# An Improved Synthesis of Pyrroles from *N*-*p*-Toluenesulfonylglycine Esters and α,β-Unsaturated Aldehydes and Ketones [1]



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*N*-*p*-Toluenesulfonylglycine esters **2** condensed with α,β-unsaturated carbonyl compounds **1** in the presence of the non-nucleophilic base DBU to give hydroxypyrrolidines **3**. Dehydration with phosphorus oxychloride-pyridine, followed by DBU mediated elimination of *p*-toluenesulfinic acid, gave a series of synthetically useful pyrrole-2-carboxylates **5**.

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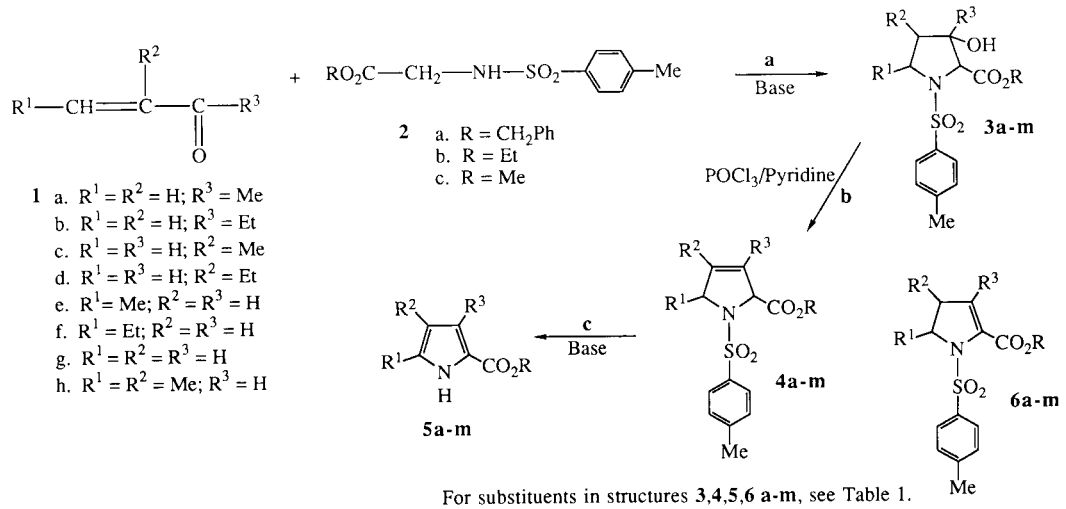
Despite the plethora of methods available for pyrrole ring synthesis, few of these approaches have been of value in porphyrin synthesis [2]. For the most part, porphyrin chemists have relied upon the Knorr pyrrole condensation and related reactions [3,4]. However, the synthesis of 5-unsubstituted pyrrole-2-carboxylates can rarely be carried out directly by using this approach. Recently, a new method for preparing these valuable intermediates, using isocyanoacetates and nitroalkenes, has been reported [5]. However, this approach cannot be utilized in the synthesis of 3-alkylpyrrole-2-carboxylates [5] and also requires the availability of relatively expensive isocyanoacetates [6,7].

In relation to our ongoing studies on the synthesis of geochemically significant cycloalkanoporphyrins [8-13], we required multigram quantities of benzyl 3-methylpyrrole-2-carboxylate (**5a**). This compound was prepared using a literature procedure [14] in three steps from readily available benzyl *N*-*p*-toluenesulfonylglycinate and methyl vinyl ketone (Scheme 1). Benzyl *N*-*p*-toluenesulfonylglycinate (**2a**) was condensed with methyl vinyl ketone (**1a**) in the presence of potassium *tert*-butoxide to give the hydroxypyrrolidine **3a**. Treatment with phosphorus oxychloride-pyridine effected a dehydration to give the 3-pyrroline **4a**. Although the related 2-pyrroline **6a** might be expected in this chemistry, on the grounds that it is a conjugated system, **4a** appears to be favored due to a decrease in the steric interaction between the *N*-tosyl substituent and the ester grouping [14]. A secondary factor may be that there is a decrease in ring strain for **4a** compared to **6a** [14]. Reaction with potassium *tert*-butoxide induced an elimination of *p*-toluenesulfinate and a subsequent tautomeric shift then yielded the desired pyrrole **5a**. In our hands, overall yields for this sequence were in the range of 30-35%. However, recrystallization of **5a** was often impeded by the presence of minor oily impurities.

