Porphyrins with Exocyclic Rings. Part 4 [1]. An Improved One Step Synthesis of Cyclopenta[*b*]pyrroles [2]

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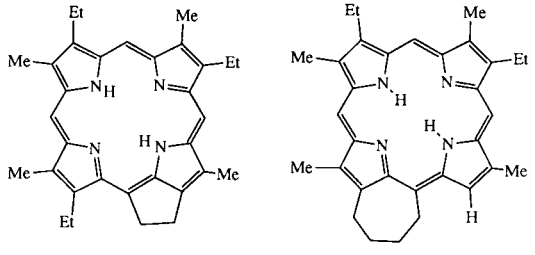
Received January 15, 1993

Cyclopentanone condensed with phenylhydrazones **5**, or oximes **6**, in the presence of zinc dust, sodium propionate and propionic acid at 150° to give cyclopenta[*b*]pyrroles **7** in good yields. This chemistry was extended to the synthesis of pyrrolic products from 1-indanone, 2-indanone and 2-methylcyclopentanone. Benzyl 3-methylcyclopenta[*b*]pyrrole-2-carboxylate was found to react regioselectively with lead tetraacetate to give the corresponding 6-acetoxy derivative and subsequent acid-catalyzed condensations with 5-unsubstituted pyrrole-2-carboxylates afforded a series of synthetically valuable dipyrroles **18a-c**.

J. Heterocyclic Chem., **30**, 477 (1993).

Cycloalkanoporphyrins (CAP's, *e.g.* **1** and **2**), usually in the form of their nickel or vanadyl complexes, are commonly present in organic-rich sediments such as oil shales

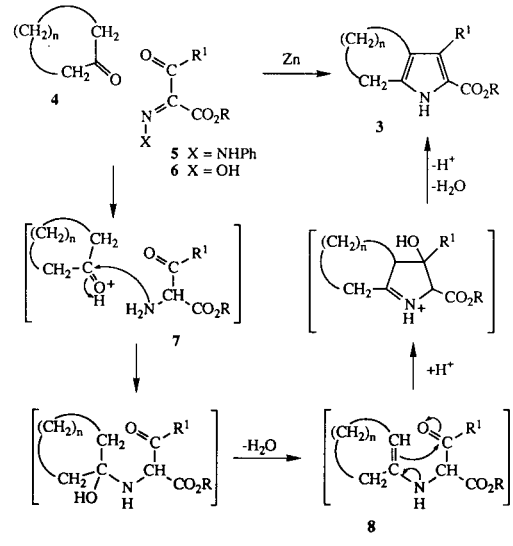


1 **2**

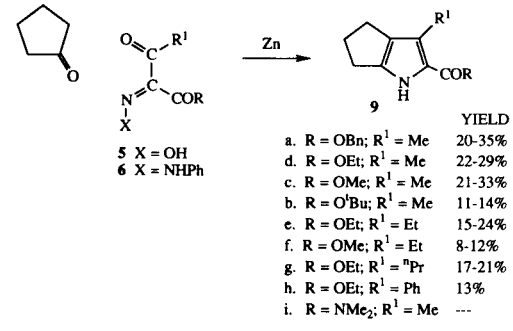
Sedimentary cycloalkanoporphyrins (CAP's)

and petroleum [3-5]. These compounds are believed to be the degradation products from biological pigments, such as the chlorophylls, that have been modified over geological time scales. Synthetic samples of geoporphyrins are of value in confirming structural assignments and in the development of new analytical procedures. We have previously reported the synthesis of CAP's from cycloalka[*b*]-pyrroles **3** [1,6-16]. These key intermediates are easily prepared by a variation on the Knorr pyrrole condensation from the corresponding cyclic ketones (Scheme 1) [6-11,13, 16-18]. Condensation of cyclic ketones **4** (n ≥ 3) with phenylhydrazones **5** or oximes **6** in the presence of zinc dust and buffered acetic acid afforded the corresponding cycloalka[*b*]pyrroles **3** (Scheme 1) in good yield. Initial *in situ* reduction of **5** or **6** leads to the formation of the aminoketones **7**. Nucleophilic attack at the carbonyl moiety of the cyclic ketone and elimination of water yields an enamine **8**, and subsequent cyclization and loss of a molecule of water then gives the pyrrolic product **3**. This chemistry has been applied to the synthesis of pyrroles fused to six- [6,8,13,17,18], seven- [6,9,10], eight- [7], nine- [19], ten- [19], twelve- [20], fifteen- [20] and sixteen- [20] membered ring systems, but our initial attempts to extend this work to the syntheis of cyclopenta[*b*]pyrroles **9** from cyclopentanone were unsuccessful (Scheme 2). Although this approach has been previously utilized in the synthesis of **9a** [17], a yield of less than 1% was reported and our attempts to reproduce this study were unsuccessful.

