6 H), 1.18 (d, J = 6.4 Hz, 3 H), 0.87 (t, J = 7 Hz, 3 H). ^{13}C NMR ($CDCl_3$): δ 145.81, 135.61, 128.28, 128.20, 127.93, 127.37, 127.02, 126.29, 125.42, 99.29, 87.38, 59.59, 32.21, 31.33, 28.71, 22.45, 15.84, 14.01. IR (neat): 2926.2, 1450.4, 1232.9, 957.3, 750.0, 702.8, 630.2 cm^{-1}. $[\alpha]_D$ = +84.3° (c = 3, $CHCl_3$). **(2*S*,3*S*,4*E*)-2-Amino-4-decen-3-ol** from **9c**. Waxy solid. ^{1}H NMR ($CDCl_3$): δ 5.72 (dt, J = 7.0, 15.4 Hz, 1 H), 5.41 (ddt, J = 1.2, 7.0, 15.4 Hz, 1 H), 3.20 (t, J = 7.0 Hz, 1 H), 2.79–2.73 (m, 1 H), 2.03–2.00 (m, 2 H), 2.00–1.77 (broad s, 3 H), 1.44–1.20 (m, 6 H), 1.08 (d, J = 6.3 Hz, 3 H), 0.88 (t, J = 6.8 Hz, 3 H). ^{13}C NMR ($CDCl_3$): δ 133.9, 130.3, 77.4, 51.3, 32.2, 31.3, 28.7, 22.5, 20.5, 13.9. IR (neat): 3600–3200, 2925.4, 1581.5, 1456.1, 1378.0, 1094.1, 1037.5, 971.5, cm^{-1}. $[\alpha]_D$ = +4.6° (c = 0.9, $CHCl_3$). MS (CI-isobutane): 172 (M + 1), 154 (M + 1 − H_2O). HRMS (CI-isobutane): M + 1 = 172.1680 (calcd for $C_{10}H_{22}NO$ (M + 1) 172.1701).

(2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-4-nonen-3-ol (9d) (oil, 10% EtOAc/petroleum ether, 73% method B). ^{1}H NMR ($CDCl_3$): δ 7.90–7.80 (m, 2 H), 7.80–7.60 (m, 2 H), 7.60–7.20 (m, 6 H), 5.71 (dt, J = 6.8, 15.3 Hz, 1 H), 5.30 (dd, J = 8.3, 15.3 Hz, 1 H), 3.80 (t, J = 8.3 Hz, 1 H), 3.00–2.90 (m, 1 H), 2.50–2.20 (broad s, 1 H), 2.10–1.90 (m, 2 H), 1.40–1.20 (m, 4 H), 1.18 (d, J = 6.3 Hz, 3 H), 0.87 (t, J = 7 Hz, 3 H). ^{13}C NMR ($CDCl_3$): δ 135.19, 130.05 128.64, 128.22, 127.93, 127.05, 126.31, 125.43, 99.25 (OCN), 87.41 (OCH), 59.59 (CNH), 31.95, 31.21, 22.18, 15.86, 13.90. IR (neat): 2957.8, 2926.2, 1726.8, 1662.3, 1450.0, 1276.5, 1067.7, 1029.1, 968.0, 749.8, 702.4, 630.0 cm^{-1}. $[\alpha]_D$ = +64.6° (c = 1.2, $CHCl_3$). **(2*S*,3*S*,4*E*)-2-Amino-4-nonen-3-ol** from **9d**. Oil. ^{1}H NMR ($CDCl_3$): δ 5.73 (ddt, J = 0.8, 6.7, 15.3 Hz, 1 H), 5.41 (ddt, J = 1.4, 7.0, 15.3 Hz, 1 H), 3.64 (t, J = 6.7 Hz, 1 H), 2.82–2.72 (m, 1 H), 2.10–2.03 (m, 5 H), 1.40–1.33 (m, 4 H), 1.21 (d, J = 6.5 Hz, 3 H), 0.90 (t, J = 7 Hz, 3 H). ^{13}C NMR APT[33] ($CDCl_3$): δ 133.61, 130.46 (HC=CH), 77.33 (OCH), 51.30 (CNH), 31.92, 31.24, 22.10 (CH_2), 20.08 (1-CH_3), 13.81 (9-CH_3). IR (neat): 3500–3000, 2926.4, 1582.7, 1453.8, 1378.3, 1141.1, 1093.4, 1037.5, 970.0, 865.8, 730.1 cm^{-1}. $[\alpha]_D$ = +10.9° (c = 3.4, $CHCl_3$). MS (CI-isobutane): 158 (M + 1), 140 (M + 1 − H_2O). HRMS (CI-isobutane): M + 1 = 158.1544 (calcd for $C_9H_{20}NO$ (M + 1) 158.1545).

