A** resulted in the 2-nitro (**21**) and 2-iodo derivatives (**23**) in 81% and 50% yields respectively. The position of the substituents was indicated by the nmr spectra (see experimental). Compound **21** was reduced to the 2-amino derivative **22** by using sodium borohydride in the presence of palladium catalyst. The 2-amino group of **22** acetylated normally with acetic anhydride. The acetamido product (**25**) on nitration (HNO_3) afforded the 3-nitro derivative **24**. The position of the nitro group was, again, deduced from the nmr spectrum.

In summary, we have explored the chemistry of a novel heterocyclic system. Although some conversions appear conventional, they do reflect on the stability of the mesoionic system toward a variety of reaction conditions.

EXPERIMENTAL

All melting points were taken in a Thomas-Hoover melting point apparatus, and are corrected. Infrared spectra were determined on a Beckmann IR-9 or a Perkin-Elmer 621 grating spectrometer, mass spectra on a Jeolco-01SG or a CEC-21-110 spectrometer, nuclear magnetic resonance spectra on a Varian A-60 or a Varian HA-100 spectrometer, using tetramethylsilane as internal standard and ultraviolet spectra with a Cary 14M or 15 recording spectrometer. Solvents used were of reagent grade purity. Petroleum ether used boils at 30-60°. Unless otherwise specified, all solvents were evaporated on a Büchi Rotavapor evaporator under water-aspirator pressure using a water bath set at 30-80°.

The progress of reactions was routinely followed by thin layer chromatography (tlc). The tlc was performed on glass plates coated with Mallinckrodt Silica 7GF5 (with fluorescent indicator) in the case of analytical tlc and Merck silica gel PF254 in the case of preparative tlc. All plates were activated by heating to 100° for 1 hour then stored at 20-50°. The chromatograms were developed over a distance of 10 cm then viewed or photographed under uv light.

2-(2-Amino-3,5-dibromobenzoyl)pyridine (**1C**) (10).

This ketone was prepared by bromination of the monobromo ketone **1B** (10). The position into which the second bromine was introduced is shown by the nmr spectrum (deuteriochloroform): δ 6.82 (broad, 2), 7.38-7.52 (m, 1), 7.70 (d, J = 2.5 Hz, 1), 7.77-7.97 (m, 3) and 8.72 ppm (broad d, 1). The presence of a hydrogen on the tetra-substituted benzene ring with *meta* coupling is indicated by the signal at 7.70 ppm.

2-(2-Azidobenzoyl)pyridine (**2A**).

A 3.5 l. beaker equipped with a stirrer was charged with 238.8 g. (1.20 moles) of 2-(2-aminobenzoyl)pyridine (**1A**) (8,9), 600 ml. of glacial acetic acid, 240 ml. of concentrated hydrochloric acid and 360 ml. of water. The mixture was stirred and was chilled in an ice bath. To the mixture (5-10°) was added slowly, with stirring, an ice cold aqueous solution of 91.0 g. (1.32 moles) of sodium nitrite in 360 ml. of water. The mixture was stirred for 10 minutes. To the mixture was added slowly (due to nitrogen evolution), with stirring, an ice-cold aqueous solution (5-10°) of 85.6 g. (1.32 moles) of sodium azide in 360 ml. of water. The mixture was stirred for 0.5 hour and allowed to stand for about 1 hour. The product was collected (17) and washed thoroughly with about 5 l. of water. The product was air dried: 203 g. (75%),

m.p. 60-70° (indefinite). Thin layer chromatogram of this material showed essentially a single spot. This material was used without recrystallization in the next step. An analytical sample of this material was obtained by recrystallizations from benzene-hexane. Light reddish-brown prisms were obtained, m.p. 51-53°; ir (potassium bromide): 2140 and 2100 (N_3) and 1670 cm^{-1} (CO); uv max (2-propanol): 242 nm (ϵ 18,300).

Anal. Calcd. for $C_{12}H_8N_4O$: C, 64.29; H, 3.60; N, 24.99. Found: C, 64.00; H, 3.54; N, 24.70.

2-(2-Azido-5-bromobenzoyl)pyridine (**2B**).

To an ice-cold solution of 166 g. (600 mmoles) of 2-(2-amino-5-bromobenzoyl)pyridine (8,9,11) in a mixture of 120 ml. of concentrated hydrochloric acid, 300 ml. of glacial acetic acid and 180 ml. of water, was added an ice cold solution of 45.6 g. (660 mmoles) of sodium nitrite in 180 ml. of water. After stirring for 10 minutes, an ice-cold solution of 42.8 g. (660 mmoles) of sodium azide in 180 ml. of water was added in portions. The mixture was stirred for 30 minutes in an ice bath, then treated with a solution of 60 g. (1.5 moles) of sodium hydroxide in 500 ml. of water. The amorphous solid was collected on a filter and washed thoroughly with water. After air-drying it weighed 173 g. (95%), m.p. 117-119°. This material was pure enough to be used without recrystallization. An analytical sample was prepared by recrystallizations from ethanol. Light yellow prisms were obtained, m.p. 117-119°; ir (potassium bromide): 2150 and 2110 (N_3) and 1675 cm^{-1} (CO).

Anal. Calcd. for $C_{12}H_7BrN_4O$: C, 47.55; H, 2.33; N, 18.48. Found: C, 47.55; H, 2.49; N, 18.58.

2-(2-Azido-3,5-dibromobenzoyl)pyridine (**2C**).

Following the procedure described for **2B** on a one-sixth scale, 35.6 g. (100 mmoles) of 2-(2-amino-3,5-dibromobenzoyl)-pyridine (**1C**) was converted to 30 g. (78%) of **2C** as an amorphous solid, m.p. 109-112°. An analytical sample was prepared by recrystallizations from ethanol: light yellow prisms, m.p. 112-114°; ir (potassium bromide): 2160 and 2130 (N_3) and 1665 cm^{-1} (CO).

Anal. Calcd. for $C_{12}H_6Br_2N_4O$: C, 37.73; H, 1.58; N, 14.67. Found: C, 37.88; H, 1.71; N, 14.85.