Scheme 1



Scheme 2

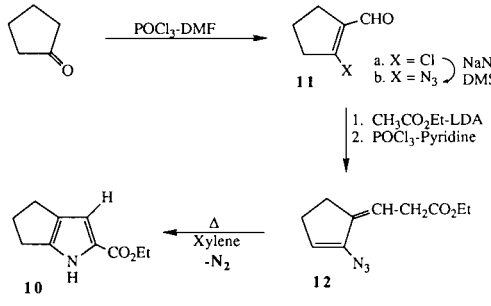


	YIELD
a. R = OBn; R^1 = Me	20-35%
d. R = OEt; R^1 = Me	22-29%
c. R = OMe; R^1 = Me	21-33%
b. R = O^{t}Bu; R^1 = Me	11-14%
e. R = OEt; R^1 = Et	15-24%
f. R = OMe; R^1 = Et	8-12%
g. R = OEt; R^1 = ^{n}Pr	17-21%
h. R = OEt; R^1 = Ph	13%
i. R = NMe_2; R^1 = Me	---

Cyclopenta[*b*]pyrroles **9** are valuable intermediates in the synthesis of meso,β-ethanoporphyrins [1,11,15] such as the widespread sedimentary porphyrin deoxophylloerythroetioporphyrin (**1**). Several of these bicyclic compounds are reported to have analgesic, antiinflammatory, and/or

antipyretic activity [21], and tetrahydro derivatives of **9** also exhibit useful pharmacological properties [22]. A number of syntheses of cyclopenta[*b*]pyrroles have been reported previously [1,9,23-25]. Cyclization of pyrroles bearing propionic acid sidechains in the presence of polyphosphoric acid affords cyclopenta[*b*]pyrroles in good yields [1,23]. However, multistep procedures are required to synthesize the precursor pyrroles and this detracts from the value of this approach. Guilard and coworkers prepared cyclopenta[*b*]pyrrole **10** (Scheme 3) in five steps from cyclopentanone [25]. Reaction of cyclopentanone with phosphorus oxychloride and dimethylformamide gave the formylation product **11a** and displacement of chloride with sodium azide in dimethyl sulfoxide yielded **11b**. Base-catalyzed condensation with ethyl acetate, followed by dehydration with phosphorus oxychloride-pyridine gave **12**. On heating in refluxing xylene, cyclization occurred *via* a nitrene intermediate to give **10**. A synthetically useful overall yield of 30% was reported for this sequence of reactions. Unfortunately, this chemistry was not completely general and 3-alkylcyclopenta[*b*]pyrroles **9** could not be prepared by this approach [25].

