steroid estrogens and the cis and trans forms of the nonsteroidal estrogens and antiestrogens, guided by detailed knowledge of receptor-binding and biological activities of all of these molecules and specially chosen active and inactive analogues.

Acknowledgment. We thank C. Weeks for providing tamoxifen coordinates. Support of this work was from the Medical Research Council of Canada and from the NIH (Grant CA 15879).

Supplementary Material Available: A list of observed and calculated structure factors, a table of anisotropic thermal parameters, and a table of hydrogen atom positional coordinates (27 pages). Ordering information is given on any current masthead page.

Experimental Antiulcer Drugs. 4. 1,3-Disubstituted 2,4,5,6-Tetrahydro-4,6,6-trimethyl-2-phenylcyclopenta[*c*]pyrrole-4-carboxamides[1]

Rudolf Oesterlin, Malcolm R. Bell,* Allan G. Hlavac, Ruthann H. McGarry, Karl O. Gelotte,

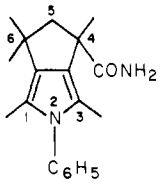
Department of Chemistry

James C. Bradford, and Janis Rozitis, Jr.

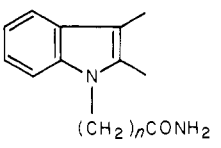
Department of Toxicology, Sterling-Winthrop Research Institute, Rensselaer, New York 12144. *Received January 10, 1980*

The synthesis of 1,3-disubstituted 2,4,5,6-tetrahydro-4,6,6-trimethyl-2-phenylcyclopenta[c]pyrrole-4-carboxamides is reported. The derivatives included $R_1 = R_3 = H$, $R_1 = CH_2OH$ with $R_3 = H$ (16) or CH_3, $R_1 = CH_3$ with $R_3 = CH_2OH$ (17), and $R_1 = R_3 = CH_2OH$. The monohydroxymethyl derivatives were as active as the parent cyclopentapyrrole, where $R_1 = R_3 = CH_3$ (1), when administered orally in the pyloric ligated rat. The compounds lacking one or both CH_3 groups at C-1 or C-3 were much less active. Compounds 16 and 17 inhibited histamine-induced gastric acid secretion in the dog.

The outstanding gastric antisecretory activity of the cyclopentapyrrole 1 in the rat and the dog has been reported in our previous publication.[2] Examination of the effect of varying the substituents at N-2 on the oral gastric antisecretory activity in the rat led to the conclusion that an unsubstituted phenyl group was the optimal substituent. We now report a study of the effect of varying the substituents at C-1 and C-3, in particular the effect of hydroxylation, homologation, and replacement by hydrogen of the methyl groups. The same modifications of the methyl groups in the 2,3-dimethylindole-1-alkanamide (2) series had demonstrated that their presence was a requirement for high oral antisecretory activity in the rat.[3]



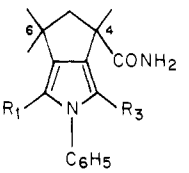
1



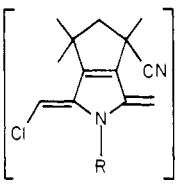
2

Chemistry. Functionalization of the C-1 and C-3 methyl groups was accomplished through chlorination with sulfuryl chloride. The chlorination products which could be prepared in good yield were the dichloro 4, tetrachloro 19, and pentachloro 7 derivatives (Schemes I and II). Solvolysis of the dichloro compound 4 in trifluoroacetic acid yielded a mixture of aldehydes consisting of three parts of the 3-aldehyde 5 and one part of the 1-aldehyde 6. Pure 5 could be isolated in about 25% yield by direct crystallization. Hydration of the mixture of nitrile aldehydes yielded a mixture of aldehyde amides from which the 1-aldehyde amide 10 could be isolated in low yield. The formation of 5 and 6 may result from the occurrence of both possible modes of elimination of HCl from 4 to give the intermediates 25 and 26. Addition of HX would give,

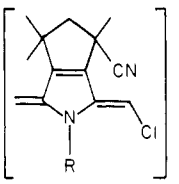
Table I. NMR Spectra of the Aldehydes in $CDCl_3$



