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The syntheses of novel 8-chloropyrazolo[1,5-*a*][1,4]benzodiazepines and of an imidazobenzodiazepinone utilizing products from the nucleophilic substitution of fluorine in 2-fluoro-5-nitrobenzophenone (**1**) by pyrazole-3,5-dicarboxylic acid, dimethyl ester (**2**) and by 2-methylimidazole-4,5-dicarboxylic acid, diethyl ester (**30**) are described.

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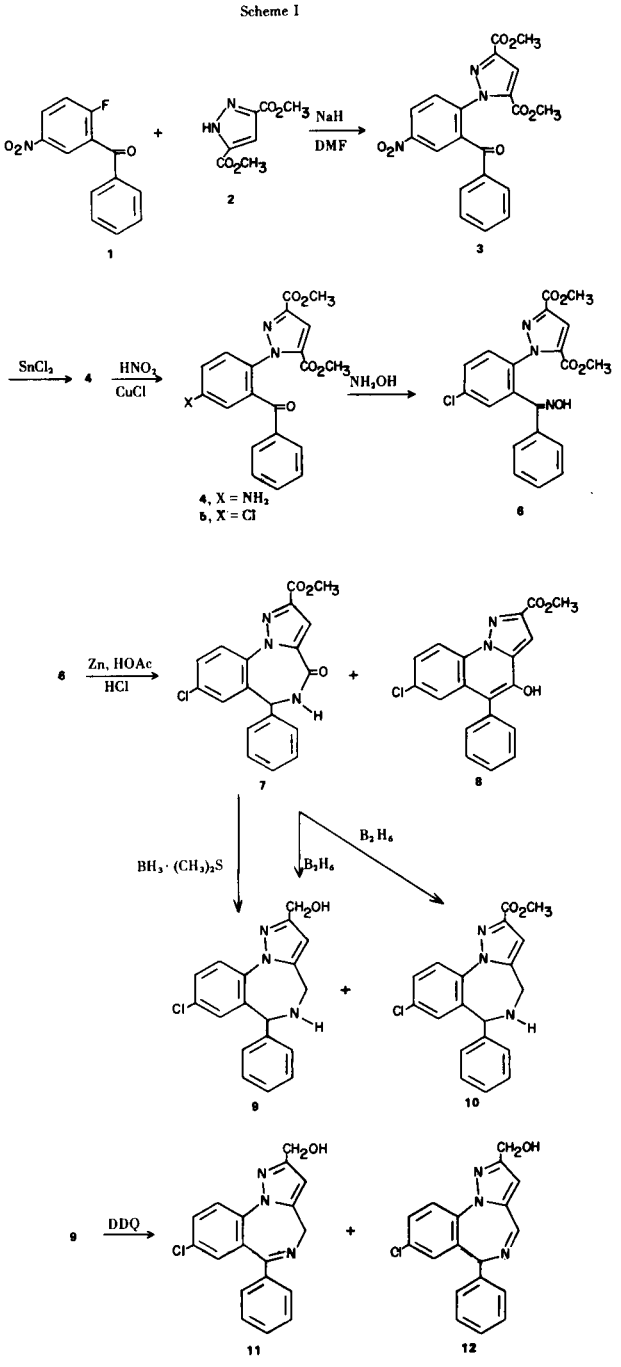
As described in the preceding paper (2), the fluorine in 2-fluoro-5-nitrobenzophenone (**1**) is readily displaced by various heterocyclic compounds leading to intermediates of potential synthetic utility in the preparation of novel 1,4-benzodiazepines. In this paper we report the synthesis of 8-chloro[1,5-*a*][1,4]benzodiazepines from one of these intermediates, **3**, and the synthesis of the imidazobenzodiazepinone, **30**, from the related intermediate, **26**.

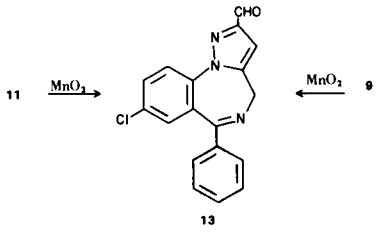
The treatment of **1** with the sodium salt of the pyrazolo diester, **2** (3), in dimethylformamide led to the benzophenone, **3**. The conversion of the nitro group to a chloro substituent was carried out by a Sandmeyer procedure involving reduction of **3** with stannous chloride to give the amino compound **4**. Diazotization with nitrous acid followed by treatment with cuprous chloride gave the chloro compound **5**. The synthesis of the pyrazolo-[1,5-*a*][1,4]benzodiazepine ring system was achieved by the oximation of **5** to compound **6** which was reductively cyclized to **7** in 55% yield by treatment with zinc in acetic acid. In addition to compound **7**, 26% of the hydroxyquinoline, **8**, was isolated. The structure of the by-product, **8**, was assigned on the basis of elemental analysis ($C_{19}H_{13}ClN_2O_3$); mass spectrum (M^+, m/e 352); ir spectrum (hydroxy and ester bands); and nmr spectrum (no CH_2, one exchangeable proton). Compounds **7** and **8** were easily separated by column chromatography.

The reduction of the lactam ester, **7**, to the dihydrobenzodiazepine, **9**, was carried out with excess borane-dimethylsulfide complex which reduced both the lactam and ester groups. The use of diborane in tetrahydrofuran gave a mixture of **9** and the partially reduced amino-ester **10**. The oxidation of **9** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) yielded 8-chloro[1,5-*a*][1,4]-benzodiazepine (**11**) in 62% yield along with 10% of the isomeric 6*H* compound, **12**. (Scheme I).

The isomers **11** and **12**, were easily distinguishable on the basis of their nmr spectra. The spectrum of **12** showed the 6*H* () proton at 5.36 ppm while the spectrum of **11** showed no evidence of this proton but had a -CH_2-signal at 4.70 ppm.

