Some Mercuration Reactions of Substituted Pyrroles

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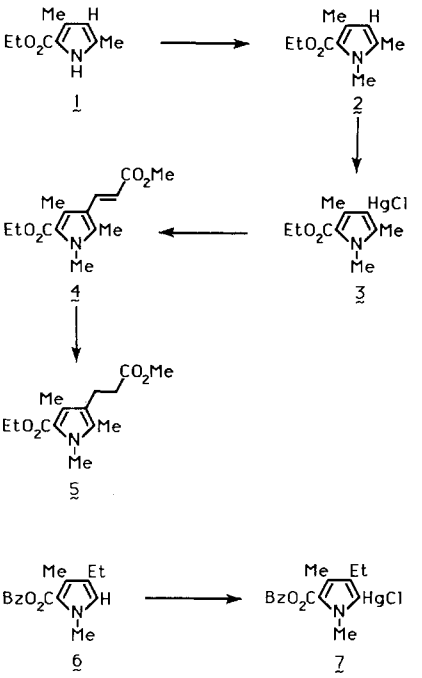
Mercuration of N-unsubstituted pyrroles with mercury(II) acetate results in immediate precipitation of the N-mercurated derivative, which is insoluble in virtually all organic solvents. If the pyrrole N atom is protected (e.g. with Me, CH_2OCH_2Ph, or CO_2t-Bu) then mercuration takes place efficiently at unsubstituted pyrrole carbons. Subsequent palladium/olefin (Heck-type) reactions afford the corresponding pyrrole acrylate when, for example, the olefin is methyl acrylate; deprotection (when the N-substituent is CH_2OCH_2Ph or CO_2t-Bu) then affords the required carbon-substituted pyrrole. Attempts to deprotect the *N*-methylpyrroles were unsuccessful.

Mercuration, followed by functionalization involving demercuration or transmetalation, has been used extensively in aromatic and heteroaromatic chemistry.[1-3] Very few published accounts of mercurated pyrroles have appeared in the literature. The earliest reports by Ciusa and Plancher,[4] between 1925–1927, indicated that pyrrole was readily permercurated, and attempts to limit the degree of mercuration failed. Söderbäck[5] reported that pyrrole was dimercurated at the two more electropositive α-carbons by treatment with mercury(II) isocyanate. Neither Ciusa nor Söderbäck mentioned N-mercuration of pyrrole, whereas Ramachandran[6] has observed that indole is readily N-mercurated. Plancher circumvented the issue by utilizing *N*-phenylpyrrole.

We have applied the Heck mercuration/palladium olefination reaction sequence[1] to the porphyrin system and have succeeded in synthesizing a variety of acrylic or propionic porphyrins which would otherwise have been difficult to obtain.[7,8] A novel mercury-promoted isocyclic ring formation in the porphyrin series was also identified[8] and exploited in the total synthesis of deoxophylloerythroetioporphyrin,[9] a chlorophyll degradation product found in shales and petroleum residues. In the present paper we describe an extension of the mercury/palladium olefination route to monopyrroles and show that with appropriate manipulation of protecting groups on the pyrrole nitrogen these heterocycles can also be efficiently functionalized.

Ethyl 3,5-dimethylpyrrole-2-carboxylate (1) was chosen as the standard pyrrole for optimization of reaction conditions. This was prepared[10] from diethyl oximinomalonate and acetylacetone by using standard Kleinspehn methodology.[11] Treatment of 1 with mercury(II) acetate (in methanol) afforded an instantaneous precipitate. This material, presumed to be the pyrrole-*N*-mercuriacetate because of the absence of the characteristic N–H stretch in the infrared spectrum, could not be dissolved in any common organic solvent. It was not clear whether α-mercuration had also occurred or not. Attempts to thermally rearrange the mercury atom from nitrogen to carbon were unsuccessful at a variety of temperatures, as evidenced by the continued insolubility of the material. Treating the mercurated pyrrole with trifluoroacetic acid regenerated the starting material 1.

At this point it was decided to continue the trial experiments using an N-protected pyrrole, and the *N*-methyl group was chosen because of its ease of synthesis. We were fully aware that this particular protecting group could not be our final choice owing to difficulty in removal. Pyrrole 1 was treated with methyl iodide in the presence of potassium hydroxide and gave a 91% yield of the *N*-methylpyrrole **2**. When **2** (in tetrahydrofuran) was treated with an excess of mercury(II) acetate (in methanol) there was no immediate precipitate, and, after a standard workup involving chloride, a 70% yield of the mercurated pyrrole **3** was obtained. The proton NMR spectrum, with no resonance at 5.75 ppm, confirmed mercuration of the 4-position. The corresponding pyrrole acrylate **4** was obtained by treatment of **4** with methyl acrylate and lithium chloride/palladium chloride ($LiPdCl_3$) in acetonitrile; disappointingly, only a 40% yield was obtained, but this material (**4**) was catalytically hydrogenated to give the propionic pyrrole **5** in almost quantitative yield. When the 5-unsubstituted *N*-methylpyrrole **6** was mercurated, a 52% yield of the 5-mercuri chloride **7** was obtained; the mercurated pyrrole was coupled with methyl acrylate via $LiPdCl_3$ in CH_3CN in a disappointing 40% yield.



Our attention next turned to use of the benzyl group for nitrogen protection. The pyrrole 1 was treated with benzyl

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(7) Smith, K. M.; Langry, K. C. *J. Chem. Soc., Chem. Commun.* **1980**, 217.
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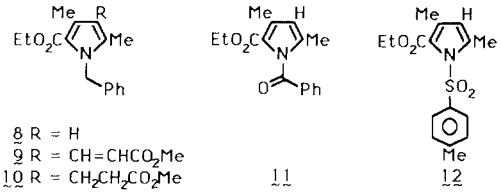
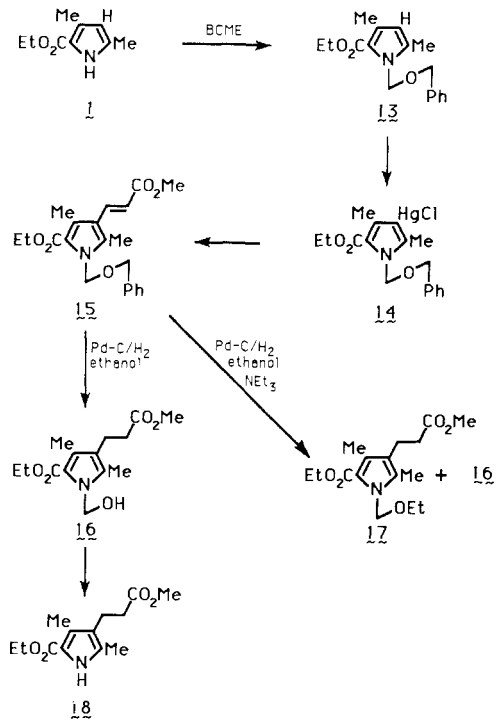
chloride in presence of potassium hydroxide and afforded a 75% yield of the required pyrrole **8**. The mercuration and palladium/acrylate sequence proceeded smoothly but in poor yield to give a 37% yield of the acrylate **9**, which was catalytically hydrogenated to provide a 95% yield of the *N*-benzyl propionic pyrrole **10**. Unfortunately, the *N*-benzyl group could not be removed by conventional means ($AlCl_3$/benzene).[12]



Further complications were encountered with the use of strongly electron-withdrawing N-protecting groups. Neither the *N*-benzoylpyrrole **11** nor the *N*-tosylpyrrole **12** could be mercurated to any measurable extent. Apparently, the electron-withdrawing power of both protecting groups thwart the electron-donating propensity of the pyrrolic nitrogen, thereby preventing mercuration from occurring.