		$\Delta\delta$ from $R_1 = R_3 = CH_3$	
R_1	R_3	C-4 CH_3	C-6 CH_3's
CH_3	CHO	−0.10	−0.03, −0.03
CHO	CH_3	−0.02	−0.18, −0.14
CHO	CHO	−0.11	−0.15, −0.17



25, R = C_6H_5



26, R = C_6H_5

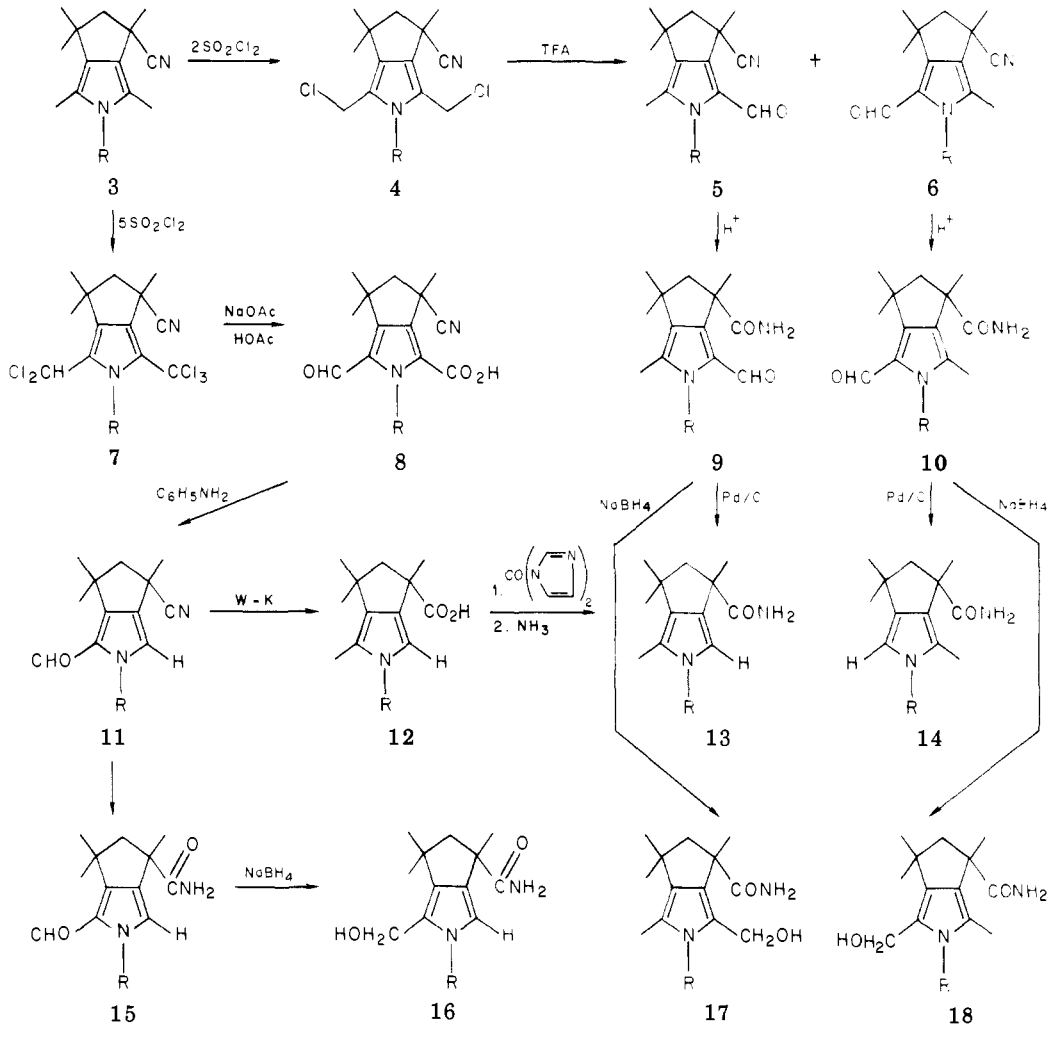
respectively, the precursors to 5 and 6. The monoaldehydes afforded the target compounds 13, 14, 17, and 18 by the routes indicated in Scheme I.