2-(2-Nitrobenzoyl)pyridine (**3**) (18).

To a solution of 2.0 g. (10.2 mmoles) of **6A** in 100 ml. of methylene chloride was added 4.40 g. (25 mmoles) of *m*-chloroperbenzoic acid. The mixture was stirred at room temperature for 6 days. *m*-Chlorobenzoic acid that crystallized from solution was removed by filtration. The filtrate was washed with saturated aqueous sodium bicarbonate followed by brine. After drying (sodium sulfate), evaporation of methylene chloride and crystallization of the oily residue from ether-petroleum ether, 1.51 g. of an amorphous solid was obtained. Tlc indicated this material to be **3** containing a small amount of an unknown by-product of much lower Rf value. Purification was readily achieved by chromatography on 50 g. of neutral alumina (activity 1) and elution with ethyl acetate (100 ml.). Evaporation of ethyl acetate and crystallization from ether-petroleum ether afforded 1.0 g. (43%) of light yellow needles, m.p. 116-118°; ir (potassium bromide): 1680 cm^{-1} (CO); uv max (CH_3OH): 235 nm (ϵ 12,800) and 268 (9150).

Anal. Calcd. for $C_{12}H_8N_2O_3$: C, 63.16; H, 3.53; N, 12.28. Found: C, 63.52; H, 3.47; N, 12.34.

2-*o*-Aminobenzylpyridine (**4**) (19).

A. From **6A**.

To a solution of 120 g. (0.61 mole) of **6A** in 280 ml. of glacial acetic acid was added 120 g. of granular zinc (20 mesh) and 1.2 l. of water. The mixture was heated on a steam bath for 8 hours. On cooling, the reaction mixture was neutralized slowly with 6 *N* aqueous sodium hydroxide until zinc hydroxide started to precipitate. The mixture was partitioned between methylene chloride and water. The methylene chloride layer was washed with water, dried (sodium sulfate) and evaporated to dryness. Crystallization of the residual oil from ether-petroleum ether afforded 78.3 g. (69%) of amber prisms, m.p. 68-70° (lit. (19) 69-70°); uv max (methanol): 236 nm (ϵ 8270), 262 (4500) and 288 (2710); nmr (DMSO-d_6): δ 3.89 ppm (s, 2, CH_2); molecular ion m/e 184 (calcd. 184).

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.21. Found: C, 78.24; H, 6.66; N, 15.21.

Dihydrochloride salt (19) of **4** was obtained by dissolving 1.0 g. (5.4 mmoles) of the free base in 10 ml. of ethanol. Addition of a slight excess of ethanolic hydrogen chloride caused an instant precipitation of the dihydrochloride salt. The salt was collected, washed with ether and recrystallized from methanol-ether. Colorless needles were obtained (1.15 g., 82%), m.p. 266-270° dec., (lit. (19) m.p. 280° dec.).

Anal. Calcd. for $C_{12}H_{14}Cl_2N_2$: C, 56.05; H, 5.49; N, 10.89; Cl^-, 27.57. Found: C, 55.92; H, 5.54; N, 10.91; Cl^-, 27.40.

B. From Thione **11A**.

A solution of 10.0 g. (47 mmoles) of **11A** in 50 ml. of tetrahydrofuran containing 5 g. of Raney nickel was hydrogenated under 1 atmosphere of hydrogen for 18 hours. The catalyst was removed by filtration and the solvent was evaporated. The residual oil on crystallization from ether-petroleum ether afforded 6.2 g. (71%) of light yellow prisms, m.p. 69-71°. This material was found identical to **4** prepared above by tlc and comparison of infrared spectra.

3-(2-Pyridyl)-2,1-benzisoxazole (**5A**).

A 2 l. round bottom flask was charged with 198 g. (0.885 mole) of **2A** and 750 ml. of toluene. The mixture was heated under reflux for 4 hours then allowed to cool. While the mixture was still warm, a small amount of solids was removed by filtration. On chilling in ice, the filtrate yielded yellow needles. After about 2 hours of chilling, the needles were collected and washed with petroleum ether (200 ml.). On drying it weighed 112.6 g., m.p. 109-112°. The combined mother liquor and washings was evaporated to near dryness. A second crop of crystals was obtained by filtration and washing with petroleum ether: 50.7 g., m.p. 108-110°. The combined material on recrystallization from methanol afforded 124 g. (71%) of yellow needles, m.p. 110-112°.

An analytical sample was obtained by recrystallization from methylene chloride-petroleum ether. Light yellow needles formed, m.p. 110-111.5°; uv max (2-propanol) 244 nm (ϵ 14,400), 250 (15,800) and 347 (16,750).

Anal. Calcd. for $C_{12}H_8N_2O$: C, 73.46; H, 4.11; N, 14.28. Found: C, 73.49; H, 4.38; N, 14.28.

5-Bromo-3-(2-pyridyl)-2,1-benzisoxazole (**5B**) (13).

A suspension of 24.7 g. (81.6 mmoles) of **2B** in 500 ml. of toluene was heated under reflux for 3 hours. The clear solution was cooled then chilled in an ice bath. The product crystallized as yellow needles: 14.2 g. (63%), m.p. 167-169°. On recrystallization from acetonitrile, yellow needles were obtained, m.p. 166-167°; uv max (methanol): 216 nm (ϵ 20,910), 245 (14,200) 253 (16,320) and 353 (16,300). This material was found identical, by tlc and comparison of infrared spectra, to that (m.p. 168-170°)

prepared by an alternate process (13,20).

5,7-Dibromo-3-(2-pyridyl)-2,1-benzisoxazole (**5C**) and 2,4-Dibromo-5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**6C**).

A solution of 300 mg. (0.785 mmole) of the azide **2C** in 25 ml. of toluene was heated under reflux for 7 hours. Toluene was evaporated. The residue was separated by preparative tlc (4 silica gel plates - 20 cm x 20 cm x 1.5 mm; 10% by volume of benzene in ether as developer). The two main products were isolated as follows:

5C: The band of silica gel at Rf 0.4 was cut out and eluted with tetrahydrofuran. Evaporation of tetrahydrofuran followed by crystallization from methylene chloride afforded 120 mg. (43%) of **5C** as yellow needles, m.p. 205-206°; uv max (methanol): 215 nm (ϵ 21,450), 257 (13,820) and 364 (16,740); molecular ion m/e 352 (Calcd. 352) with isotope peaks indicating presence of two bromine atoms.