Although this method provides the only known viable synthesis for benzyl 3-methylpyrrole-2-carboxylate, this approach has seen little application. The original procedure required the use of excess α,β-unsaturated ketones (generally two equivalents) and α,β-unsaturated aldehydes

## SCHEME 1




For substituents in structures **3,4,5,6 a-m**, see Table 1.

Table 1

| Product | Substituents | | | | % Yield | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 5 | $R^1$ | $R^2$ | $R^3$ | R | Part a [a] | Part b [a] | Part c [a] | Overall | mp (bp) | lit mp |
| a | H | H | Me | $CH_2Ph$ | 78 | 80 | 78 | 53 | 85-87.5° | 89-90° [14] |
| b | H | H | Me | Et | 90 | (100) | 78 | 70 | 53-55° | 56° [14], 56-58° [21] |
| c | H | H | Et | $CH_2Ph$ | 74 | 73 | 95 | 51 | Oil [b] | -- |
| d | H | Me | H | $CH_2Ph$ | 82 | 61 | 76 | 38 | 44.5-45.5° | 40-42° [15] |
| e | H | Me | H | Et | 57 | 79 | 27 | 12 | 38-40° (102-104° at 1 torr) | 37-38° [22] |
| f | H | Me | H | Me | 50 | 53 | 41 | 11 | 71-72° | 73-74° [23], 74-75° [24] 72.5-73.5° [18], 72-73° [5] |
| g | H | Et | H | $CH_2Ph$ | 77 | 64 | 81 | 40 | 56-58 [c] | -- |
| h | Me | H | H | $CH_2Ph$ | 70 | 59 | 73 | 30 | 95-96° | 96-97° [25] |
| i | Me | H | H | Et | 76 | 71 | 36 | 20 | 92-95° | 97-99° [14], 100° [26] |
| j | Et | H | H | $CH_2Ph$ | 74 | 49 | 40 | 13 | 75-78° [d] | -- |
| k | H | H | H | $CH_2Ph$ | 52 | 78 | 84 | 34 | 53-54.5° | 54-55° [27] |
| l | H | H | H | Et | 76 | (100) | 30 | 23 | 40-42° (82° at 1 torr) | 38-40° [28a], 40-42° [28b] |
| m | Me | Me | H | $CH_2Ph$ | 49 | 35 | -- | <5 (product impure by nmr spectroscopy) | | |

[a] Since intermediates 3 and 4 are not purified, these yield values serve only to give the reader a rough idea of the quantities carried through in each step of the procedure. However, overall yields were calculated for pure, isolated pyrrole products. [b] >95% pure by proton nmr spectroscopy. An analytical sample was obtained by crystallization from hexane, mp 26-26.5°. [c] Further recrystallization from hexane gave an analytical sample, mp 60.5-61.5°. [d] Further recrystallization from hexane gave an analytical sample, mp 80-80.5°.

were reported to give little or no product [14]. We speculated that a relatively non-nucleophilic base, such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), would be less likely to induce polymerization of the $\alpha,\beta$-unsaturated carbonyl compounds and might thereby allow us to extend the utility of this condensation. Methyl vinyl ketone (1 equivalent) and benzyl *N*-tosylglycinate in tetrahydrofuran were treated with 2 equivalents of DBU at room temperature and gave, after workup, the related hydroxypyrrolidine **3a** in 78% yield. Dehydration with phosphorus oxychloride/pyridine afforded the crude pyrroline **4a** and subsequent reaction with DBU in refluxing THF gave the required pyrrole **5a** in an overall yield of 53% from **2a**. The related pyrrole ethyl ester **5b** was also obtained in excellent yield (Table 1) from ethyl *N*-*p*-toluenesulfonylglycinate **2b**. Attempts to carry out these reactions in a single, one pot procedure have so far been unsuccessful. However, since the intermediary pyrrolidines **3** and pyrrolines **4** do not need to be purified, this study provides superior conditions for the synthesis of **5a** and **5b**.

In order to examine the generality of these condensations, the reactions of a series of $\alpha,\beta$-unsaturated aldehydes and ketones were examined. Ethyl vinyl ketone **1b** reacted with **2a** to give benzyl 3-ethylpyrrole-2-carboxylate (**5c**) in good overall yield (Table 1). We were also interested in the synthesis of 4-alkylpyrrole-2-carboxylates, which are valuable intermediates in porphyrin synthesis [15,16]. Methacrolein (**1c**) condensed with **2a** to give benzyl 4-methylpyrrole-2-carboxylate **5d** in 38% overall yield. We had hoped to extend this study to the synthesis of the corresponding methyl ester **5f**, since this is the trail marker for the Texas leaf-cutting ant (*Atta texana*) [17-19]. However, relatively poor yields were obtained from the condensation of **1c** and **2c**, possibly due in part to losses in extracting the initial hydroxypyrrolidine **3f**. Attempts to prepare the ethyl ester **5e** also resulted in relatively low yields (Table 1). Superior methods are available for the synthesis of the insect pheromone **5f** [5,18]. However, the benzyl ester **5d**, which is far more useful in porphyrin synthesis, is conveniently prepared by our approach. The previously unknown 4-ethylpyrrole **5g** was also prepared in good yield from ethacrolein **1d** (Table 1).