The 3-unsubstituted 1-hydroxymethyl derivative 16 proved to be readily available from the pentachloro compound 7. A noteworthy step in this sequence is the excellent decarboxylation procedure utilizing aniline in boiling dimethylaniline. This reagent combination has been reported to be effective in the decarboxylation of 3-formylindole-2-carboxylic acid.[4] The 1,3-bis(hydroxy-

(1) For Part 3, see M. R. Bell, R. Oesterlin, K. O. Gelotte, A. G. Hlavac, and A. V. R. Crain, Jr., *J. Heterocycl. Chem.*, 14, 1059 (1977).
(2) R. Oesterlin, M. R. Bell, R. H. McGarry, and A. G. Hlavac, *J. Med. Chem.*, 20, 1068 (1977).
(3) M. R. Bell, A. W. Zalay, R. Oesterlin, S. D. Clemans, D. J. Dumas, J. C. Bradford, and J. Rozitis, Jr., *J. Med. Chem.*, 20, 537 (1977).
(4) A. C. Shabica, E. E. Howe, J. B. Ziegler, and M. Tishler, *J. Am. Chem. Soc.*, 68, 1156 (1946).

0022-2623/80/1823-0945$01.00/0

Scheme I[a]



[a] R = C_6H_5.

methyl) derivative **22** and compound **24** were synthesized from the tetrachloro derivative **19** as outlined in Scheme II.

The assignment of structure to the unsymmetrical derivatives in Scheme I depended on a determination of the structures of the aldehydes **9** and **10**. A comparison of the chemical shifts in the NMR spectra of the C-4 and C-6 methyl signals in the dialdehyde **23** and the monoaldehydes **9** and **10** with the dimethyl derivative **1** and the sequence **11** → **12** → **13** permitted an unambiguous assignment of structure (Table I).

The 1,3-diethyl derivative **27** was prepared by the sequence outlined in Scheme III.

Discussion

The results of screening the new compounds and the parent cyclopentapyrrole **1** in the pyloric ligated rat are presented in Table II. A marked reduction in activity was observed upon removal of either one or both methyl groups at C-1 and C-3 (**13**, **14**, and **24**) or homologation to the ethyl derivative (**27**). These results parallel those reported for the indoles **2**.[3] The hydroxymethyl derivatives **16**–**18** were approximately as active as the parent substance **1**, an observation which contrasts with the results of testing the 3-(hydroxymethyl)indoles by the oral route.[3] The latter compounds are highly active when administered by a parenteral route but apparently do not survive in rat stomach acid. As a result, they do not exhibit oral activity. 3-(Hydroxymethyl)indoles and hydroxymethylpyrroles are known to be unstable in an acid environment. The presence of the electron-attracting phenyl groups at N-2 in the cyclopentapyrroles may lend sufficient stability to the hydroxymethyl derivatives to allow their survival in the highly acidic rat stomach. There is no obvious explanation for the failure of the bis(hydroxymethyl) compound **22** to exhibit activity. It was also inactive when administered by parenteral routes.