Anal. Calcd. for $C_{12}H_6Br_2N_2O$: C, 40.71; H, 1.71; N, 7.91. Found: C, 40.67; H, 1.91; N, 7.92.

6C: The band of silica gel at Rf 0.1 was cut out and eluted with tetrahydrofuran. Evaporation of solvent followed by crystallization from acetonitrile afforded 114 mg. (41%) of yellow needles, m.p. 248-251°; ir (potassium bromide) no NH stretching band, 1640 (weak) and 1600 cm^{-1} (strong); uv max (methanol): 216 nm (ϵ 17,120), 241 (32,000), 389 (21,350), 412 (15,500), 435 (13,480) and 461 (9180); molecular ion m/e 352 (Calcd. 352) with isotope peaks indicating presence of two bromine atoms.

Anal. Calcd. for $C_{12}H_6Br_2N_2O$: C, 40.71; H, 1.71; N, 7.91; Br, 45.15. Found: C, 40.94; H, 1.82; N, 8.17; Br, 44.95.

Larger quantities of **5C** and **6C** have been obtained by a scale-up of this procedure and using column chromatography (neutral alumina of activity 1, ether as eluent).

5,11-Dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**6A**).

A solution of 157.7 g. (0.803 mole) of the anthranil **5A** in 500 ml. of 1,2,4-trichlorobenzene was heated under reflux for 18 hours. On cooling, brown needles that crystallized from a dark solution were collected and washed with petroleum ether: 148.8 g. (94%), m.p. 219-222°. On recrystallization from glacial acetic acid, 118.8 g. (75%) of yellow needles were obtained, m.p. 220-222°; ir (potassium bromide) 1635 (weak) and 1595 cm^{-1} (strong); uv max (methanol): 234 nm (ϵ 38,200), 312 (2500) 381 (20,500), 422 (10,700) and 447 (5550).

Anal. Calcd. for $C_{12}H_8N_2O$: C, 73.46; H, 4.11; N, 14.28. Found: C, 73.15; H, 4.28; N, 14.15.

PKa of **6A**(21).

The basicity of **6A** has been determined by a standard uv spectroscopic method (22). Using acidity functions of sulfuric acid solutions taken from the literature (23), the p*K*a of **6A** was found to be -0.25. The uv spectrum of protonated **6A** [9*M* aqueous sulfuric acid: max 225 nm (ϵ 29,000), 250 sh (17,120), 283 (14,120), 337 (8000) and 394 (8200)] was found to be almost identical to that of the *N*-methyl salt **7** and different from those of the compounds such as **14A**, **15** and **19**. On this basis, it appears that protonation occurs predominantly on the 5-nitrogen and not on oxygen.

2-Bromo-5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**6B**).

A solution of 2.75 g. (10.0 mmoles) of anthranil **5B** in 20 ml. of 1,2,4-trichlorobenzene was heated under reflux for 16 hours. On cooling, yellow needles that crystallized were collected and washed with petroleum ether: 2.58 g. (93%), m.p. 222-224°. An analytical sample was prepared by recrystallizations from acetonitrile affording golden yellow prisms, m.p. 224-226°, ir (potassium bromide): 1635 (medium), 1600 (strong) and 1585 cm^{-1} (strong); uv max (methanol): 240 nm (ϵ 36,500), 315 (1500), 385 (21,600), 428 (11,500) and 453 (6100); nmr (DMSO-d_6): δ 7.58 (d, J = 9 Hz, 1, H-4), 7.7-8.1 (m, 3, H-3, 8, 9), 8.22 (d, J = 2.5 Hz, 1, H-1), 8.37 (m, 1, H-10) and 8.90 ppm (m, 1, H-7).

Anal. Calcd. for $C_{12}H_7BrN_2O$: C, 52.39; H, 2.57; N, 10.18; Br, 29.05. Found: C, 52.25; H, 2.48; N, 10.14; Br, 29.11.

2,4-Dibromo-5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**6C**).

A. From Toluene.

The isolation of **6C** from the pyrolysis of the azide **2C** in toluene is described above.

B. From 1,2,4-Trichlorobenzene.

A suspension of 5.0 g. (13 mmoles) of the azide **2C** in 30 ml. of 1,2,4-trichlorobenzene was heated to reflux for 24 hours. On cooling 3.98 g. (85%) of **6C** crystallized, m.p. 240-243°. This material was brownish although it appeared quite pure by tlc. After decolorization by passage of a methylene chloride solution of this material through a pad of cellulose filter-aid, followed by evaporation of methylene chloride and recrystallization from acetonitrile, yellow needles were obtained, m.p. 243-245°. Infrared spectrum of this material is identical to that of the material obtained from toluene.

5,11-Dihydro-5-methyl-11-oxopyrido[1,2-*b*]cinnolin-6-ium Methylsulfate (**7**).

A solution of 1.00 g. (5.10 mmoles) of **6A** and 2.8 g. (22 mmoles) of dimethyl sulfate in 20 ml. of toluene was heated under reflux for 17 hours. On cooling, analytically pure **7** crystallized as yellow prisms. On collection and washing with methylene chloride, it weighed 1.25 g. (76%), m.p. indefinite, in the range of 230-238°; ir (potassium bromide): 1655 (strong), 1605 (strong) and 1580 cm^{-1} (weak); uv max (methanol): 227 nm (ϵ 29,100), 250 sh (13,100), 283 (10,800), 335 (7000) and 395 (7800).

Anal. Calcd. for $C_{14}H_{14}N_2O_5S$: C, 52.17; H, 4.38; N, 8.69. Found: C, 51.83; H, 4.27; N, 8.62.

o-Methylamino-alpha-(2-pyridyl)benzyl Alcohol (**8**) from the Reduction of **7**.