Requirements for an acceptable pyrrole N-protecting group should include ease of attachment and subsequent removal, inertness toward the reagents in question, and availability. Pyrroles have been protected by a variety of methods.[13] Anderson and Groves[14] have reported benzyl methyl ether (BME) to be a robust, easily appended and removed protecting group for pyrrole. Since BME is an electron-donating substrate, we felt that the nucleophilicity of pyrrole would be enhanced, hopefully increasing the reaction rate for mercuration of the pyrrole. Moreover since removal of BME initially requires hydrogenolysis, we saw an opportunity to reduce the acrylate side chain with concomitant deprotection of the pyrrole nitrogen.

Utilizing the same model β-free pyrrole **1**, benzyl chloromethyl ether (BCME) was reacted with pyrrole and KOH in dimethyl sulfoxide to give a 78% yield of the *N*-BME pyrrole **13**. The β-position of **13** was mercurated by treatment with 2 equiv of mercury(II) acetate in methanol/tetrahydrofuran at room temperature. After treatment with chloride, an 81% yield of the β-(chloromercuri)pyrrole **14** was isolated. ^{1}H NMR spectroscopy indicated that the benzyl group was *not* mercurated. Transmetalation with $LiPdCl_3$ in acetonitrile in the presence of methyl acrylate gave 86% of the protected pyrrole–acrylate **15**, this yield being far in excess of that achieved with the previous pyrrole acrylate **4**. Removal of the protecting group from the pyrrole nitrogen was accomplished by catalytic hydrogenation in absolute ethanol, this reaction concomitantly accomplishing reduction of the acrylate to propionate, to furnish a 95% yield of the *N*-(hydroxymethyl)pyrrole **16**. The choice of absolute alcohol as the hydrogenation solvent was important because the same reaction in tetrahydrofuran was prohibitively slow. After 24 h in tetrahydrofuran, only 40% of the acrylate had been reduced, and none of the benzyl ether had been cleaved. A further complication resulted from addition of triethylamine to the ethanolic



solution; following hydrogenolysis, NMR spectroscopy indicated that partialy transetherification had occurred, resulting in a mixture of the *N*-(ethoxymethyl)pyrrole **17** and the desired *N*-(hydroxymethyl)pyrrole **16**. Deprotection of *N*-(hydroxymethyl)pyrrole **16** was carried out to give **18** in 95% yield by treatment with a catalytic amount of Triton B in refluxing acetonitrile. Use of more than catalytic quantities of Triton B resulted in partial hydrolysis of the propionic ester.

Grehn and Ragnarsson[15] recently published a method for linking the *tert*-butoxycarbonyl (t-Boc) group to pyrrole, based on a method developed by Bohlmann[16] for the preparation of *N*-acetylpyrroles. Kaiser and Muchowski have also shown[17] that the same reaction can be readily achieved with t-Boc-anhydride and a catalytic amount of *tert*-butoxide. We considered the *N*-t-Boc functionality to be an ideal choice for preparation of acrylate side chains via mercurated pyrroles. Thus, pyrrole **1** was treated with t-Boc anhydride and (dimethylamino)pyridine to afford a 74% yield of the *N*-t-Boc pyrrole **19** as a viscous oil. This was taken up in methanol and mercurated at room temperature to give a 91% yield of the β-mercurated pyrrole **20** as a white crystalline solid. The electron-withdrawing power of the *tert*-butyl carboxylate group is obviously far less troublesome to the successful mercuration of pyrrole than *N*-benzoyl or *N*-tosyl. Transmetalation and acrylation proceeded smoothly to give an 84% yield of the low-melting acrylate pyrrole **21**. Deprotection was carried out in one of two ways; conventional trifluoroacetic acid catalyzed cleavage of the *tert*-butoxy moiety followed by decarboxylation gave an 86% isolated yield of the deprotected acrylate pyrrole **22**. However, if the pyrrole was simply heated[18] at 180 °C under argon, quantitative thermolytic removal of the *tert*-butyloxycarbonyl group to give **22** was observed. This method provides an alternative for pyrroles bearing acid-sensitive groups.

(12) Murakami, Y.; Watanabe, T.; Kobayashi, A.; Yokoyama, Y. *Synthesis* **1984**, 738.
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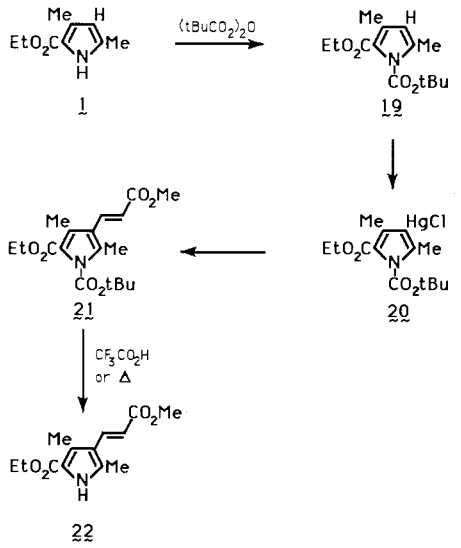
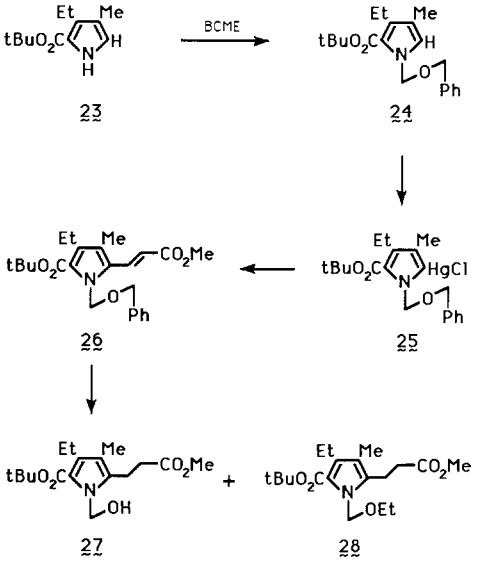
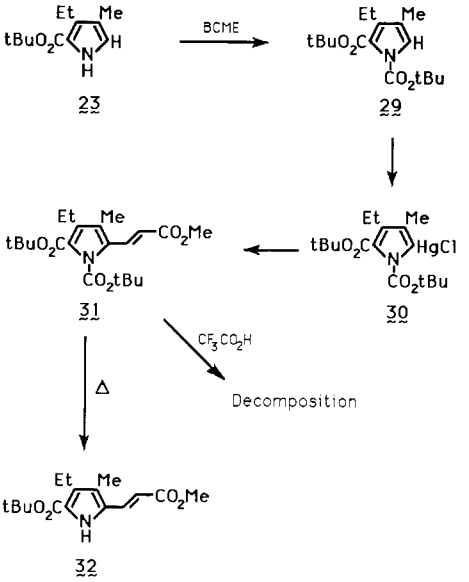


The same series of transformations were also carried out on an α-unsubstituted pyrrole. A quantitative yield was obtained in the preparation of the *N*-BME derivative **24** of the parent pyrrole **23**. Mercuration of **24** gave a 64% yield of **25**, which with methyl acrylate gave a 97% yield of the acrylate pyrrole **26**. Unfortunately, attempts to hydrogenolyze the benzyl ether in ethanol *without* triethylamine gave a mixture of (ethoxymethyl)pyrrole **28** (56%) and desired (hydroxymethyl)pyrrole **27**. This etherification or transetherification reaction is not well understood at the present time.