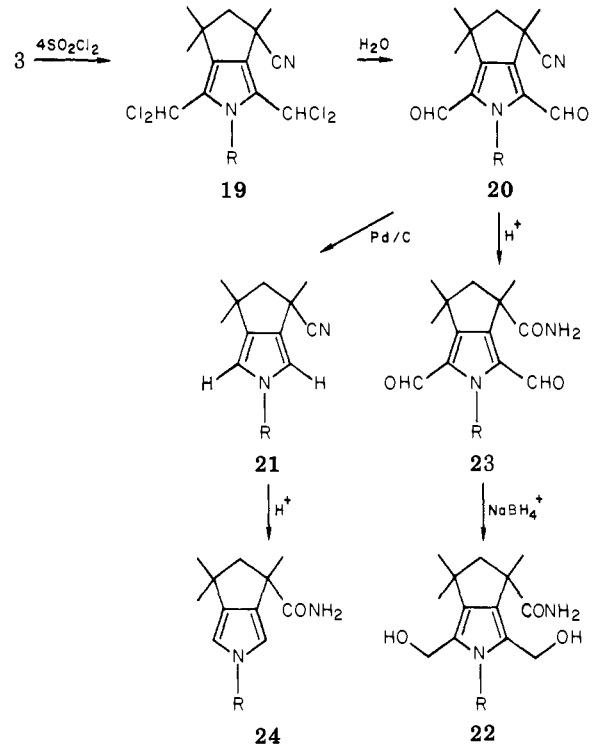
Compounds **16** and **17** did not appear to possess anticholinergic properties. The procedure used for a preliminary evaluation of this property is the mouse mydriasis test.[5] It has been described in a previous publication.[2] Both compounds were active in inhibiting histamine-induced gastric acid secretion in the dog when given by the oral route. The details of this procedure have also been reported earlier.[2] When compound **17** was administered 18 and 2 h prior to histamine injection at a dose of 50 mg/kg, the pH of the gastric secretions ranged from 7.1 to 7.9 over the 5-h collection period. Compound **16** was somewhat less active in this test. At the same dose and under the same conditions the pH values were in the 5 range.

Chronic administration of **1** to rats, dogs, and monkeys resulted in a bone marrow depression in all three species.

(5) We are indebted to Dr. Bertram A. Spilker for these results. See ref 2 for a description of the experimental procedures used to evaluate these properties.

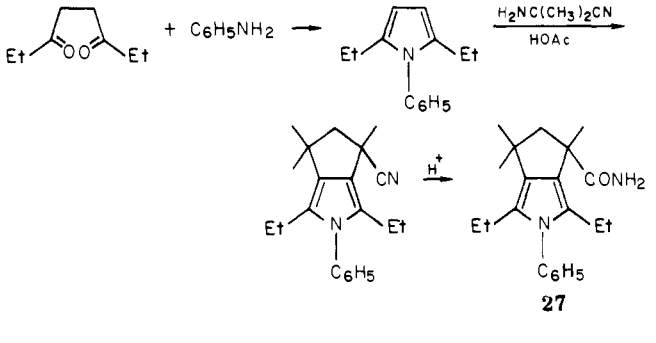
(6) H. Reinheckel and D. Iahnke, *Chem. Ber.*, **97**, 2661 (1969).

Scheme II[a]



[a] R = C_6H_5.

Scheme III



The phenomenon exhibited itself by a depression of hematologic parameters and was confirmed at autopsy upon examination of the bone marrow. For example, when 1 was administered to rats at 250 and 1250 mg/kg po for 14 weeks, a decreased red blood cell count, hemoglobin concentration, and hematocrit was observed. Bone marrow changes at the high dose consisted of an increase in the number of blast cells and a decrease in the number of mature cells, particularly the heterophils, along with a decrease of overall cellularity. Monkeys which had been treated with 17 over a period of several weeks also showed evidence of bone marrow depression. The derivative 16 did not appear to affect the blood-producing organs in the moneky but did induce convulsions in dogs at doses not far removed from the doses required to inhibit gastric acid secretion.

Experimental Section

Where analyses are indicated by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values. The amides were prepared from the nitriles in 91% H_2SO_4 at room temperature. Reduction of the aldehydes to the hydroxymethyl derivatives was accomplished by $NaBH_4$ in EtOH at room temperature.