(4*S*,5*S*)-5-((*E*)-Dec-1-en-1-yl)-4-methyl-2-oxazolidinone (11). To a flame-dried reaction flask was added amino alcohol 10 (119 mg, 0.56 mmol), carbonyldiimidazole (118 mg, 0.73 mmol), and 2 mL of freshly distilled THF. The resulting solution was stirred for 2 h at rt. The THF was evaporated, the resulting residue was dissolved in Et_2O, washed (3 × 1 N HCl, 1 × saturated $NaHCO_3$), and dried (K_2CO_3), and the solvent was removed under reduced pressure to provide crude material. Chromatography[29] (50% EtOAc/hexanes) provided 93 mg of pure product (70%, 0.39 mmol) as an oil. ^{1}H NMR ($CDCl_3$): δ 6.20 (broad s, 1 H), 5.85 (dd, J = 6.8, 15.4 Hz, 1 H), 5.50 (ddt, J = 7.9, 15.4, 1.4 Hz, 1 H), 4.43 (apparent t, J = 7.6 Hz, 1 H), 3.70–3.50 (m, 1 H), 2.10–2.00 (m, 2 H), 1.25 (broad s, 12 H), 0.88 (t, J = 6.6 Hz, 3 H). ^{13}C NMR APT[33] ($CDCl_3$): δ 159.31 (C=O), 137.75, 125.31 (HC=CH), 85.21 (OCH), 54.27 (CNH), 32.10, 31.80, 29.33, 29.17, 29.04, 28.63, 22.60 (CH_2), 19.22 (4-CH_3), 14.06 (CH_3). $[\alpha]_D$ = −29.9° (c = 1.6, $CHCl_3$).

(4*S*,5*S*)-2,2-Diphenyl-5-((*E*)-dec-1-en-1-yl)-4-((*tert*-butyldimethylsiloxy)methyl)-*N*-(phenylcarbamoyl)oxazolidine (12). (2*S*,3*S*,4*E*)-2-[*N*-(Diphenylmethylene)amino]-1-*O*-(*tert*-butyldimethylsilyl)-4-tridecene-1,3-diol (**8b**) (421 mg, 0.83 mmol) in dry pyridine (2 mL) was treated with PhN=C=O (1.8 mmol, 2.2 equiv) and stirred at rt overnight. Pyridine and unreacted phenyl isocyanate were removed under reduced pressure, and chromatography[29] (20% EtOAc/petroleum ether) provided 409 mg of the pure product (78% yield, 0.65 mmol) as an oil. ^{1}H NMR ($CDCl_3$): δ 7.70–7.60 (m, 2 H), 7.50–7.20 (m, 9 H), 7.20–7.10 (m, 2 H), 6.90–6.80 (m, 2 H), 6.43 (broad s, 1 H), 5.83 (dt, J = 6.4, 15.4 Hz, 1 H), 5.66 (dd, J = 7.1, 15.4 Hz, 1 H), 4.25 (apparent t, J = 7.7 Hz, 1 H), 4.18–4.12 (m, 1 H), 3.92 (dd, J = 3.9, 10.5 Hz, 1 H), 3.84 (dd, J = 4.7, 10.5 Hz, 1 H), 2.10–2.0 (m, 2 H), 1.40–1.20 (broad s, 12 H), 0.90–0.80 (m, 12 H), 0.01 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR APT[33] ($CDCl_3$): δ 152.69 (C=O), 141.70, 140.58, 138.37 (quaternary, aromatic), 136.63, 128.52 (HC=CH), 128.46, 128.37, 128.23, 128.12, 126.70, 122.76, 119.49 (aromatic), 98.08 (OCN), 79.12 (OCH), 64.65 (HC-N), 62.65 (CH_2O), 32.19, 31.74, 29.30, 29.08, 28.69 (CH_2), 25.80 ($SiCCH_3$), 22.54 ($SiCCH_3$), 14.01 (CH_3), −5.40 ($SiCH_3$). IR (neat): 1673.6, 1596.9, 1528.7, 1441.9, 1332.1, 1249.5, 1102.7, 836.9, 751.6, 700.1 cm^{-1}. $[\alpha]_D$ = −14.1° (c = 1.2, $CHCl_3$).

