Anal. Calcd for $C_{12}H_{16}N_2S$: C, 65.41; H, 7.32; N, 12.71. Found: C, 65.46; H, 7.18; N, 12.53.

6-Dimethylaminomethylthieno[3,2-b]pyrrole (XV).—A suspension of 0.750 g of chromatographically pure 6-dimethylaminomethyl-5-carbethoxythieno[3,2-b]pyrrole (IX),[4] mp 94–95°, in 500 ml of water was refluxed for 6 hr. Since no significant precipitate formed when this cloudy solution was cooled to 0°, the solution was concentrated to 100 ml, cooled to room temperature, and filtered. The light tan filtrate was acidified to pH 5 with 3 *N* HCl solution and subjected to the same conditions of decarboxylation used for XI. After the ether extracts had been dried over anhydrous sodium sulfate, the ether was removed *in vacuo* to leave 375 mg of crude product which was recrystallized from methylcyclohexane and decolorized with Darco to afford 270 mg (50%) of 6-dimethylaminomethylthieno[3,2-b]pyrrole as buff-colored prisms, mp 117–120°. An infrared spectrum (KBr disk) of this product showed no carbonyl absorption.

Anal. Calcd for $C_9H_{12}N_2S$: C, 59.86; H, 6.71; N, 15.53. Found: C, 60.21; H, 6.89; N, 15.30.

2-Dimethylaminomethyl-5-carbethoxythieno[3,2-b]pyrrole (XVI).—The crude product obtained from the reaction of I with formaldehyde and dimethylamine by the method of Gale, Scott, and Snyder[4] was recrystallized once from methylcyclohexane. A 5.0-g sample of this material, mp 90–92°, was suspended in 1.8 l. of water and the aqueous mixture refluxed for 6 hr. When this solution was filtered hot to remove traces of solid and cooled to 0° in an ice bath, a white crystalline precipitate formed which was collected on a Büchner funnel and recrystallized from methylcyclohexane to afford 3.5 g (70%) of XVI as white needles, mp 132–133°. A mass spectrum of this product run at low ionization voltage showed a parent ion peak at *m/e* 252, as expected for an isomer of IX. An infrared spectrum of XVI in chloroform was similar to that of IX, but the two spectra were not superimposable.

Anal. Calcd for $C_{12}H_{16}N_2O_2S$: C, 57.12; H, 6.39; N, 11.10. Found: C, 57.45; H, 6.51; N, 10.50.

When 200 mg of XVI was suspended in 100 ml of water and the resulting suspension was refluxed for 6 hr, the solution became homogeneous. Upon cooling of this solution to 0°, 194 mg (97%) of XVI, mp 131–133°, precipitated.

When 3.0 g of the once-recrystallized product from the preparation of IX was placed on a column of acid-washed alumina 28 cm in height and 3.5 cm in diameter and the column was eluted with a 50% ethanolic benzene solution, only 750 mg (25%) of pure 6-dimethylaminomethyl-5-carbethoxythieno[3,2-b]pyrrole (IX), mp 94–95°, was obtained. Subsequent elution of the column failed to yield any pure material.

Attempted Hydrolysis of 5-Carbethoxythieno[3,2-b]pyrrole (I).—A mixture of 0.292 g of 5-carbethoxythieno[3,2-b]pyrrole and 150 ml of water was refluxed for 24 hr. The solution was cooled to room temperature and extracted with an equal volume of diethyl ether. The ether extract was dried over anhydrous sodium sulfate and filtered, and the ether was removed on a rotary evaporator to yield 0.215 g (74%) of 5-carbethoxythieno-[3,2-b]pyrrole, mp 132–133° (lit.[4] mp 132.5–133°). The recovered material had the same R_f value as that of the starting material when compared by tlc.

Registry No.—VI, 15819-12-2; IX, 15811-13-9; X, 15811-14-0; X p-chloroanil derivative, 16315-46-1; XI, 15811-16-2; XIII, 15811-17-3; XIV, 15811-18-4; XV, 15811-19-5; XVI, 15811-20-8.

The Synthesis of Polycyclic Fused [1,2-a]Pyrroles

EDWARD E. GARCIA, J. G. RILEY, AND R. IAN FRYER

Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

Received October 25, 1967

The condensation of 2,5-dimethoxytetrahydrofuran with 2-amino-5-chlorobenzophenone and its two oxime forms afforded the 2-(1-pyrrolyl)benzophenone derivatives **4**, **5**, and **6**. These compounds were converted into the corresponding 2-substituted Mannich bases by treatment with formaldehyde and dimethylamine. Subsequent quaternization with methyl iodide followed by heating led to intramolecular condensations to give the pyrrolo[1,2-a]quinoline **8**, the pyrrolo[1,2-a]benzoxadiazocine **13**, and the pyrrolo[1,2-a]benzodiazepine **14**, respectively. Compound **6** with electrophiles in acid gave pyrrolo[1,2-a]quinazolines. Attempted formylation of **6** with dimethylformamide–phosphorus oxychloride yielded the pyrrolo[1,2-a]quinoxaline **21**.

The ready availability of *o*-aminobenzophenones[1] has, in the past few years, led to the synthesis of several heterocyclic systems. Thus, quinazolines,[2] benzodiazepines,[3] quinolones,[4] and indoles[5] have all been prepared from various *o*-aminobenzophenones.

As an extension of this work, and employing 2-amino-5-chlorobenzophenone **1** and its *syn*- and *anti*-oximes (**2** and **3**, respectively[6]) as starting materials, we wish to report a general synthetic approach for the preparation of derivatives of fused [1,2-a]pyrrolo quinolines, quinazolines, benzodiazepines, benzoxadiazocines, and quinoxalines.