Scheme I



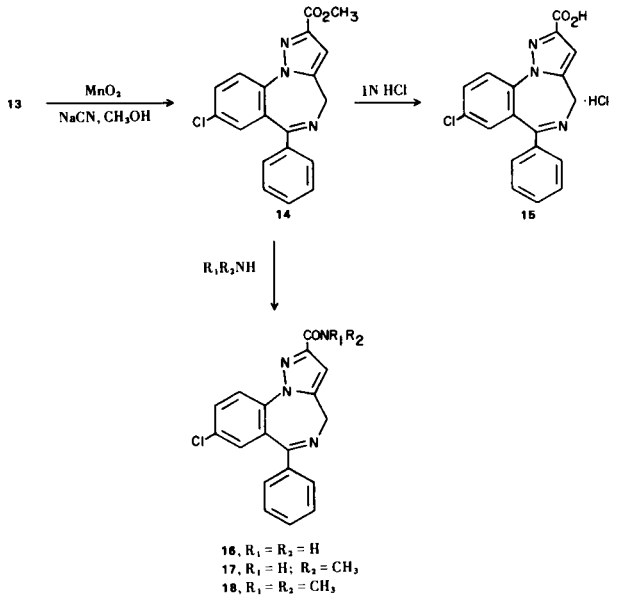


The alcohol **11** was oxidized to the aldehyde, **13**, with manganese dioxide. Attempts to oxidize the dihydro-alcohol, **9**, directly to **13** resulted in lower overall yields.

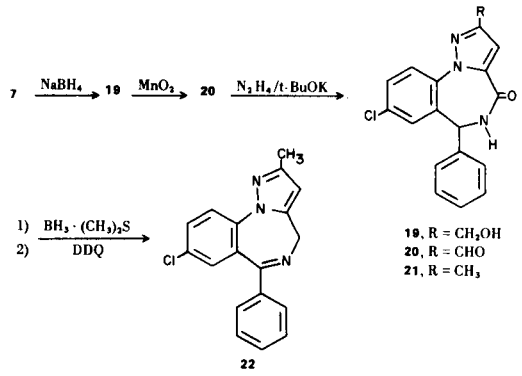
The aldehyde, **13**, proved to be a versatile intermediate for the preparation of various 2-substituted pyrazolo-benzodiazepines (Scheme II). The carboxylic ester, **14**, was prepared from **13** by treatment with manganese dioxide in methanol in the presence of sodium cyanide (4). The ester was subsequently converted either to the acid, **15**, by acid hydrolysis or to the amides, **16**, **17** and **18**, by treatment with ammonia, methylamine and dimethyl-amine, respectively.

An additional pyrazolobenzodiazepine, the 2-methyl analog, was prepared starting with compound **7**. The ester function was reduced with sodium borohydride to the alcohol **19**. Oxidation with manganese dioxide gave the aldehyde **20** which under Wolff-Kishner conditions gave the methyl compound **2**. The product **22** was obtained by reduction of the amide group of **21** followed by DDQ oxidation.

Scheme II

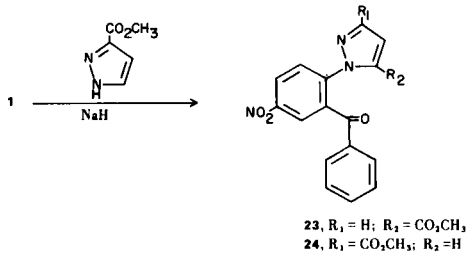


In an attempt to prepare an unsubstituted pyrazolo-benzodiazepine, it was of interest to note that when compound **1** was reacted with pyrazole-3(5)carboxylic acid, methyl ester, only one product was isolated from the reaction mixture.



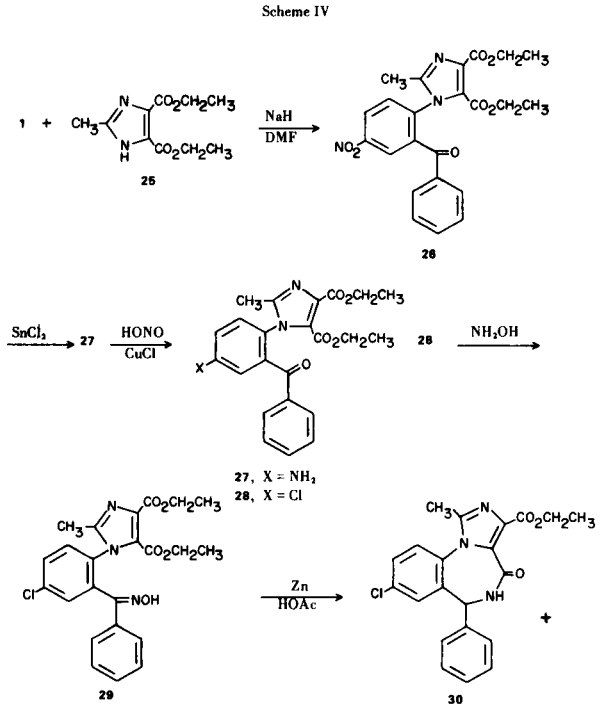
Application of the chemistry in Scheme I to this product failed to produce a tricyclic derivative. Accordingly we assigned it structure **24** (2) rather than **23**.

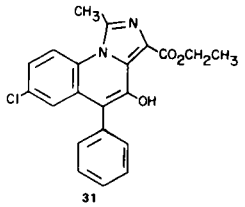
Scheme III



The displacement of fluoride from **1** by the anion of 2-methyl-4,5-imidazole dicarboxylic acid, diethyl ester (**25**) (5) gave **26** which was converted to the benzo-diazepinone **30** by the sequence of reactions outlined in Scheme IV.