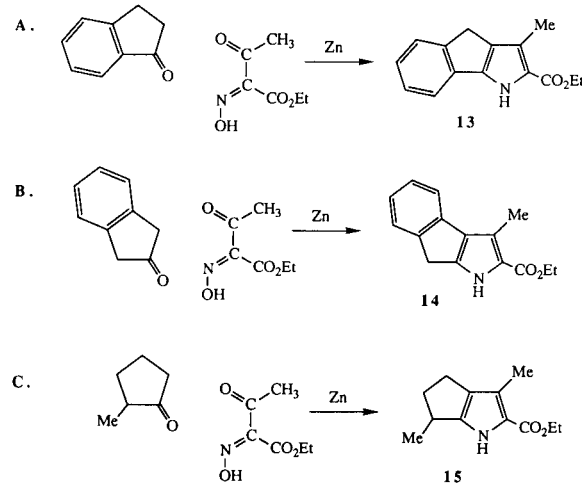
Scheme 3



We have reinvestigated the synthesis of cyclopenta[*b*]-pyrroles using the chemistry outlined in Scheme 2. Although no more than a trace of pyrrole product was obtained under conventional conditions using acetic acid as a solvent, low yields of the ethyl ester **9a** were obtained using phenylhydrazones **5a** [13], or oximes **6a**, when propionic acid was substituted as a solvent. The reaction conditions were further modified and superior results were obtained when the chemistry was carried out under relatively dilute conditions in the presence of a high concentration of sodium propionate at 150°. The benzyl, ethyl and methyl esters of 3-methylcyclopenta[*b*]pyrrole-2-carboxylic acid, **9a-c**, were prepared from readily available phenylhydrazones **5a-c** [13], or oximes **6a-c**, in reproducible yields in the range of 20-35% (Scheme 2). When one considers that this chemistry is carried out using inexpensive reagents such as ethyl acetoacetate and cyclopentanone, this scheme provides an excellent method for preparing these compounds. Comparable yields were obtained in these reactions using phenylhydrazones **5** or oximes **6**, and for simplicity all of the subsequent studies were carried out using the oximes. Oximes **6a, 6b, 6c, 6d, 6e, 6f, 6g** and **6h** were prepared by reaction of the corresponding β-ketoesters with sodium nitrite in acetic acid; **6i** was prepared by the reaction of *N,N*-dimethylacetoacetamide with butyl nitrite and hydrochloric acid. The oxime derived from *tert*-butyl acetoacetate (**6d**) gave a somewhat lower yield of **9d**, but this was not unexpected given the acid lability of the *tert*-butyl ester function. Oxime **6e** gave a good yield of the corresponding 3-ethylcyclopenta-[*b*]pyrrole **9e**, but the related methyl ester **6f** gave an inferior yield of **9f**. Oximes **6g** and **6h** similarly gave the related 3-propyl- and 3-phenylcyclopenta[*b*]pyrroles **9g** and **9h**, respectively. The 3-phenyl substituent appeared to lower the yield somewhat, perhaps due to steric effects, and a similar trend had been noted previously in the synthesis of 4,5,6,7-tetrahydroindoles (**3**, n = 3) [13]. The oxime derived from *N,N*-dimethylacetoacetamide has been previously utilized in the synthesis of pyrroles [26,27], but in this case none of the required product **9i** could be isolated (Scheme 2). We presently have no explanation for the low yields observed for **9f** and **9i**.

The generality of this chemistry was further investigated by condensing 1-indanone, 2-indanone, and 2-methylcyclopentanone with oxime **6b** in the presence of zinc dust, sodium propionate and propionic acid (Scheme 4). In each case, the expected cyclopenta[*b*]pyrroles **13, 14** and **15**, respectively, were obtained in good yields and these results further demonstrated the versatility of this reaction.

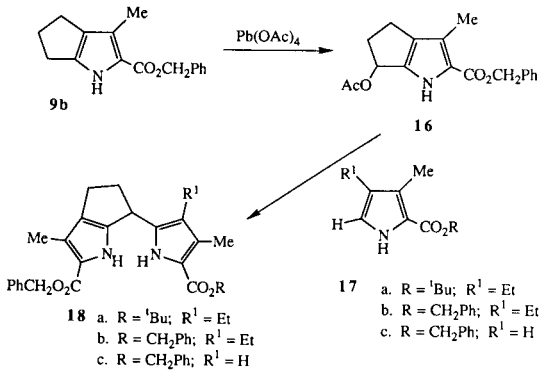
Scheme 4



The value of cyclopenta[*b*]pyrroles in porphyrin synthesis is dependant upon the utility of these compounds in the preparation of dipyrrolic structures [1,15]. In particular, it is necessary to generate intermediates with a second pyrrole unit attached at the 6-position of the cyclopenta[*b*]-pyrrole system (Scheme 5). Benzyl ester **9b** was found to react regiospecifically with lead tetraacetate in acetic acid

to give the labile 6-acetoxy derivative **16** in excellent yield (Scheme 5). The acetate could be isolated and fully characterized, but it was found to be more convenient to use the crude product in the preparation of the required dipyrroles. Condensation of the crude acetoxy compound **16** with 5-unsubstituted pyrrole **17a** in the presence of *p*-toluenesulfonic acid in acetic acid gave the corresponding dipyrrole **18a** in excellent yield. Similarly, **17b** reacted with **16** to afford the mixed ester dipyrrole **18b**. Poorer, more variable yields, were obtained in the reaction of **16** with **17c**, and dipyrrole **18c** was isolated in 38-52% yield. This inferior result was attributed in part to the lower reactivity of pyrrole **17c** due to the absence of an alkyl substituent at the 4-position.

Scheme 5



This study provides a simple direct route to cyclopenta[*b*]pyrroles from inexpensive starting materials. Furthermore, these bicyclic compounds can be elaborated to pyrrolylcyclopenta[*b*]pyrroles **18a-c** in excellent yields. These compounds show the potential to be valuable intermediates in the total synthesis of geochemically significant cycloalkanoporphyrins [15,16,28].