Acknowledgment. We would like to thank the University of Arizona for a Biomedical Research Support Grant (BRSG No. S07RR07002), the University of Arizona Foundation, and the American Cancer Society or an Institutional Cancer Research Grant Award. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. Ms. Lynn DeYoung would like to thank the National Science Foundation and the Howard Hughes Medical Institute for partial support of this work.

Supplementary Material Available: ^{1}H NMR (250 MHz) and ^{13}C NMR (62.5 MHz) spectra of compounds **2a–14** and amino alcohols (sphingosines) derived from the hydrolysis of compounds **8a–d** and **9a–d** (59 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

An Efficient, Regiocontrolled Synthesis of 5-Aryl-2-carbethoxypyrroles from 3-Aryl-3-chloropropeniminium Salts[1]

John T. Gupton,* Dale A. Krolikowski, Richard H. Yu, and Phong Vu

Department of Chemistry, University of Central Florida, Orlando, Florida 32816

James A. Sikorski,* Maria L. Dahl, and Claude R. Jones

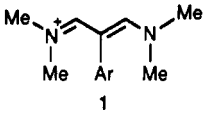
Monsanto Agricultural Co., New Products Division, A Unit of Monsanto Co., 700 Chesterfield Village Parkway, St. Louis, Missouri 63198

Received April 21, 1992

A variety of 3-aryl-3-chloropropeniminium salts react with α-amino acid esters under basic conditions to produce 2-carbethoxy-5-arylpyrroles in a regioselective manner. The overall process represents a short, efficient, and convergent synthesis of 2,5-disubstituted pyrroles, and azomethine ylides or azapentadienyl anions may be involved as intermediates.

We have recently reported[2] a short, convergent and regiocontrolled synthesis of 4-aryl-2-carbethoxypyrroles from the condensation of 2-arylvinamidinium salts (1) with either glycine ethyl ester or sarcosine ethyl ester.

0022-3263/92/1957-5480$03.00/0



1

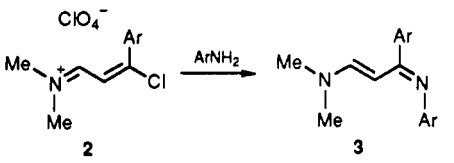
The reactions are thought to proceed through either an azomethine ylide or an azapentadienyl anion intermediate after an initial amine exchange reaction between the vinamidinium salt and the amino acid ester has taken place. Recently, Thal[3] and co-workers have used this methodology for the synthesis of analogs of the antitubulin agent, Rhazinilam.

In related work, Wilkinson[4] and co-workers have pointed out the importance of being able to prepare the isomeric 5-substituted 2-carbethoxypyrroles, and they have demonstrated that β-keto acetals and N,N-protected glycines could be used in such an application. In addition Paine,[5] Barluenga,[6] Tashiro,[7] and Boukou-Poba[8] have also developed useful synthetic methodologies toward this end. The common theme that exists in most of the methods involves the use of a 1,3-dicarbonyl compound or its masked equivalent and its reaction with an α-amino ester analog. If one is to generate the proper regiochemistry in such a reaction, there must be some controlling factors which will allow for selective formation of the 5-substituted pyrrole over the alternative condensation product, the 3-substituted pyrrole. One of the reasons for the interest in the synthesis of such compounds stems from the wide range of biological properties that this class of substances exhibits.[9,10] In our search for other applications of vinamidinium salts and analogous compounds to the regiochemically controlled preparation of pyrroles and related materials, it appeared that 3-chloro-2-propeniminium salts might serve as useful building blocks. Liebscher and Hartmann[11] have reviewed the chemistry surrounding this class of compounds, and a wide variety of important and useful transformations are evident. It is significant to note that the 3-aryl-3-chloro-2-propeniminium salts (2) are conveniently prepared[11] in one step from aryl methyl ketones, phosphorus oxychloride and *N,N*-dimethylformamide. This reaction is thought to proceed through the formation of an enamino ketone under Vilsmier–Haack conditions.[11]

Results and Discussion

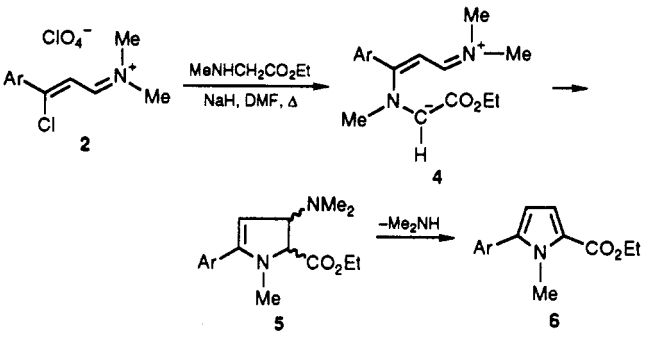
We anticipated that the electrophilic character of such a chloropropeniminium salt would be chemodifferentiated[11] since Liebscher[11] has demonstrated that simple aromatic amines react with chloropropeniminium salts regioselectively at the chlorovinyl carbon.