Scheme IV





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The reduction of the nitro group in **26** was carried out with stannous chloride to give the amine **27**. A Sandmeyer reaction on **27** gave the chloro compound, **28**. The oxime **29** was prepared by oximation of **28** with hydroxylamine in pyridine. Reduction of **29** with zinc in acetic acid gave a mixture of the imidazobenzodiazepinone **30** and the quinoline **31**. The structure of **31** was assigned on the basis of microanalytical and spectral data in comparison with the data obtained from the quinoline **8**.

EXPERIMENTAL

Melting points were determined with a Thomas-Hoover capillary apparatus and are corrected. The ir spectra were recorded on a Digilab FTS14 or a Perkin-Elmer 621 spectrometer, mass spectra on a Varian MAT CH5 or a CEC 21-110 instrument, and nmr spectra on a Jeolco C-60H, a Varian XL-100 or HA-100 instrument, using tetramethylsilane as an internal standard. Silica gel 60 (Merck, 60-230 mesh) was used for chromatography and either anhydrous sodium sulfate or magnesium sulfate was used for drying organic solutions.

1-(2-Benzoyl-4-aminophenyl)-3,5-pyrazoledicarboxylic Acid, Dimethyl Ester (**4**).

A solution of 33.0 g. (150 mmoles) of stannous chloride dihydrate in 65 ml. of 6*N* hydrochloric acid and 200 ml. of acetic acid was added to a warm solution of 17.5 g. (42.7 mmoles) of **3** (2) in 225 ml. of acetic acid. After cooling to room temperature and stirring for 16 hours, the reaction was poured into an ice-water slurry and made very basic ($pH > 13$) with sodium hydroxide pellets, keeping the temperature of the mixture below 20° with extra additions of ice. The basic mixture was extracted thoroughly with dichloromethane. The combined extracts were washed with brine, dried and concentrated *in vacuo* to give 14.5 g. (90%) of **4**. Recrystallization from dichloromethane/hexane gave an analytical sample of **4** as pale yellow needles, m.p. 171-172°; ir (potassium bromide): 3460, 3320 cm^{-1} (NH).

Anal. Calcd. for $C_{20}H_{15}N_3O_7$: C, 58.68; H, 3.69; N, 10.26. Found: C, 58.98; H, 3.67; N, 10.21.

1-(2-Benzoyl-4-chlorophenyl)-3,5-pyrazoledicarboxylic Acid, Dimethyl Ester (**5**).

To a solution of 13.1 g. (34.5 mmoles) of **4** in 50 ml. of acetic acid and 75 ml. of 3*N* hydrochloric acid, stirred at 3°, was added dropwise so as to maintain a temperature of 3-6°, a solution of 2.50 g. (36.3 mmoles) of sodium nitrite in 25 ml. of water. When the addition was complete, the reaction was stirred at 3° for 20 minutes. A fresh solution of cuprous chloride in concentrated hydrochloric acid (prepared from 27 g. of cupric sulfate pentahydrate (6)) was mixed with an equal volume of water and cooled to 3°. The diazotized solution, which had to be kept cold (<5°) at all times, was slowly poured into the vigorously stirred cuprous chloride solution, in several portions in order to control foaming. When addition was complete, the reaction was stirred for one hour while slowly warming to room temperature, then heated on a steam bath to an internal temperature of 95°. After cooling to room temperature, the reaction was made basic with ammonium hydroxide and extracted well with dichloromethane. The combined extracts were washed with brine, dried and concentrated *in vacuo* to a brown oil. This crude product was chromatographed on silica gel using a 2% ethyl acetate in benzene solution as eluent to give 8.26 g. (60%) of **5**. An analytical sample was prepared by recrystallization from ether/hexane and was obtained as colorless crystals, m.p. 118-120°; ir (potassium bromide): 1730, 1745 cm^{-1} (C=O), no N-H; nmr (deuteriochloroform): δ 3.63 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 7.08 (1H, s, C_3N_2H), 7.46 (8H, m, C_6H_5 and C_6H_3).

Anal. Calcd. for $C_{20}H_{15}N_2O_5Cl$: C, 60.24; H, 3.79; N, 7.02; Cl, 8.89. Found: C, 60.25; H, 3.84; N, 7.28; Cl, 8.82.

1-[4-Chloro-2-(α-hydroxyiminobenzyl)phenyl]-3,5-pyrazoledicarboxylic Acid, Dimethyl Ester (**6**).

A mixture of 11.2 g. (28 mmoles) of **5**, 5.80 g. (84 mmoles) of hydroxylamine hydrochloride and 180 ml. pyridine was heated to reflux for 6.5 hours. After cooling to room temperature the reaction was concentrated *in vacuo*. The crude product was then chromatographed on silica gel, using 10% ethyl acetate in benzene as eluent, to give 6.79 g. (59%) of **6**. Recrystallization from ethanol/water gave an analytical sample of **6** as colorless prisms, m.p. 177-179°; ir (potassium bromide): 3410 (OH), 1743, 1722 cm^{-1} (C=O of ester); nmr (dimethyl sulfoxide-d_6): δ 3.53 (3H, s, OCH_3), 3.68 (3H, s, OCH_3), 7.08 (6H, m, C_6H_5, C_3N_2H), 7.50 (3H, m, C_6H_3), 11.33 (1H, s, NOH).

Anal. Calcd. for $C_{20}H_{16}ClN_3O_5$: C, 58.05; H, 3.90; N, 10.15. Found: C, 58.30; H, 3.83; N, 9.99.