Acrolein (**1g**) gave no trace of pyrrolic products in the original work [14], due to extensive polymerization under the reaction conditions. However, using our procedure, we were able to prepare the benzyl **5k** and ethyl **5l** esters of pyrrole-2-carboxylic acid in reasonable yields (Table 1). In the original publication [14], the condensation of crotonaldehyde (**1e**) with ethyl *N*-tosylglycinate (**2b**) was investigated but very poor yields (approximately 3%) of pyrrole **5i** were achieved. Using our modified procedure, ethyl 5-methylpyrrole-2-carboxylate **5i** was obtained in nearly 20% yield. The corresponding benzyl ester **5h** was again obtained in higher yield (30%) and *trans*-2-pentenal (**1f**) similarly condensed with **2a** to give benzyl 5-ethylpyrrole-2-carboxylate **5j** in 13% yield. None-the-less, this chemistry was less successful for these cases and extractions were often hampered by the formation of intractible black tarry biproducts.

Finally, the condensation of 2-methyl-2-butenal **1h** with

benzyl *N*-tosylglycinate **2a** in the presence of DBU was investigated. The reaction was very slow in this case and prolonged reaction times (> 1 week) were required for most of the $\alpha,\beta$-unsaturated aldehyde to be consumed. Very poor yields of impure benzyl 4,5-dimethylpyrrole-2-carboxylate **5m** resulted from this reaction sequence. It seems likely

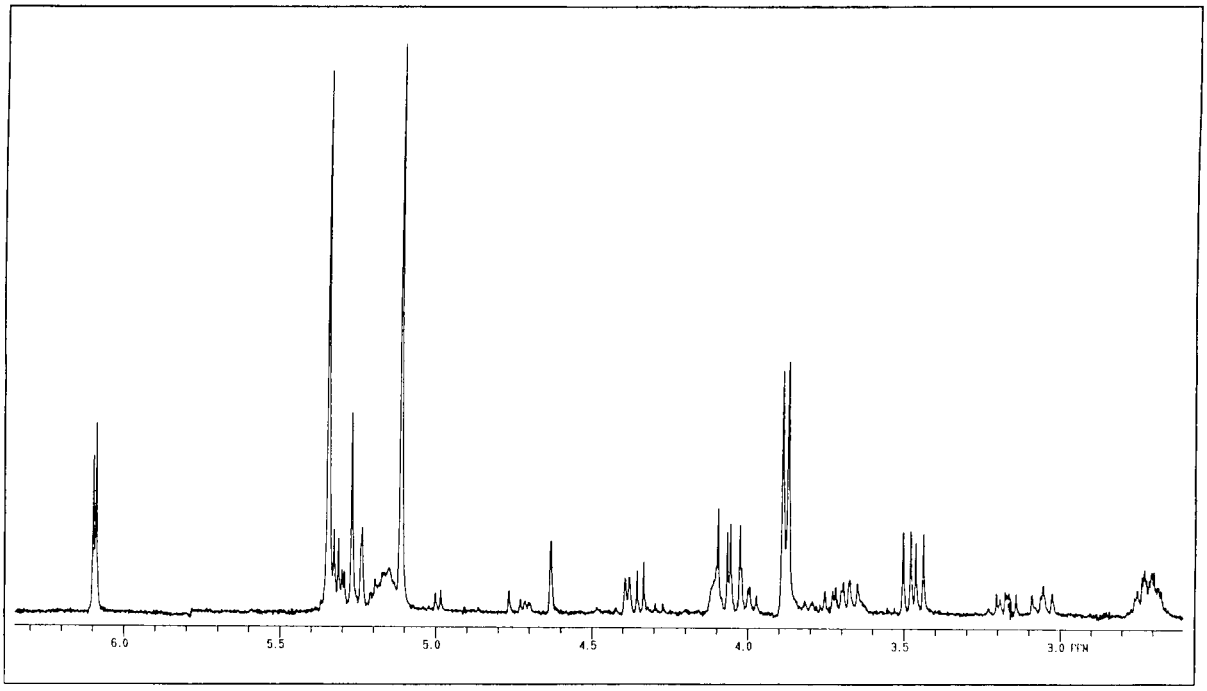



Figure 1. Partial 300 MHz proton nmr spectrum of the crude intermediary pyrroline(s) derived from methacrolein (**1c**) and benzyl *N*-*p*-toluenesulfonylglycinate (**2a**).