EXPERIMENTAL

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. The ir spectra were obtained on a Perkin-Elmer 1600 Series FTIR spectrometer as liquid films or Nujol mulls. The nmr spectra were recorded on a Hitachi-Perkin Elmer R24B 60 MHz nmr spectrometer or a Varian Gemini-300 nmr spectrometer using deuteriochloroform as the solvent and tetramethylsilane as a reference. Ethyl acetoacetate, *tert*-butyl acetoacetate, methyl acetoacetate, ethyl butyrylacetate, ethyl benzoylacetate, propionic acid, cyclopentanone, sodium propionate and lead tetraacetate were purchased from Aldrich Chemical Company; benzyl acetoacetate was obtained from Lancaster Synthesis. All of these reagents were used without further purification. Ethyl propionylacetate was prepared from Meldrum's acid [29] using the procedure of Oikawa *et al.* [30]. Mass spectral determinations were made at the Midwest Center for Mass Spectrometry at the University of Nebraska-Lincoln with partial support by the National Science Foundation, Biology Division (Grant No DIR9017262). Analytical data were obtained from Micro-analysis, Inc., Wilmington, DE 19808.

Ethyl 3-Ethylcyclopenta[*b*]pyrrole-2-carboxylate (**9e**).

A solution of sodium nitrite (18.85 g) in water (52 ml) was added dropwise to a stirred solution of ethyl propionylacetate (27.99 g) and glacial acetic acid (52 ml) in a 250 ml Erlenmeyer flask, maintaining the temperature below 10°. The resulting orange-red solution was stirred at room temperature for 1 hour and then diluted with an equal volume of water. The organic layer was separated and the aqueous layer extracted with dichloromethane (3 x 30 ml). The combined organic extracts were washed with water, 5% sodium bicarbonate solution and water. The organic layer was dried over magnesium sulfate, filtered, and the solvent removed under reduced pressure to give oxime **6e** as a yellow oil in quantitative yield (33.56 g); ir (Nujol mull): ν 3340 (br, OH), 1747, 1694 (st, sh, C=O) cm^{-1}.

In a 2 ℓ Erlenmeyer flask, cyclopentanone (10.15 g) and sodium propanoate (150 g) were dissolved in propionic acid (500 ml). The mixture was stirred and heated on an oil bath until the internal temperature reached 150°. A solution of oxime **6e** (17.3 g) in propionic acid (500 ml) was added dropwise to the stirred mixture, while simultaneously adding small portions of zinc dust (60 g) and maintaining the temperature of the reaction mixture at 150°. Once the addition was complete, the mixture was stirred at 120° for 1 hour. The mixture was cooled to 70°, poured into an ice/water slurry and the resulting mixture allowed to stand overnight. The precipitate was filtered and washed with water until the presence of propionic acid could no longer be detected. The product was dissolved in chloroform and any inorganic solids were filtered off. The chloroform was evaporated under reduced pressure and the residue recrystallized from ethanol to yield the desired pyrrole **9e** as an off-white solid (4.96 g, 24%), mp 111.5-112.5°. In some cases the crude pyrrole was chromatographed on silica, eluting with dichloromethane, prior to recrystallization. Polar by-products tended to stick to the top of the column and were conveniently removed in this way; ir (Nujol mull): ν 3296 (NH str), 1658 (C=O str) cm^{-1}; pmr: δ 1.17 (3H, t, J = 7.5 Hz, CH_2CH_3), 1.33 (3H, t, J = 7.1 Hz, $CO_2CH_2CH_3$), 2.36-2.45 (2H, m), 2.59-2.70 (4H, m) ($CH_2CH_2CH_2$), 2.78 (2H, q, J = 7.5 Hz, CH_2CH_3), 4.28 (2H, q, J = 7.1 Hz, $CO_2CH_2CH_3$), 8.66 (1H, br, NH); cmr: δ 14.56, 19.68, 24.55, 25.12, 29.00, 29.72, 59.52, 120.91, 129.23, 130.09, 141.34, 161.67.

Anal. Calcd. for $C_{12}H_{17}NO_2$ (207.27): C, 69.54; H, 8.27; N, 6.76. Found: C, 69.52; H, 8.02; N, 6.60.

Oximes **6a, 6b, 6c, 6d, 6f, 6g** and **6h** were prepared from the corresponding β-keto esters in quantitative yields by the procedure detailed above and were used in the synthesis of pyrroles **9a, 9b, 9c, 9d, 9f** and **9g** without further purification.

Ethyl 3-Methylcyclopenta[*b*]pyrrole-2-carboxylate (**9a**).