Scheme I



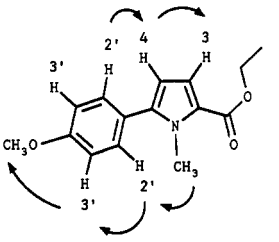
2 3

Scheme II



2 4 5 6

Chart I. NOESY NMR Experiment Results for 2-Carbethoxy-5-(4-methoxyphenyl)-1-methylpyrrole (6d)



		OCH_3	H3′	H2′	H3	H4	NCH_3
	ppm	3.82	7.03	7.40	6.92	6.18	3.80
OCH_3	3.82	....	xxx	....	....	....	....
H3′	7.03	xxx	....	xxx	....	....	....
H2′	7.40	....	xxx	....	....	xxx	xxx
H3	6.92	....	....	....	....	xxx	....
H4	6.18	....	....	xxx	xxx	....	....
NCH_3	3.80	....	....	xxx	....	....	....

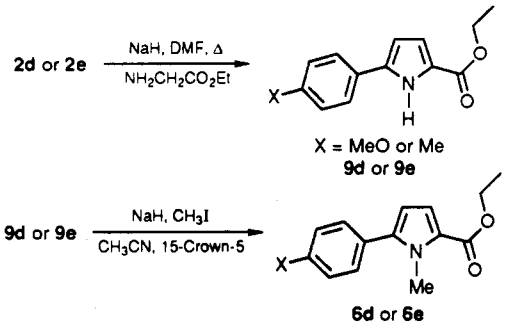
This would imply that reaction of a chloropropeniminium salt such as 2 with an α-amino acid ester should generate an intermediate such as 4 (Scheme II) in a regioselective manner. Subsequent ring closure of 4 and elimination of a dimethylamino group from 5 would then lead to a 5-aryl-2-carbethoxypyrrole (6) in a clean and selective fashion.

The Ar substituent can be represented by a variety of aromatic groups such as phenyl, 4-chlorophenyl, 4-nitrophenyl, 4-methoxyphenyl, 4-methylphenyl, and 4-fluorophenyl. When such a reaction was conducted in the presence of sodium hydride and DMF, good yields of the anticipated 2,5-disubstituted pyrroles were obtained.

The assignment of the 2,5-substitution pattern for the isolated pyrrole products was determined in the following manner. The well-documented ^1H coupling constants[12] for pyrrole hydrogens at the 3 and 4 positions (2,5 isomer) are in the range of 3.5 Hz, whereas similar ^1H couplings for the 4 and 5 hydrogens (2,3 isomer) are in the range of 2.5 Hz. The experimentally determined analogous ^1H couplings for the pyrroles prepared are in the range of 3.7–4.0 Hz. In addition a NOESY NMR experiment was run on compound **6d**, and the subsequent results are consistent

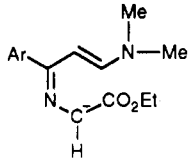
(1) Dedicated to Professor Drury S. Caine on the occasion of his 60th birthday.
(2) Gupton, J. T.; Krolikowski, D. A.; Yu, R. H.; Riesinger, S. W.; Sikorski, J. A. *J. Org. Chem.* **1990**, *55*, 4735.
(3) Thal, C.; Alazard, J.; Millet-Paillusson, C.; Guenard, D.; Chiaroni, A.; Riche, C. *Bioorg. Med. Chem. Lett.* **1991**, *1*, 725.
(4) Elder, T.; Gregory, L. C.; Orozca, A.; Pflug, J. L.; Wiens, P. S.; Wilkinson, T. J. *Synth. Commun.* **1989**, *19*, 763.
(5) Paine, J. B.; Brough, J. R.; Buller, K. K.; Erikson, E. E. *J. Org. Chem.* **1987**, *52*, 3986.
(6) Barluenga, J.; Rubio, V.; Gotor, V. *J. Org. Chem.* **1982**, *47*, 1696.
(7) Mataka, S.; Takahashi, K.; Tsuda, Y.; Tashiro, M. *Synthesis* **1982**, 157.
(8) Boukou-Poba, J. P.; Farnier, M.; Guillard, R. *Tetrahedron Lett.* **1979**, *19*, 1717.
(9) Roth, B. D.; Blankley, C. J.; Chucolowski, A. W.; Ferguson, E.; Hoefle, M. L.; Ortwine, D. F.; Newton, R. S.; Sekerke, C. S.; Sliskovic, D. R.; Stratton, C. D.; Wilson, M. W. *J. Med. Chem.* **1991**, *34*, 357.
(10) Corelli, F.; Garofalo, A.; Massa, S.; Silvestri, R.; Prosini, P.; Artico, M. *J. Heterocycl. Chem.* **1990**, *27*, 1489.
(11) Liebscher, J.; Hartmann, H. *Synthesis* **1979**, *241*.
(12) Pretsch, E.; Seibl, J.; Simon, W.; Clerc, T. *Spectral Data for Structure Determination of Organic Compounds*, 2 ed.; Springer-Verlag: New York, 1989.