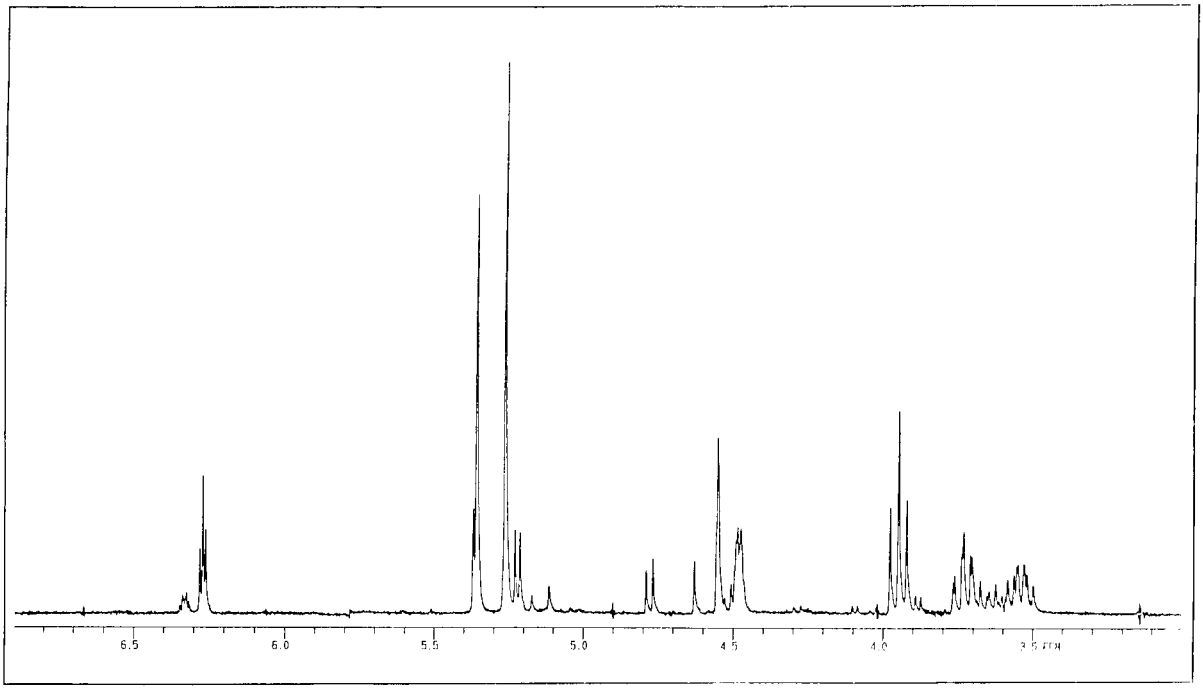



Figure 2. Partial 300 MHz proton nmr spectrum of the crude intermediary pyrroline(s) derived from acrolein (**1g**) and benzyl *N*-*p*-toluenesulfonylglycinate (**2a**).

that the alkyl substituents exert a deleterious influence on the cyclization reaction, presumably due to a combination of steric and inductive factors. Similar effects are probably responsible for the lower yields obtained in the synthesis of **5h**, **5i** and **5j**. Pyrrole **5m** may be prepared [20] by a variation of the Knorr pyrrole condensation, although in practice this procedure is complicated by the formation of two pyrrolic biproducts. Hence, a new synthesis of **5m** is needed, although the chemistry described in this paper does not appear to offer a viable alternative.

The intermediary pyrrolidines and pyrrolines in these reactions were not purified. The proton nmr spectra of these compounds were generally too complex to be fully interpreted and did not appear to correspond to single compounds. The complexity of these spectra arose, in part, from the presence of diastereomers. However, the pyrrolines derived from aldehydes **1c-g** all showed an absorption between 6.0 and 6.34 ppm in their proton nmr spectra which was consistent with the presence of 2-pyrroline structures **6**. For instance, the pyrroline derived from methacrolein (**1c**) and **2a** gave a doublet at 6.03 ppm (J = 2.7 Hz), which was consistent with the presence of the conjugated alkene unit in **6d** (Figure 1). In addition, the presence of a doublet at 0.81 ppm (J = 7 Hz) also provided evidence for the 2-pyrroline structure. Similarly, the pyrroline derived from acrolein (**1g**) and **2a** showed a triplet at 6.21 ppm (J = 2.8 Hz) (Figure 2), which is consistent with the presence of the 2-pyrroline **6k**. Although the 2-pyrrolines **6** were minor biproducts in many of these reactions, they were major components for the benzyl esters derived from **1c**, **1d** and **1g**. The intermediacy of 2-pyrrolines in these reactions was not problematical, however, since the intermediates **4** and **6** would both be expected to eliminate *p*-toluenesulfinic acid to give the pyrroles **5**.