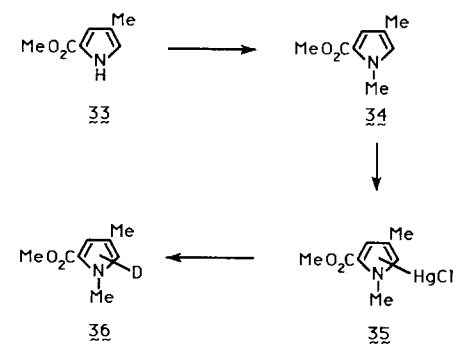
Preparation of the *N*-t-Boc-pyrrole **29** was equally facile and resulted in a 99% yield of product. Lower steric crowding is probably the cause for the higher yield. An 86% yield of the corresponding mercurated pyrrole **30** was isolated and this was efficiently converted (90%) to the acrylate pyrrole **31**. As expected, treatment of the bis(t-Boc)pyrrole **31** with trifluoroacetic acid resulted in formation of a multitude of uncharacterizable products. However, we were fortunate to discover in initial experiments that thermolysis was sufficient for the removal of the N-protecting group; a brief study was required to determine the exact window of experimental conditions necessary for complete removal of the *N*-t-Boc group while retaining the 2-t-Boc group.

Proton NMR spectroscopy indicated that heating the sample at 130 °C under argon for 30 min caused deprotection of neither t-Boc functionality. Heating the sample



at 150 °C for the same period resulted in a mixture of pyrroles. NMR integration showed a 58:42 mixture of N-deprotected pyrrole **32**: *N*-t-Boc pyrrole **31**, unequivocally demonstrating that the *N*-t-Boc group is lost more easily than the 2-t-Boc. Heating the sample for a total of 1.5 h at 150 °C resulted in formation of a 72:28 mixture of **32**:**31** without any sign of 2-t-Boc deprotection. After 2.5 h at 160 °C, the NMR spectrum indicated that all the *N*-t-Boc was lost and a small quantity (96:4) of the bis-deprotected material began to appear. Optimum conditions for selective N-deprotection of this pyrrole were 155 °C for 3.5 h, and with use of these parameters the desired pyrrole **32** was isolated in 96% yield.

Although we suspected from standard pyrrole chemistry[10] that α-mercuration would predominate over β-pyrrole mercuration, an experiment was designed to illustrate the site-propensity for mercuration. An ideal model for this study would be *N*-methylpyrrole, but every attempt to monomercurate this pyrrole and reduce it with sodium borodeuteride (to establish the site of mercuration) failed. We chose instead to N-methylate the already available α,β-unsubstituted pyrrole **33**. Following protection of the pyrrole with methyl iodide, the resultant bis-unsubstituted pyrrole **34** was mercurated with 1 equiv of mercury(II) acetate. Reduction of this aryl mercurial **35** with sodium borodeuteride to give **36** indicated (^{1}H NMR spectroscopy) that the α-position was 94% deuterated and the β-position was only 10% deuterated (indicating partial dimercuration). An NOE experiment was performed to prove that



the α-proton appears upfield (δ 6.564 ppm) from the β-proton (δ 6.735 ppm). We must acknowledge, however, that differential conjugation of both the methyl and methoxycarbonyl groups in **34** with the α and β unsubstituted positions renders **34** a less than perfect vehicle for

estimation of reactivity. It does, however, seem that the mercuration/transmetalation methodology developed above for pyrroles should be extendable to all current variations of the Heck reaction, and work along these lines is in hand.

Finally, it should be mentioned that Heck-type reactions of *iodinated* monopyrroles are successful and have been reported in the literature.[19]

Experimental Section

General. Melting points are uncorrected and were measured on a Thomas/Bristoline hot stage apparatus. Electronic absorption spectra were measured on a Hewlett-Packard 8450A spectrophotometer using solutions in dichloromethane. Mass spectra were obtained on a VG Analytical ZAB-HS instrument (70 eV, EI, mss reference perfluorokerosene). Proton NMR spectra (^{1}H NMR) were obtained in $CDCl_3$) either at 90 MHz (Varian EM390) or at 300 MHz (GE QE300) with chemical shifts reported in ppm relative to internal standards of tetramethylsilane (0 ppm, 90 MHz spectra) or chloroform (7.258 ppm, 300 MHz). Elemental analyses were performed at the Microchemical Analysis Laboratory, UC Berkeley. Reactions were monitored by thin-layer chromatography (TLC) using commercially available Eastman-Kodak 13181 (100 μm thick) silica sheets. Gravity and flash column chromatography employed either Merck neutral alumina (70–230 mesh) or Merck silica gel 60. The alumina was usually deactivated with 6% water (Brockmann Grade III) before use.

Ethyl 1,3,5-Trimethylpyrrole-2-carboxylate (2). Ethyl 3,5-dimethylpyrrole-2-carboxylate (3.00 g) was added to dimethyl sulfoxide (50 mL) containing potassium hydroxide (2.80 g) and stirred for 30 min under nitrogen. Methyl iodide (3 mL) was then added, and stirring was continued for a further 30 min before addition of ether (100 mL). The mixture was washed with water (2 × 150 mL), and the ether layer was dried over Na_2SO_4 and evaporated to dryness. The residue was passed through a short column of silica gel, eluting with dichloromethane, and the appropriate eluates were collected and evaporated to give the title pyrrole (2.96 g, 91%) with mp 38–39 °C after crystallization from dichloromethane/hexane. ^{1}H NMR ($CDCl_3$): δ 1.32 (t, 3 H, OCH_2CH_3), 2.20, 2.30 (each s, 3 H, CH_3), 3.75 (s, 3 H, NCH_3), 4.22 (q, 2 H, OCH_2CH_3), 5.75 (s, 1 H, 4-H). Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.07; H, 8.45; N, 7.59.

Ethyl 4-(Chloromercuri)-1,3,5-trimethylpyrrole-2-carboxylate (3). The foregoing pyrrole **2** (1.5 g, 8.3 mmol) in tetrahydrofuran (5 mL) was added to a solution of mercury(II) acetate (5.4 g, 17 mmol) in methanol (35 mL) and stirred for 50 min. The reaction was monitored by analytical TLC for formation of the polar mercury salt. A saturated solution of sodium chloride (100 mL) was added, and the mixture was stirred vigorously for 10 min. It was extracted with dichloromethane (2 × 250 mL), which was then washed with water, dried over Na_2SO_4, and evaporated to dryness to give 2.40 g (70%) of the title compound after crystallization from dichloromethane/hexane with mp 195–196 °C. ^{1}H NMR ($CDCl_3$): δ 1.31 (t, 3 H, OCH_2CH_3), 2.28, 2.32 (each s, 3 H, CH_3), 3.80 (s, 3 H, NCH_3), 4.28 (q, 2 H, OCH_2CH_3). Anal. Calcd for $C_{10}H_{14}ClHgNO_2$: C, 28.85; H, 3.39; N, 3.36. Found: C, 29.02; H, 3.45; N, 3.38.

