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Research Articles

Quinazolines and 1,4-Benzodiazepines XVII

Synthesis of 1,3-Dihydro-5-pyridyl-2*H*-1,4-benzodiazepine Derivatives

By R. IAN FRYER, R. A. SCHMIDT, and L. H. STERNBACH

The synthesis of a series of 5-pyridyl analogs of the psychopharmacologically active class of compounds, 1,4-benzodiazepines, is described. These compounds are being screened for psychosedative, muscle relaxant, and anticonvulsant activity.

THE NEW PSYCHOTHERAPEUTIC agents of the 1,4-benzodiazepine class of compounds, chlordiazepoxide[1] and diazepam,[2] have received wide attention in recent years (1, 2). As a continuation of our earlier work on the synthesis of analogs of 1,4-benzodiazepines (3), we have prepared for pharmacological evaluation several derivatives of 1,3-dihydro-5-(2-pyridyl)-2*H*-1,4-benzodiazepin-2-one and 1,3-dihydro-5-(4-pyridyl)-2*H*-1,4-benzodiazepin-2-one.

The 2-aminobenzoylpyridines III*a,b* (H)[3] used as starting materials for these syntheses are described by Schofield and co-workers (4, 5). However, as recent work by Raynolds and Levine (6) makes 4-phenacyl pyridine readily available, we were able to prepare 4-(2-aminobenzoyl)pyridine III*b* (H) by the much easier route used by Schofield and Ockenden for the synthesis of 2-(2-aminobenzoyl)pyridine III*a* (H).[4] These workers utilized the oxidative fission of the 2,3-double bond of the appropriate indole I*a* (H), followed by hydrolysis of the 2-(2-benzamidobenzoyl)-pyridine II*a* (H) thus obtained.

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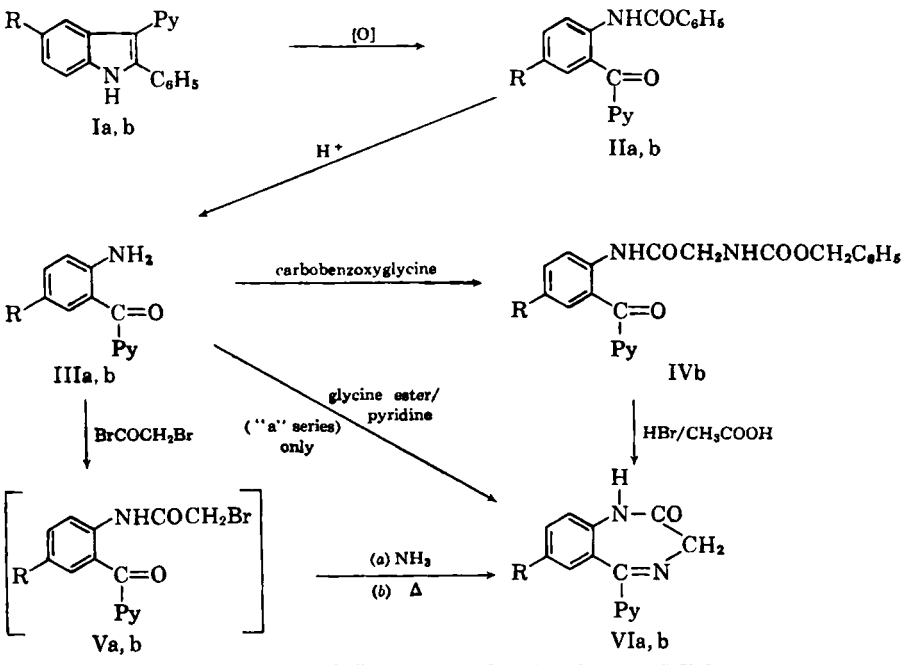
[1] Marketed as Librium by Hoffmann-La Roche, Inc., Nutley, N. J.

[2] Marketed as Valium by Hoffmann-La Roche, Inc., Nutley, N. J.

[3] III*a* (H) indicates compound III*a*, R = H (Scheme I); III*a* (Br) indicates compound III*a*, R = Br, etc.