## EXPERIMENTAL

Methyl vinyl ketone, ethyl vinyl ketone, methacrolein, ethacrolein, crotoaldehyde, *trans*-2-pentenal, *trans*-2-methyl-2-butenal and 1,8-diazabicyclo[5.4.0]undec-7-ene were purchased from Aldrich Chemical Company; acrolein was purchased from Fluka Chemie AG. All of these reagents were used without further purification. Pyridine and phosphorus oxychloride were distilled prior to use. Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 1600 Series FTIR spectrometer. 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 solvent and tetramethylsilane as a reference. Assignment of the carbon-13 nmr spectra for pyrroles **5a-l** was aided by consideration of substituent and additive chemical shift effects [29]. Analytical data were obtained from Micro-analysis, Inc., Wilmington, DE 19808.

Benzyl *N*-*p*-Toluenesulfonylglycinate (**2a**).

Benzyl alcohol (64.0 g), *N*-*p*-toluenesulfonylglycine (85.9 g) and *p*-toluenesulfonic acid (4.0 g) were dissolved in toluene and refluxed under a Dean and Stark apparatus for 3 hours. The solvent was removed under reduced pressure and the residue dissolved in a mixture of toluene-petroleum ether (60-90°). After standing overnight, the resulting crystals were filtered off to give the desired product (102.3 g, 86%) as white needles, mp 84-86° (lit mp [30] 82-84°); pmr: δ 2.38 (3H, s, $C_6H_4CH_3$), 3.80 (2H, d, J = 4.7 Hz, $CH_2NH$), 5.03 (2H, s, $OCH_2Ph$), 5.51 (1H, br, NH), 7.2-7.4 (7H, m, $C_6H_5$ and *ortho* tosyl), 7.73 (2H, d, J = 8.2 Hz, *meta* tosyl); cmr: 21.50 ($CH_3$), 44.22 ($CH_2NH$), 67.38 ($OCH_2$), 127.17 (2 x tosyl CH), 128.34 (*o*- and *p*-Ph), 128.56 (*m*-Ph), 129.69 (2 x tosyl CH), 134.79 (Ph-$C_{att}$), 136.23 (tosyl C-2), 143.67 (tosyl C-4), 168.82 (C=O).

Methyl *N*-*p*-Toluenesulfonylglycinate (**2c**).

*N*-*p*-Toluenesulfonylglycine (50.0 g) was refluxed with methanol (400 ml) and concentrated sulfuric acid (4 ml) for 5 hours. The mixture was cooled to room temperature and neutralized to *p*H 7 with concentrated aqueous ammonia. The mixture was filtered to remove precipitated ammonium sulfate, concentrated by evaporation under reduced pressure and cooled in ice. The resulting precipitate was filtered off and recrystallized from methanol to give the title compound as white crystals (42.9 g, 81%), mp 92-93° (lit mp [31] 92-93°); pmr: δ 2.42 (3H, s, $C_6H_4CH_3$), 3.63 (3H, s, $OCH_3$), 3.77 (2H, d, J = 3.9 Hz, $NHCH_2$), 5.48 (1H, br, NH), 7.30 (2H, d, J = 8.3 Hz, 2 x *meta*-H), 7.75 (2H, d, J = 8.3 Hz, 2 x *ortho*-H); cmr: 21.52 ($C_6H_5CH_3$), 44.08 ($CH_2NH$), 52.55 ($OCH_3$), 127.23, 129.74 (4 x tosyl CH), 136.27 (tosyl C-2), 143.79 (tosyl C-4), 169.41 (C=O).

Ethyl *N*-*p*-Toluenesulfonylglycinate (**2b**).