To a solution of 2.0 g. (6.0 mmoles) of **7** in 6 ml. of glacial acetic acid was added 20 ml. of water and 3.0 g. of granular zinc (20 mesh). The mixture was heated on a steam bath for 2 hours. On cooling the reaction mixture was filtered through a plug of cotton and partitioned between methylene chloride and water. The methylene chloride layer was washed with water, dried (sodium sulfate) and evaporated. The residual oil was separated by preparative tlc. The alcohol **8**, occurring as the major product, having an Rf value of 0.5 (silica gel, ether) was isolated. After crystallization from ether-petroleum ether, light yellow prisms weighing 486 mg. (36%) were obtained, m.p. 90-92°; ir (potassium bromide): 3410, 3380, 3160 cm^{-1} (broad); uv max (methanol): 246 nm (ϵ 10,660) and 301 (3020); nmr (DMSO-d_6) in addition to aromatic protons, signals at δ 2.72 (d, J = 5 Hz, 3, CH_3), 5.74 (exchangeable, 1, NH), 5.72 (d, J = 4 Hz, 1, CH) and 5.99 (d, J = 4 Hz, 1, OH, exchangeable).

Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.88; H, 6.59; N, 13.07. Found: C, 72.99; H, 6.61; N, 13.14.

Hydrogenation of **6A** over Palladium on Carbon. 5,7,8,9,10,11-Hexahydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**9**) and 1,2,3,4,5,7,8,9,10,11-Decahydro-11-oxopyrido[1,2-*b*]-cinnolin-6-ium Hydroxide Inner Salt (**10**).

A solution of 1.0 g. (5.2 mmoles) of **6A** in 150 ml. of tetrahydrofuran containing 750 mg. of 10% palladium-on-carbon catalyst, was hydrogenated at room temperature, under 1 atmosphere of hydrogen. After 21 hours, the catalyst was removed by filtration through a pad of filter aid (Celite). Solvent was evaporated. The residual oil was separated on twelve 20 cm x 20 cm x 1.5 mm silica gel plates, using a mixture of equal volumes of ethanol and ethyl acetate as developer. Compounds **9** and **10** occurring as the main components of this product mixture were isolated as shown below.

Compound **9**.

The band of silica gel at Rf 0.5 was isolated and eluted with a mixture of methanol and ethyl acetate. Evaporation of solvents followed by crystallization from methylene chloride-petroleum ether afforded 386 mg. (37%) of **9** as yellow prisms, m.p. 149-151°; ir (potassium bromide): 1570 cm^{-1} (strong); uv max (methanol): 213 nm (ϵ 35,490) 254 (10,730), 322 (6600), 355 (14,950) and 372 (16,280); molecular ion m/e 200 (Calcd. 200); nmr (DMSO-d_6): δ 1.7-2.3 (m, 4, CH_2CH_2), 2.96 (t, 2, $CH_2\overset{|}{C}=$), 4.52 (t, 2, $CH_2\overset{+}{N}$) and 7.2-8.2 ppm (m, 4, aromatic).

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 72.19; H, 6.01; N, 14.10.

Compound **10**.

The band of silica gel at Rf 0.3 was isolated and eluted with ethyl acetate containing methanol. Evaporation of solvents followed by crystallization from methylene chloride-petroleum ether afforded 136 mg. (13%) of **10** as colorless prisms, m.p. 193-195°; ir (potassium bromide): 1570 cm^{-1} (strong); uv max in methanol: 219 nm (ϵ 19,800), 265 (4720) and 308 (8000); in 0.1 *N* HCl: 205 nm (ϵ 23,700) and 269 (6800); in 0.1 *N* KOH: 218 nm (ϵ 19,500), 268 (4650) and 301 (8500); nmr (DMSO-d_6): δ 1.5-2.1 (m, 8, $4CH_2$), 2.3-2.7 (m, 4, $2CH_2$), 2.79 (t, 2, CH_2) and 4.25 ppm (t, 2, $CH_2\overset{+}{N}$); molecular ion m/e 204 (Calcd. 204).

Anal. Calcd. for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71. Found: C, 70.67; H, 7.93; N, 13.64.

Hydrogenation of **6A** over Raney Nickel. Compound **10**.

A solution of 1.00 g. (5.04 mmoles) of **6A** in 130 ml. of tetrahydrofuran containing 2 g. of Raney nickel was hydrogenated (1 atmosphere) at room temperature, for 6 hours. Catalyst was removed by filtration. Evaporation of solvent followed by crystallization from acetonitrile afforded 700 mg. (68%) of colorless prisms, m.p. 196-198°. This material was found to be identical to **10** obtained above by mixture m.p. and tlc.

Perchlorate Salt (**12**) of **10** was obtained by adding 0.10 ml. of 70% perchloric acid (1.1 mmoles) to a solution of 204 mg. (1.0 mmole) of **10** in 2 ml. of methylene chloride. The solution was allowed to evaporate slowly to dryness by allowing to stand at room temperature in a small loosely covered Erlenmeyer flask. Colorless prisms that formed were collected and washed with tetrahydrofuran: 285 mg. (93%), m.p. 223-225°; ir (potassium bromide): 3150 cm^{-1} (broad, OH), clear in the region between 1500-2000 cm^{-1} except for weak aromatic absorptions at 1600 and 1565 cm^{-1}.

Anal. Calcd. for $C_{12}H_{17}ClN_2O_5$: C, 47.30; H, 5.62; N, 9.19; Cl, 11.63. Found: C, 47.17; H, 5.68; N, 9.11; Cl, 11.75.

11-Mercaptopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**11A**).

A mixture of 5.0 g. (25 mmoles) of **6A**, 7.5 g. (34 mmoles) of phosphorus pentasulfide and 100 ml. of pyridine was heated on the steam bath for 1 hour. The solution was allowed to cool then was poured into 250 ml. of ice-cold water and allowed to stand until precipitation of an amorphous solid was complete (20 minutes). The solid was collected on a filter and washed with water. The wet filter cake was partitioned between methylene chloride and brine. The methylene chloride layer was washed with water, dried (sodium sulfate) and evaporated. The residue crystallized from ether to afford 4.20 g. (77%) of brown prisms, m.p. 214-216°. The m.p. remained unchanged after recrystallization from methylene chloride-petroleum ether; uv max (methanol): 226 nm (ϵ 26,300), 252 (24,500), 279 (18,200), 419 (7150), 480 (13,100) and 502 (12,800); molecular ion m/e 212 (Calcd. 212).