Using the method of Clauson-Kaas for the synthesis of 1-substituted pyrroles,[7,8] compounds **1**, **2**, and **3** were treated with 2,5-dimethoxytetrahydrofuran to give the corresponding 2-(1-pyrrolyl)benzophenone derivatives **4**, **5**, and **6**, respectively (Scheme I).

The ketone **4** was then treated with formaldehyde and dimethylamine to give the corresponding Mannich base. This compound was not isolated, but alkylated with methyl iodide to give directly the quaternary salt **7** (Scheme II). When a solution of **7** in aqueous dimethylformamide was then treated with sodium cyanide, trimethylammonium iodide was displaced by cyanide ion and the carbonyl function underwent intramolecular cyclization to give the pyrrolo[1,2-a]-quinoline, compound **8**.

Similar treatment of the oximes **5** and **6** with formaldehyde and dimethylamine gave the Mannich bases **9** and **10**, respectively (Scheme III), which were also alkylated with methyl iodide to afford the corresponding quaternary salts **11** and **12**. When a solution of

(1) (a) L. H. Sternbach, E. Reeder, O. Keller, and W. Metlesics, *J. Org. Chem.*, **26**, 4488 (1961); (b) L. H. Sternbach, R. I. Fryer, W. Metlesics, G. Sach, and A. Stempel, *ibid.*, **27**, 3781 (1962).

(2) (a) L. H. Sternbach, S. Kaiser, and E. Reeder, *J. Amer. Chem. Soc.*, **82**, 475 (1960); (b) G. F. Field, W. J. Zally, and L. H. Sternbach, *J. Org. Chem.*, **30**, 3957 (1965).

(3) L. H. Sternbach, R. I. Fryer, W. Metlesics, E. Reeder, G. Sach, G. Saucy, and A. Stempel, *ibid.*, **27**, 3788 (1962).

(4) R. I. Fryer, B. Brust, and L. H. Sternbach, *J. Chem. Soc.*, 3097 (1964).

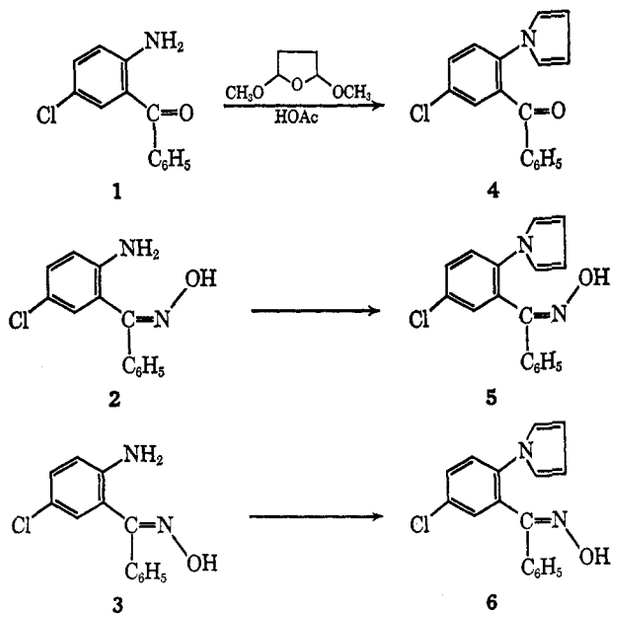
(5) R. I. Fryer, J. V. Earley, and L. H. Sternbach, *J. Org. Chem.*, **32**, 3798 (1967).

(6) The *syn* isomer is defined as that isomer in which the hydroxy group is *syn* to the phenyl ring bearing the 2-amino group. See, also, A. Stempel, I. Douvan, E. Reeder, and L. H. Sternbach, *ibid.*, **32**, 2417 (1967), footnote 7.

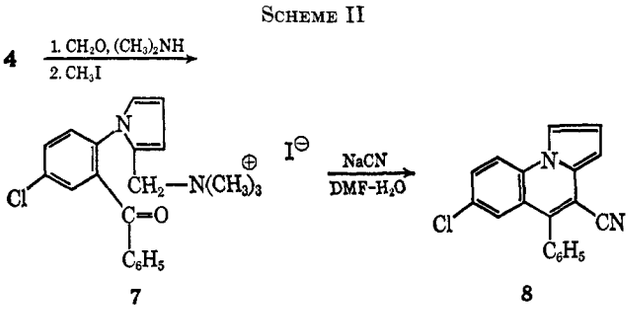
(7) (a) N. Clauson-Kaas and Z. Tyle, *Acta Chem. Scand.*, **6**, 667 (1952); (b) E. Elming and N. Clauson-Kaas, *ibid.*, **6**, 867 (1952).

(8) A. D. Josey and E. L. Jenner [*J. Org. Chem.*, **27**, 2466 (1962)] recognized the potential of this reaction in the synthesis of a pyrrolo[1,2-a]indole.