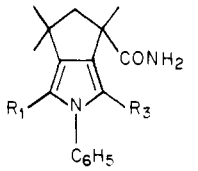
1,3-Bis(chloromethyl)-2,4,5,6-tetrahydro-4,6,6-trimethyl-2-phenylcyclopenta[*c*]pyrrole-4-carbonitrile (4). To 278 g (1 mol) of **3** in 3.5 L of CCl_4 at 0 °C was added 162 mL (2 mol) of SO_2Cl_2 dropwise, and the temperature was kept at or below 0 °C by external cooling. After completion of the addition, the dark solution was left at room temperature overnight. The reaction mixture was divided into two equal portions. Each portion was poured on to 1.5 L of ice–H_2O, the layers were separated, and the organic phase was washed with water (3 × 1 L) and brine (2 × 0.5 L). Concentration of the combined dried ($MgSO_4$) extracts left a brown oil, which crystallized on trituration with a limited quantity of Et_2O to give 250 g (72%) of an unstable gray solid: mp 126–128.5 °C; NMR ($CDCl_3$) δ 1.47 (3 H, s), 1.50 (3 H, s), 1.80 (3 H, s), 2.35 (1 H, d, J = 13 Hz), 2.85 (1 H, d, J = 12 Hz), 4.35 (2 H, s), 4.22 (1 H, d, J = 12 Hz), 4.58 (1 H, d, J = 12 Hz), 7.50 (5 H, s); MS m/e 346 (M^+).

1,3-Bis(dichloromethyl)-2,4,5,6-tetrahydro-4,6,6-trimethyl-2-phenylcyclopenta[*c*]pyrrole-4-carbonitrile (19). To a stirred solution of nitrile **3** (41.7 g, 0.15 mol) in 600 mL of absolute Et_2O was added dropwise over 1.5 h at −5 to 0 °C 53.4 mL (0.66 mol) of SO_2Cl_2. The mixture was left at room temperature overnight. The solution was poured into ice–H_2O, and the organic phase was separated. It was washed (H_2O, brine), dried ($MgSO_4$), and evaporated to dryness in vacuo. The residue (60 g) was triturated with ca. 50 mL of Et_2O to furnish 38.1 g (61%) of off-white **19**: mp 186–188.5 °C; NMR ($CDCl_3$) δ 1.62 (3 H, s), 1.64 (3 H, s), 2.01 (3 H, s), 2.42 (1 H, d, J = 13 Hz), 2.89 (1 H, d, J = 13 Hz), 6.28 (1 H, s), 6.39 (1 H, s), 7.35–7.8 (5 H, m); MS m/e 414 (M^+).

1-(Dichloromethyl)-2-phenyl-2,4,5,6-tetrahydro-3-(trichloromethyl)-4,6,6-trimethylcyclopenta[*c*]pyrrole-4-carbonitrile (7). This compound was prepared in the same manner as **19** from the nitrile **3** (44.5 g, 0.16 mol) and 70 mL (0.88 mol) of SO_2Cl_2 in 640 mL of absolute Et_2O. The precipitate from the reaction mixture was filtered and washed (Et_2O) to give 44.5 g (62%) of **7**: mp 181–184 °C; NMR ($CDCl_3$) δ 1.71 (6 H, s), 1.93 (3 H, s), 2.44 (1 H, d, J = 13 Hz), 2.93 (1 H, d, J = 13 Hz), 6.17 (1 H, s), 7.35–7.5 (5 H, m); MS m/e 448 (M^+).

3-Formyl-2-phenyl-2,4,5,6-tetrahydro-1,4,6,6-tetramethylcyclopenta[*c*]pyrrole-4-carbonitrile (5). A solution of 50 g of **4** in 500 mL of TFA was refluxed for 3 h, cooled, and poured into 1 L of ice–H_2O. The layers were separated and the aqueous phase was extracted with Et_2O (4 × 300 mL). The combined organic phases were washed with H_2O, aqueous $NaHCO_3$, and