Ethyl 4-[2-(Methoxycarbonyl)vinyl]-1,3,5-trimethylpyrrole-2-carboxylate (4). The foregoing pyrrole **3** (1.00 g, 2.4 mmol) in tetrahydrofuran (30 mL) and methyl acrylate (60 mL) was stirred under nitrogen for 5 min at 50 °C. To this was added $LiPdCl_3$ in acetonitrile [prepared by refluxing LiCl (75 mg, 1.84 mmol) and $PdCl_2$ (722 mg, 4.07 mmol) in acetonitrile (40 mL) for 30 min under nitrogen]. The mixture was stirred for 40 min at 50 °C, cooled, and filtered through a bed of Celite. The filtrate was diluted with dichloromethane (250 mL), which was washed with water (2 × 100 mL), dried over Na_2SO_4, and evaporated to dryness. The brown residue was chromatographed on a sort silica gel column, eluting with 30% ethyl acetate in cyclohexane, and the appropriate eluates were collected. Evaporation under vacuum gave a residue, which was crystallized from dichloromethane/hexane to give the title pyrrole (255 mg, 40%), mp 54–57 °C. ^{1}H NMR ($CDCl_3$): δ 1.40 (t, 3 H, OCH_2CH_3), 2.32, 2.46 (each s, 3 H, CH_3), 3.80 (s, 6 H, NCH_3 and OCH_3), 4.30 (q, 2 H, OCH_2CH_3), 6.12, 7.80 (each d, 1 H, $CO_2CH{=}CH$). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.55; H, 7.11; N, 4.91.

Ethyl 4-[2-(Methoxycarbonyl)ethyl]-1,3,5-trimethylpyrrole-2-carboxylate (5). The foregoing pyrrole **4** (100 mg) in tetrahydrofuran (20 mL) and triethylamine (0.1 mL) was hydrogenated at room temperature and atmospheric pressure over 10% Pd–C (10 mg) until uptake of hydrogen ceased. The solution was filtered through a pad of Celite, and the filtrate was evaporated to give the title pyrrole (96 mg, 96%) after crystallization from dichloromethane/hexane, mp 85–89 °C. ^{1}H NMR ($CDCl_3$): δ 1.42 (t, 3 H, OCH_2CH_3), 2.10, 2.22 (each s, 3 H, CH_3), 2.4–2.8 (m, 4 H, CH_2CH_2CO), 3.62, 3.72 (each s, 3 H, NCH_3 and OCH_3), 4.25 (q, 2 H, OCH_2CH_3). Anal. Calcd for $C_{14}H_{21}NO_4$: C, 62.90; H, 7.92; N, 5.24. Found: C, 62.63; H, 7.91; N, 5.04.

Benzyl 5-(Chloromercuri)-4-ethyl-1,3-dimethylpyrrole-2-carboxylate (7). Benzyl 4-ethyl-1,3-dimethylpyrrole-2-carboxylate (**6**) (1.50 g) [prepared from benzyl 4-ethyl-3-methylpyrrole-2-carboxylate (502 mg) with potassium hydroxide (245 mg) in dimethyl sulfoxide (25 mL) and methyl iodide (619 mg), as described in the synthesis of pyrrole **2**] in tetrahydrofuran (10 mL) was added to a solution of mercury(II) acetate (4.6 g) in methanol (30 mL) and allowed to stir at room temperature under nitrogen for 15 h. Saturated sodium chloride solution (100 mL) was then added, and the mixture was stirred vigorously for 10 min before being extracted with dichloromethane (2 × 100 mL), which was washed with water (2 × 100 mL) and then dried over Na_2SO_4. The solution was then evaporated to dryness, and the residue was chromatographed on a column of silica gel, eluting with dichloromethane. Evaporation of the appropriate eluates gave a residue which was crystallized from dichloromethane/hexane to give the title pyrrole (1.50 g, 52%), mp >150 °C dec. ^{1}H NMR ($CDCl_3$): δ 1.30 (t, 3 H, CH_2CH_3), 2.11 (s, 3 H, CH_3), 2.30 (q, 2 H, CH_2CH_3), 3.80 (s, 3 H, NCH_3), 5.14 (s, 2 H, CH_2Ph), 7.33 (s, 5 H, Ph). Anal. Calcd for $C_{16}H_{18}ClHgNO_2$: C, 39.03; H, 3.69; N, 2.85. Found: C, 39.13; H, 3.68; N, 2.88.

Ethyl 1-Benzyl-2-ethyl-3,5-dimethylpyrrole-2-carboxylate (8). This pyrrole was prepared, as described above for compound **2**, using pyrrole **1** (2.00 g), potassium hydroxide (1.40 g), and dimethyl sulfoxide (25 mL) containing benzyl chloride (1.52 mL). The residue after workup was chromatographed on silica gel, eluting with 30% ethyl acetate in cyclohexane, and evaporation of the appropriate eluates gave a residue which was crystallized from dichloromethane/hexane to give 3.00 g (75%) of the title pyrrole, mp 41–45 °C. ^{1}H NMR ($CDCl_3$): δ 1.28 (t, 3 H, OCH_2CH_3), 2.12, 2.32 (each s, 3 H, CH_3), 4.20 (q, 2 H, OCH_2CH_3), 5.55 (s, 2 H, NCH_2Ph), 5.85 (s, 1 H, 4-H), 6.75–7.45 (m, 5 H, Ph). Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.84; H, 7.43; N, 5.26.

Ethyl 1-Benzyl-4-[2-(methoxycarbonyl)vinyl]-3,5-dimethylpyrrole-2-carboxylate (9). This compound was prepared, as described for synthesis of pyrrole **4** via **3**, by mercuration of the foregoing pyrrole **8** (1.20 g) in tetrahydrofuran (10 mL) with mercury(II) acetate (1.60 g) in methanol (30 mL). The usual workup gave 1.72 g (75%) of the mercurated pyrrole after crystallization from dichloromethane/hexane and with mp 106–108 °C. ^{1}H NMR ($CDCl_3$): δ 1.25 (t, 3 H, OCH_2CH_3), 2.20, 2.40 (each s, 3 H, CH_3), 4.18 (q, 2 H, OCH_2CH_3), 5.56 (s, 2 H, NCH_2Ph), 6.95 (m, 2 H, Ph), 7.25 (br s, 3 H, Ph). This mercurated pyrrole (1.00 g) was converted into the title pyrrole by dissolving in tetrahydrofuran (30 mL) and treatment with methyl acrylate (60 mL) and $LiPdCl_3$ in acetonitrile (40 mL), as described for synthesis of pyrrole **4**. The usual workup gave a residue which was crystallized from dichloromethane/hexane to give the title pyrrole (256 mg, 37%) as a viscous oil. ^{1}H NMR ($CDCl_3$): δ 1.34 (t, 3 H, OCH_2CH_3), 2.30, 2.55 (each s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 4.30 (q, 2 H, OCH_2CH_3), 5.65 (s, 2 H, NCH_2Ph), 6.15, 7.30 (each d, 1 H, $CO_2CH{=}CH$), 6.98 (m, 2 H, Ph), 7.30 (m, 3 H, Ph). HR mass spectrum: $C_{20}H_{23}NO_4$ requires 341.1627, found 341.1633.