The title cyclopenta[*b*]pyrrole was prepared by the condensation of cyclopentanone (5.04 g) and oxime **9a** (7.96 g) by the previously described procedure. Recrystallization from ethanol afforded the title product as an off-white solid (2.69, 28%); mp 145-147° (lit mp [17] 147°); ir (Nujol mull): ν 3325 (NH str), 1667 (C=O str) cm^{-1}; pmr: δ 1.34 (3H, t, J = 7.1 Hz, CH_2CH_3), 2.27 (3H, s, pyrrole-CH_3), 2.35-2.44 (2H, m), 2.51-2.56 (2H, m), 2.65-2.70 (2H, m) ($CH_2CH_2CH_2$), 4.29 (2H, q, J = 7.1 Hz, CH_2CH_3), 8.70 (1H, br, NH); cmr: δ 11.65, 14.61, 23.82, 25.36, 28.91, 59.54, 121.71, 123.47, 130.24, 141.07, 161.87.

Benzyl 3-Methylcyclopenta[*b*]pyrrole-2-carboxylate (**9b**).

The title pyrrole was synthesized from cyclopentanone (5.04 g) and oxime **6b** (11.1 g) by the procedure detailed above. Recrystallization from ethanol gave pyrrole **9b** as an off-white solid (3.09 g, 24%); mp 125.5-126.5°; ir (Nujol mull): ν 3318 (NH str), 1651 (C=O str) cm^{-1}; pmr: δ 2.28 (3H, s, CH_3), 2.35-2.42 (2H, m), 2.51-2.58 (2H, m), 2.62-2.67 (2H, m) ($CH_2CH_2CH_2$), 5.28 (2H, s, CH_2Ph), 7.3-7.4 (5H, m, Ph), 8.8 (1H, br, NH); cmr: δ 11.79, 23.78, 25.33, 28.88, 65.32, 121.25, 123.99, 127.95, 128.16, 128.49, 130.33, 136.76, 141.62, 161.47.

Anal. Calcd. for $C_{16}H_{17}NO_2 \cdot 1/5\ H_2O$ (258.92): C, 74.22; H, 6.77; N, 5.41. Found: C, 74.46; H, 6.69; N, 5.42.

Methyl 3-Methylcyclopenta[*b*]pyrrole-2-carboxylate (**9c**).

The title cyclopenta[*b*]pyrrole was synthesized from cyclopentanone (5.04 g) and oxime **9c** (7.25 g) by the procedure detailed for **9e**. Recrystallization from ethanol gave the title compound as a yellow powder (1.92 g, 22%), mp 138.5-139.5°; ir (Nujol mull): ν 3294 (NH str), 1663 (C=O str) cm^{-1}; pmr: δ 2.26 (3H, s, CH_3), 2.37-2.44 (2H, m), 2.52-2.56 (2H, m), 2.65-2.70 (2H, m) ($CH_2CH_2CH_2$), 3.81 (3H, s, CO_2CH_3), 8.85 (1H, br, NH); cmr: δ 11.65, 23.79, 25.32, 28.88, 50.82, 121.40, 123.57, 130.19, 141.43, 162.30.

Anal. Calcd. for $C_{10}H_{13}NO_2$ (179.22): C, 67.02; H, 7.31; N, 7.81. Found: C, 66.66; H, 7.13; N, 7.63.

tert-Butyl 3-Methylcyclopenta[*b*]pyrrole-2-carboxylate (**9d**).

Cyclopenta[*b*]pyrrole **9d** was prepared from the condensation of cyclopentanone (5.04 g) and oxime **6d** (9.35 g) by the method described for **9e**. Recrystallization from ethanol afforded **9d** as an off-white solid (1.19 g, 11%), mp 166-167°; ir (Nujol mull): ν 3294 (NH str), 1656 (C=O str) cm^{-1}; pmr: δ 1.56 (9H, s, ^tBu), 2.24 (3H, s, CH_3), 2.33-2.40 (2H, m), 2.50-2.56 (2H, m), 2.65-2.70 (2H, m) ($CH_2CH_2CH_2$), 9.06 (1H, br, NH); cmr: δ 11.81, 23.84, 25.37, 28.60, 28.91, 79.96, 122.51, 122.93, 129.96, 140.56, 161.71.

Anal. Calcd. for $C_{13}H_{19}NO_2 \cdot 1/8\ H_2O$ (223.55): C, 69.85; H, 8.68; N, 6.26. Found: C, 69.89; H, 8.68; N, 6.26.

Methyl 3-Ethylcyclopenta[*b*]pyrrole-2-carboxylate (**9f**).