Anal. Calcd. for $C_{12}H_8N_2S$: C, 67.90; H, 3.79; N, 13.20; S, 15.10. Found: C, 67.92; H, 3.53; N, 13.00; S, 14.88.

2-Bromo-11-mercaptopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**11B**).

Following the procedure described for **11A**, 5.0 g. (18 mmoles) of **6B** afforded 4.44 g. (84%) of **11B**, m.p. 240-245°. On recrystallization from acetonitrile, brown plates were obtained, m.p. 240-244°; uv max (1,4-dioxane): 237 nm (ϵ 25,600), 264 (26,900), 284 (21,700), 382 (4800), 432 (8600), 462 (8800), 491 (16,150) and 525 (23,500); molecular ion m/e 290 (Calcd. 290).

Anal. Calcd. for $C_{12}H_7BrN_2S$: C, 49.50; H, 2.42; N, 9.62; S, 11.01. Found: C, 49.62; H, 2.20; N, 9.60; S, 11.23.

11-Ethoxycarbonylmethylthiopyrido[1,2-*b*]cinnolin-6-ium Bromide (**13A**).

A suspension of 15.0 g. (70 mmoles) of **11A** in 40 ml. of ethyl bromoacetate was heated on a steam bath for 3 hours. On cooling, the nearly solid mass was triturated with two portions of 200 ml. each of tetrahydrofuran. Yellow prisms were collected and washed with tetrahydrofuran: 25 g. (94%), m.p. 168-170°. The m.p. was unchanged after recrystallization from acetonitrile; ir (potassium bromide): 1730 cm^{-1} (ester); uv max (water): 220 nm (ϵ 16,400), 258 (42,500), 298 (11,600), 343 (4500), 359 (4000) and 413 (6000).

Anal. Calcd. for $C_{16}H_{15}BrN_2O_2S$: C, 50.67; H, 3.99; N, 7.39. Found: C, 50.57; H, 3.85; N, 7.36.

Hydrolysis of **13A** to **11A**.

A solution of 1.65 g. (5.0 mmoles) of **13A** and 891 mg. (10 mmoles) of β-alanine in 20 ml. of water was allowed to stand at room temperature overnight. The reaction mixture was extracted with methylene chloride. The methylene chloride layer was washed with water and dried (sodium sulfate). The residue obtained after evaporation of methylene chloride crystallized from acetonitrile affording 195 mg. (15%) of the mercapto inner salt **11A** as red prisms, m.p. 212-216°.

2-Bromo-11-ethoxycarbonylmethylthiopyrido[1,2-*b*]cinnolin-6-ium Bromide (**13B**).

Following the procedure as described for **13A**, 1.46 g. (5.0 mmoles) of **11B** afforded, after recrystallization from methanol-ether, 1.3 g. (56%) of **13B** as yellow prisms, m.p. indefinite above 240°; ir (potassium bromide): 1735 cm^{-1} (ester); uv max (water): 243 nm (ϵ 24,400), 269 (35,350), 296 (21,600), 350 (4700), 370 (4200), 416 (8100) and 437 (7700).

Anal. Calcd. for $C_{16}H_{14}Br_2N_2O_2S$: C, 41.94; H, 3.08; N, 6.11. Found: C, 41.90; H, 2.94; N, 6.04.

11-Anilinopyrido[1,2-*b*]cinnolin-6-ium Bromide (**14a**).

A solution of 1.0 g. (2.63 mmoles) of the 11-ethoxycarbonylmethylthio salt **13A** and 1.0 g. (10.8 mmoles) of aniline in 5.0 ml. of methanol was allowed to stand at room temperature. After 10 minutes, the yellow needles that formed were collected and recrystallized from ethanol: 0.50 g. (70%) of yellow needles, m.p. 292-294°. The m.p. was raised to 296-299° by recrystallization from acetonitrile; uv max 241 nm (ε 29,900), 261 (22,100), 336 (3570), 388 (10,000) and 440 (12,200).

Anal. Calcd. for $C_{18}H_{14}BrN_3$: C, 61.38; H, 4.00; N, 11.93; Br, 22.69. Found: C, 61.56; H, 4.00; N, 11.85; Br, 22.89.

11-(4-Chloroanilino)pyrido[1,2-*b*]cinnolin-6-ium Bromide (**14b**).

A solution of 1.0 g. (2.63 mmoles) of **13A** and 0.40 g. (3.1 mmoles) of *p*-chloroaniline in 5 ml. of methanol was allowed to stand at room temperature. After 2 days, the yellow precipitate formed was collected and recrystallized from acetonitrile affording 0.67 g. (83%) of **14b** as yellow prisms, m.p. 300-302°; uv max (methanol): 241 nm (ε 33,300), 265 (23,400), 336 (4170), 385 (9500) and 442 (12,800).

Anal. Calcd. for $C_{18}H_{13}BrClN_3$: C, 55.91; H, 3.39; N, 10.87; Cl, 9.17; Br, 20.67. Found: C, 56.01; H, 3.28; N, 10.84; Cl, 9.12; Br, 20.54.

11-(2-Hydroxyanilino)pyrido[1,2-*b*]cinnolin-6-ium Bromide (**14c**).

Reaction of **13A** (2.0 g., 5.3 mmoles) with *o*-aminophenol (0.70 g., 6.4 mmoles) in methanol (10 ml., room temperature, 30 minutes) afforded **14c** (1.46 g., 75%) as yellow flakes, m.p. 296-299° (2-propanol-petroleum ether); uv max (methanol): 241 nm (ε 29,900), 265 (20,400), 335 (3350), 387 (11,200), 415 (10,300) and 435 (11,000).