[4] We found chromium trioxide preferable to ozone as an oxidant for *Ia, b* (H). For example, see Schofield, K., and Theobald, R. S., *J. Chem. Soc.*, **1949**, 796.



a series, Py = 2-C_5H_4N *b* series, Py = 4-C_5H_4N

Scheme I

Attempts to convert III*a* and *b* into benzodiazepinones by condensation with glycine ester hydrochloride showed a significant difference in their reactivity. III*a* (H) reacted readily and gave the desired product VI*a* (H), whereas attempts to form VI*b* (H) by this method were not successful. The second method (III→V→VI) used for the synthesis of these benzodiazepinones gave the desired result for both isomers. The first intermediates, the two bromoacetamido derivatives V*a,b* (H), were prepared in an acid medium to avoid quaternization of the pyridine nitrogen. Two methods were generally employed. The first consisted of treating the dihydrobromide of the aminobenzoyl pyridine in *N,N*-dimethylformamide with 1 mole of bromoacetyl bromide and slowly titrating the mixture with two equivalents of pyridine. The second procedure, which was preferred, consisted of treating III*a,b* (H) in acetic acid with bromoacetyl bromide. Since attempts to obtain the pure bromoacetamido derivatives, V*a,b* (H), as crystalline compounds were unsuccessful, the crude bromoacetyl compounds were converted directly to VI*a,b* (H) by reaction with ammonia. The intermediate aminoacetamidobenzoylpyridines were not isolated. An alternative method for the synthesis of VI*b* (H) proceeded *via* the carbobenzoxyglycyl derivative IV*b*. This compound was prepared using essentially the method that Sheehan and Hess devised for the synthesis of peptides (7, 8). Cleavage of the carbobenzoxy group with hydrogen bromide in glacial acetic acid (9) gave VI*b* (H) directly without isolation of the intermediate, 4-(2-aminoacetamidobenzoyl)pyridine.

The 5-bromo-2-phenyl-3-(2-pyridyl)indole I*a* (Br) and the 1-acetyl derivative of 5-bromo-2-phenyl-3-(4-pyridyl)indole I*b* (Br), prepared by Fischer syntheses, gave the (2-benzamido-5-bromobenzoyl)pyridines II*a,b* (Br) after oxidation. The acetyl derivative of I*b* (Br) was utilized since we were unable to oxidize the parent indole I*b* (Br) successfully in this instance.

Hydrolysis of these compounds afforded the two 2-amino-5-bromobenzoylpyridines, III*a,b* (Br). A simpler method for the preparation of these 5-bromo compounds was the direct bromination of the 2-aminobenzoylpyridines, III*a,b* (H), with bromine in acetic acid.[5] This yielded products which were in every respect identical with the one synthesized by the above unequivocal method. Chlorination of III*a* (H) with chlorine in acetic acid gave a chloro derivative which, by analogy, would be III*a* (Cl).

A dibromo compound was isolated as a by-product from the bromination of III*b* (H). By analogy with similar bromination reactions of 2-aminoacetophenone (10), it is believed to be 4-(2-amino-3,5-dibromobenzoyl)pyridine; but this structure was not established conclusively.

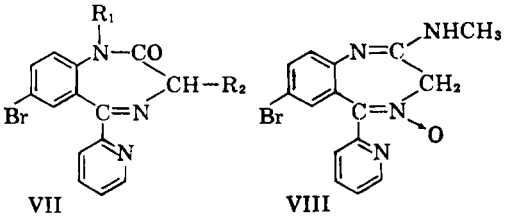
The three halogenated aminobenzoyl pyridines,

[5] Bromination of the acetyl or benzoyl derivatives of III*a,b* (H) proceeded very slowly or not at all, and the yields of the bromo compounds were extremely small when isolated.

IIIa,b (Br), and IIIa (Cl), were converted to the corresponding 7-halo-1,3-dihydro-5-pyridyl-2*H*-1,4-benzodiazepin-2-ones, VIa,b (Br) and VIa (Cl)—as described above—*via* the bromoacetyl derivatives Va,b (Br) and Va (Cl), respectively.