Scheme III

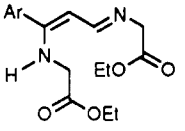


with this assignment. The summary of results for this experiment is listed in Chart I.

In addition to studying sarcosine as a potential condensing agent, we also have examined glycine ethyl ester itself. It is important to recognize that this is a significant change since from a mechanistic standpoint we would predict an azapentadienyl anion (7) as an intermediate instead of an azomethine ylide. In addition, primary



7



8

amines can rapidly exchange both amino groups of a vinamidinium salt in which case an imino enamine (8) would be produced and this could be the intermediate which would potentially lead to either isomer of the pyrrole. These potential considerations make the question of regiochemical outcome less than straightforward, a priori. However, upon conducting such a reaction, the 2,5-disubstituted pyrrole was found to be the only product produced. The same arylchloropropeniminium salts which were evaluated in the sarcosine condensations were also evaluated in the glycine condensations and were found to work equally well.

As was the case for the *N*-methylpyrroles, the experimentally determined coupling constants for the hydrogens at the 3 and 4 positions of the N–unsubstituted pyrroles was in the range of 3.5–4 Hz which is consistent with the 2,5-disubstitution pattern. The 2-carbethoxy-5-phenylpyrrole (**9a**) is a known compound, and the physical properties of the compound prepared by our method compares favorably with those reported in the literature.[4] In order to further establish the structural relationship between the N-methylated and the N-unmethylated pyrroles, we decided to use the method of Guida[13] to alkylate several of the unsubstituted pyrroles (compounds **9d** and **9e**) and thereby convert them to compounds (Scheme III) prepared directly from the sarcosine condensations.

The above reactions gave the anticipated products, and these results firmly establish the regiochemistry of the pyrroles prepared by chloropropeniminium salt methodology.

In summary, we have demonstrated that 3-aryl-3-chloropropeniminium salts can be used as three-carbon building blocks for the regioselective, convergent synthesis of 5-aryl-2-carbethoxypyrroles in one step by reaction with either glycine or sarcosine. This methodology should be applicable to the preparation of bioactive pyrroles which exhibit the 2,5-disubstitution pattern and should also complement our previous work on the synthesis of 2,4-disubstituted pyrroles.

(13) Guida, W. C.; Mathre, D. J. *J. Org. Chem.* **1980**, *45*, 3172.

Experimental Section[14]

The following procedures are typical of the experimental conditions used for the reaction of 3-aryl-3-chloropropeniminium salts with α-amino acid esters. The requisite chloropropeniminium salts were prepared by standard methods.[11] The difference in yield between crude and pure materials is at least in part due to physical losses incurred during the handling of the samples and the removal of some unreacted chloropropeniminium salt. All purified compounds gave a single spot on TLC analysis on silica gel 7GF with an ethyl acetate/hexane mixture as the eluant.