The title pyrrole was prepared by the condensation of cyclopentanone (5.04 g) and oxime **6f** (7.95 g) using the method described for **9e**. Recrystallization from ethanol gave **9f** as an off-white solid (0.83 g, 9%), mp 98-99°; ir (Nujol mull): ν 3312 (NH str), 1667 (C=O str) cm^{-1}; pmr: δ 1.17 (3H, t, J = 7.3 Hz, CH_2CH_3), 2.35-2.45 (2H, m), 2.58-2.69 (4H, m) ($CH_2CH_2CH_2$), 2.77 (2H, q, J = 7.3 Hz, CH_2CH_3), 3.81 (3H, s, CH_3), 8.82 (1H, br, NH); cmr: δ 14.49, 19.66, 24.57, 25.10, 29.00, 50.80, 120.61, 129.21, 130.24, 141.73, 162.15.

Anal. Calcd. for $C_{11}H_{15}NO_2$ (193.24): C, 68.37; H, 7.82; N, 7.25. Found: C, 68.60; H, 7.64; N, 7.18.

Ethyl 3-Propylcyclopenta[*b*]pyrrole-2-carboxylate (**9g**).

The cyclopenta[*b*]pyrrole **9g** was synthesized from cyclopentanone (5.04 g) and oxime **6g** (9.35 g) by the procedure detailed for **9e**. Recrystallization from ethanol gave the title compound as an off-white solid (2.31 g, 21%), mp 113-114°; ir (Nujol mull): ν 3293 (NH str), 1657 (C=O str) cm^{-1}; pmr: δ 0.93 (3H, t, J = 7.4 Hz, $-CH_2CH_2CH_3$), 1.33 (3H, t, J = 7.1 Hz, OCH_2CH_3), 1.59 (2H, m, $CH_2CH_2CH_3$), 2.35-2.44 (2H, m), 2.55-2.60 (2H, m), 2.65-2.74 (4H, m) ($CH_2CH_2CH_3$ and $CH_2CH_2CH_2$), 4.28 (2H, q, J = 7.1 Hz, OCH_2CH_3), 8.7 (1H, br, NH); cmr: δ 14.12, 14.56, 23.44, 24.57, 25.21, 28.43, 28.99, 59.50, 121.36, 128.60, 129.67, 141.19, 161.75.

Anal. Calcd. for $C_{13}H_{19}NO_2$ (221.30): C, 70.56; H, 8.65; N, 6.33. Found: C, 70.67; H, 8.48; N, 6.33.

Ethyl 3-Phenylcyclopenta[*b*]pyrrole-2-carboxylate (**9h**).

The title compound was prepared from cyclopentanone (5.04 g) and oxime **6h** (11.1 g) by the method detailed for **9e**. Recrystallization from ethanol gave the title cyclopenta[*b*]pyrrole as an off-white solid (1.70 g, 13%), mp 160.5-161.5°; ir (Nujol mull): ν 3297 (NH str), 1647 (C=O str) cm^{-1}; pmr: δ 1.22 (3H, t, J = 7.1 Hz, CH_2CH_3), 2.38-2.47 (2H, m), 2.65-2.76 (4H, m) ($CH_2CH_2CH_2$), 4.22 (2H, q, J = 7.1 Hz, CH_2CH_3), 7.23-7.28 (1H, m, *para*-H), 7.32-7.37 (2H, m, 2 x *meta*-H), 7.51-7.54 (2H, m, 2 x *ortho*-H), 9.16 (1H, br, NH); cmr: δ 14.26, 25.04, 25.29, 28.93, 59.90, 120.34, 126.59, 127.51, 129.60, 129.91, 135.05, 141.52, 161.38.

Anal. Calcd. for $C_{16}H_{17}NO_2$ (255.32): C, 75.27; H, 6.71; N, 5.49. Found: C, 75.14; H, 6.71; N, 5.49.

Ethyl 3-Methylindano[1,2-*b*]pyrrole-2-carboxylate (**13**).

The title cyclopenta[*b*]pyrrole was prepared from 1-indanone (7.93 g) and oxime **6a** (7.95 g) using the method described for **9e**. Recrystallization from ethanol gave **13** as an off-white solid (2.69 g, 22%), mp 203-204°; ir (Nujol mull): ν 3293 (NH str), 1657 (C=O str) cm^{-1}; pmr: δ 1.40 (3H, t, J = 7.1 Hz, CH_2CH_3), 2.42 (3H, s, CH_3), 3.47 (2H, s, CH_2), 4.38 (2H, q, J = 7.1 Hz, CH_2CH_3), 7.16-7.21 (1H, m), 7.29-7.32 (1H, m), 7.45-7.48 (2H, m) (4 x aromatic-H), 9.34 (1H, br, NH); cmr: δ 11.74, 14.66, 29.63, 60.00, 117.93, 122.16, 123.79, 125.21, 125.67, 126.71, 130.82, 134.08, 140.40, 148.10, 162.38.