8-Chloro-5,6-dihydro-4-oxo-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]-benzodiazepine-2-carboxylic acid, Methyl Ester (**7**) and 7-Chloro-4-hydroxy-5-phenylpyrazolo[1,5-*a*]quinoline-2-carboxylic Acid, Methyl Ester (**8**).

To a mixture of 13.5 g. (33 mmoles) of **6**, 10.7 g. (165 mmoles) of zinc dust and 85 ml. of acetic acid, was added 1 ml. of concentrated hydrochloric acid. The reaction mixture was then heated in a 70° oil bath for 5.75 hours, cooled to room temperature and filtered through diatomaceous earth (Hyflo Supercel®). The collected solids were washed thoroughly with dichloromethane and the combined filtrate and washings concentrated *in vacuo*.

The residue was cautiously neutralized and made basic with saturated sodium carbonate solution; sodium ethylenediaminetetraacetate was added to complex the zinc salts and the mixture was extracted well with dichloromethane. The combined extracts were washed with saturated sodium bicarbonate solution, then with brine, dried and concentrated. The residue was triturated with acetone to give 4.10 g. of **7**. The concentrated mother liquor was chromatographed on silica gel packed in benzene, using benzene containing gradually increasing amounts of ethyl acetate (5-40%) as eluent. The side product **8**, 3.02 g. (26%) was eluted first and then the desired product **7**, 2.54 g. (total yield 6.64 g., 55%) was obtained. A small amount of **8** was recrystallized from acetone/hexane to give an analytical sample as colorless needles, m.p. 236.5-238°; ir (potassium bromide): 3375 (OH), 1720 cm^{-1} (ester C=O), nmr (deuteriochloroform): δ 4.01 (3H, s, OCH_3), 7.26-7.68, (8H, m, C_6H_4, C_6H_3 and C_3N_2H), 8.58 (1H, d, C_6H), 9.22 (1H, bm, OH).

Anal. Calcd. for $C_{19}H_{13}ClN_2O_3$: C, 64.69; H, 3.71; N, 7.94; Cl, 10.05. Found: C, 64.53; H, 3.70; N, 7.82; Cl, 9.88.

An analytical sample of **7** was prepared by recrystallization from acetone/hexane and was obtained as colorless crystals, m.p. 222-224°; ir (potassium bromide): 3340, 3320 (NH), 1740

(ester C=O), 1670 cm^{-1} (lactam C=O); nmr (deuteriochloroform): δ 3.84 (3H, s, OCH_3), 5.51 (1H, d, CH), 6.90-7.90 (9H, m, C_6H_5, C_6H_3 and C_3N_2H), 8.50 (1H, d, NH).

Anal. Calcd. for $C_{19}H_{14}ClN_3O_3$: C, 62.05; H, 3.84; N, 11.43. Found: C, 61.97; H, 3.86; N, 11.33.

8-Chloro-5,6-dihydro-5-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine-2-methanol (**9**) and 8-Chloro-5,6-dihydro-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine-2-carboxylic Acid Methyl Ester (**10**).

Method A.

To a solution of 6.72 g. (18.3 mmoles) of **7** in 190 ml. of dry tetrahydrofuran cooled to 3° and under argon was added dropwise 91.5 ml. (91.5 mmoles) of 1*M* diborane in tetrahydrofuran, while maintaining a temperature of less than 5°. When addition was complete, the reaction was stirred at 3-5° for 10 minutes. After slowly warming to room temperature, the reaction was heated to reflux for 16 hours, then cooled to 5°, and 40 ml. of 3*N* hydrochloric acid was added dropwise to quench the reaction. The acidic reaction mixture was stirred 40 minutes at room temperature, then made basic with ice and 3*N* sodium hydroxide and extracted well with dichloromethane. The combined extracts were dried and concentrated to give 7 g. of foamy white solid. This crude product was chromatographed on silica gel packed in benzene, using benzene containing 0-100% ethyl acetate as eluent. The partially reduced side product **10**, 650 mg. (10%) was eluted first and then the more polar product **9**, 3.3 g. (55%).

A small amount of **10** was recrystallized from acetone/ether/hexane to give an analytical sample as colorless crystals, m.p. 160-161°; ir (potassium bromide): 3290, 3185 (NH), 1740 cm^{-1} (C=O); mass spectrum: m/e 353 (M^+).

Anal. Calcd. for $C_{19}H_{16}ClN_3O_2$: C, 64.50; H, 4.56; N, 11.88. Found: C, 64.59; H, 4.50; N, 11.91.

A small amount of **9** was recrystallized twice from acetone/hexane to give an analytical sample as colorless needles, m.p. 117-119°; ir (potassium bromide): 3305 cm^{-1} (OH), no C=O bands.

Anal. Calcd. for $C_{18}H_{16}ClN_3O$: C, 66.36; H, 4.95; N, 12.90. Found: C, 66.53; H, 4.83; N, 12.80.

Method B.

To a solution of 12.1 g. (32.9 mmoles) of **7** in 310 ml. of dry tetrahydrofuran under argon, was added dropwise *via* syringe over a 15-minute time period, 13.1 ml. (131 mmoles) of borane-methyl sulfide (BMS). The reaction was stirred at room temperature for 1.25 hours. After replacing the argon supply with a drying tube, the reaction was heated to reflux for 19 hours. A tlc analysis done at that time indicated no starting material remained, nor was any of the side product **10** present. Methanol (150 ml.) was added dropwise (very slowly at first, 15 minutes for the first 5 ml.), to quench the reaction, keeping the temperature below 30°. When the addition was complete, the reaction was stirred 2 hours at room temperature, cooled to 5° and dry gaseous hydrogen chloride bubbled into the reaction (keeping the temperature below 10°) until a *p*H of < 2 was reached. The acidic solution was heated to reflux for 2.5 hours, cooled and concentrated *in vacuo*. The residue was taken up in methanol (500 ml.) and reconcentrated to dryness. The residue was mixed with ice, dichloromethane and 3*N* sodium hydroxide. The two phases were separated, and the aqueous phase extracted well with dichloromethane. The combined organic phases were washed with brine, dried and concentrated *in vacuo* to give 11.8 g. of semipure **9**, which by tlc analysis (comparison with authentic sample) was shown to be greater than 80% pure (> 80% yield). This crude product was then used as isolated in the DDQ oxidation.