2-Carbethoxy-5-(4-chlorophenyl)-1-methylpyrrole (6b). A 250-mL, round-bottomed flask was equipped with a condenser, magnetic stirring bar, and mineral oil bubbler and was placed under a nitrogen atmosphere. Into the flask was placed 0.49 g (0.012 mol) of a 60% mineral oil dispersion of sodium hydride. The dispersion was washed with several portions of dry hexane, and the hexane was removed via cannula. To the flask was added 40 mL of dry DMF, sarcosine ethyl ester hydrochloride (0.73 g, 0.0046 mol), and 3-chloro-3-(4-chlorophenyl)prop-2-en-1-ylidenedimethylaniminium perchlorate (1.0 g, 0.0031 mol) in that order. The reaction mixture was refluxed for several hours, and the solvent was removed in vacuo. The residue was partioned between water and chloroform, and the aqueous phase was re-extracted several times. The combined chloroform extracts were dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude material was dissolved in a 70:30 mixture of hexane/ethyl acetate and passed through a short column of silica gel to remove polar impurities. The eluants were concentrated in vacuo to leave 0.65 g of an oil which was subjected to radial chromatography on a Harrison Chromatotron with a 2-mm-thick plate of silica gel. Elution with a 70:30 mixture of hexane/ethyl acetate gave a liquid (0.54 g, 67% yield) which exhibited the following properties: bp 75–76 °C (1 mTorr); ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3 H), 3.84 (s, 3 H), 4.29 (q, J = 7.1 Hz, 2 H), 6.17 (d, J = 4.0 Hz, 1 H), 7.01 (d, J = 4.0 Hz, 1 H), 7.30 (d, J = 8.7 Hz, 2 H), and 7.40 (d, J = 8.7 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.7, 34.7, 60.2, 109.9, 118.1, 124.6, 129.3, 131.1, 134.6, 140.7, and 162.1; IR (Nujol) 1702 cm^{-1}; mass spectrum, m/z 263, 265 (M^+). Anal. Calcd for $C_{14}H_{14}ClNO_2$: C, 63.75; H, 5.36; N, 5.31. Found: C, 64.01; H, 5.10; N, 5.51.

Preparation of 2-Carbethoxy-5-(4-methoxyphenyl)-1-methylpyrrole (6d) from 2-Carbethoxy-5-(4-methoxyphenyl)pyrrole (9d). A 250-mL, round-bottomed flask was equipped with a magnetic stirring bar and was placed under a nitrogen atmosphere. Into the flask was placed sodium hydride (0.016 g, 0.0004 mol of a 60% mineral oil dispersion) which was subsequently washed with hexane, and the hexane was removed via cannula. Acetonitrile (30 mL) was added along with 0.010 g of 15-crown-5 as a catalyst. The appropriate pyrrole (0.050 g, 0.000119 mol) was added along with 0.12 g of iodomethane, and the resulting mixture was stirred overnight at room temperature. The solvent was removed in vacuo, the residue was partitioned between water and chloroform, and the combined chloroform extracts were dried and concentrated in vacuo to leave a 100% yield of compound **6d**.

2-Carbethoxy-5-phenyl-1-methylpyrrole (6a). A 100% crude yield and 44% purified yield of this compound was obtained, and the following physical properties were observed: bp 75–77 °C (1 mmHg); ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3 H), 3.80 (s, 3 H), 4.29 (q, J = 7.1 Hz, 2 H), 6.19 (d, J = 4.0 Hz, 1 H), 7.02 (d, J = 4.0 Hz, 1 H), 7.39 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.7, 34.7, 60.1, 109.5, 118.0, 128.5, 129.0, 129.9, 132.7, 142.1, and 162.2; IR (Nujol) 1699 cm^{-1}; mass spectrum, m/z 229 (M^+). Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.33; H, 6.61; N, 6.11. Found: C, 73.60; H, 6.42; N, 5.84.

2-Carbethoxy-5-(4-nitrophenyl)-1-methylpyrrole (6c). A 100% crude yield and a 51% purified yield of this compound was

(14) Infrared spectra were recorded on a Perkin-Elmer 1600 FT-IR as either thin films, KBr disks, or Nujol mulls. NMR spectra were obtained in $CDCl_3$ or DMSO-d_6 with a Varian Gemini 200 spectrometer. All melting points and boiling points are uncorrected.

obtained, and the following physical properties were observed: mp 119–121 °C; ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J = 7.1 Hz, 3 H), 3.91 (s, 3 H), 4.30 (q, J = 7.1 Hz, 2 H), 6.30 (d, J = 4.0 Hz, 1 H), 7.03 (d, J = 4.0 Hz, 1 H), 7.56 (d, J = 9.0 Hz, 2 H), and 8.29 (d, J = 9.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.6, 35.0, 60.5, 111.1, 118.2, 124.4, 130.2, 130.3, 139.0, 139.3, 147.6, and 161.9: IR (KBr) 1700 cm^{-1}; mass spectrum, m/z 274 (M^+). Anal. Calcd for $C_{14}H_{14}N_2O_4$: C, 61.30; H, 5.15; N, 10.22. Found: C, 61.39; H, 4.95; N, 10.16.