Anal. Calcd. for $C_{15}H_{15}NO_2 \cdot 1/5\ H_2O$ (244.89): C, 73.57; H, 6.34; N, 5.72. Found: C, 73.77; H, 6.24; N, 5.63.

Ethyl 3-Methylindano[2,1-*b*]pyrrole-2-carboxylate (**14**).

The title cyclopenta[*b*]pyrrole was synthesized from 2-indanone (7.93 g) and oxime **6a** (7.95 g) using the method detailed for **9e**. Recrystallization from ethanol gave **14** as an off-white solid (4.13 g, 34%), mp 197-198°; ir (Nujol mull): ν 3274 (NH str), 1657 (C=O str) cm^{-1}; pmr: δ 1.39 (3H, t, J = 7.1 Hz, CH_2CH_3), 2.60 (3H, s, CH_3), 3.61 (2H, s, CH_2), 4.35 (2H, q, J = 7.1 Hz, CH_2CH_3), 7.08-7.13 (1H, m), 7.25-7.31 (1H, m), 7.37-7.40 (1H, m), 7.50-7.53 (1H, m) (4 x aromatic-H), 9.18 (1H, br, NH); cmr: δ 11.61, 14.58, 30.54, 59.97, 118.85, 121.32, 122.61, 123.56, 125.05, 126.96, 130.75, 139.34, 142.12, 143.05, 162.13.

Anal. Calcd. for $C_{15}H_{15}NO_2 \cdot 1/5\ H_2O$ (244.89): C, 73.57; H, 6.34; N, 5.72. Found: C, 73.22; H, 6.12; N, 5.87.

Ethyl 3,6-Dimethylcyclopenta[*b*]pyrrole-2-carboxylate (**15**).

Cyclopenta[*b*]pyrrole **15** was prepared by the condensation of 2-methylcyclopentanone (5.89 g) and oxime **6a** (7.95 g) using the procedure detailed for **9e**. Recrystallization from ethanol afforded the title compound as an off-white solid (2.01 g, 20%), mp 103-104°; ir (Nujol mull): ν 3309 (NH str), 1666 (C=O str) cm^{-1}; pmr: δ 1.22 (3H, t, J = 6.7 Hz, 6-CH_3), 1.34 (3H, t, J = 7.1 Hz, CH_2CH_3), 2.26 (3H, s, pyrrole-CH_3), 1.92 (1H, m), 2.4-2.7 (3H, m), 3.10 (1H, m) (5 x cyclopentane ring protons), 4.30 (2H, q, J = 7.1 Hz, CH_2CH_3), 9.06 (1H, br, NH); cmr: δ 11.65, 14.62, 19.75, 23.04, 33.15, 38.43, 59.60, 121.56, 123.39, 129.06, 145.82, 162.18.

Anal. Calcd. for $C_{12}H_{17}NO_2$ (207.27): C, 69.54; H, 8.27; N, 6.76. Found: C, 69.41; H, 8.02; N, 6.72.

Benzyl 6-Acetoxy-3-methylcyclopenta[*b*]pyrrole-2-carboxylate (**16**).

Lead tetraacetate (0.913 g) was added in several portions to a stirred solution of benzyl 3-methylcyclopenta[*b*]pyrrole-2-carboxylate **9b** (0.50 g) in acetic acid (10 ml) and acetic anhydride (0.5 ml), and the resulting mixture was stirred for an additional 2 hours. The mixture was diluted with dichloromethane and washed with water, 5% sodium bicarbonate solution, and water. The solution was dried over sodium sulfate and evaporated under reduced pressure to give the crude acetoxy derivative **16** as a pale yellow oil that solidified on standing. The residue was recrystallized from hexane to give the acetoxy compound as an off-white solid (0.521 g, 85%), mp 98-100°. Further recrystallization from carbon tetrachloride gave an analytical sample of **16** as a pale yellow powder, mp 101-102°, ir (Nujol mull): ν 3300 (NH str), 1725 (acetoxy C=O str), 1664 (pyrrole C=O str) cm^{-1}; pmr: δ 2.02 (3H, s, $OCOCH_3$), 2.27 (3H, s, pyrrole-CH_3), 2.48 (2H, m, 5-CH_2), 2.74 (2H, m, 4-CH_2), 5.23-5.34 (2H, AB quartet, OCH_2), 5.68 (1H, m, CHOAc), 7.3-7.45 (5H, m, Ph), 8.9 (1H, br, NH); cmr: δ 11.47, 21.05, 21.95, 35.34, 65.63, 72.45, 122.80, 123.52, 128.10, 128.53, 132.54, 136.41, 137.84, 161.27, 172.19.