Table II. Gastric Antisecretory Activity in the Pyloric Ligated Rat



no.	R_1	R_3	pH[a]	mp, °C	formula[b]
1	CH_3	CH_3	6.2		
9	CH_3	CHO	1.2	207-209	$C_{19}H_{22}N_2O_2$
10	CHO	CH_3	1.5	123-126	$C_{19}H_{22}N_2O_2$
13	CH_3	H	2.6	185-202	$C_{18}H_{22}N_2O$
14	H	CH_3	1.2	186-190	$C_{18}H_{22}N_2O$
15	CHO	H	1.5	190-192	$C_{18}H_{20}N_2O_2$
16	CH_2OH	H	6.4	170-171	$C_{18}H_{22}N_2O_2$
17	CH_3	CH_2OH	7.0	173-176	$C_{19}H_{24}N_2O_2$
18	CH_2OH	CH_3	5.7	184-185	$C^c_{19}H^c_{24}N_2O_2$
22	CH_2OH	CH_2OH	1.2	115-120	$C_{19}H_{24}N_2O_3 \cdot C_2H_5OH$
23	CHO	CHO	1.2	164.5-166.5	$C_{19}H_{20}N_2O_3$
24	H	H	1.1	192-194	$C_{17}H_{20}N_2O$
27	C_2H_5	C_2H_5	1.1	152-153	$C_{21}H_{28}N_2O$

[a] pH of gastric contents after administration of the drug at 100 mg/kg po 1 h prior to the 5-h pyloric ligation period. See ref 3 for the details of the procedure. pH values are reproducible to within 1 unit. A value of < 2 is considered to indicate the compound is inactive. [b] Elemental analyses for C, H, and N were within 0.4% of the calculated values unless otherwise noted. [c] C: calcd, 73.04; found, 71.94; H: calcd, 7.74; found, 7.24.

brine. Concentration of the dried (Na_2SO_4) extracts and recrystallization of the residue from *i*-PrOH afforded 10.7 g (25%) of **5**: mp 125–128 °C; NMR ($CDCl_3$) δ 1.41 (3 H, s), 1.47 (3 H, s), 1.86 (3 H, s), 2.40 (1 H, d, J = 13 Hz), 2.90 (1 H, d, J = 13 Hz), 7.1–7.7 (5 H, m), 9.31 (1 H, s). Anal. ($C_{19}H_{20}N_2O$) C, H, N.

1-Formyl-2-phenyl-2,4,5,6-tetrahydro-1,4,6,6-tetramethylcyclopenta[*c*]pyrrole-4-carboxamide (10). The mixture of aldehyde nitriles remaining after isolation of pure 3-aldehyde nitrile **5** was converted to the corresponding mixture of aldehyde amides with 91% H_2SO_4 at room temperature. From the product mixture by fractional crystallization from benzene could be isolated a quantity of 1-aldehyde amide **10**: NMR ($CDCl_3$) δ 1.46 (3 H, s), 1.50 (3 H, s), 1.58 (3 H, s), 2.30 (3 H, s), 2.78 (1 H, d, J = 13 Hz), 2.30 (1 H, d, J = 13 Hz), 5.87 (1 H, br), 6.35 (1 H, br), 7.1–7.6 (5 H, m), 9.32 (1 H, s).

2-Phenyl-2,4,5,6-tetrahydro-1,4,6,6-tetramethylcyclopenta[*c*]pyrrole-4-carboxamide (13). A. From Carboxylic Acid 12. A solution of 6.2 g (21.8 mmol) of **12** and 4.2 g (26 mmol) of *N,N'*-carbonyldiimidazole in 70 mL of tetrahydrofuran was stirred at room temperature for 6 h and treated with 5 mL of liquid NH_3 in 20 mL of tetrahydrofuran, and the mixture was stirred for 18 h. A white solid was filtered off, the filtrate was concentrated, and the brown solid residue was slurried in H_2O, collected, and dissolved in EtOAc. This solution was washed with alkali, H_2O, and brine and dried ($MgSO_4$). Concentration of the extract afforded 6 g of a yellow solid, which was recrystallized from EtOAc and then MeOH: mp 185–202 °C; NMR ($CDCl_3$) δ 1.20 (3 H, s), 1.30 (3 H, s), 1.47 (3 H, s), 2.06 (3 H, s), 2.12 (1 H, d, J = 7 Hz), 2.68 (1 H, d, J = 7 Hz), 5.64 (1 H, br), 6.16 (1 H, br), 6.42 (1 H, s), 7.1–7.48 (5 H, m).