2-Carbethoxy-5-(4-methoxyphenyl)-1-methylpyrrole (6d). A 100% crude yield and a 50% purified yield of this compound was obtained, and the following physical properties were observed: mp 69–71 °C; ^{1}H NMR ($CDCl_3$) δ 1.34 (t, J = 7.0 Hz, 3 H), 3.83 (s, 6 H, NCH_3 and OCH_3), 4.28 (q, J = 7.0 Hz, 2 H), 6.13 (d, J = 4.0 Hz, 1 H), 6.95 (d, J = 8.9 Hz, 2 H), 7.00 (d, J = 4.0 Hz, 1 H), and 7.27 (d, J = 8.9 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.7, 34.6, 55.7, 60.1, 109.1, 114.4, 118.0, 123.8, 125.1, 131.2, 142.0, 160.1, and 162.2; IR (Nujol) 1706 cm^{-1}; mass spectrum, m/z 259 (M^+). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.47; H, 6.62; N, 5.40. Found: C, 69.20; H, 6.42: N, 5.28.

2-Carbethoxy-5-(4-methylphenyl)-1-methylpyrrole (6e). A 100% crude yield and a 50% purified yield of this compound was obtained, and the following physical properties were observed: bp 80–81 °C (1 mmHg); ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J = 7.0 Hz, 3 H), 2.39 (s, 3 H), 3.86 (s, 3 H), 4.29 (q, J = 7.0 Hz, 2 H), 6.16 (d, J = 4.0 Hz, 1 H), 7.02 (d, J = 4.0 Hz, 1 H), 7.23 (d, J = 8.4 Hz, 2 H), and 7.28 (d, J = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.7, 21.5, 34.6, 60.1, 109.3, 118.0, 124.0, 129.7, 129.8, 138.5, 142.3, and 162.2; IR (Nujol) 1699 cm^{-1}; mass spectrum, m/z 243 (M^+). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.04; H, 7.06; N, 5.76. Found: C, 73.83; H, 7.24; N, 5.51.

2-Carbethoxy-5-(4-fluorophenyl)-1-methylpyrrole (6f). A 92% crude yield and a 76% purified yield of this compound was obtained, and the following physical properties were observed: mp 54–56 °C; ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J = 7.5 Hz, 3 H), 3.83 (s, 3 H), 4.29 (q, J = 7.5 Hz, 2 H), 6.15 (d, J = 3.7 Hz, 1 H), 7.00 (d, J = 3.7 Hz, 1 H), 7.11 (t, J = 8.6 Hz, 2 H), and 7.33 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.7, 34.6, 60.2, 109.5, 116.0 (d, J = 21.8 Hz), 117.9, 124.2, 128.8, 131.7 (d, J = 8.5 Hz), 141.0, 162.1, and 163.2 (d, J = 248.9 Hz); IR (Nujol) 1708 cm^{-1}; mass spectrum, m/z 247 (M^+). Anal. Calcd for $C_{14}H_{14}FNO_2$: C, 67.99; H, 5.72; N, 5.67. Found: C, 67.72; H, 5.85; N, 5.53.

2-Carbethoxy-5-phenylpyrrole (9a). A 100% crude yield and a 44% purified yield of this compound was obtained, and the following physical properties were observed: mp 115–116 °C (lit.[4] mp 121–122 °C).

2-Carbethoxy-5-(4-chlorophenyl)pyrrole (9b). A 100% crude yield and a 57% purified yield of this compound was obtained, and the following physical properties were observed: mp 125–126 °C; ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J = 7.5 Hz, 3 H), 4.33 (q, J = 7.5 Hz, 2 H), 6.50 (t, J = 3.4 Hz, 1 H), 6.93 (t, J = 3.4 Hz, 1 H), 7.37 (d, J = 9.0 Hz, 2 H), 7.50 (d, J = 9.0 Hz, 2 H), and 9.30 (broad s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.7, 61.0, 108.7, 117.4, 124.2, 126.7, 129.6, 130.5, 133.9, 136.5, and 162.2; IR (Nujol) 3310 and 1687 cm^{-1}; mass spectrum, m/z 249 and 251 (M^+). Anal. Calcd for $C_{13}H_{12}ClNO_2$: C, 63.75; H, 5.36; N, 5.31. Found: C, 64.01; H, 5.10; N, 5.51.