Nitration of the two 1,3-dihydro-5-pyridyl-2*H*-1,4-benzodiazepin-2-ones, VIa,b (H), with potassium nitrate in cold concentrated sulfuric acid gave the two corresponding 1,3-dihydro-7-nitro-5-pyridyl-2*H*-1,4-benzodiazepin-2-ones, VIa,b (NO_2). The nitro group was assumed to be in position 7, based on analogous reactions carried out on 1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-ones described in an earlier paper (11).

Using known procedures (12), IIIa (Br) was converted to the three 5-(2-pyridyl)-1,4-benzodiazepine derivatives VII (R_1 = CH_3, R_2 = H), VII (R_1 = H, R_2 = CH_3), and VIII.



VII VIII

PHARMACOLOGICAL RESULTS

Preliminary screening data indicate that a number of these compounds are nontoxic centrally acting agents with anticonvulsant and psychosedative properties. As other results become available, it is anticipated that they will be reported as an integral part of an overall study of the 1,4-benzodiazepine class of compounds.

EXPERIMENTAL[6]

All melting points are corrected. The infrared absorption spectra of starting materials and reaction products were compared wherever necessary in order to establish structural changes. The infrared spectra were determined in 0.3 to 0.4% chloroform solutions using a Perkin-Elmer model 21 spectrophotometer.

1,3-Dihydro-5-(2-pyridyl)-250-1,4-benzodiazepin-2-one, VIa (H).—*A.* Bromoacetyl bromide (9 ml., 0.1 mole) was added dropwise (15 minutes) to a stirred solution of 2-(2-aminobenzoyl)pyridine IIIa (H) (4), (19.8 Gm., 0.1 mole), in glacial acetic acid (1 L.). The mixture was stirred at room temperature for 2 hours, then concentrated to a gum under reduced pressure. Liquid ammonia (approximately 500 ml.) was carefully added to the residue and allowed to evaporate slowly. The crude product was stirred for 2 hours with 500 ml. of water and filtered. Recrystallization of the precipitate from acetone gave 16.4 Gm. (69%) of VIa (H) as white prisms, m.p. 232–234° dec.

Anal.—Calcd. for $C_{14}H_{11}N_3O$: C, 70.87; H, 4.67. Found: C, 71.18; H, 4.98.

B.—A mixture of 2-(2-aminobenzoyl)pyridine (2.0 Gm., 0.01 mole), glycine ethyl ester hydrochloride (4.2 Gm., 0.03 mole), and pyridine (100 ml.) was refluxed for 8 hours. The solvent was removed under reduced pressure, and the residue was partitioned between water (50 ml.) and benzene (50 ml.). The aqueous layer was extracted with benzene (2 × 50 ml.). The organic layers were combined, washed with water (2 × 25 ml.), and concentrated to 25 ml. The addition of 25 ml. of petroleum ether (b.p. 30–60°) gave 0.5 Gm. (21%) of crystalline material on standing, m.p. 231–232°.

2-(2-Amino-5-bromobenzoyl)pyridine, IIIa (Br).—*A.*—*From 2-Phenacylpyridine.*—2-Phenacylpyridine *p*-bromophenylhydrazone was cyclized with concentrated hydrochloric acid to give 5-bromo-2-phenyl-3-(2-pyridyl)indole Ia (Br) (colorless prisms from ethanol, m.p. 175–177°). This compound was not purified further but oxidized with chromium trioxide (4) to give 2-(2-benzamido-5-bromobenzoyl) pyridine IIa (Br), m.p. 138–140° dec., (yellow prisms from ethanol).

Anal.—Calcd. for $C_{19}H_{13}BrN_2O_2$: C, 59.86; H, 3.44. Found: C, 59.88; H, 3.65.

Hydrolysis of IIa (Br) with concentrated hydrochloric acid gave, after recrystallization from ligroin (b.p. 90–120°), IIIa (Br) as yellow needles, m.p. 96–98°.