8-Chloro-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine-2-methanol (**11**) and 8-Chloro-6-phenyl-6*H*-pyrazolo[1,5-*a*][1,4]-benzodiazepine-2-methanol (**12**).

A solution of 8.96 g. (39.5 mmoles) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in 450 ml. of benzene was added dropwise to a solution of 11.8 g. (> 26.3 mmoles) of semipure **9** (from the BMS reduction) in 325 ml. of benzene. When addition was complete, the dark green solution was heated to reflux for 30 minutes to yield an orange mixture. After cooling to room temperature, the mixture was filtered and the collected solids washed thoroughly with benzene. The combined filtrate and washings were concentrated *in vacuo* and the residue taken up in ethyl acetate and washed twice with water. The organic phase was then extracted six times with 3*N* hydrochloric acid and the combined acidic phases were washed with ethyl acetate and then made basic. The basic solution was extracted four times with dichloromethane and the combined extracts washed with brine, dried and concentrated *in vacuo*. The crude product was chromatographed on silica gel packed in benzene, using 25% ethyl acetate in benzene to elute the unwanted isomer, **12** and then with ethyl acetate to elute the desired isomer **11**.

The purification yielded 1.10 g. (10%) of **12**; an analytical sample was prepared by recrystallization from ether/hexane and obtained as colorless needles, m.p. 147-149°; ir (potassium bromide): 1625 cm^{-1} (C=N); nmr (deuteriochloroform): δ 3.00 (1H, bs, OH), 4.84 (2H, bs, CH_2OH), 5.36 (1H, bs, CHN), 6.78 (1H, s, C=CH), 6.80 (1H, s, C=CH), 7.40-8.05 (7H, bm, C_6H_5, C_6H_2), 8.56 (1H, d, N=CH); mass spectrum: m/e 323 (M^+).

Anal. Calcd. for $C_{18}H_{14}ClN_3O$: C, 66.77; H, 4.36; N, 12.98. Found: C, 67.01; H, 4.22; N, 13.03.

The desired product **11** was isolated in a yield of 62% (6.6 g.). An analytical sample was prepared by recrystallization from acetone/hexane and was obtained as colorless needles, m.p. 174-176°; ir (potassium bromide): 1633 cm^{-1} (C=N); nmr (deuteriochloroform): δ 3.40 (1H, bm, OH), 4.70 (4H, bd, CH_2OH, CH_2), 6.32 (1H, s, C_3N_2H), 7.48 (8H, bm, C_6H_5, C_6H_3); mass spectrum: m/e 323 (M^+).

Anal. Calcd. for $C_{18}H_{14}ClN_3O$: C, 66.77; H, 4.36; N, 12.98. Found: C, 66.97; H, 4.34; N, 13.00.

8-Chloro-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine-2-carboxyaldehyde (**13**).

A. From Compound **9**.

To a solution of 400 mg. (1.23 mmoles) of **9** in 40 ml. of dichloromethane, was added 1.50 g. of manganese dioxide. The mixture was stirred for 1.75 hours at 5°, then warmed to room temperature with stirring for 1 hour. After being stored at 10° for 68 hours, the mixture was warmed to room temperature and filtered through diatomaceous earth (Hyflo Supercel®). The collected solids were washed thoroughly with dichloromethane and the combined filtrate and washings concentrated *in vacuo*. The residue was taken up in 40 ml. of dichloromethane and a fresh 1.6 g. sample of manganese dioxide was added. After stirring for 0.5 hour at room temperature, a tlc indicated no starting material remained. The reaction was worked up as described above to give 335 mg. of foamy yellow solid, which was shown by tlc analysis to be a very complex mixture.

Chromatography of the crude product on silica gel packed in benzene, using 4% ethyl acetate in benzene as the eluent yielded

120 mg. (30%) of **13**. An analytical sample was prepared by recrystallization from acetone/hexane and was obtained as light yellow needles, m.p. 170-172°; ir (potassium bromide): 1700 cm^{-1} (C=O aldehyde); nmr (deuteriochloroform): δ 4.68 (2H, bm, CH_2) 6.83 (1H, s, C_3N_2H), 7.40 (6H, m, C_6H_5 and C_6HCl), 7.65 (1H, abq, C_6HCl), 8.02 (1H, d, C_6HCl), 10.08 (1H, s, CHO); mass spectrum: m/e 321 (M^+).

Anal. Calcd. for $C_{18}H_{12}ClN_3O$: C, 67.19; H, 3.76; N, 13.06. Found: C, 67.12; H, 3.67; N, 13.01.

B. From Compound **11**.

A mixture of 7.7 g. (23.8 mmoles) of **11**, 30.8 g. of activated manganese dioxide and 850 ml. of dichloromethane was heated at reflux for 18 hours. After cooling to room temperature, the mixture was filtered through diatomaceous earth (Hyflo Supercel®) and the collected solids washed thoroughly with dichloromethane. The combined filtrate and washings were concentrated *in vacuo* to leave 6.6 g. (87%) of the aldehyde **13**, which was identical with the product obtained in procedure A.

8-Chloro-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine-2-carboxylic Acid, Methyl Ester (**14**).