Ethyl 1-Benzyl-4-[2-(methoxycarbonyl)ethyl]-3,5-dimethylpyrrole-2-carboxylate (10). The foregoing pyrrole **9** (150 mg) was hydrogenated in tetrahydrofuran (20 mL) and triethylamine (0.1 mL) over 10% Pd–C (15 mg) as described for

(19) Demopoulos, B. J.; Anderson, H. J.; Loader, C. E.; Faber, K. *Can. J. Chem.* **1983**, *61*, 2415. Faber, K.; Anderson, H. J.; Loader, C. E.; Daley, A. S. *Can. J. Chem.* **1984**, *62*, 1046.

synthesis of pyrrole 5. The usual workup gave the title pyrrole (144 mg, 95%) as a viscous oil. ^{1}H NMR ($CDCl_3$): δ 1.22 (t, 3 H, OCH_2CH_3), 2.08, 2.30 (each s, 3 H, CH_3), 2.46, 2.76 (each t, 2 H, CH_2CH_2CO), 3.60 (s, 3 H, OCH_3), 4.28 (q, 2 H, OCH_2CH_3), 5.54 (s, 2 H, NCH_2Ph), 6.88 (m, 2 H, Ph), 7.20 (m, 3 H, Ph). HR mass spectrum: $C_{20}H_{25}NO_4$ requires 343.1784, found 373.1773.

Ethyl 1-(Benzyloxymethyl)-3,5-dimethylpyrrole-2-carboxylate (13). Ethyl 3,5-dimethylpyrrole-2-carboxylate (1) (3.0 g, 0.018 mol) was added to a solution of KOH (1.96 g, 0.035 mol) in dimethyl sulfoxide (50.0 mL) and stirred for 15 min at room temperature under nitrogen atmosphere. The solution was cooled to 10 °C, to it was added benzyl chloromethyl ether (4.89 mL, 0.035 mol), and the mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with diethyl ether (10 mL), and the mixture was washed twice with water and then with brine. The ether layer was dried over Na_2SO_4 before the solvent was removed by evaporation. The yellow residue was applied to a 5 × 50 cm alumina column (Brockmann Grade III) and eluted with cyclohexane/toluene/ethyl acetate (70:20:10). The appropriate eluates were combined and evaporated under vacuum to give the title pyrrole (4.0 g, 78% yield) as an oil which hardened upon cooling, mp 20.5–21.5 °C. ^{1}H NMR ($CDCl_3$): δ 1.31 (t, 3 H, CH_2CH_3), 2.25, 2.32 (each s, 3 H, ring methyl), 4.28 (q, 2 H, CH_2CH_3), 4.52 (s, 2 H, OCH_2Ph), 5.80 (s, 2 H, NCH_2O), 5.80 (s, 1 H, β-H), 7.30 (m, 5 H, Ph). LR mass spectrum: *m/e* 287 (2), 181 (71), 91 (100).

Ethyl 1-(Benzyloxymethyl)-4-(chloromercuri)-3,5-dimethylpyrrole-2-carboxylate (14). The foregoing pyrrole 13 (2.85 g, 0.01 mol) in freshly distilled tetrahydrofuran (15 mL) was added to a solution of mercury(II) acetate (6.38 g, 0.02 mol) in dry methanol (75 mL), and the mixture was stirred at room temperature. Silica gel TLC (cyclohexane/ethyl acetate, 70:30) indicated the reaction was complete after 1 h. The mixture was diluted with dichloromethane in a separatory funnel and shaken vigorously for 10 min with a saturated aqueous solution of NaCl. The layers were separated, and the organic layer was shaken once again with brine. The organic layer was separated, dried over Na_2SO_4, and evaporated under vacuum. Recrystallization of the resulting yellow-white solid from dichloromethane/petroleum ether afforded the title pyrrole as white crystals (4.12 g, 81% yield), mp 122.5–123.5 °C. ^{1}H NMR ($CDCl_3$): δ 1.35 (t, 3 H, CH_2CH_3), 2.35 (s, 6 H, 2 × ring methyl), 4.26 (q, 2 H, CH_2CH_3), 4.51 (s, 2 H, OCH_2Ph), 5.77 (s, 2 H, NCH_2O), 7.30 (m, 5 H, Ph). Anal. Calcd for $C_{17}H_{20}ClHgNO_3$: C, 39.09;; H, 3.86; N, 2.68. Found: C, 38.97; H, 3.82; N, 2.63.

Ethyl 1-(Benzyloxymethyl)-4-[2-(methoxycarbonyl)-ethenyl]-3,5-dimethylpyrrole-2-carboxylate (15). The foregoing pyrrole 14 (951 mg, 1.8 mmol), methyl acrylate (50 mL), and triethylamine (1.0 mL) in freshly distilled tetrahydrofuran (40 mL) were stirred under a nitrogen atmosphere at 50 °C for 5 min before the addition of $LiPdCl_3$ in acetonitrile dropwise over a period of 10 min. [The palladium catalyst was preprepared by refluxing LiCl (160 mg, 3.8 mmol) and $PdCl_2$ (545 mg, 3.1 mmol) in acetonitrile (20 mL) for 1 h under N_2.] The mixture was stirred at this temperature for an additional 45 min before being cooled to room temperature and filtered through a bed of Celite, to remove Pd^0, and rinsing the Celite with dichloromethane. The organic layer was washed twice with water and then with brine and finally dried over Na_2SO_4. The solvent was removed under vacuum by evaporation, leaving a dark, viscous oil which was chromatographed on a 2 × 40 cm silica gel gravity column, eluting with cyclohexane/ethyl acetate (70/30). The appropriate eluates were combined and evaporated to give the title pyrrole (582 mg, 86.2%) as a viscous oil. ^{1}H NMR ($CDCl_3$): δ 1.35 (t, 3 H, CH_2CH_3), 2.40, 2.45 (each s, 3 H, ring methyl), 3.78 (s, 3 H, OCH_3), 4.26 (q, 2 H, CH_2CH_3), 4.47 (s, 2 H, OCH_2Ph), 5.78 (s, 2 H, NCH_2O), 6.03 (d, 1 H, $CH{=}CHCO_2Me$, J_{HH} = 15 Hz), 7.27 (m, 5 H, Ph), 7.68 (d, 1 H, $CH{=}CHCO_2Me$, J_{HH} = 15 Hz). LR mass spectrum: *m/e* 371 (4), 340 (2), 265 (44), 91 (100).

Ethyl 1-(Hydroxymethyl)-4-[2-(methoxycarbonyl)-ethyl]-3,5-dimethylpyrrole-2-carboxylate (16). The foregoing pyrrole 15 (182 mg, 0.5 mmol) in absolute ethanol (20 mL) was hydrogenated at room temperature and atmospheric pressure over Pd–C (50 mg) until the uptake of hydrogen had ceased (~18 h). Care was taken not to use triethylamine because transetherification of ethanol with the benzyl ether was shown to occur. The solution was filtered through a pad of Celite to remove Pd–C, and the pad was rinsed with dichloromethane. The organic phase was dried over Na_2SO_4 before stripping off the solvent under vacuum. The white product was solidified by cooling in the refrigerator, and the resulting solid was not easily recrystallized, mp 60.5–61.0 °C. ^{1}H NMR ($CDCl_3$): δ 1.35 (t, 3 H, CH_2CH_3), 2.25 (s, 6 H, 2 × ring methyl), 2.85–2.25 (m, 4 H, $CH_2CH_2CO_2Me$), 3.65 (s, 3 H, methyl ester), 4.30 (q, 2 H, CH_2CH_3), 5.38 (s, 2 H, CH_2OH). LR mass spectrum: *m/e* 283 (7), 253 (82), 208 (27), 180 (100), 134 (77). HR mass spectrum $C_{14}H_{21}NO_5$ requires 283.14197, found 283.14197. Anal. Calcd for $C_{14}H_{21}NO_5$: C, 59.35; H, 7.47; N, 4.94. Found: C, 59.21; H, 7.54; N, 4.84.