Prepared from *N*-*p*-toluenesulfonylglycine (49 g) and ethanol (425 ml) by the procedure detailed above. Recrystallization from ethanol gave the ethyl ester as white crystals (37.87 g, 69%), mp 62-64° (lit mp [32] 64-65°); pmr: δ 1.17 (3H, t, J = 7 Hz, $OCH_2CH_3$), 2.42 (3H, s, $C_6H_4CH_3$), 3.77 (2H, d, J = 5.3 Hz, $NHCH_2$), 4.08 (2H, q, J = 7 Hz, $OCH_2CH_3$), 5.46 (1H, br, NH), 7.30 (2H, d, J = 8.3 Hz, 2 x *meta*-H), 7.76 (2H, d, J = 8.3 Hz, 2 x *ortho*-H); cmr: 13.96 ($CH_2CH_3$), 21.51 ($C_6H_4CH_3$), 44.24 ($CH_2NH$), 61.83 ($OCH_2$), 127.25, 129.72 (4 x tosyl CH), 136.30 (tosyl C-2), 143.75 (tosyl C-4), 168.92 (C=O).

Benzyl 3-Ethylpyrrole-2-carboxylate (**5c**).

Step a.

DBU (19.8 g) was added to a stirred solution of ethyl vinyl ketone (5.0 g, 59 mmoles) and benzyl *N*-*p*-toluenesulfonylglycinate (18.8 g, 59 mmoles) in tetrahydrofuran (50 ml). The resulting dark brown mixture was stirred overnight at room temperature. The mixture was diluted with ether, washed with 5% hydrochloric acid, 5% sodium bicarbonate solution and water. The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure to give the crude pyrrolidine **3c** (17.59 g, 74%) as a yellow oil.

Step b.

The foregoing pyrrolidine oil (17.59 g, 44 mmoles) was dissolved in pyridine (115 ml). Phosphorus oxychloride (17.0 g) was added dropwise over 5-10 minutes and the resulting mixture stirred overnight at room temperature. The mixture was poured over ice, extracted with ether and washed with 5% hydrochloric

acid, 5% sodium bicarbonate solution and water. The etherial layer was dried over sodium sulfate, filtered and evaporated under reduced pressure to give the crude oily 3-pyrroline **4c** (12.22 g, 73%).

Step c.

The foregoing pyrroline (12.00 g) was dissolved in toluene (75 ml), DBU (11.0 g) was added over several minutes and the resulting solution stirred under reflux overnight. The mixture was cooled to room temperature, diluted with ether and washed with 10% hydrochloric acid, 5% sodium bicarbonate solution and water. The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure to give a brown oil. The oil was dissolved in dichloromethane and chromatographed on silica, eluting with dichloromethane. A yellow fraction was collected and the solvent removed under reduced pressure to give benzyl 3-ethylpyrrole-2-carboxylate **5c** as a yellow oil (6.79 g, 95%). A sample was crystallized from hexane to give white needles, mp 26-26.5°; ir: $\nu$ 3321 (NH str), 1674 (C=O str); pmr: $\delta$ 1.19 (3H, t, J = 7.5 Hz, $CH_2CH_3$), 2.83 (2H, q, J = 7.5 Hz, $CH_2CH_3$), 5.30 (2H, s, $OCH_2Ph$), 6.13 (1H, m, 4-H), 6.79 (1H, m, 5-H), 7.3-7.45 (5H, m, $C_6H_5$), 9.2 (1H, br, NH); cmr: 14.93 ($CH_3$), 20.26 (Pyrrole-$CH_2$), 65.74 ($OCH_2$), 110.75 (C-4), 118.12 (C-2), 122.06 (C-5), 128.10 (*o*- and *p*-Ph), 128.53 (*m*-Ph), 135.33 (C-3), 136.35 (Ph-$C_{att}$), 161.37 (C=O).

*Anal.* Calcd. for $C_{14}H_{15}NO_2$ (229.30): C, 73.33; H, 6.61; N, 6.11. Found: C, 73.52; H, 6.52; N, 6.36.

The following pyrroles were prepared by the procedure detailed above with minor modifications. Pyrroles **5a** and **5b** were not chromatographed prior to crystallization. All the remaining pyrroles were chromatographed on silica gel, eluting with dichloromethane. Polar biproducts tended to stick to the top of the column and were conveniently removed at this stage. Chloroform was used instead of ether for all the extractions in the preparation of pyrroles **5b**, **5e**, **5f**, **5i**, **5j** and **5l**. Tetrahydrofuran was used as the reaction solvent in step c for compounds **5a**, **5b**, **5d**, **5e** and **5l**.

Benzyl 3-Methylpyrrole-2-carboxylate (**5a**).