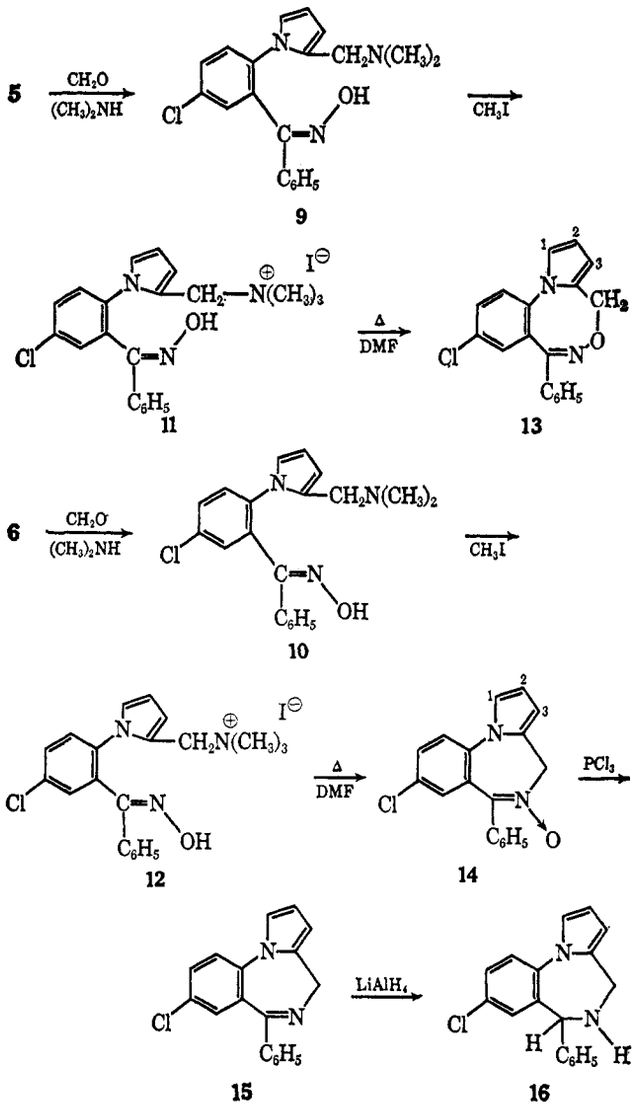
SCHEME I



SCHEME II



SCHEME III



either of these latter compounds in dimethylformamide was warmed on the steam bath, intramolecular condensation took place with the loss of trimethylamine hydriodide to afford, from **11**, the pyrrolo[1,2-*a*]-benzoxadiazocine **13** and, from **12**, the pyrrolo[1,2-*a*]-benzodiazepine **14**.[9] (This is a further example of the O-alkylation of a *syn*-oxime and the N-alkylation of an *anti*-oxime.[7,10]) Phosphorus trichloride readily converted **14** into the corresponding desoxy derivative **15** and this was then converted into the tetrahydro derivative **16** by treatment with lithium aluminum hydride.

As a further extension of reactions which would convert the *anti*-oxime **6** into tricyclic products, we investigated the behavior of this substance with electrophiles in acidic media. Thus, we found that treatment of compound **6** with a molar equivalent of bromine in acetic acid at room temperature gave a bromine-free substance to which we have assigned the phenylpyrrolo[1,2-*a*]quinazoline 4-oxide structure **17** (Scheme IV). The N-oxide structure was established both by its mass spectrum which in addition to the parent ion (294) showed the strong loss of **16** (278, parent less oxygen) characteristic of N-oxides,[11] and by its conversion into the desoxy derivative **18** with hydrogen and Raney nickel. The formation of **17** from **6** may be envisioned as proceeding *via* a brominated dihydro intermediate such as A, which could cyclize with the elimination of bromide ion as shown (Scheme IV), to give the final product. A similar reaction sequence was observed when we treated an acetic acid solution of **6** with formaldehyde. In this instance, we isolated 7-chloro-1-methyl-5-phenylpyrrolo[1,2-*a*]quinazoline 4-oxide (**19**). The methyl substituent was assigned at position 1 and not at 3 on the basis of the nmr spectrum and also by analogy with the site of alkylation observed in the conversion of **6** into **10**. Reduction of **19** with Raney nickel gave the corresponding desoxy derivative **20**. The formation of **19** can be rationalized by a pathway analogous to that given for the formation of **17**, *i.e.*, *via* an intermediate such as B.

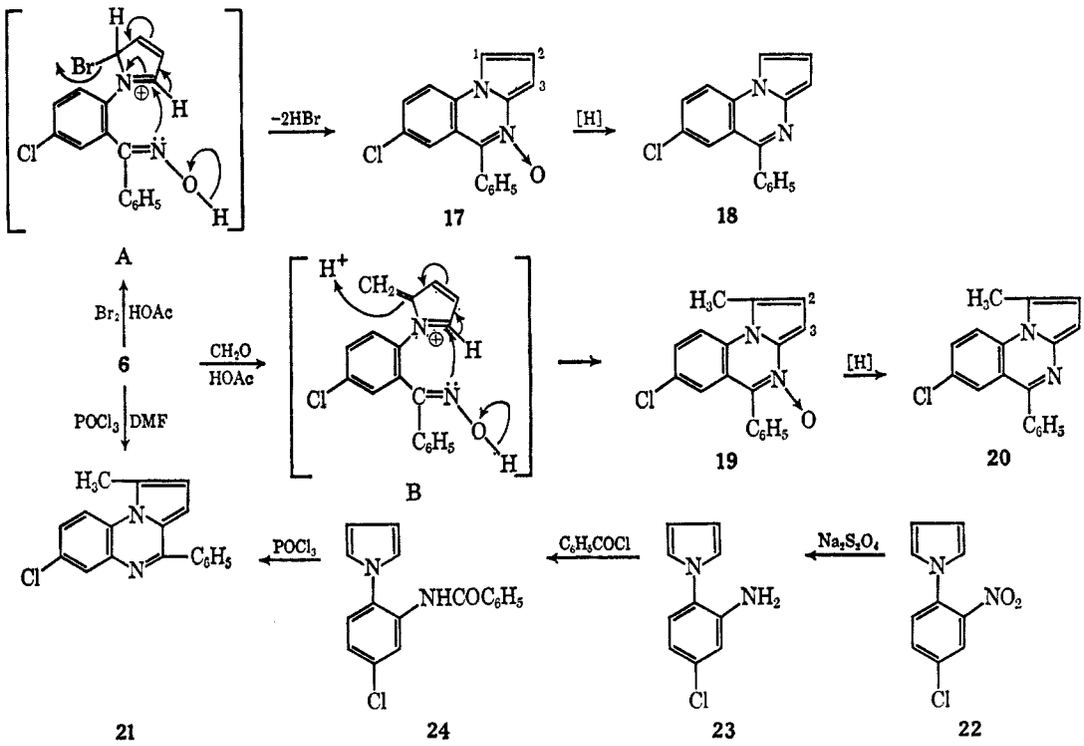
In an attempt to formylate one of the pyrrole oximes, **6** was treated together with a mixture of phosphorus oxychloride and dimethylformamide. Instead of the anticipated product, we obtained the pyrrolo[1,2-*a*]-quinoxaline **21**. In addition to compatible spectra, the structure of **21** was confirmed by the following synthesis. A solution of 4-chloro-2-nitroaniline in acetic acid was treated with dimethoxytetrahydrofuran to give the nitrophenylpyrrole **22**. Reduction of **22** with sodium hydrosulfite yielded the amino compound **23** which was then acylated with benzoyl chloride to give **24**. Treatment of **24** with boiling phosphorus