Anal. Calcd. for $C_{18}H_{14}BrN_3O$: C, 58.72; H, 3.83; N, 11.41. Found: C, 58.68; H, 3.95; N, 11.29.

11-(2-Aminoanilino)pyrido[1,2-*b*]cinnolin-6-ium Bromide (**14d**).

Reaction of **13A** (1.00 g., 2.63 mmoles) with *o*-phenylenediamine (310 mg., 2.83 mmoles) in methanol (5 ml., room temperature, 1 hour) afforded 640 mg. (67%) of **14d** as yellow flakes (methanol-ether), m.p. 270-273°; uv max (water): 238 nm (ε 27,420), 382 (10,000) and 432 (7400).

Anal. Calcd. for $C_{18}H_{15}BrN_4$: C, 58.87; H, 4.12; N, 15.26. Found: C, 58.95; H, 4.23; N, 15.21.

11-(3-Dimethylaminopropylamino)pyrido[1,2-*b*]cinnolin-6-ium Bromide Hydrobromide (**14e**).

Reaction of **13A** (1.00 g., 2.63 mmoles) with 3-dimethylaminopropylamine (0.32 g., 3.1 mmoles) in methanol (room temperature, 20 minutes) followed by addition of ether (15 ml.) afforded 0.50 g. of yellow needles, m.p. 243-247°. Yellow needles obtained after two recrystallizations from methanol-ether, weighed 430 mg. (36%), m.p. 253-256°; uv max (water): 238 nm (ε 32,500), 267 (19,400), 313 (4520), 380 (14,300), 408 (9980) and 431 (9520).

Anal. Calcd. for $C_{17}H_{21}BrN_4 \cdot HBr \cdot 0.5H_2O$: C, 45.25; H, 5.14; N, 12.42; Br, 35.42. Found: C, 45.24; H, 5.21; N, 12.46; Br, 35.52.

11-Thiosemicarbazidopyrido[1,2-*b*]cinnolin-6-ium Bromide (**14f**).

A mixture of 1.00 g. (2.63 mmoles) of **13A**, 300 mg. (3.28 mmoles) of thiosemicarbazide and 5 ml. of methanol was heated on the steam bath for 10 minutes. After standing at room temperature for 1 hour, the precipitated salt was collected and recrystallized from methanol-ether. Yellow prisms weighed 650 mg. (70%), m.p. 204-206°. Further recrystallizations raised the m.p. to 213-215°; uv max (methanol): 234 nm (ε 32,200), 293 (16,500), 355 (9800) and 468 (16,400).

Anal. Calcd. for $C_{13}H_{12}BrN_5S$: C, 44.58; H, 3.45; N, 20.00. Found: C, 44.49; H, 3.37; N, 20.11.

11-(2-Acetylhydrazino)pyrido[1,2-*b*]cinnolin-6-ium Bromide (**14g**).

Solution of **13A** (0.95 g., 2.5 mmoles) and acetylhydrazine (0.40 g., 5.4 mmoles) in 5 ml. methanol deposited 14 g. almost instantly. After recrystallizations from methanol-ether, 0.67 g. (80%) of yellow needles were obtained, m.p. 273-277°; uv max 235 nm (ε 32,000), 359 (6080) and 430 (13,000).

Anal. Calcd. for $C_{14}H_{13}BrN_4O$: C, 50.47; H, 3.93; N, 16.82. Found: C, 50.32; H, 3.89; N, 16.83.

11-Carboxymethylthiopyrido[1,2-*b*]cinnolin-6-ium Bromide (**15**).

A solution of 1.50 g. (4.0 mmoles) of **13A** in 3.0 ml. of 1 *N* aqueous hydrobromic acid was allowed to stand at room temperature for 2 days. The precipitate (1.5 g.) was collected and washed with tetrahydrofuran. On crystallization from methanol-tetrahydrofuran, 1.06 g. (76%) of yellow prisms were obtained, m.p. 208-211° dec.; ir (potassium bromide): 1785 (weak) and 1745 cm^{-1} (strong); uv max (water): 222 nm (ε 16,300), 258 (42,000), 298 (11,000), 342 (4400), 359 (4300) and 416 (5800).

Anal. Calcd. for $C_{14}H_{11}BrN_2O_2S$: C, 47.88; H, 3.16; N, 7.98; Br, 22.75; S, 9.13. Found: C, 47.74; H, 3.26; N, 7.81; Br, 22.89; S, 8.87.

5,11-Dihydro-11-[bis(methoxycarbonyl)methylene]pyrido[1,2-*b*]-cinnolin-6-ium Hydroxide Inner Salt (**16A**).

To a suspension of 66.0 g. (0.20 mole) of **13A** in 100 ml. of dimethylmalonate was added, slowly with stirring, 500 ml. of 1.0 *N* sodium hydroxide. The dark mixture was stirred further for 1 hour. After addition of 500 ml. of water, the dark solid was collected and washed thoroughly with water. Upon drying and recrystallizations from methanol-ether, 40 g. (80%) of purple needles were obtained, m.p. 251-253°; ir (potassium bromide): 1700 cm^{-1} (esters), uv max (methanol): 247 nm (ε 50,110), 393 (5900) and 565 (4100); molecular ion m/e 310 (Calcd. 310).

Anal. Calcd. for $C_{17}H_{14}N_2O_4$: C, 65.80; H, 4.55; N, 9.03. Found: C, 65.66; H, 4.47; N, 8.93.

2-Bromo-5,11-dihydro-11-[bis(methoxycarbonyl)methylene]-pyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**16B**).

Following the procedure described for the preparation of **16A**, **13B** afforded **16B** in 28% yield. It was obtained as purple prisms (methanol-ether), m.p. 215-217° (softening above 205°); ir (potassium bromide): 1695 cm^{-1} (ester); uv max (methanol): 249 nm (ε 44,350), 395 (8240) and 580 (4300).

Anal. Calcd. for $C_{17}H_{13}BrN_2O_4$: C, 52.46; H, 3.37; N, 7.20. Found: C, 52.30; H, 3.42; N, 7.06.

5,11-Dihydro-11-(3-dimethylaminopropylimino)pyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**17e**).