Anal.—Calcd. for $C_{12}H_9BrN_2O$: C, 52.01; H, 3.27. Found: C, 52.03; H, 3.57.

B.—*From 2-(2-Aminobenzoyl)pyridine.*—A solution of bromine (35 ml., 0.70 mole) in glacial acetic acid (600 ml.) was added dropwise to a stirred solution of 2-(2-aminobenzoyl)pyridine IIIa (H) (131 Gm., 0.66 mole) kept at 15–17° with an ice bath. The reaction mixture was allowed to warm to room temperature and stirred for 20 hours. The red crystalline hydrobromide was separated by filtration and washed with cold glacial acetic acid. The base was liberated by decomposition of the salt with water (2.5 L.). The product was separated by filtration, dried, and recrystallized from ligroin (b.p. 90–120°). By making the filtrate basic with sodium hydroxide solution, additional product was obtained which was filtered, dried, recrystallized, and added to the first crop. The product (154.5 Gm., 84%) was obtained as bright yellow needles, melting point and mixed melting point with the product obtained by *Method A*, 96–98°.

2-(2-Amino-5-chlorobenzoyl)pyridine, IIIa (Cl).—A solution of chlorine (1.36 Gm., 0.019 mole) in glacial acetic acid (50 ml.) was added over a 15-minute period to a cold, stirred solution of IIIa (H) (3.57 Gm., 0.018 mole) in glacial acetic acid (25 ml.). The mixture was stirred for 15 minutes and allowed to stand overnight at room temperature. The solvent was removed under reduced pressure, and the residue was digested with hot water (50 ml.) and allowed to cool. After 3 days of standing, the solution deposited 1.0 Gm. of yellow crystalline solid which was filtered and recrystallized from ligroin (b.p. 90–120°) to give 0.84 Gm. (20%) of product as yellow prisms, m.p. 99–101°.

Anal.—Calcd. for $C_{12}H_9ClN_2O$: C, 61.94; H, 3.90. Found: C, 62.09; H, 4.04.

7-Bromo-1,3-dihydro-5-(2-pyridyl)-2H-1,4-benzodiazepin-2-one, VIa (Br).—A mixture of IIIa (Br) (1.0 Gm., 3.6 mmole), glycine ethyl ester hydrochloride (0.75 Gm., 5.4 mmoles) and pyridine (100 ml.) was refluxed and worked up as described for

[6] The *Experimental* was performed in part with Mr. R. Czajkowski.

the *preparation of VIa (H) Method B* to give, after recrystallization from acetone, 235 mg. (20%) of VIa (Br) as colorless prisms, m.p. 237 to 238.5°.

Anal.—Calcd. for $C_{14}H_{10}BrN_3O$: C, 53.18; H, 3.19. Found: C, 53.36; H, 3.38.

7 - Chloro - 1,3 - dihydro - 5 - (2 - pyridyl) - 2H - 1,4-benzodiazepin-2-one, VIa (Cl).—Using the procedure described for the *preparation of VIa (H) Method A*, 4.66 Gm. of IIIa (Cl) gave, after recrystallization from ethanol, 3.1 Gm. (57%) of VIa (Cl) as yellow prisms, m.p. 225–226° dec.

Anal.—Calcd. for $C_{14}H_{10}ClN_3O$: C, 61.88; H, 3.71. Found: C, 61.92; H, 3.91.

1,3 - Dihydro - 7 - nitro - 5 - (2 - pyridyl) - 2H - 1,4-benzodiazepin-2-one, VIa (NO_2).—A solution of potassium nitrate (5.04 Gm., 0.05 mole) in concentrated sulfuric acid (30 ml.) was added dropwise at 5° to a solution of VIa (H) (11.2 Gm., 0.047 mole) in concentrated sulfuric acid (100 ml.). The reaction mixture was stirred at 5° for 2 hours, then poured onto ice in a vessel cooled by an ice-salt bath. The solution was kept at 0° and made alkaline (pH 8) by the addition of ammonium hydroxide (450 ml.). The product was filtered and recrystallized from acetone to give 6 Gm. (45%) of VIa (NO_2) as colorless prisms, m.p. 254–255° dec.