(9) For a discussion of condensation reactions of pyrrole Mannich bases, see H. Hellmann and G. Opitz, "α-Aminoalkylierung," Verlag Chemie, G.m.b.H., Weinheim, Berstr., Germany, 1960.

(10) L. H. Sternbach and E. Reeder, *J. Org. Chem.*, **26**, 4936 (1961).

(11) T. A. Bryce and J. R. Maxwell, *Chem. Commun.*, 206 (1965).

SCHEME IV



oxychloride gave **21**, identical in all respects with the product obtained by the attempted Vilsmeier reaction.[12] The formation of **21** from **6** would appear to be the result of a Beckmann type of rearrangement catalyzed by phosphorus oxychloride. Thus, compound **6** could then be converted into the amide **24**, which under the reaction conditions would cyclize to the quinoxaline **21**.

Experimental Section[13]

5-Chloro-2-(1-pyrrolyl)benzophenone (4).—To a solution of 41.8 g (0.18 mol) of 2-amino-5-chlorobenzophenone (**1**) in 200 ml of glacial acetic acid was added 21.4 g (0.20 mol) of dimethoxytetrahydrofuran. After heating on the steam bath for 25 min, the solution was poured into 800 ml of water and extracted with carbon tetrachloride. The addition of 10% sodium hydroxide facilitated the separation of the layers. The organic phase was separated, washed with brine, dried over sodium sulfate, and concentrated to a dark brown oil. This residue was covered with 600 ml of hexane, heated to boiling, and filtered while hot from some undissolved oil (discarded). The hexane filtrate was concentrated to small volume and cooled. The precipitated oily solid was recrystallized several times from hexane to yield 23.4 g (46%) of colorless prisms: mp 86–87°; infrared absorption ($CHCl_3$) at 1665 cm^{-1} (C=O).

Anal. Calcd for $C_{17}H_{12}ClNO$: C, 72.47; H, 4.29; N, 4.97. Found: C, 72.24; H, 4.43; N, 5.09.

5-Chloro-2-(1-pyrrolyl)benzophenone *syn*-Oxime (5).—A solution of 45 g (0.18 mol) of 2-amino-5-chlorobenzophenone *syn*-oxime[14] (**2**) in 200 ml of glacial acetic acid was treated with 26.5 g (0.2 mol) of dimethoxytetrahydrofuran, heated on the steam bath for 25 min, and poured into 500 ml of water. The mixture was extracted with benzene and the organic layer was separated, washed with water, dried over sodium sulfate, and concentrated to dryness. This residue was dissolved in a small amount of hot carbon tetrachloride and refrigerated. Filtration gave 27 g (50%) of the product as a cream-colored solid, mp 146–148°. Recrystallization from carbon tetrachloride yielded white plates: mp 146–147° (sintered prior to melting); ultraviolet maximum (2-propanol) at 250 mμ (ε 23,500).[15]

Anal. Calcd for $C_{17}H_{13}ClN_2O$: C, 68.80; H, 4.42; N, 9.44. Found: C, 69.06; H, 4.47; N, 9.49.

5-Chloro-2-(1-pyrrolyl)benzophenone *anti*-Oxime (6).—A solution of 45 g (0.18 mol) of 2-amino-5-chlorobenzophenone *anti*-oxime[16] (**3**) in 200 ml of glacial acetic acid was treated with 26.5 g (0.2 mol) of 2,5-dimethoxytetrahydrofuran and heated on the steam bath for 15 min. The reaction mixture was cooled to room temperature, poured into 500 ml of water, and extracted with benzene. The organic layer was separated, aided by the addition of 10% sodium hydroxide, washed with water, dried over anhydrous sodium sulfate, and concentrated to dryness. The residue was covered with a small amount of carbon tetrachloride, heated on the steam bath until a solid began to separate, and then refrigerated. Filtration gave 25 g (46%) of a cream-colored solid, which softened from 130° until completely melted at 168: ultraviolet maxima (2-propanol) at 227 mμ (infl) (ε 22,700) and 250 mμ (sh) (ε 19,600).[17]

Anal. Calcd for $C_{17}H_{13}ClN_2O$: C, 68.80; H, 4.42; N, 9.44. Found: C, 69.07; H, 4.31; N, 9.41.

7-Chloro-4-cyano-5-phenylpyrrolo[1,2-a]quinoline (8).—To a cooled, stirred solution of 20 g (0.068 mol) of **4** in 225 ml of glacial acetic acid was added 13.2 g (0.16 mol) of 37% formaldehyde followed by 28.8 g (0.16 mol) of 25% dimethylamine in water. The solution was stirred overnight at room temperature and poured into 600 ml of water. The mixture was filtered to separate a small amount of undissolved solid (discarded) and the filtrate was basified with sodium hydroxide and extracted with ethyl acetate. The organic layer was separated, washed with water, dried over sodium sulfate, and concentrated to a viscous oil. This oil was dissolved in ether and, while stirring, was treated with 20 ml of methyl iodide. A precipitate formed

(12) The cyclization of 1-(2-acylaminophenyl)pyrroles as a facile, general method for the preparation of pyrrolo[1,2-a]quinoxalines has been reported by G. W. H. Cheeseman and B. Tuck [*J. Chem. Soc.*, 852 (1966)].