The hydrobromide salt **14e** (1.1 g., 2.5 mmoles) was partitioned between methylene chloride and 0.5 *N* sodium hydroxide. The methylene chloride layer was washed with water, dried (sodium sulfate) and evaporated to dryness. The residual oil crystallized from ether-petroleum ether affording 490 mg. (70%) of yellow needles, m.p. 103-105°. The m.p. remained unchanged after recrystallization; uv max (methanol): 215 nm (ε 18,500), 240 (30,500), 266 (17,500), 318 (3300), 390 (14,600), 412 (12,300), 435 (11,250) and 455 (7100); nmr (deuteriochloroform): δ 2.27 (s, 6, CH_3), 1.8-2.7 (m, 4, CH_2), 3.94 (t, 2, $=NCH_2$) and 6.7-8.6

ppm (m, 8, aromatic); molecular ion m/e 280 (Calcd. 280).

Anal. Calcd. for $C_{17}H_{20}N_4$: C, 72.83; H, 7.19; N, 19.98. Found: C, 73.12; H, 6.98; N, 20.17.

5,11-Dihydro-11-thiosemicarbazonopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**17f**).

A mixture of 1.50 g. (3.97 mmoles) of **13A**, 0.50 g. (5.5 mmoles) of thiosemicarbazide and 8 ml. of methanol was heated on a steam bath for 20 minutes. Methanol was evaporated. The residual mixture was partitioned between methylene chloride and 1 *N* sodium hydroxide. The methylene chloride layer was washed with water, dried (sodium sulfate) and evaporated. Trituration of the residue with a small volume of tetrahydrofuran afforded amorphous **17f** which on crystallization from chloroform-petroleum ether gave 460 mg. (43%) of red prisms, m.p. 196-198°; uv max (methanol): 233 nm (ϵ 29,000), 292 (14,400), 354 (8500) and 465 (14,250).

Anal. Calcd. for $C_{13}H_{11}N_5S$: C, 57.97; H, 4.12; N, 26.00. Found: C, 57.68; H, 4.27; N, 25.78.

11-Methylpyrido[1,2-*b*]cinnolin-6-ium Chloride (**18**).

A solution of 1.00 g. (3.95 mmoles) of **16A** in 7 ml. of 2 *N* hydrochloric acid was heated under reflux for 4 hours. The reaction mixture was evaporated (70-90°) to dryness. Water present in the residual mixture was azeotroped with 5 ml. of ethanol. Crystallization from ethanol-ether afforded 0.70 g. (76%) of **18** as hygroscopic yellow prisms, m.p. 134-140°. The m.p. sharpened to 137-140° after repeated recrystallizations from the same solvent; ir (potassium bromide): no carbonyl band; uv max (water, *p*H 1, 7 or 10) 253 nm (ϵ 38,400), 289 (11,300), 336 (4400), 353 (5600) and 390 (4800); at *p*H above 11, the uv spectrum changed irreversibly; nmr (deuterium oxide, external TMS) δ 3.66 ppm (s, 3, CH_3).

Anal. Calcd. for $C_{13}H_{11}ClN_2 \cdot 0.15H_2O$: C, 66.90; H, 4.88; N, 12.00; Cl, 15.19. Found: C, 66.70; H, 4.83; N, 11.98; Cl, 15.52.

The sample was highly hygroscopic.

2-Cyano-5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**19**).

A mixture of 1.0 g. (3.6 mmoles) of the 2-bromo analog **6B**, 0.65 g. (7.2 mmoles) of cuprous cyanide and 10 ml. of dimethylformamide was heated under nitrogen at a reflux for 5 hours. The dark mixture was poured into a mixture of 25 ml. of methylene chloride and 50 ml. of an aqueous solution of 1.0 g. of sodium cyanide. The two phased mixture was stirred vigorously for 1 hour at room temperature. The methylene chloride layer was separated, washed with water, dried (sodium sulfate) and evaporated to dryness. The residue crystallized from ether affording 0.37 g. (46%) of yellow needles, m.p. 267-270°. Recrystallizations of this material from acetonitrile afforded yellow flakes, m.p. 273-277°; ir (potassium bromide): 2220 (medium), 1645 (medium) and 1605 cm^{-1} (strong); uv max (2-propanol): 240 nm (ϵ 39,300), 390 (22,250), 407 (19,800), 430 (18,400) and 455 (14,000); molecular ion m/e 221 (Calcd. 221).

Anal. Calcd. for $C_{13}H_7N_3O$: C, 70.59; H, 3.19; N, 19.00. Found: C, 70.15; H, 3.13; N, 19.09.

2-Carboxy-5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**20**).

A solution of 1.0 g. (4.5 mmoles) of the 2-cyano compound **19** in 100 ml. of concentrated hydrochloric acid was heated on a steam bath for 4 hours. On cooling, the precipitated product was collected and washed with water. Recrystallizations from dimethylformamide-ethanol afforded 0.89 g. (82%) of yellow needles, m.p. > 350°; ir (potassium bromide): 1700 cm^{-1} (CO_2H); molecular ion m/e 240 (Calcd. 240).

Anal. Calcd. for $C_{13}H_8N_2O_3$: C, 65.00; H, 3.36; N, 11.66. Found: C, 64.84; H, 3.16; N, 11.58.

5,11-Dihydro-2-nitro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**21**).

To an ice-chilled suspension of 10.0 g. (5.1 mmoles) of **6A** in 30 ml. of glacial acetic acid was added a mixture of 4 ml. of 90% nitric acid and 10 ml. of glacial acetic acid. The red paste was stirred at room temperature for 30 minutes, then diluted with water (50 ml.). The red precipitate was collected and washed thoroughly with water. Recrystallizations from dimethylformamide-ethanol afforded 10.0 g. (81%) of red prisms m.p. 306-308°; nmr (DMSO-d_6): δ 7.73 (d, J = 9 Hz, 1, H-4), 8.08 (m, 2, H-8, 9), 8.37 (d of d, J = 2 and 9 Hz, 1, H-3), 8.66 (m, 1, H-10), 8.93 (d, J = 2 Hz, 1, H-1) and 9.14 (m, 1, H-7).