This compound had ir (Nujol mull): $\nu$ 3282 (NH str), 1663 (C=O str); pmr: $\delta$ 2.37 (3H, s, pyrrole-$CH_3$), 5.30 (2H, s, $CH_2Ph$), 6.08 (1H, m, 4-H), 6.78 (1H, m, 5-H), 7.3-7.45 (5H, m, $C_6H_5$), 9.1 (1H, br, NH); cmr: 12.91 ($CH_3$), 65.72 ($OCH_2$), 112.66 (C-4), 118.97 (C-2), 121.93 (C-5), 128.08 (*o*- and *p*-Ph), 128.54 (*m*-Ph), 136.37 (Ph-$C_{att}$), 161.48 (C=O).

Ethyl 3-Methylpyrrole-2-carboxylate (**5b**) (with T. H. Nguyen).

This compound had ir (Nujol mull): $\nu$ 3304 (NH str), 1681 (C=O str); pmr: $\delta$ 1.35 (3H, t, J = 7 Hz, $CH_2CH_3$), 2.36 (3H, s, pyrrole-$CH_3$), 4.32 (2H, q, J = 7 Hz, $OCH_2$), 6.08 (1H, m, 4-H), 6.81 (1H, m, 5-H), 9.1 (1H, br, NH); cmr: 12.79 (Pyrrole-$CH_3$), 14.52 ($CH_2CH_3$), 59.95 ($OCH_2$), 112.56 (C-4), 119.37 (C-2), 121.56 (C-5), 127.94 (C-3), 161.85 (C=O).

Benzyl 4-Methylpyrrole-2-carboxylate (**5d**).

This compound had ir (Nujol mull): $\nu$ 3302 (NH str), 1678 (C=O str); pmr: $\delta$ 2.19 (3H, s, $CH_3$), 5.26 (2H, s, $OCH_2$), 6.66 (1H, m), 6.77 (1H, m) (2 x pyrrole-H), 7.3-7.45 (5H, m, $C_6H_5$), 9.4 (1H, br, NH); cmr: 11.65 ($CH_3$), 65.84 ($OCH_2$), 116.41 (C-3), 120.99 (C-2), 121.57 (C-5), 122.10 (C-4), 128.09 (*o*- and *p*-Ph), 128.54 (*m*-Ph), 136.29 (Ph-$C_{att}$), 161.00 (C=O).

Methyl 4-Methylpyrrole-2-carboxylate (**5e**).

This compound had ir (Nujol mull): $\nu$ 3280 (NH str), 1672 (C=O str); pmr: $\delta$ 2.10 (3H, s, pyrrole-$CH_3$), 3.83 (3H, s, $OCH_3$), 6.72 (2H, m, 2 x pyrrole-H), 9.3 (1H, br, NH); cmr: 11.65 (Pyrrole-$CH_3$), 51.31 ($OCH_3$), 116.14 (C-3), 120.94 (C-2), 121.48 (C-5), 122.23 (C-4), 161.77 (C=O).

Ethyl 4-Methylpyrrole-2-carboxylate (**5f**).

This compound had ir (Nujol mull): $\nu$ 3310 (NH str), 1684 (C=O str); pmr: $\delta$ 1.33 (3H, t, J = 7 Hz, $CH_2CH_3$), 2.10 (3H, s, pyrrole-$CH_3$), 4.30 (2H, q, J = 7 Hz, $OCH_2CH_3$), 6.72 (2H, m, 2 x pyrrole-H), 9.4 (1H, br, NH); cmr: 11.66 (Pyrrole-$CH_3$), 14.46 ($CH_2CH_3$), 60.18 ($OCH_2$), 115.96 (C-3), 120.80 (C-2), 121.41 (C-5), 122.51 (C-4), 161.45 (C=O).

Benzyl 4-Ethylpyrrole-2-carboxylate (**5g**).

This compound had ir (Nujol mull): $\nu$ 3324 (NH str), 1675 (C=O str); pmr: $\delta$ 1.18 (3H, t, J = 7.5 Hz, $CH_2CH_3$), 2.48 (2H, q, J = 7.5 Hz, $CH_2CH_3$), 5.28 (2H, s, $OCH_2Ph$), 6.71 (1H, m), 6.82 (1H, m) (2 x pyrrole-H), 7.3-7.45 (5H, m, $C_6H_5$), 9.2 (1H, br, NH); cmr: 15.18 ($CH_3$), 19.85 (Pyrrole-$CH_2$), 65.86 ($OCH_2$), 114.99 (C-3), 120.62 (C-5), 122.03 (C-2), 126.98 (C-4), 128.11 (*o*- and *p*-Ph), 128.53 (*m*-Ph), 136.30 (Ph-$C_{att}$), 161.14 (C=O).