(13) All melting points are corrected. Infrared spectra were determined using a Beckman IR-9 spectrophotometer, nmr spectra with a Varian A-60 spectrometer, mass spectra with a CEC 21-100 spectrometer, and ultraviolet spectra with a Cary Model 14 spectrophotometer. The dimethoxytetrahydrofuran used in these experiments was obtained from the Aldrich Chemical Co.

(14) The ultraviolet spectrum indicated that the starting material was contaminated with less than 1% of the *anti* isomer. The characteristic differences in the ultraviolet spectra of pairs of oximes has been reported by J. G. Pritchard, G. F. Field, K. Koch, G. Raymond, L. H. Sternbach, and S. Traiman [*Appl. Spectry.*, **20**, 363 (1966)].

(15) The ultraviolet spectrum of this material is vastly different from that of the starting material but very similar to that observed for 2-methylbenzophenone *syn*-oxime. For an interpretation of these differences, see ref 14.

(16) This material was shown to be contaminated with less than 4% of the *syn* isomer by ultraviolet spectroscopy (*cf.* ref 14).

(17) This absorption is about the same as that observed with 2-methylbenzophenone *anti*-oxime.

immediately. After standing at room temperature for 3 hr, the solid was filtered to give 30.9 g (94%) of **7** as a cream-colored solid. Recrystallization of a small sample from methanol–ether gave off-white prisms, mp 165° with slow decomposition. Upon vacuum drying the sample turned green and consequently satisfactory microchemical data could not be obtained for this substance.

To a solution of 150 ml of water in 350 ml of dimethylformamide was added 25 g (0.052 mol) of **7** and 25 g (large excess) of sodium cyanide. After being heated on the steam bath for 8 hr, the mixture was poured into 1.5 l. of water and filtered. The precipitate was washed with water and dissolved in benzene. After drying, the benzene was concentrated to dryness and the residue triturated with a small amount of hot 2-propanol and refrigerated. Filtration gave 2.6 g (17%) of **8** as yellow-green crystals, mp 180–183°. The analytical sample was recrystallized from 2-propanol to yield bright, yellow plates: mp 182–183°; infrared absorption ($CHCl_3$) at 2225 cm^{-1} (CN); ultraviolet maxima (2-propanol) at 240 mμ (ε 36,700), 252 (32,500), 259 (34,000), 288 (11,000), 299 (9200), 327 (sh) (1250), 343 (2700), 360 (4000), and at 406 (5200).

Anal. Calcd for $C_{19}H_{11}ClN_2$: C, 75.37; H, 3.66; N, 9.25. Found: C, 75.39; H, 3.56; N, 9.42.

5-Chloro-2-(2-dimethylaminomethyl-1-pyrrolyl)benzophenone *syn*-Oxime (9).—To an ice-cooled, sitrred solution of 29.7 g (0.1 mol) of **5** in 300 ml of glacial acetic acid was added 22.2 g (0.2 mol) of 37% formaldehyde and 45 g (0.2 mol) of 25% dimethylamine in water. After stirring for 22 hr at room temperature, the solution was poured into 800 ml of water and basified with 20% sodium hydroxide. The precipitate was filtered, washed with water, and recrystallized from methanol–acetone to yield 23.7 g (66%) of white crystals, mp 203–204° dec.

Anal. Calcd for $C_{20}N_{20}ClN_3O$: C, 67.84; H, 5.70; N, 11.81. Found: C, 68.03; H, 5.77; N, 11.66.

5-Chloro-2-(2-dimethylaminomethyl-1-pyrrolyl)benzophenone *anti*-Oxime (10).—To an ice-cooled, stirred solution of 29.67 g (0.1 mol) of **6** in 300 ml of acetic acid was added 22.2 g (0.2 mol) of 37% formaldehyde and then, portionwise, 45 g (0.2 mol) of 25% dimethylamine in water. After stirring at room temperature for 20 hr, the solution was poured into 700 ml of water, basified with concentrated ammonia, and extracted with ethyl acetate. The organic layer was separated, washed with water, dried over sodium sulfate, and concentrated to dryness. The residue was recrystallized from methanol to give 20.8 g (58%) of white crystals, mp 173–179°. An additional recrystallization from methanol gave colorless prisms: mp 175–179°; nmr peaks ($CDCl_3$) at δ 5.72, 5.84, 6.35 (3 H, ABX pattern, pyrrole H's 5, 4, and 3, had respectively, $J_{3,4}$ = 3.5 cps, $J_{4,5}$ = 2.8 cps, and $J_{3,5}$ = 1.7 cps).[18]

Anal. Calcd for $C_{20}H_{20}ClN_3O$: C, 67.84; H, 5.70; N, 11.81. Found: C, 67.80; H, 5.50; N, 11.95.

5-Chloro-2-(2-dimethylaminomethyl-1-pyrrolyl)benzophenone *syn*-Oxime Methyl Iodide (11).—To a stirred solution of 13.8 g (0.039 mol) of **9** in 150 ml of tetrahydrofuran was added 11 g (0.078 mol) of methyl iodide. After stirring for 3 hr at room temperature, the suspension was refrigerated overnight. Filtration and recrystallization of the product from methanol–ether gave 17 g (88%) of white crystals, mp 145–155° dec.

Anal. Calcd for $C_{21}H_{23}ClIN_3O$: C, 50.87; H, 4.68; N, 8.48. Found: C, 50.66; H, 4.70; N, 8.18.