Ethyl 4-[2-(Methoxycarbonyl)ethyl]-3,5-dimethylpyrrole-2-carboxylate (18). To the foregoing pyrrole **16** (30 mg, 0.11 mmol) in dry acetonitrile (5 mL) was added 1 drop of a diluted (10:1, methanol:Triton B) solution of Triton B (40% in methanol; Aldrich). The mixture was refluxed for 2.5 h, whereupon silica gel TLC (cyclohexane/ethyl acetate, 70:30) showed that none of the more polar starting material was present. The mixture was cooled to room temperature before taking up in dichloromethane. The organic layer was washed twice with water and then with brine and dried over Na_2SO_4 before stripping off the solvent under vacuum. The yield of the title pyrrole following crystallization from dichloromethane/petroleum ether was 77% (20 mg), mp 100–101 °C (lit.[20] mp 100–102 °C). ^{1}H NMR ($CDCl_3$): δ 1.35 (t, 3 H, CH_2CH_3), 2.22, 2.30 (each s, 3 H, ring methyl), 2.85–2.30 (m, 4 H, $CH_2CH_2CO_2Me$), 3.70 (s, 3 H, OCH_3), 4.28 (q, 2 H, CH_2CH_3), 8.85 (s, 1 H, NH). LR mass spectrum: *m/e* 251 (100), 220 (28), 205 (27), 174 (67), 146 (48). Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.36; H, 7.47; N, 5.58.

Ethyl 1-(*tert*-Butoxycarbonyl)-3,5-dimethylpyrrole-2-carboxylate (19). Ethyl 3,5-dimethylpyrrole-2-carboxylate (1) (1.0 g, 6 mmol) was dissolved in dry dichloromethane, and to the stirring solution at room temperature and under nitrogen were added (dimethylamino)pyridine (74 mg, 0.6 mmol) and triethylamine (6.1 g, 8.4 mL, 60 mmol). To this solution was added t-BOC anhydride (2.0 g, 9.0 mmol); within 10 min the solution began to darken from pale yellow to golden yellow. After stirring overnight (15 h) under N_2 the solution was diluted with dichloromethane and washed three times with water and once with brine. The organic layer was dried over Na_2SO_4, and the solvent was stripped off under vacuum to yield a light-red viscous oil. This was chromatographed on a 2 × 85 cm silica gel gravity column, and the desired pyrrole was eluted from the column with 70:30 cyclohexane/ethyl acetate. The appropriate fractions were combined, and the solvent was removed to give the title pyrrole as a light-yellow viscous oil (1.18 g, 74% yield). ^{1}H NMR ($CDCl_3$): δ 1.34 (t, 3 H, CH_2CH_3), 1.56 (s, 9 H, t-Bu), 2.20, 2.32 (each s, 3 H, ring methyl), 4.30 (q, 2 H, CH_2CH_3), 5.75 (s, 1 H, β-H). LR mass spectrum: *m/e* 267 (4), 194 (4), 167 (32), 138 (16), 121 (22), 57 (100). ^{13}C NMR ($CDCl_3$): δ 12.37, 13.97, 14.33, 27.50, 60.12, 84.05, 112.90, 121.19, 130.36, 135.52, 149.59, 161.38.

Ethyl 1-(*tert*-Butoxycarbonyl)-4-(chloromercuri)-3,5-dimethylpyrrole-2-carboxylate (20). The foregoing pyrrole **19** (945 mg, 3.5 mmol) in freshly distilled tetrahydrofuran (3 mL) was added to a solution of mercury(II) acetate (1.6 g, 5.3 mmol) in dry methanol (20 mL), and the mixture was stirred at room temperature. Silica gel TLC (cyclohexane/ethyl acetate, 70:30) indicated the reaction was complete after 1 h. The mixture was diluted with dichloromethane in a separatory funnel and shaken vigorously for 10 min with a saturated aqueous solution of sodium chloride. The layers were separated, and the organic layer was shaken once again with brine. The organic layer was separated, dried over Na_2SO_4, and evaporated under vacuum. Recrystallization of the resulting off-white powder from dichloromethane/petroleum ether afforded the title pyrrole as white crystals (1.78 g, 91% yield), mp 149–150 °C. ^{1}H NMR ($CDCl_3$): δ 1.34 (t, 3 H, CH_2CH_3), 1.56 (s, 9 H, t-Bu), 2.23, 2.40 (each s, 3 H, ring methyl), 4.30 (q, 2 H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 14.28, 15.18, 16.29, 27.44, 60.40, 84.78, 121.67, 133.06, 134.00, 139.13, 149.29, 161.08. LR mass spectrum: *m/e* 503 (4, cluster), 430 (6, cluster), 403 (62), 374 (22), 357 (34). Anal. Calcd for

(20) Hayes, A.; Kenner, G. W.; Williams, N. R. *J. Chem. Soc. C* **1985**, 3782.

$C_{14}H_{20}ClHgNO_4$: C, 33.47; H, 4.01; N, 2.79. Found: C, 33.53; H, 4.20; N, 2.85.

Ethyl 1-(*tert*-Butoxycarbonyl)-4-[2-(methoxycarbonyl)ethenyl]-3,5-dimethylpyrrole-2-carboxylate (21). The foregoing pyrrole **20** (1.37 g, 2.7 mmol), methyl acrylate (12.3 mL), and triethylamine (4.0 mL) in freshly distilled tetrahydrofuran (20 mL) were stirred under a nitrogen atmosphere at 50 °C for 5 min before the addition of $LiPdCl_3$ in acetonitrile [prepared by refluxing LiCl (174 mg, 4.1 mmol) and $PdCl_2$ (612 mg, 3.4 mmol) in acetonitrile (10 mL) for 1 h under N_2] dropwise over a period of 10 min. The mixture was stirred at this temperature for an additional 60 min before being cooled to room temperature, filtered through a bed of Celite, to remove Pd^0, and rinsing the Celite with dichloromethane. The organic layer was washed twice with water and brine and then dried over Na_2SO_4. The solvent was removed under vacuum to leave a dark viscous oil, which was chromatographed on a 3 × 80 cm silica gel gravity column, eluting with cyclohexane/ethyl acetate (70/30). The appropriate eluates were combined and evaporated to give the title compound (802 mg, 84%) as a viscous oil which hardened upon cooling, mp 60–63 °C. ^1H NMR ($CDCl_3$): δ 1.36 (t, 3 H, CH_2CH_3), 1.57 (s, 9 H, t-Bu), 2.34, 2.44 (each s, 3 H, ring methyl), 3.78 (s, 3 H, OCH_3), 4.32 (q, 2 H, CH_2CH_3), 6.12 (d, 1 H, CH=C*H*CO_2Me, J_{HH} = 16.0 Hz), 7.65 (d, 1 H, C*H*=$CHCO_2Me$, J_{HH} = 16.0 Hz). ^{13}C NMR ($CDCl_3$): δ 11.77, 12.12, 14.35, 27.55, 48.38, 50.21, 51.53, 60.75, 85.35, 116.64, 118.50, 128.32, 136.65, 136.71, 136.76, 167.97. LR mass spectrum: *m/e* 351 (3), 278 (3), 251 (39), 220 (10), 205 (11), 57 (100).