B. By Decarbonylation of 9. The aldehyde **9** (0.2 g), 10% Pd/C (50 mg), and diethylene glycol monoethyl ether (2 mL) were refluxed for 2 h. The mixture was diluted with EtOH, filtered, and concentrated. The residue was diluted with H_2O and extracted with Et_2O. Concentration of the dried ($MgSO_4$) extracts and addition of pentane to the residue yielded 0.1 g of dark yellow crystals, mp 175–178 °C. This sample was shown to be identical with that prepared from **8** via **11** and **12** by comparison of their NMR, MS, and IR spectra, as well as their gas chromatographic behavior.

4-Cyano-1-formyl-2,4,5,6-tetrahydro-4,6,6-trimethyl-2-phenylcyclopenta[*c*]pyrrole-3-carboxylic Acid (8). A mixture of 190 g of **7**, which contained approximately 10% (NMR) of the tetrachloro derivative **19** and 230 g of potassium acetate in 2 L of AcOH, was refluxed for 2.5 h, cooled, poured into 4 L of H_2O, and the precipitate was collected. The product was slurried with 2 L of 10% Na_2CO_3, which had been diluted with 4 L of H_2O, the aqueous phase was extracted once with benzene and acidified with HOAc, and the product was collected. It was washed with H_2O and dissolved in $CHCl_3$, and the dried (Na_2SO_4) solution was concentrated. The residue was triturated with hot CCl_4 to give essentially pure aldehyde acid: yield 101 g (74%); mp 213–214 °C. When recrystallized from *i*-PrOH, it formed an isopropanolate: mp 209–211 °C dec; NMR ($CDCl_3$) δ 1.05 (6 H, d, J = 6 Hz), 1.47 (3 H, s), 1.50 (3 H, s), 1.82 (3 H, s), 2.45 (1 H, d, J = 13 Hz), 2.95 (1 H, d, J = 13 Hz), 3.97 (1 H, q, J = 6 Hz), 7.22 (1 H, s), 7.2–7.6 (5 H, m), 9.27 (1 H, s). Anal. ($C_{19}H_{18}N_2O_3 \cdot C_3H_8O$) C, H, N.

1-Formyl-2-phenyl-2,4,5,6-tetrahydro-4,6,6-trimethylcyclopenta[*c*]pyrrole-4-carbonitrile (11). A solution of 50 g (0.155 mol) of **8**, 21.6 g (0.232 mol) of aniline, and 500 mL of dimethylaniline was refluxed for 45 min under a Dean–Stark trap. Approximately the theoretical amount of water was collected. The cooled solution in 1 L of CH_2Cl_2 was washed with 6 N HCl (2 × 500 mL, 6 × 250 mL), the organic phase was washed with $NaHCO_3$ and H_2O, dried (Na_2SO_4), and concentrated, and the residue was crystallized from MeOH to give the product: yield 36.1 g (84%); mp 129–130 °C; NMR ($CDCl_3$) δ 1.55 (6 H, s), 1.71 (3 H, s), 2.33 (1 H, d, J = 13 Hz), 2.90 (1 H, d, J = 13 Hz), 6.82 (1 H, s), 7.40 (5 H, s), 9.51 (1 H, s); MS m/e 278 (M^+). Anal. ($C_{19}H_{20}N_2O$) H, N; C: calcd, 77.67; found, 76.12.

2-Phenyl-2,4,5,6-tetrahydro-1,4,6,6-tetramethylcyclopenta[*c*]pyrrole-4-carboxylic Acid (12). The aldehyde (8.35 g) was reduced by the Huang–Minlon modification of the Wolff–Kishner reduction utilizing 5.25 g of KOH, 4.55 mL of 85% $N_2H_4 \cdot H_2O$, and 50 mL of 2-(2-ethoxyethoxy)ethanol. The reaction mixture was poured into H_2O, and the solution was extracted with EtOAc and acidified with dilute H_2SO_4 to give an oil which solidified: yield 6.2 g (73%); MS m/e 283 (M^+). This carboxylic acid was not further characterized but was converted to the amide **13** (vide supra).