Anal. Calcd. for $C_{12}H_7N_3O_3$: C, 59.76; H, 2.93; N, 17.42. Found: C, 59.87; H, 2.77; N, 17.18.

2-Amino-5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**22**).

To a stirring mixture of 10.0 g. (41.4 mmoles) of the 2-nitro compound **21**, 1.0 g. of 10% palladium-on-carbon catalyst, 50 ml. of water and 1.0 l. of methanol, was added under nitrogen, in 4 portions over 2 hours, 10.0 g. of sodium borohydride. Stirring at room temperature was continued for 2 hours. The catalyst was removed by filtration. Evaporation of methanol yielded a solid (6.0 g.) which was collected and washed with water followed by methylene chloride. Recrystallizations from methanol afforded 4.5 g. (51%) of red needles, m.p. 275-277°; ir (potassium bromide): 3330 and 3210 cm^{-1} (NH_2); uv max (methanol): 251 nm (ϵ 35,600) and 418 (21,900); molecular ion m/e 211 (Calcd. 211).

Anal. Calcd. for $C_{12}H_9N_3O$: C, 68.23; H, 4.30; N, 19.90. Found: C, 68.52; H, 4.40; N, 19.80.

2-Iodo-5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**23**).

To a solution of 4.24 g. (22 mmoles) of **6A** in 125 ml. of dimethylformamide was added a solution of 7.33 g. (45 mmoles) of iodine mono chloride in 10 ml. of dimethylformamide. After standing at room temperature for 1 day, 3.5 g. (50%) of yellow prisms were collected, m.p. 235-240°. Recrystallizations from tetrahydrofuran raised the m.p. to 245-247°; ir (potassium bromide) spectrum nearly identical to that of the 2-bromo analog **6B**; nmr (DMF-d_7): δ 7.55 (d, J = 9 Hz, 1, H-4), 7.9-8.2 (m, 3, H-3, 8, 9), 8.61 (d, J = 2 Hz, 1, H-1), 8.70 (m, 1, H-10) and 9.12 ppm (m, 1, H-7).

Anal. Calcd. for $C_{12}H_7IN_2O$: C, 44.75; H, 2.19; N, 8.70; I, 39.40. Found: C, 44.78; H, 2.14; N, 8.69; I, 39.37.

2-Acetamido-5,11-dihydro-3-nitro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**24**).

To an ice-chilled suspension of 300 mg. (1.18 mmoles) of **25** in 2 ml. of glacial acetic acid was added a mixture of 1 ml. each of 90% nitric acid and glacial acetic acid. The mixture was stirred in ice bath for 20 minutes. Addition of 20 ml. of ether precipitated 270 mg. of the product, m.p. > 350°. Recrystallization from dimethylformamide-ethanol afforded 170 mg. (48%) of red needles, m.p. > 350°; nmr (DMSO-d_6): δ 2.12 (s, 3, CH_3), 7.94 (m, 2, H-8 and 9), 8.62 (s, 2, H-1 and 4), 8.63 (m, 1, H-10) and 9.00 (m, 1, H-7).

Anal. Calcd. for $C_{14}H_{10}N_4O_4$: C, 56.39; H, 3.38; N, 18.79. Found: C, 56.37; H, 3.26; N, 18.82.

2-Acetamido-5,11-dihydro-11-oxopyrido[1,2-*b*]cinnolin-6-ium Hydroxide Inner Salt (**25**).

A suspension of 1.0 g. (4.7 mmoles) of the 2-amino compound **22** in 5 ml. of acetic anhydride was heated on a steam bath for 2 hours. On cooling the product crystallized. It was collected and washed with ether: 1.1 g. (92%) of red prisms, m.p. 307-312°. On recrystallization from dimethylformamide-ethanol, it turned to golden flakes, m.p. 311-314°; uv max (10% DMF in methanol): 250 nm (ϵ 27,580), 307 (1550) and 395 (16,900).

Anal. Calcd. for $C_{14}H_{11}N_3O_2$: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.17; H, 4.39; N, 16.29.

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(1) Presented in part at the Fourth International Congress of Heterocyclic Chemistry held in Salt Lake City, Utah, U.S.A., July, 1973.

(2) We thank Dr. Kurt L. Loening, Director of Nomenclature, Chemical Abstracts Service, ACS, for suggesting this name.

(3) While this work was in progress, some related unusual transformations and their products in the papaverine series were described. M. P. Cava, M. J. Mitchell and D. T. Hill, *Chem. Commun.*, 1601 (1970).

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(16) This crystallographic analysis was conducted in our Physical Chemistry Department by Dr. J. F. Blount. Prisms grown in tetrahydrofuran were used. We are grateful to Dr. Blount for the following summary of his results.

Crystals of **6B** are monoclinic, space group A2/a, with a = 18.91 (2), b = 10.539 (6), c = 10.827 (6) Å, β = 107.58 (4)°, d_{obs} = 1.78, d_{calc} = 1.776 g cm^{-3} for Z = 8. The intensity data were measured on a four-circle diffractometer from a crystal approximately 0.12 x 0.15 x 0.4 mm in size. The data were corrected for absorption [μ(CuKα) = 58.2 cm^{-1}]. The structure was solved by the heavy atom method and the hydrogen atoms were located from a difference Fourier calculated after preliminary refinement. The final refinement was by full matrix least squares with anisotropic thermal parameters for all atoms except the hydrogens which had isotropic temperature factors. The final unweighed discrepancy factor is R = 0.030 for 1520 observed data. The molecule is nearly planar although there is slight folding of the molecule along the axes of the junction of the rings. The maximum deviations from the planes of the six-membered rings are 0.005, 0.013, 0.012 A for rings A, B, C respectively. The angles between the normals to the three rings are 1.6 (A, B), 3.2 (B, C), and 4.8° (A, C).

(17) The product was in the form of a mixture of needles and cake which solidified in the bottom of the beaker. The cake was broken up into small lumps with a spetula before transferring into the funnel. Due to their *potential* explosive properties heating and grinding of dry, solid azides must be performed with caution.

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