5-Chloro-(2-dimethylaminomethyl-1-pyrrolyl)benzophenone *anti*-Oxime Methyl Iodide (12).—A mixture of 13 g (0.036 mol) of **10** and 50 ml of methyl iodide was stirred at room temperature for 15 min, 100 ml of ether was added, and the suspension was allowed to stand for an additional 3.5 hr. Filtration yielded 17 g (95%) of off-white colored crystals, mp 140–146°. Recrystallization from methanol–ether gave white needles, mp 140–145° (foamed).

Anal. Calcd for $C_{21}H_{23}ClIN_3O$: C, 50.87; H, 4.68; N, 8.48. Found: C, 50.47; H, 4.76; N, 8.36.

9-Chloro-7-phenyl-4H-pyrrolo[1,2-*a*][4.1.5]benzoxadiazocine (13).—A solution of 40 g (0.085 mol) of **11** in 150 ml of dimethylformamide was heated on the steam bath for 2.5 hr under nitrogen. The solution was poured into water, stirred for 15 min, and filtered. The precipitate was collected, dried at room temperature, and then extracted with 400 ml of hot benzene. The benzene solution, filtered from 16.5 g of unreacted starting material, was washed with water, dried over sodium sulfate, and concentrated. The residual orange oil was triturated with 10 ml of 2-propanol and scratched to induce crystallization. The solid was collected and recrystallized twice from 2-propanol to give 7.8 g (50%, based upon starting material consumed) of tan rods: mp 137–138.5°; nmr peaks ($CDCl_3$) at δ 6.70, 6.18, 6.08 (3 H, ABX pattern, pyrrole H's 1, 2, 3, respectively)[19] and at 5.38 (2 H, AB quartet, J = 14 cps, CH_2).

Anal. Calcd for $C_{18}H_{13}ClN_2O$: C, 70.02; H, 4.24; N, 9.07. Found: C, 70.06; H, 4.31; N, 9.09.

8-Chloro-6-phenyl-4H-pyrrolo[1,2-*a*][1,4]benzodiazepine 5-Oxide (14).—A solution of 18 g (0.036 mol) of **12** in 80 ml of dimethylformamide was heated under nitrogen on the steam bath for 3 hr and then poured into 300 ml of water. The precipitate was filtered, washed with water, and dissolved in benzene (a small amount of undissolved residual oil was discarded). The benzene extract was washed with water, dried over sodium sulfate, and concentrated. The residue was dissolved in chloroform and filtered over 75 g of alumina[20] with the aid of additional chloroform. The eluate was treated with Darco G charcoal and filtered and the filtrate concentrated to an orange oil. The oil was crystallized from a small amount of 2-propanol to give 4.4 g (40%) of orange-brown crystals, mp 180–186°. The analytical sample was recrystallized from 2-propanol–methylene chloride to give chunky, pale orange prisms: mp 191–193° (sintered at 185°); nmr peaks ($CDCl_3$) at δ 6.42 (2 H doublet, J = 2 cps, pyrrole H's 2 and 3), at 7.15 (1 H multiplet J = 2 cps, pyrrole H 1), and at 5.07 (2 H singlet, CH_2).

Anal. Calcd for $C_{18}H_{13}ClN_2O$: C, 70.02; H, 4.24; N, 9.07. Found: C, 70.30; H, 4.44; N, 8.89.

8-Chloro-6-phenyl-4H-pyrrolo[1,2-*a*][1.4]benzodiazepine (15).—To a solution of 7 g (0.022 mol) of **14** in 150 ml of chloroform was added 3.6 ml (0.042 mol) of phosphorus trichloride. The solution was heated under reflux for 30 min and poured into 300 ml of 1 *N* sodium hydroxide. The organic phase was separated, washed with brine, and dried over sodium sulfate. This solution was filtered through 150 g of alumina and the alumina washed with chloroform until the eluate was colorless. Evaporation of the solvent gave a reddish oil which was covered with 275 ml of hexane, heated to reflux, and filtered while hot to remove some oily solid (discarded). The filtrate was concentrated to 85 ml and refrigerated. Filtration gave 3.6 g of amber crystals, mp 122–124°. Concentration of the filtrate gave an additional 0.3 g of product to yield 3.9 g (61%). The analytical sample was recrystallized from hexane to give pale, amber prisms: mp 125–126°; nmr peaks (DMSO-d_6) at δ 7.33, 6.28, 6.17 (3 H, ABX pattern, pyrrole H's 1, 2, 3, respectively, $J_{1,2}$ = 3 cps, $J_{2,3}$ = 3.5 cps, $J_{1,3}$ = 1.5 cps), and 4.52 (2 H, AB quartet, J = 13 cps, CH_2).

Anal. Calcd for $C_{18}H_{13}ClN_2$: C, 73.84; H, 4.48; N, 9.57. Found: C, 74.11; H, 4.32; N, 9.63.

8-Chloro-5,6-dihydro-6-phenyl-4H-pyrrolo[1,2-*a*][1.4]benzodiazodiazepine (16).—To a suspension of 3.5 g of lithium aluminum hydride in 200 ml of tetrahydrofuran was added 11.8 g of **15**. After refluxing overnight a few milliliters of aqueous tetrahydrofuran was added slowly and the mixture was filtered. The solution was concentrated and the resultant oil recrystallized several times from a large volume of hexane to give tan rods: mp 145–146°; nmr peaks ($CDCl_3$) at δ 6.95, 6.30, 6.17 (3 H, ABX pattern, pyrrole H's 1, 2, 3, respectively, $J_{1,2}$ = 3 cps, $J_{2,3}$ = 3.5 cps, $J_{1,3}$ = 1.5 cps), and 3.81 (2 H, AB quartet, J = 15 cps, CH_2).

Anal. Calcd for $C_{18}H_{15}ClN_2$: C, 73.34; H, 5.13; N, 9.50. Found: C, 73.55; H, 5.35; N, 9.62.