Ethyl 4-[2-(Methoxycarbonyl)ethenyl]-3,5-dimethylpyrrole-2-carboxylate (22). Method A. Pyrolysis. The foregoing pyrrole **21** (30 mg, 0.084 mmol) was placed in a 10-mL round-bottom flask equipped with a condenser and rubber septum. The flask was purged with argon for 5 min before heating the flask to 180 °C in a silicon oil bath. The pyrrole melted at a bath temperature of ~72 °C, and slight discoloration occurred near 180 °C. The sample was heated at this temperature for 30 min to ensure complete decarboxylation of the *N*-t-BOC-pyrrole. The vessel was cooled to room temperature, the darkened pyrrole was dissolved in dichloromethane, and the title deprotected pyrrole (quantitative yield by TLC) was crystallized from this solution with petroleum ether (85% yield). **Method B. Acid Catalysis.** The foregoing pyrrole **21** (266 mg, 0.76 mmol) was dissolved in freshly distilled dichloromethane, and to the solution under nitrogen was added trifluoroacetic acid (1.6 mL, 16 mmol). The initial yellow solution darkened very quickly to an orange color and, over the course of 1 h, became orange-brown. At this time silica gel TLC (70:30 cyclohexane/ethyl acetate) indicated the reaction to be complete. The mixture was diluted with dichloromethane and poured into ice water; the organic layer was washed twice with water and once with brine, followed by drying over Na_2SO_4. A solid pyrrolic product remained in the flask following evaporation of the solvent, and this was recrystallized from CH_2Cl_2/petroleum ether to afford 163 mg (86% yield) of the desired pyrrole, mp 149–150 °C. ^1H NMR ($CDCl_3$): δ 1.36 (t, 3 H, CH_2CH_3), 2.39, 2.44 (each s, 3 H, ring methyl), 3.78 (s, 3 H, OCH_3), 4.32 (q, 2 H, CH_2CH_3), 6.07 (d, 1 H, CH=C*H*CO_2Me, J_{HH} = 16.2 Hz), 7.69 (d, 1 H, C*H*=$CHCO_2Me$, J_{HH} = 16.2 Hz), 9.37 (br s, 1 H, NH). ^{13}C NMR ($CDCl_3$): δ 11.39, 12.61, 14.20, 51.20, 60.14, 113.15, 117.35, 118.19, 128.06, 135.66, 137.60, 162.05, 168.42. Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 61.83; H, 6.52; N, 5.56.

***tert*-Butyl 1-(Benzyloxymethyl)-3-ethyl-4-methylpyrrole-2-carboxylate (24).** *tert*-Butyl 3-ethyl-4-methylpyrrole-2-carboxylate (**23**) (986 mg, 4.7 mmol) was dissolved in dry dimethylformamide, and to the resulting solution was added hexane washed sodium hydride (300 mg of 60% in mineral oil, 7.5 mmol). Bubbling occurred upon addition, and the mixture was stirred at room temperature under nitrogen for 30 min. After the mixture was cooled to 0 °C benzyl chloromethyl ether (0.80 mL, 5.8 mmol) was slowly added via a pipette. The solution was stirred at the reduced temperature for an additional 10 min and then at room temperature for another 1 h. The mixture was diluted with dichloromethane, and the organic phase was washed four times with water and once more with brine; the mixture was dried over Na_2SO_4, and the solvent was removed under vacuum to give 1.55 g (100% yield) of the title N-protected pyrrole as a viscous oil. ^1H NMR ($CDCl_3$): δ 1.12 (t, 3 H, CH_2CH_3), 1.58 (s, 9 H, t-Bu), 2.00 (s, 3 H, ring methyl), 2.71 (q, 2 H, CH_2CH_3), 4.48 (s, 2 H, OCH_2Ph), 5.64 (s, 2 H, OCH_2N), 6.68 (s, 1 H, α-H), 7.30 (m, 5 H, Ph).

***tert*-Butyl 1-(Benzyloxymethyl)-3-ethyl-5-(chloromercuri)-4-methylpyrrole-2-carboxylate (25).** The foregoing pyrrole **24** (1.42 g, 4.3 mmol) in freshly distilled tetrahydrofuran (10 mL) was added to a solution of mercury(II) acetate (2.10 g, 6.6 mmol) in dry methanol (30 mL), and the mixture was stirred at room temperature. Silica gel TLC (cyclohexane/ethyl acetate, 70:30) indicated the reaction was complete after 30 min. The mixture was quenched with dichloromethane in a separatory funnel and shaken vigorously for 10 min with a saturated aqueous solution of sodium chloride. The layers were separated, and the organic layer was shaken once again with brine. The organic layer was separated, dried over Na_2SO_4, and evaporated under vacuum. Recrystallization of the resulting off-white powder from dichloromethane/petroleum ether afforded the title pyrrole as white crystals (1.53 g, 64% yield), mp 82–84 °C. ^1H NMR ($CDCl_3$): δ 1.13 (t, 3 H, CH_2CH_3), 1.59 (s, 9 H, t-Bu), 2.10 (s, 3 H, ring methyl), 2.70 (q, 2 H, CH_2CH_3), 4.54 (s, 2 H, OCH_2Ph), 5.77 (s, 2 H, OCH_2N), 7.33 (m, 5 H, Ph). Anal. Calcd for $C_{20}H_{26}ClHgNO_3$: C, 42.56; H, 4.64; N, 2.48. Found: C, 42.51; H, 4.71; N, 2.23.

***tert*-Butyl 1-(Benzyloxymethyl)-3-ethyl-5-[2-(methoxycarbonyl)ethenyl]-4-methylpyrrole-2-carboxylate (26).** The foregoing pyrrole **25** (1.45 g, 2.6 mmol), methyl acrylate (3.5 mL, 39 mmol), and triethylamine (0.4 mL) in freshly distilled tetrahydrofuran (20 mL) were stirred under a nitrogen atmosphere at 50 °C for 5 min before the addition of $LiPdCl_3$ in acetonitrile [prepared by refluxing LiCl (334 mg, 8.0 mmol) and $PdCl_2$ (593 mg, 3.3 mmol) in acetonitrile (10 mL) for 1 h under N_2] dropwise over a period of 10 min. The mixture was stirred at this temperature for an additional 90 min and then cooled to room temperature before the solution was filtered through a bed of Celite, to remove Pd^0, and the Celite was rinsed with dichloromethane. The organic layer was washed four times with water and twice with brine and finally dried over Na_2SO_4. The solvent was removed under vacuum, leaving a golden, viscous oil which was chromatographed on a 2 × 20 cm silica gel gravity column with cyclohexane/ethyl acetate (70/30). The appropriate eluates were combined and evaporated to give the title compound (1.02 g, 97%) as a colorless gum. ^1H NMR ($CDCl_3$): δ 1.16 (t, 3 H, CH_2CH_3), 1.65 (s, 9 H, t-Bu), 2.20 (s, 3 H, ring methyl), 2.76 (q, 2 H, CH_2CH_3), 3.85 (s, 3 H, OCH_3), 4.61 (s, 2 H, OCH_2Ph), 5.92 (s, 2 H, OCH_2N), 6.35 (d, 1 H, CH=C*H*CO_2Me, $J_{\alpha\beta}$ = 16.2 Hz), 7.34 (m, 5 H, Ph), 7.85 (d, 1 H, C*H*=$CHCO_2Me$, $J_{\alpha\beta}$ = 16.2 Hz). ^{13}C NMR ($CDCl_3$): δ 10.48, 15.06, 18.63, 28.15, 51.41, 69.89, 72.93, 81.12, 117.96, 123.06, 123.40, 127.39, 127.42, 128.07, 130.84, 132.07, 134.36, 137.48, 160.90, 167.50.