2,4,5,6-Tetrahydro-1,3-diformyl-4,6,6-trimethyl-2-phenylcyclopenta[*c*]pyrrole-4-carbonitrile (20). The nitrile **19** (36 g, 86.5 mmol) in 400 mL of 50% aqueous EtOH was refluxed with stirring under N_2 for 1 h. When the solution cooled, a sticky solid separated, which was filtered and washed (H_2O). It was dissolved in $CHCl_3$, and the solution was washed (H_2O, saturated $NaHCO_3$). The dried ($MgSO_4$) filtrate was evaporated in vacuo to yield 28 g of crude dialdehyde. Recrystallization from *i*-PrOH afforded 19.8 g (75%) of **20**: mp 135–136.5 °C (sealed evacuated cap); NMR ($CDCl_3$) δ 1.52 (6 H, s), 1.85 (3 H, s), 2.48 (1 H, d, J = 13 Hz), 2.98 (1 H, d, J = 13 Hz), 7.58 (5 H, m), 9.49 (2 H, s). Anal. ($C_{19}H_{18}N_2O_2$) C, H, N.

2,4,5,6-Tetrahydro-4,6,6-trimethyl-2-phenylcyclopenta-[*c*]pyrrole-4-carbonitrile (21). The dialdehyde **20** (20 g, 65.5 mmol), 10% Pd/C (2.5 g), and diethylene glycol monoethyl ether (200 mL) were refluxed with stirring under N_2 for 24 h. The mixture was diluted with MeOH (200 mL) and filtered, and the MeOH was removed in vacuo. The residual solution was diluted with H_2O to 600 mL volume and was extracted with EtOAc (3 × 100 mL). The combined organic fractions were washed (H_2O, brine) and dried ($MgSO_4$). Evaporation afforded a solid (20.5 g) which was recrystallized (80 mL of *i*-PrOH) to yield 6.5 g (39.5%) of **21**: mp 139–141 °C; NMR ($CDCl_3$) δ 1.34 (3 H, s), 1.43 (3 H, s), 1.68 (3 H, s), 2.25 (1 H, d, J = 13 Hz), 2.75 (1 H, d, J = 13 Hz), 6.65 (1 H, d, J = 1.5 Hz), 6.82 (1 H, d, J = 1.5 Hz), 7.1–7.45 (5 H, m). Anal. ($C_{17}H_{18}N_2$) H; C: calcd, 81.56; found, 80.94; N: calcd, 11.19; found, 10.25.

2,4,5,6-Tetrahydro-3,4,6,6-tetramethyl-2-phenylcyclopenta[*c*]pyrrole-4-carboxamide (14). A solution of 10 g of **10** in 100 mL of 2-(2-ethoxyethoxy)ethanol and 1 g of 10% Pd/C was refluxed for 8 h. The product (0.9 g, 10%) crystallized from benzene: NMR ($CDCl_3$) δ 1.29 (3 H, s), 1.32 (3 H, s), 1.60 (3 H, s), 2.18 (3 H, s), 2.20 (1 H, d, J = 13 Hz), 2.75 (1 H, d, J = 13 Hz), 6.12, 6.40, 6.42 (3 H, s), 7.37 (5 H, m).

1,3-Diethyl-2-phenyl-2,4,5,6-tetrahydro-4,6,6-trimethylcyclopenta[*c*]pyrrole-4-carboxamide (27). A solution of octane-3,6-dione[6] (7.6 g), aniline (5.6 g), and *p*-toluenesulfonic acid monohydrate (50 mg) in 100 mL of benzene was refluxed under a Dean–Stark trap for 18 h. The solution was washed with $NaHCO_3$ and brine, dried (K_2CO_3), concentrated, and distilled to give 8.1 g, bp 134–136 °C (8 mmHg), of **2,5-diethyl-1-phenylpyrrole**. The pyrrole was converted to **1,3-diethyl-2-phenyl-2,4,5,6-tetrahydro-4,6,6-trimethylcyclopenta[*c*]-pyrrole-4-carbonitrile** in the usual manner.[2] This nitrile was not characterized but converted directly to the amide **27**.