7-Chloro-5-phenylpyrrolo[1,2-*a*]quinazoline 4-Oxide (17).—To a stirred solution of 3 g (0.01 mol) of **6** in 500 ml of glacial acetic acid was added dropwise 1.8 g (0.011 mol) of bromine and the resultant mixture stirred for 2 hr at room temperature. The resultant suspension was filtered to give a brown solid, which rendered water strongly acidic to pH paper. This solid was stirred in excess 1 *N* sodium hydroxide for a few minutes, filtered, and then thoroughly washed with water. After trituration with a small amount of acetone the product was recrystallized twice from carbon tetrachloride to give 1.5 g (50%) of pale yellow prisms: mp 226–229° dec (changed to needles *ca.* 200°); ultraviolet maxima (2-propanol) at 241 mμ (ε 29,250), 252 (infl) (31,500), 256 (32,500), 282 (18,250), 343 (infl) (5200), 360

(18) For a listing of pyrrole coupling constants, see S. Gronowitz, *et al.*, *Ark. Kemi*, **18**, 133 (1961).

(19) The J values for these pyrrole hydrogens were not clearcut within 1 cps.

(20) Alumina refers to Woelm alumina, activity I.

(6600), and 385 (sh) (6200); nmr peaks (DMSO-d_6) at δ 5.17 (2 H doublet, J = 2.5 cps, pyrrole H's 2 and 3) and at 8.22 (1 H triplet, J = 2.5 cps, pyrrole H 1).

Anal. Calcd for $C_{17}H_{11}ClN_2O$: C, 69.27; H, 3.76; N, 9.50. Found: C, 69.72; H, 3.81; N, 9.49.

7-Chloro-5-phenylpyrrolo[1,2-a]quinazoline (18).—A solution of 4.7 g (0.015 mol) of **17** in 100 ml of dioxane was shaken under 1 atm of pressure and 24° in an atmosphere of hydrogen using *ca.* 6 g of Raney nickel as catalyst. After the uptake of hydrogen reached 359 ml (theory 370 ml), the mixture was filtered and the catalyst washed with 50 ml of dioxane and 50 ml of methanol. Evaporation of the solvent gave a yellow oil which crystallized upon standing. After several recrystallizations from ethanol, yellow needles were obtained, mp 149–150°.

Anal. Calcd for $C_{17}H_{11}ClN_2$: C, 73.25; H, 3.98; N, 10.05. Found: C, 72.96; H, 4.02; N, 9.93.

7-Chloro-1-methyl-5-phenylpyrrolo[1,2-a]quinazoline 4-Oxide (19).—A solution of 12 g (0.04 mol) of **6** in 100 ml of acetic acid was treated with 6 g (0.074 mol) of 37% formaldehyde and the mixture was allowed to stir at room temperature for 24 hr. The solution was poured into 300 ml of water and extracted with chloroform. The organic layer was separated (aided by the addition of alkali to the aqueous phase), washed with water, dried over sodium sulfate, and passed through 250 g of Florisil.[21] The Florisil was washed with chloroform and the eluate concentrated to dryness. The residue was dissolved in hot carbon tetrachloride and filtered from a small amount of undissolved solid (discarded); the filtrate was refrigerated. Filtration yielded 3 g (24%) of pale orange crystals: mp 220–223° dec; mass spectrum (m/e), 308 (p), 292 (p − 16); nmr peaks ($CDCl_3$) at δ 6.55, 7.05 (2 H, AB quartet, J = 4 cps, pyrrole H's 2 and 3),[22] and 2.97 (3 H singlet, CH_3).

Anal. Calcd for $C_{18}H_{13}ClN_2O$: C, 70.02; H, 4.24; N, 9.07. Found: C, 70.32; H, 4.19; N, 9.26.

7-Chloro-1-methyl-5-phenylpyrrolo[1,2-a]quinazoline (20).—A solution of 3 g (0.01 mol) of **19** in a mixture of 25 ml of methanol and 50 ml of dioxane was shaken under 1 atm of pressure at 24° in an atmosphere of hydrogen using 6.5 g of Raney nickel as a catalyst. After the uptake of hydrogen reached 231 ml, the mixture was filtered and the filtrate concentrated to a viscous, yellow oil. This oil, which contained some starting material (determined by tlc), was dissolved in carbon tetrachloride and placed on 150 g of alumina. Elution with 1:1 ethyl acetate–hexane gave, upon evaporation, a yellow solid which was recrystallized from ethanol to give yellow prisms, mp 139–141°.

Anal. Calcd for $C_{18}H_{13}ClN_2$: C, 73.84; H, 4.48; N, 9.57. Found: C, 73.92; H, 4.68; N, 9.44.

7-Chloro-4-phenylpyrrolo[1,2-a]quinoxaline (21). A. From 6.—To 4 g (0.055 mol) of dimethylformamide, cooled in ice, was added dropwise with stirring, 8.5 g (0.055 mol) of phosphorus oxychloride. After stirring for 15 min at room temperature, 25 ml of ethylene dichloride was added and the solution cooled to 5°. A suspension of 15 g (0.05 mol) of **6** in 60 ml of ethylene dichloride was then added portionwise during 1 hr. After stirring at room temperature for 20 min, the mixture was refluxed for 15 min and then hydrolyzed at room temperature by the dropwise addition of a solution of 37.5 g of sodium acetate trihydrate in 50 ml of water. The resultant mixture was heated to gentle reflux for 15 min and then the organic layer was separated. The aqueous phase was extracted with ether and the organic layers were combined, washed, dried over sodium sulfate, and concentrated to a dark brown solid. Trituration with hot ethanol gave 6.1 g of yellow solid, mp 150–159°. This solid was dissolved in methylene chloride and passed through 100 g of Florisil. After eluting with *ca.* 750 ml of additional methylene chloride, evaporation gave 5.4 g (38%) of product as a pale yellow solid, mp 152–155°. The analytical sample was recrystallized from methanol–methylene chloride to give pale yellow needles: mp 154–156°; ultraviolet maxima (2-propanol) at 215 mμ (infl) (ϵ 2600), 233 (27,000), 247 (infl) (35,000), 250 (36,300), 271 (23,400), 279 (infl) (2000), 327 (infl) (5900), 343 (8000), and 355 (8250); nmr peaks ($CDCl_3$) at δ 7.82, 6.80, 6.96 (3 H, ABX pattern, pyrrole H's 1, 2, and 3, respectively, $J_{1,2}$ = 2.7 cps, $J_{2,3}$ = 4.1 cps, $J_{1,3}$ = 1.3 cps).[23]

Anal. Calcd for $C_{17}H_{11}ClN_2$: C, 73.25; H, 3.98; N, 10.05. Found: C, 73.54; H, 3.84; N, 9.98.