*Anal.* Calcd. for $C_{14}H_{15}NO_2$ (229.30): C, 73.33; H, 6.61; N, 6.11. Found: C, 73.06; H, 6.56; N, 6.07.

Benzyl 5-Methylpyrrole-2-carboxylate (**5h**).

This compound had ir (Nujol mull): $\nu$ 3298 (NH str), 1677 (C=O str); pmr: 2.27 (3H, s, pyrrole-$CH_3$), 5.30 (2H, s, $CH_2Ph$), 5.94 (1H, m, 4-H), 6.88 (1H, m, 3-H), 7.3-7.45 (5H, m, $C_6H_5$), 9.6 (1H, br, NH); cmr: 13.10 ($CH_3$), 65.69 ($OCH_2$), 109.01 (C-4), 116.72 (C-3), 120.83 (C-2), 127.95 (*p*-Ph), 128.07 (*o*-Ph), 128.51 (*m*-Ph), 134.51 (C-5), 136.40 (Ph-$C_{att}$), 161.21 (C=O).

Ethyl 5-Methylpyrrole-2-carboxylate (**5i**).

This compound had ir (Nujol mull): $\nu$ 3292 (NH str), 1678 (C=O str); pmr: $\delta$ 1.35 (3H, t, J = 7 Hz, $CH_2CH_3$), 2.31 (3H, s, pyrrole-$CH_3$), 4.31 (2H, q, J = 7 Hz, $OCH_2CH_3$), 5.94 (1H, m, 4-H), 6.82 (1H, m, 3-H), 9.75 (1H, br, NH); cmr: 13.09 (Pyrrole-$CH_3$), 14.49 ($CH_2CH_3$), 60.08 ($OCH_2$), 108.82 (C-4), 116.13 (C-3), 121.26 (C-2), 134.19 (C-5), 161.62 (C=O).

Benzyl 5-Ethylpyrrole-2-carboxylate (**5j**).

This compound had ir (Nujol mull): $\nu$ 3308 (NH str), 1681 (C=O str); pmr: $\delta$ 1.22 (3H, t, J = 7.5 Hz, $CH_2CH_3$), 2.61 (2H, q, J = 7.5 Hz, $CH_2CH_3$), 5.30 (2H, s, $OCH_2$), 5.97 (4-H), 6.90 (1H, m, 3-H), 7.29-7.42 (5H, m, $C_6H_5$), 9.7 (1H, br, NH); cmr: 13.42 ($CH_3$), 20.97 (Pyrrole-$CH_2$), 65.66 ($OCH_2$), 107.38 (C-4), 116.54 (C-3), 120.68 (C-2), 127.91 (*p*-Ph), 128.05 (*o*-Ph), 128.51 (*m*-Ph), 136.44 (Ph-$C_{att}$), 140.95 (C-5), 161.38 (C=O).

*Anal.* Calcd. for $C_{14}H_{15}NO_2$ (229.30): C, 73.33; H, 6.61; N, 6.11. Found: C, 72.95; H, 6.53; N, 6.13.

Benzyl Pyrrole-2-carboxylate (**5k**).

This compound had ir (Nujol mull): $\nu$ 3317, 3275 (NH str), 1688 (C=O str); pmr: $\delta$ 5.30 (2H, s, $CH_2Ph$), 6.25 (1H, m, 4-H), 6.92 (1H, m), 6.97 (1H, m) (3- and 5-H), 7.3-7.45 (5H, m, $C_6H_5$), 9.46 (1H, br, NH); cmr: 65.99 ($OCH_2$), 110.46 (C-4), 115.69 (C-3), 122.51 (C-2), 123.21 (C-5), 128.13 (*o*-Ph), 128.21 (*p*-Ph), 128.55 (*m*-Ph), 136.17 (Ph-$C_{att}$), 161.09 (C=O).

Ethyl Pyrrole-2-carboxylate (**5l**).

This compound had ir (Nujol mull): $\nu$ 3312, 3250 (NH str), 1685 (C=O str); pmr: $\delta$ 1.34 (3H, t, J = 7 Hz, $CH_2CH_3$), 4.32 (2H, q, J = 7 Hz, $OCH_2CH_3$), 6.23 (1H, m, 4-H), 6.85-6.95 (2H, m, 3- and 5-H), 9.9 (1H, br, NH); cmr: 14.45 ($CH_3$), 60.39 ($OCH_2$), 110.26 (C-4), 115.33 (C-3), 122.91 (C-2), 123.24 (C-5), 161.71 (C=O).

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