A solution of 5.03 g. (102.5 mmoles) of sodium cyanide in 503 ml. methanol was added to 6.6 g. (20.5 mmoles) of **13** with stirring; 35.6 g. (410 mmoles) of manganese dioxide was added to the reaction and the mixture stirred at room temperature for 6 hours. The mixture was filtered through diatomaceous earth (Hyflo Supercel®), and the collected solids washed thoroughly with methylene chloride. The combined filtrates and washings were cautiously concentrated *in vacuo* using a 30° water bath. The residue was mixed with water and extracted well with dichloromethane. The combined extracts were dried and concentrated *in vacuo* to give 6.5 g. of crude product. Recrystallization from dichloromethane/hexane yielded 5.3 g. (73%) of **14**, m.p. 208-210°. An analytical sample was prepared by recrystallization from acetone/hexane and obtained as light yellow needles, m.p. 209-211°; ir (potassium bromide): 1730 cm^{-1} (C=O); nmr (deuteriochloroform): δ 3.92 (3H, s, OCH_3), 4.20-5.00 (2H, bs, CH_2), 6.83 (1H, s, C_3N_2H), 7.32 (1H, d, C_6H) 7.39 (5H, m, C_6H_5), 7.59 (1H, abq, C_6H), 8.02 (1H, d, C_6H); mass spectrum: m/e 351 (M^+).

Anal. Calcd. for $C_{19}H_{14}ClN_3O_2$: C, 64.87; H, 4.01; N, 11.59. Found: C, 65.01; H, 4.20; N, 12.01.

8-Chloro-6-phenyl-4*H*-pyrazolo-[1,5-*a*][1,4]benzodiazepine-2-carboxylic Acid Hydrochloride Monohydrate (**15**).

A mixture of 1.05 g. (3 mmoles) of **14** in 3 ml. of acetone and 30 ml. of 1*N* hydrochloric acid was heated to reflux for 2 hours. After cooling to room temperature, the mixture was concentrated *in vacuo* and the residue recrystallized twice from water/acetone/ether to give 470 mg. (40%) of analytically pure **15** as off-white prisms, m.p. 268-269°; ir (potassium bromide): 3300 (OH), 2960-2500, 1920 ($C=NH^+$), 1735, 1717 (C=O of CO_2H), 1635 cm^{-1} ($C=N^+$); nmr (dimethylsulfoxide-d_6): δ 4.90 (2H, bs, CH_2), 6.98 (1H, s, C_3N_2H), 7.40 (1H, s, C_6H), 7.55 (5H, m, C_6H_5), 8.07 (2H, m, C_6H_2Cl), 9.53 (4H, bs, COOH, HCl, H_2O).

Anal. Calcd. for $C_{18}H_{15}Cl_2N_3O_3$: C, 55.12; H, 3.85; N, 10.71. Found: C, 55.19; H, 3.94; N, 10.82.

8-Chloro-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine-2-carboxamide (**16**).

A solution of 750 mg. (2.13 mmoles) of **14** in 50 ml. of methanol in a glass bomb was cooled to 3° and saturated with ammonia. The glass bomb was then sealed and the reaction heated to 70° with stirring, for 16 hours. After cooling to 5°, the bomb was opened, the contents transferred to a round-bottomed flask and concentrated *in vacuo*. Recrystallization from acetone/hexane yielded 630 mg. (88%) of product, m.p. 216-218°. An analytical sample of **16** was prepared by an additional recrystallization from acetone/hexane and obtained as pale yellow needles, m.p. 217-219°; ir (potassium bromide): 1680, 1613 cm^{-1} (1° amide); nmr (deuteriochloroform): δ 4.67 (2H, bs, CH_2), 6.42 (1H, bs, NH), 6.88 (1H, bs, NH), 6.90 (1H, s, C_3N_2H), 7.45 (6H, m, C_6H_5, C_6H), 7.63 (1H, abq, C_6H), 8.02 (1H, d, C_6H).

Anal. Calcd. for $C_{18}H_{13}ClN_4O$: C, 64.20; H, 3.89; N, 16.64. Found: C, 63.98; H, 4.12 N, 16.67.

8-Chloro-*N*-methyl-5-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine-2-carboxamide (**17**).

This compound was prepared from 1.48 g. (4.2 mmoles) of **14** and monomethylamine according to the procedure described above for **16**. Recrystallization from acetone/ether/hexane gave 1.25 g. (85%) of product, m.p. 170-172°. An analytical sample was prepared by recrystallization from the same solvent system and isolated as colorless needles, m.p. 170-172°; ir (potassium bromide) 3375 (NH), 1660, 1545 cm^{-1} (2° amide); nmr (deuteriochloroform): δ 2.96 (3H, d, NCH_3), 4.60 (2H, bs, CH_2), 6.82 (1H, s, C_3N_2H), 6.92 (1H, bs, NH), 7.24-7.51 (6H, m, C_6H_5, C_6H), 7.57 (1H, abq, C_6H), 7.88 (1H, d, C_6H).

Anal. Calcd. for $C_{19}H_{15}ClN_4O$: C, 65.05; H, 4.31; N, 15.97. Found: C, 65.26; H, 4.35; N, 16.14.

8-Chloro-*N*,*N*-dimethyl-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine-2-carboxamide (**18**).

This compound was prepared from 700 mg. (1.99 mmoles) of **14** and dimethylamine according to a procedure similar to that described above for **16**. The reaction mixture was heated at 60-65° in a sealed glass bomb for 16 hours. Recrystallization from acetone/ether/hexane yielded 580 mg. (80%) of product, m.p. 176-178°; ir (potassium bromide): 1622 cm^{-1} (C=O); nmr (deuteriochloroform): δ 3.09 (3H, s, NCH_3), 3.31 (3H, s, NCH_3), 4.60 (2H, bs, CH_2), 6.67 (1H, s, C_3N_2H), 7.24-7.54 (6H, m, C_6H_5, C_6H), 7.56 (1H, abq, C_6H), 7.89 (1H, d, C_6H).