B. From 5′-Chloro-2′-(1-pyrrolyl)benzanilide (24).—A solution of 2.6 g of **24**, prepared as described below, in 18 ml of redistilled phosphorus oxychloride was refluxed for 20 min. The excess phosphorus oxychloride was removed at reduced pressure and the residue treated with water and then basified with sodium carbonate. After extraction with chloroform, the organic phase was separated, washed, dried, and concentrated to an oil. This oil was dissolved in benzene and filtered over 80 g of alumina and the alumina washed with *ca.* 700 ml of benzene. Removal of the solvent gave a pale yellow solid, mp 150–153°. This product was identical in all respects (infrared spectra and mixture melting point) with the substance obtained from procedure A.

1-(4-Chloro-2-nitrophenyl)pyrrole (22).—A solution of 17.2 g (0.1 mol) of 4-chloro-2-nitroaniline in 100 ml of glacial acetic acid was treated with 18.8 g (0.15 mol) of dimethoxytetrahydrofuran and then heated on the steam bath for 30 min. The hot solution was filtered from a small amount of undissolved solid (discarded) and the filtrate poured into 500 ml of water. After extraction with carbon tetrachloride, the organic phase was separated, washed, dried, and filtered over 100 g of Florisil. Continued elution with carbon tetrachloride gave, upon concentration, an orange oil. The oil was dissolved in ethyl ether and the solution diluted with petroleum ether (bp 30–60°). After refrigeration, filtration gave 15.6 g (70%) of yellow-amber crystals, mp 53–54°. Recrystallization from ether–petroleum ether raised the melting point to 55–56°. The product was light sensitive becoming dark red upon exposure to overhead light.

Anal. Calcd for $C_{10}H_7ClN_2O_2$: C, 53.95; H, 3.17; N, 12.58. Found: C, 53.79; H, 3.15; N, 12.87.

1-(4-Chloro-2-aminophenyl)pyrrole (23).—To a stirred solution of 10 g (0.045 mol) of **22** dissolved in a mixture of 200 ml of tetrahydrofuran and 100 ml of water was added, portionwise, 10 g of sodium hydrosulfite. After heating on the steam bath for 5 min, an additional 10 g of sodium hydrosulfite was added. The mixture was again placed on the steam bath for 5 min after which it was treated with 23 g of additional sodium hydrosulfite and a solution of 200 ml of ethanol in 250 ml of water. After 5 min of further heating the organic solvents were removed at reduced pressure; the resultant precipitate was filtered and washed with water. Recrystallization from hexane gave 4.5 g (46%) of white needles, mp 87–88°.

Anal. Calcd for $C_{10}H_9ClN_2$: C, 62.34; H, 4.71; N, 14.54. Found: C, 62.59; H, 4.76; N, 14.59.

5′-Chloro-2′-(1-pyrrolyl)benzanilide (24).—To a solution of 6 ml of benzoyl chloride in 30 ml of pyridine, cooled in ice, was added 6.1 g (0.03 mol) of **23**. The resultant mixture was heated gently on the steam bath for 1 hr and the excess pyridine removed at reduced pressure. The residue was covered with water and the mixture extracted with ethyl ether. The organic layer was separated, washed twice with 50-ml portions of 2 N hydrochloric acid and with water, and then dried over sodium sulfate. Removal of the ether gave a sticky, brown solid which was recrystallized from ethanol to give 4 g (45%) of cream-colored needles, mp 124–125.5°.

Anal. Calcd for $C_{17}H_{13}ClN_2O$: C, 68.80; H, 4.42; N, 9.44. Found: C, 68.81; H, 4.17; N, 9.50.

Registry No.—**4,** 15707-36-5; **5,** 15893-36-4; **6,** 15707-37-6; **8,** 15707-38-7; **9,** 15707-39-8; **10,** 15707-40-1; **11,** 15707-41-2; **12,** 15707-42-3; **13,** 15707-44-5; **14,** 15707-43-4; **15,** 15707-45-6; **16,** 15707-46-7; **17,** 15707-47-8; **18,** 15814-72-9; **19,** 15814-73-0; **20,** 15814-75-2; **21,** 15814-74-1; **22,** 15893-38-6; **23,** 15814-76-3; **24,** 15893-37-5.

Acknowledgment.—We are indebted to Dr. T. Williams for the nmr spectra, to Dr. V. Toome for the ultraviolet spectra, to Dr. F. Vane for the mass spectra, to Mr. S. Traiman for the infrared spectra, and to Dr. A. Steyermark and Dr. F. Scheidl for the microanalyses.

(21) Florisil (Floridin Co.) is a synthetic magnesium silicate adsorbent.

(22) The value for the spin coupling constant for these pyrrole hydrogens is consistent with the $J_{3,4}$ noted for 2,5-disubstituted pyrroles (*cf.* ref 18).

(23) Similar nmr data for a series of 4-substituted pyrrolo[1,2-a]quinoxalines have been reported by G. W. H. Cheeseman and B. Tuck [*J. Chem. Soc.*, 1164 (1967)].