Anal.—Calcd. for $C_{14}H_{10}N_4O_3$: C, 59.57; H, 3.57; N, 19.85. Found: C, 60.00; H, 4.06; N, 20.04.

7 - Bromo - 1,3 - dihydro - 1 - methyl - 5 - (2 - pyridyl)-2H-1,4-benzodiazepin-2-one, VII (R_1 = CH_3, R_2 = H).—Alkylation of VIa (Br) (7.5 Gm., 0.024 mole) with methyl iodide by a previously described procedure (3) gave 5.51 Gm. (70%) of VII (R_1 = CH_3, R_2 = H) as pale yellow crystals, m.p. 136–137°.

Anal.—Calcd. for $C_{16}H_{12}BrN_3O$: C, 54.56; H, 3.66. Found: C, 54.71; H, 3.73.

7 - Bromo - 1,3 - dihydro - 3 - methyl - 5 - (2 - pyridyl)-2H-1,4-benzodiazepin-2-one, VII (R_1 = H, R_2 = CH_3).—By substituting α-bromopropionyl bromide for bromoacetyl bromide and 2-(2-amino-5-bromobenzoyl)pyridine for 2-(2-aminobenzoyl)pyridine in the procedure described for the *preparation of VIa (H) Method A*, a 30% yield of VII (R_1 = H, R_2 = CH_3) was obtained as cream-colored crystals from acetone, m.p. 228–229°.

Anal.—Calcd. for $C_{16}H_{12}BrN_3O$: C, 54.66; H, 3.66. Found: C, 54.51; H, 3.39.

7 - Bromo - 2 - methylamino - 5 - (2 - pyridyl) - 3H-1,4-benzodiazepine 4-oxide, VIII.—2-(2-Amino-5-bromobenzoyl)pyridine was converted to the oxime(12), m.p. 163–166°.

Anal.—Calcd, for $C_{12}H_{10}BrN_3O$: C, 49.33; H, 3.45. Found: C, 49.41; H, 3.33.

Then, by treating with chloroacetyl chloride, it was converted to 2-chloromethyl-4-(2-pyridyl)-6-bromoquinazoline 3-oxide (12), m.p. 206° dec.

Anal.—Calcd. for $C_{14}H_9BrClN_3O$: C, 47.96; H, 2.59. Found: C, 48.07; H, 2.65.

Reaction of the quinazoline derivative with methylamine in methanol (12) resulted in ring enlargement and formation of the 5-pyridyl-1,4-benzodiazepine 4-oxide, which was isolated in the usual manner (12). It formed cream-colored prisms after recrystallization from acetone, m.p. 231–233° dec.

Anal.—Calcd. for $C_{15}H_{12}BrN_4O$: C, 52.19; H, 3.79. Found: C, 52.46; H, 4.04.

4-(2-Aminobenzoyl)pyridine, IIIb (H).—Using the methods described by Ockenden and Schofield (4), 4-phenacylpyridine (6) was converted *via* the phenylhydrazone into 2-phenyl-3-(4-pyridyl)indole *Ib* (H), m.p. 257–258°, colorless prisms from acetic acid.

Anal.—Calcd. for $C_{19}H_{14}N_2$: C, 84.42; H, 5.22. Found: C, 84.57; H, 5.57.

The indole was oxidized with chromium trioxide to give 4-(2-benzamidobenzoyl)pyridine II*b* (H), m.p. 129–130°, (colorless prisms from ethanol).

Anal.—Calcd. for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67. Found: C, 75.61; H, 4.51.

This was hydrolyzed with concentrated hydrochloric acid to give III*b* (H). This crystallized from methanol as yellow needles melting at 159.5 to 160°.[7]

Anal.—Calcd. for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09. Found: C, 72.56; H, 4.66.