Anal. Calcd. for $C_{20}H_{17}ClN_4O$: C, 65.84; H, 4.70; N, 15.36. Found: C, 65.93; H, 4.72; N, 15.34.

8-Chloro-5,6-dihydro-4-oxo-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]-benzodiazepine-2-methanol (**19**).

To a slurry of 4.63 g. (122.4 mmoles) of sodium borohydride in 525 ml. of dry tetrahydrofuran under argon, was added 6.25 g. (17 mmoles) of **7**. The mixture was heated to reflux for 6 hours, then cooled to 5° and 160 ml. of 1*N* hydrochloric acid added dropwise to hydrolyze the excess borohydride. When addition was complete, the mixture was concentrated *in vacuo* to remove the tetrahydrofuran. The remaining aqueous phase was made basic (*p*H ~ 8) with saturated sodium bicarbonate solution and extracted thoroughly with dichloromethane. The combined extracts were dried and concentrated *in vacuo* to give 5.85 g. (100%) of product. Two recrystallizations from acetone/hexane gave an analytical sample of **19** as a colorless solid, m.p. 260-262°; ir (potassium bromide): 3420 (OH), 1665 cm^{-1} (2° amide); nmr (dimethylsulfoxide-d_6): δ 4.35 (2H, d, CH_2), 5.09 (1H, t, OH), 5.65 (1H, d, CH), 6.69 (1H, s, C_3N_2H), 6.90-7.28 (5H, m, C_6H_5) 7.55 (1H, abq, C_6H), 7.56 (1H, m, C_6H), 7.77 (1H, d, C_6H), 9.33 (1H, d, NH).

Anal. Calcd. for $C_{18}H_{14}ClN_3O_2$: C, 63.63; H, 4.15; N, 12.37. Found: C, 63.77; H, 4.22; N, 12.32.

8-Chloro-5,6-dihydro-4-oxo-5-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]-benzodiazepine-2-carboxaldehyde (**20**).

A solution of 5.85 g. (17 mmoles) of **19** in 600 ml. of dry tetrahydrofuran was mixed with 24 g. of activated manganese dioxide and heated at reflux for 17 hours. The mixture was cooled, filtered and the collected solids washed thoroughly with tetrahydrofuran. The combined filtrate and washings were concentrated *in vacuo*. Recrystallization of this crude product from tetrahydrofuran/hexane yielded 3.43 g. (60%) of **20**. An analytical sample was prepared by an additional recrystallization from tetrahydrofuran/hexane and was obtained as colorless plates, m.p. 276-278°; ir (potassium bromide): 1708 (C=O of CHO), 1675 cm^{-1} (C=O of CON); nmr (dimethylsulfoxide-d_6): δ 5.77 (1H, d, CH), 6.84-7.38 (6H, m, C_6H_5, C_3N_2H), 7.64 (1H, abq, C_6H), 7.79 (1H, m, C_6H), 7.86 (1H, d, C_6H), 9.64 (1H, d, NH), 9.80 (1H, s, CHO).

Anal. Calcd. for $C_{18}H_{12}ClN_3O_2$: C, 64.01; H, 3.58; N, 12.44. Found: C, 64.26; H, 3.61; N, 12.54.

8-Chloro-2-methyl-5,6-dihydro-4-oxo-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine (**21**).

To a solution of 3.43 g. (10.15 mmoles) of **20** in 60 ml. ethanol was added 12 ml. of hydrazine hydrate. The reaction was heated at reflux for 17 hours, then cooled and concentrated *in vacuo*. The residue was taken up in 60 ml. of toluene; 1.0 g. of potassium *t*-butoxide added and the mixture heated to reflux for 8 hours, then cooled to room temperature and stirred for 9 hours. The reaction mixture was poured over ice and brine and extracted with toluene, followed by extraction with dichloromethane. The extracts were combined, dried, and concentrated. The crude product was recrystallized from tetrahydrofuran/hexane to give 2.52 g. (76%) of **21**, m.p. 258-261°. An analytical sample of **21** was prepared by an additional recrystallization from tetrahydrofuran/hexane and was obtained as colorless crystals, m.p. 259-261°; ir (potassium bromide): 3280, 3190 (NH), 1658 cm^{-1} (amide); nmr (dimethylsulfoxide-d_6): δ 2.11 (3H, s, CH_3), 5.61 (1H, s, CHN), 6.51 (1H, s, C_3N_2H), 7.05 (5H, m, C_6H_5), 7.65 (3H, m, C_6H_3), 9.13 (1H, d, NH).

Anal. Calcd. for $C_{18}H_{14}ClN_3O$: C, 66.77; H, 4.36; N, 12.98. Found: C, 66.88; H, 4.61; N, 12.80.

8-Chloro-2-methyl-6-phenyl-4*H*-pyrazolo[1,5-*a*][1,4]benzodiazepine (**22**).

A solution of 2.52 g. (7.8 mmoles) of **21** in 75 ml. of dry tetrahydrofuran was reduced with 3.12 ml. (31.2 mmoles) of BMS according to the procedure described above for **9**, Method B. The crude product from this reduction was then treated with 2.15 g. (9.4 mmoles) of DDQ according to the oxidation procedure described above for **11** and **12**. The crude oxidation product, 1.54 g., was chromatographed on silica gel packed in benzene and eluted first with 3% ethyl acetate in benzene and then 5% ethyl acetate in benzene. Recrystallization from methanol/water of the material isolated from the column yielded 550 mg. (23%) of analytically pure **22**, as colorless needles, m.p. 105-107°; ir (potassium bromide): 1613 cm^{-1} (C=N); nmr (deuteriochloroform): δ 2.31 (3H, s, CH_3), 4.58 (2H, bs, CH_2), 6.10 (1H, s, C_3N_2H), 7.26-7.64 (7H, m, C_6H_5, C_6H_2), 7.90 (1H, d, C_6H).