2-Carbethoxy-5-(4-nitrophenyl)pyrrole (9c). A 100% crude yield and a 46% purified yield was obtained for this compound, and the following physical properties were observed: mp 191–192 °C; ^{1}H NMR ($CDCl_3$) δ 1.37 (t, J = 7.5 Hz, 3 H), 4.35 (q, J = 7.5 Hz, 2 H), 6.70 (dd, J = 2.3 Hz, J = 3.9 Hz, 1 H), 6.98 (dd, J = 2.3 Hz, J = 3.9 Hz, 1 H), 7.72 (d, J = 10 Hz, 2 H), 8.28 (d, J = 10 Hz, 2 H) and 9.72 (broad s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.4, 60.1, 111.1, 117.0, 124.4, 125.8, 126.0, 134.8, 138.0, 146.1, and 160.6; IR ($CHCl_3$) 3325 and 1682 cm^{-1}; HRMS (FAB, M + 1) for $C_{13}H_{12}N_2O_4$ calcd 261.0875, found 261.0874. Anal. Calcd for $C_{13}H_{12}N_2O_4$: C, 59.99; H, 4.66; N, 10.77. Found: C, 58.67; H, 4.68; N, 10.25.

2-Carbethoxy-5-(4-methoxyphenyl)pyrrole (9d). A 100% crude yield and a 59% purified yield was obtained for this compound, and the following physical properties were observed: mp 120–121 °C; ^{1}H NMR ($CDCl_3$) δ 1.35 (t, J = 7.3 Hz, 3 H), 3.82 (s, 3 H), 4.31 (q, J = 7.3 Hz, 2 H), 6.42 (dd, J = 2.6 Hz, J = 3.8 Hz, 1 H), 6.92 (m, 3 H), 7.49 (d, J = 10 Hz, 2 H), and 9.30 (broad s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.7, 55.7, 60.7, 107.5, 114.8, 117.3, 123.3, 124.8, 126.7, 137.5, 159.9, and 162.1; IR (Nujol) 3319 and 1683 cm^{-1}; mass spectrum, m/z 245 (M^+). Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.54; H, 6.18; N, 5.71. Found: C, 68.38; H, 6.20; N, 5.60.

2-Carbethoxy-5-(4-methylphenyl)pyrrole (9e). A 100% crude yield of this material was obtained, and the following physical properties were observed: mp 120–121 °C; ^{1}H NMR ($CDCl_3$) δ 1.36 (t, J = 7.5 Hz, 3 H), 2.37 (s, 3 H), 4.33 (q, J = 7.5 Hz, 2 H), 6.50 (dd, J = 2.8 Hz, J = 3.9 Hz, 1 H), 6.95 (dd, J = 2.8 Hz, J = 3.9 Hz, 1 H), 7.20 (d, J = 9 Hz, 2 H), 7.49 (d, J = 9 Hz, 2 H) and 9.50 (broad s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.7, 21.4, 60.7, 108.0, 117.2, 123.5, 125.2, 129.1, 130.2, 137.5, 138.2 and 162.0; IR (Nujol) 3332 and 1675 cm^{-1}; HRMS (FAB, M + 1) for $C_{14}H_{15}NO_2$ calcd 230.1181, found 230.1182. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.33; H, 6.66; N, 6.11. Found: C, 73.83; H, 7.24; N, 5.51.

2-Carbethoxy-5-(4-fluorophenyl)pyrrole (9f). A 40% purified yield of this material was obtained, and the following physical properties were observed: mp 147–148 °C; ^{1}NMR ($CDCl_3$) δ 1.37 (t, J = 7.5 Hz, 3 H), 4.33 (q, J = 7.5 Hz, 2 H), 6.46 (dd, J = 2.4 Hz, J = 3.9 Hz, 1 H), 6.93 (dd, J = 2.4 Hz, J = 3.9 Hz, 1 H), 7.10 (t, J = 9.0 Hz, 2 H), 7.53 (m, 2 H), and 9.25 (broad s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.7, 21.4, 60.9, 108.3, 116.4 (d, J = 17.2 Hz), 117.4, 123.9, 127.2 (d, J = 8.2 Hz), 128.4, 136.7, 162.2, and 162.9 (d, J = 248.6 Hz); IR (KBr) 3321 and 1685 cm^{-1}; mass spectrum, m/z 233 (M^+). Anal. Calcd for $C_{13}H_{12}FNO_2$: C, 66.93; H, 5.20; N, 6.01. Found: C, 66.50; H, 5.15: N, 6.20.

Acknowledgment. We thank the National Science Foundation for an equipment grant (CHE-8068881) which was made for the purchase of a Varian Gemini 200 NMR spectrometer. Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, the National Institutes of Health (grant no. 1R15GM46078-01A1), and Monsanto Agricultural Products Co. for support of this research.