[2 - (4 - Pyridylcarbonyl)phenyl]carbamoylmethylcarbamic Acid Benzyl Ester, IVb (H).—A mixture of 4-(2-aminobenzoyl)pyridine (5.0 Gm., 0.025 mole) and carbobenzoxy glycine (5.3 Gm., 0.025 mole) in methylene chloride (200 ml.) was cooled to 19°. *N,N'*-Dicyclohexylcarbodiimide (5.2 Gm., 0.025 mole) was added, and the solution stirred for 2 hours. The mixture was refrigerated (+5°) for 3 days; *N,N'*-dicyclohexyl urea was removed by filtration and discarded. The methylene chloride solution was concentrated *in vacuo* at room temperature. The residue was dissolved in benzene and was chromatographed through a column of florisil (90 Gm.) after filtration. The benzene fractions were discarded, and the eluant changed to ether. The ether fractions gave 3.5 Gm. (35.7%) of white needles which were recrystallized from a benzene–petroleum ether mixture, m.p. 130 to 130.5°.

Anal.—Calcd. for $C_{22}H_{19}N_3O_4$: C, 67.85; H, 4.92. Found: C, 68.03; H, 4.99.

1,3 - Dihydro - 5 - (4 - pyridyl) - 2H - 1,4-benzodiazepin-2-one, VIb (H).—*A.—From the Carbobenzoxyglycine Derivative, IVb (H).*—A solution of hydrogen bromide in glacial acetic acid (33% w/w), (20 ml.) was added dropwise at room temperature to a stirred solution of the carbobenzoxy compound IV*b* (H) (3.5 Gm., 9.0 mmole) in glacial acetic acid (10 ml.). The mixture was stirred for an additional 4 hours and diluted with 1 L. of diethyl ether. The precipitated hydrobromide (2.8 Gm., m.p. 254–255°) was separated by filtration and dissolved in water (100 ml.). The solution was made alkaline (pH 8) with concentrated ammonium hydroxide; the resulting precipitate was separated by filtration and recrystallized from benzene to give 1.6 Gm. (75%) of white needles, m.p. 206–207°.

Anal.—Calcd. for $C_{14}H_{11}N_3O$: C, 70.87; H, 4.67. Found: C, 71.00; H, 4.82.

B.—From 4-(2-Aminobenzoyl)pyridine, IIIb (H).—1. A solution of 4-(2-aminobenzoyl)pyridine III*b* (H) (5.0 Gm., 0.025 mole) in *N,N*-dimethylformamide (20 ml.) was saturated with hydrogen bromide. Excess hydrogen bromide was removed by warming under reduced pressure. Bromoacetyl bromide (5.1 Gm., 0.024 mole, 2.2 ml.) was added dropwise to the resulting mixture with stirring. A solution of pyridine (4.0 Gm., 0.05 mole, 4.0 ml.) in *N,N*-dimethylformamide (5 ml.) was added over a 5-minute period. The mixture was stirred for a few hours; approximately 300 ml. of liquid ammonia was carefully added. The ammonia was allowed to

[7] Schofield (5) reports m.p. 160–161°

evaporate overnight, and the reaction mixture was taken up in benzene (100 ml.). Ammonium bromide was removed by filtration. The benzene solution was washed with water (3 × 100 ml.) and concentrated under reduced pressure. Recrystallization of the residue from an acetone–hexane mixture gave 2.5 Gm. (41%) of white needles, m.p. 206–207°.

2. A solution of 4-(2-aminobenzoyl)pyridine III*b* (H), (16 Gm., 0.08 mole) in glacial acetic acid, was treated with bromoacetyl bromide and then with ammonia as described for the *preparation of VIa (H), Method A* to give 7.0 Gm. (36.5%) of crude VI*b* (H), melting at 203–205°.

4-(2-Amino-5-bromobenzoyl)pyridine IIIb (Br) and 4-(2-Amino-3,5-dibromobenzoyl)-pyridine.—*A. —From 4-Phenacylpyridine.*—The crude *p*-bromophenylhydrazone of 4-phenacylpyridine was cyclized in hydrochloric acid to give 5-bromo-2-phenyl-3(4-pyridyl)indole, I*b* (Br), m.p. 312–313° (yellow prisms from acetic acid).