Anal. Calcd. for $C_{18}H_{19}NO_4$ (313.35): C, 68.99; H, 6.11; N, 4.47. Found: C, 68.76; H, 6.08; N, 4.46.

Benzyl 6-(5-*tert*-Butoxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[*b*]pyrrole-2-carboxylate (**18b**).

Lead tetraacetate (7.30 g, 1.05 equivalents) was added in several portions to a stirred solution of benzyl 3-methylcyclopenta[*b*]pyrrole-2-carboxylate **9b** (4.00 g) in acetic acid (80 ml) and acetic anhydride (4 ml) and the resulting mixture was stirred for an additional 2 hours. The mixture was diluted with dichloromethane and washed with water, 5% sodium bicarbonate solution, and water. The solution was dried over sodium sulfate and evaporated under reduced pressure to give the crude acetoxy derivative **9b** as a yellow oil that solidified on standing. The residue and *tert*-butyl 4-ethyl-3-methylpyrrole-2-carboxylate **17b** [1,31] (3.12 g) were dissolved in glacial acetic acid (110 ml). *p*-Toluenesulfonic acid (180 mg) was added and the resulting mixture stirred at room temperature for 2 hours. The dark solution was diluted with chloroform, washed with water (500 ml) and the aqueous solutions back extracted with chloroform. The combined organic phases were washed with 10% sodium bicarbonate solution and evaporated under reduced pressure. The dark residue was chromatographed on silica, eluting with dichloromethane. Recrystallization from ethanol gave an off-white solid (5.04 g, 72%), mp 133-134° (lit mp [1] 135-136°).

Benzyl 6-(5-Benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[*b*]pyrrole-2-carboxylate (**18a**).

The title compound was prepared from **9b** (2.00 g) and benzyl 4-ethyl-3-methylpyrrole-2-carboxylate **17a** [1,32] (1.81 g) by the procedure described above. Recrystallization from ethanol gave the dipyrrole **18a** as white crystals (2.65 g, 72%), mp 149-150° (lit mp [1] 149-150°).

Benzyl 6-(5-Benzyloxycarbonyl-4-methyl-2-pyrrolyl)-3-methylcyclopenta[*b*]pyrrole-2-carboxylate (**18c**).

Prepared from **9b** (1.00 g) and benzyl 3-methylpyrrole-2-carboxylate **17c** [33] (0.80 g) by the procedure detailed for **18b**. The crude product was chromatographed on a silica column, eluting first with toluene to remove unreacted **17c**. Elution with dichloromethane gave the product fraction and crystallization from ethanol afforded **18c** as a white solid (0.91 g, 52%), mp 166-168°, with softening at 162°. Further recrystallization from ethanol gave an analytical sample as white crystals, mp 168-169°; eims: (relative intensity) m/z 468 (M^+, 52%), 333 (55%), 225 (35%), 91 (100%); pmr: δ 2.26 (3H, s), 2.27 (3H, s) (2 x pyrrole-CH_3), 2.3-2.85 (4H, m, ring CH_2CH_2), 4.14 (1H, t, bridge-CH), 5.2 (4H, m, 2 x OCH_2Ph), 5.81 (1H, d, J = 2.4 Hz, pyrrole-H), 7.25-7.4 (10H, m, 2 x Ph), 9.4 (1H, br), 9.5 (1H, br) (2 x NH); cmr: δ 11.82, 13.16, 23.22, 37.36, 38.23, 65.62, 65.70, 110.06, 118.25, 122.12, 123.68, 127.90, 128.46, 129.07, 130.23, 136.31, 136.41, 138.46, 141.03, 161.87.

Anal. Calcd. for $C_{29}H_{28}N_2O_4$ (468.55): C, 74.33; H, 6.03; N, 5.98. Found: C, 73.94; H, 6.01; N, 5.91.

Acknowledgements.

This material is based upon work supported by the National Science Foundation under Grant No. CHE-9201149, the Donors of the Petroleum Research Fund, administered by the American Chemical Society, and the University Research Fund of Illinois State University. We also thank the National Science Foundation (Grant No. CHE-9001175) for providing funds to purchase a Varian 300 MHz NMR spectrometer.

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