Anal. Calcd. for $C_{18}H_{14}ClN_3$: C, 70.24; H, 4.59; N, 13.65. Found: C, 70.47; H, 4.69; N, 13.76.

1-(2-Benzoyl-4-aminophenyl)-2-methyl-4,5-dicarboxylic Acid, Diethyl Ester (**27**).

To a warm solution of 902 mg. (2 mmoles) of **26** (2) in 10 ml. of acetic acid, was added 1.35 g. (6 mmoles) of stannous chloride dihydrate dissolved in 10 ml. of acetic acid and 3 ml. of 6*N* hydrochloric acid. After stirring at room temperature overnight, the mixture was poured into water, made basic with ammonium hydroxide and extracted with dichloromethane. The extracts were combined, dried and concentrated. The residue was triturated with ether and filtered to give 740 mg. (88%) of **27**. The analytical sample was obtained as pale yellow needles by recrystallization from dichloromethane/petroleum ether, m.p. 157.5-158.5°.

Anal. Calcd. for $C_{23}H_{23}N_3O_5$: C, 65.55; H, 5.50; N, 9.97. Found: C, 64.91; H, 5.46; N, 10.02.

1-(2-Benzoyl-4-chlorophenyl)-2-methyl-4,5-imidazoledicarboxylic Acid, Diethyl Ester (**28**).

To a solution of 350 mg. (0.83 mmole) of **27** in 10 ml. of 3*N* hydrochloric acid, stirred in an ice bath, was added dropwise a solution of 58 mg. (0.83 mmole) of sodium nitrite in 3 ml. of water. After stirring for 5 minutes, a mixture of 198 mg. (2 mmoles) of cuprous chloride and 5 ml. of 5*N* hydrochloric acid was added. After heating on the steambath for 10 minutes, the reaction was cooled, poured into ice-water, made basic with 3*N* ammonium hydroxide and extracted with ethyl acetate. The organic phase was dried, concentrated and the residue filtered through silica gel with ethyl acetate to give 154 mg. (42%) of **28**. The analytical sample was prepared by recrystallization from methanol/water and obtained as off-white plates, m.p. 118-120°.

Anal. Calcd. for $C_{23}H_{21}ClN_2O_5$: C, 62.63; H, 4.80; N, 6.35. Found: C, 62.73; H, 4.68; N, 6.51.

1-[4-Chloro-2-(α-hydroxyiminobenzyl)phenyl]-2-methyl-4,5-imidazoledicarboxylic Acid, Diethyl Ester (**29**).

A solution of 10.5 g. (23 mmoles) of **28**, 4.96 g. (71 mmoles) of hydroxylamine hydrochloride in 130 ml. of pyridine was refluxed fro 5 hours and then concentrated *in vacuo*. The residue was recrystallized from ethanol/water to give 8.1 g. (77%) of **29**. The analytical sample was obtained as colorless prisms by recrystallization from ethanol, m.p. 195-197°.

Anal. Calcd. for $C_{23}H_{22}ClN_3O_5$: C, 60.60; H, 4.86; N, 9.22. Found: C, 60.68; H, 4.79; N, 9.19.

8-Chloro-5,6-dihydro-1-methyl-4-oxo-6-phenyl-4*H*-imidazo[1,5-*a*][1,4]benzodiazepine-3-carboxylic Acid, Ethyl Ester (**30**) and 7-Chloro-4-hydroxy-1-methyl-5-phenylimidazo[1,5-*a*]quinoline-3-carboxylic Acid, Ethyl Ester (**31**).

A mixture of 7.5 g. (16.4 mmoles) of **29**, 5.3 g. (82.2 mmoles) of zinc dust, 2 ml. of concentrated hydrochloric acid and 100 ml. of acetic acid was stirred and refluxed for 18 hours. After cooling, the zinc was removed by filtration and washed with dichloromethane. The filtrates were made basic with concentrated sodium hydroxide and extracted with dichloromethane. The extracts were dried and concentrated. The residue was recrystallized from dichloromethane/petroleum ether to give 1.7 g. (27%) of **31**. The analytical sample was obtained as off-white plates by recrystallization from the same solvents, m.p. 263-266°; ir (chloroform): no N-H bands, 2750 (associated OH), 1663 cm^{-1} (hydrogen bonded ester); nmr (deuteriochloroform): δ 1.47 (3H, t, CH_3 of ester), 3.13 (3H, s, CH_3), 4.51 (2H, q, CH_2), 7.25-7.70 (7H, m, aromatics), 8.21 (1H, d, aromatic), and 12.34 (1H, s, OH).

Anal. Calcd. for $C_{21}H_{17}ClN_2O_3$: B, 66.23; H, 4.50; N, 7.36. Found: C, 66.18; H, 4.40; N, 7.46.

The filtrates from the above recrystallization were concentrated and the residue filtered through silica gel with benzene-ethyl acetate (1:1) to give 1.7 g. (26%) of **30**. The analytical sample was obtained as colorless prisms by recrystallization from dichloromethane/petroleum ether, m.p. 295°; ir (chloroform): 3405, 3200 (NH), 1725 (CO_2Et) and 1672 cm^{-1} (-NHC=O).

Anal. Calcd. for $C_{21}H_{18}ClN_3O_3$: C, 63.72; H, 4.58; N, 10.62. Found: C, 63.59; H, 4.53; N, 10.51.

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