Anal.—Calcd. for $C_{19}H_{13}BrN_2$: C, 65.34; H, 3.75. Found: C, 65.04; H, 3.96.

Acetylation of the indole was accomplished by treating the compound under reflux in a mixture of acetic anhydride and potassium acetate for 3 hours. The reaction mixture was cooled, poured into water. and the product extracted into ether. Removal of the solvent and recrystallization of the residue from acetone gave 1-acetyl-5-bromo-2-phenyl-3(4-pyridyl) indole as white prisms, m.p. 172–173°.

Anal.—Calcd. for $C_{21}H_{15}BrN_2O$: C, 64.46; H, 3.86. Found: C, 64.16; H, 3.84.

This product was then oxidized with trifluoroperacetic acid (13, 14). The crude product was hydrolyzed with 50% (v/v) sulfuric acid to give III*b* (Br). After crystallization from chloroform, yellow prisms were obtained melting at 213–214°.

Anal.—Calcd. for $C_{12}H_9BrN_2O$: C, 52.01; H, 3.27. Found: C, 51.95; H, 3.13.

B.—From 4-(2-Aminobenzoyl)pyridine.—A solution of bromine (25 Gm., 0.16 mole, 8 ml.) in glacial acetic acid (5 ml.) was added dropwise with stirring to a solution of 4-(2-aminobenzoyl)pyridine, III*b* (H), (30 Gm., 0.15 mole) in glacial acetic acid (200 ml.) cooled in an ice bath. The mixture was stirred for 10 minutes, diluted with water (300 ml.), and made alkaline with solid sodium hydroxide. The crystalline residue was separated by filtration, washed with water, then dissolved in benzene. Residual water was removed by azeotropic distillation. The benzene solution was concentrated to a small volume and chromatographed on grade I neutral alumina (300Gm.).

Elution of the column with chloroform gave the dibromo compound (8.3 Gm.), m.p. 139–140°, which gave yellow needles on recrystallization from ether, m.p. 141–142°.

Anal.—Calcd. for $C_{12}H_8Br_2N_2O$: C, 40.37; H, 2.54. Found: C, 40.13; H, 2.38.

Eluting with 50% benzene/ether (v/v) gave 15.8 Gm. of the monobromo derivative III*b* (Br). Further elution of the column with methanol gave 4 Gm. of starting material. The dibromo ketone could also be prepared by further bromination of III*b* (Br) under the conditions described above.

7 - Bromo - 1,3 - dihydro - 5 - (4 - pyridyl) - 2H - 1,4-benzodiazepin-2-one, VIb (Br).—The 1,4-benzodiazepinone was prepared from 13 Gm. (0.36 mole) of III*b* (Br) as described for *IIIb(H), Procedure B.1.* The crude product (8.8 Gm.) was purified by crystallization and yielded 3 Gm. of starting material and 4.5 Gm. (39%) of the desired product. Recrystallization from acetone gave white needles, m.p. 228 to 228.5°.

Anal.—Calcd. for $C_{14}H_{10}BrN_3O$: C, 53.18; H, 3.19. Found: C, 53.09; H, 3.38.

1,3 - Dihydro - 7 - nitro - 5 - (4 - pyridyl) - 2H - 1,4-benzodiazepin-2-one, VIb (NO_2).—A solution of 5-(4-pyridyl)-1,4-benzodiazepinone, VI*b* (H), (6.0 Gm., 0.025 mole) in concentrated sulfuric acid (30 ml.) was nitrated as described under the *preparation of VIa (NO_2).* The reaction mixture was worked up as described above and gave 3.0 Gm. (42.5%) of pale yellow needles after recrystallization from acetone, m.p. 242 to 242.5°.

Anal.—Calcd. for $C_{14}H_{10}N_4O_3$: C, 59.57; H, 3.57. Found: C, 59.71; H, 3.26.

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