***tert*-Butyl 1-(*tert*-Butoxycarbonyl)-3-ethyl-4-methylpyrrole-2-carboxylate (29).** *tert*-Butyl 3-ethyl-4-methylpyrrole-2-carboxylate (1.49 g, 7.1 mmol) was dissolved in dry dichloromethane, and to the stirring solution at room temperature and under nitrogen were added (dimethylamino)pyridine (87 mg, 0.71 mmol) and triethylamine (10 mL, 72 mmol). The solution was cooled to 0 °C before the addition of t-BOC anhydride (2.5 mL, 11 mmol); after addition was complete, the solution was warmed to room temperature. After being stirred overnight (15 h) under N_2 the solution was diluted with dichloromethane and washed with water, 1 N HCl, twice with water, and then once with brine. The organic layer was dried over Na_2SO_4, and the solvent was stripped off under vacuum to yield a golden viscous oil. This was chromatographed on a 3 × 20 cm silica gel gravity column, and the desired pyrrole was eluted from the column with 70:30 cyclohexane/ethyl acetate. The appropriate fractions were combined, and the solvent was removed under high vacuum to give the title pyrrole as a light-yellow viscous oil (2.21 g, 100% yield): ^1H NMR ($CDCl_3$): δ 1.11 (t, 3 H, CH_2CH_3), 1.56 (s, 9 H, t-Bu), 1.565 (s, 9 H, t-Bu), 1.97 (s, 3 H, ring methyl), 2.55 (q, 2 H, CH_2CH_3), 6.95 (s, 1 H, α-H). ^{13}C NMR ($CDCl_3$): δ 9.64, 14.86, 18.08, 27.77, 27.17, 76.57, 77.42, 80.96, 83.50, 120.21, 122.14, 122.88, 160.92.

***tert*-Butyl 1-(*tert*-Butoxycarbonyl)-3-ethyl-5-(chloromercuri)-4-methylpyrrole-2-carboxylate (30).** The foregoing pyrrole **29** (2.15 g, 6.9 mmol) in freshly distilled tetrahydrofuran (10 mL) was added to a solution of mercury(II) acetate (4.0 g, 12.5 mmol) in dry methanol (30 mL), and the mixture was stirred

at room temperature. Silica gel TLC (cyclohexane/ethyl acetate, 70:30) indicated the reaction was complete after 5.5 h. The mixture was diluted with dichloromethane in a separatory funnel and shaken vigorously for 10 min with a saturated aqueous solution of sodium chloride. The layers were separated, and the organic layer was shaken once again with brine. The organic layer was separated, dried over Na_2SO_4, and evaporated under vacuum. Recrystallization of the resulting yellow-white powder from dichloromethane/petroleum ether afforded the title pyrrole as white crystals (3.25 g, 86% yield), mp 147 °C. ^1H NMR ($CDCl_3$): δ 1.10 (t, 3 H, CH_2CH_3), 1.56 (s, 18 H, 2 t-Bu), 2.07 (s, 3 H, Me), 2.52 (q, 2 H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 12.46, 14.73, 18.68, 81.52, 85.77, 128.71, 135.90, 145.03, 160.68. Anal. Calcd for $C_{17}H_{26}ClHgNO_4$: C, 37.50; H, 4.81; N, 2.57. Found: C, 37.31; H, 4.54; N, 2.25.

***tert*-Butyl 1-(*tert*-Butoxycarbonyl)-3-ethyl-5-[2-(methoxycarbonyl)ethenyl]-4-methylpyrrole-2-carboxylate (31).** The foregoing pyrrole **30** (1.20 g, 2.2 mmol), methyl acrylate (3.0 mL, 33 mmol), and triethylamine (0.4 mL) in freshly distilled tetrahydrofuran (20 mL) were stirred under a nitrogen atmosphere at 50 °C for 5 min before the addition of $LiPdCl_3$ in acetonitrile [prepared by refluxing LiCl (298 mg, 7.1 mmol) and $PdCl_2$ (502 mg, 2.8 mmol) in acetonitrile (10 mL) for 1 h under N_2] dropwise over a period of 10 min. The mixture was stirred at this temperature for an additional 30 min before being cooled to room temperature and left in the refrigerator overnight (~15 h). The mixture was warmed to room temperature before the solution was fitted through a bed of Celite, to remove Pd^0, and the Celite was rinsed with dichloromethane. The organic layer was washed five times with water and once with brine and then dried over Na_2SO_4. The solvent was removed under vacuum, leaving a dark viscous oil which was chromatographed on a 3 × 30 cm silica gel gravity column eluting with cyclohexane/ethyl acetate (70/30). The appropriate eluates were combined and evaporated under high vacuum to give the title product (1.02 g, 97%) as a colorless gum which eventually solidified upon standing. Attempts at recrystallization proved fruitless. Mp: 89–93 °C. ^1H NMR ($CDCl_3$): δ 1.07 (t, 3 H, CH_2CH_3), 1.53 (s, 9 H, t-Bu), 1.57 (s, 9 H, t-Bu), 2.08 (s, 3 H, ring methyl), 2.58 (q, 2 H, CH_2CH_3), 3.75 (s, 3 H, OCH_3), 6.08 (d, 1 H, CH=C*H*CO_2Me, $J_{\alpha\beta}$ = 16.2 Hz), 7.83 (d, 1 H, C*H*=$CHCO_2Me$, $J_{\alpha\beta}$ = 16.2 Hz).

***tert*-Butyl 3-Ethyl-5-[2-(methoxycarbonyl)ethenyl]-4-methylpyrrole-2-carboxylate (32).** Attempts to deprotect pyrrole **31** with trifluoroacetic acid failed; therefore, the pyrolysis method (vide supra, for **22**) was used. It was determined empirically that the *N*-t-BOC could be cleaved at temperatures above 130 °C while retaining the *C*-t-BOC functionality. At temperatures above 160 °C, loss of *C*-t-BOC was detected by NMR spectroscopy. The ideal combination of temperature and time for the pyrrole in question was determined to be 155 °C for 3.5 h, resulting in a 96% yield of the title deprotected pyrrole **32**, mp 126–127 °C. ^1H NMR ($CDCl_3$): δ 1.09 (t, 3 H, CH_2CH_3), 1.56 (s, 9 H, t-Bu), 2.10 (s, 3 H, ring methyl), 2.68 (q, 2 H, CH_2CH_3), 3.76 (s, 3 H, OCH_3), 6.08 (d, 1 H, CH=C*H*CO_2Me, $J_{\alpha\beta}$ = 16.2 Hz), 7.57 (d, 1 H, C*H*=$CHCO_2Me$, $J_{\alpha\beta}$ = 16.2 Hz), 9.18 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$): δ 8.98, 15.00, 18.10, 28.28, 51.53, 81.35, 113.21, 122.67, 124.63, 127.46, 131.94, 133.01, 160.81, 167.65.

Methyl 1,4-Dimethylpyrrole-2-carboxylate (34). Benzyl 1,4-dimethylpyrrole-2-carboxylate (197 mg, 0.86 mmol) was added to a mixture of sodium metal (300 mg, 130 mmol) in methanol (40 mL), and the mixture was refluxed under N_2 for 7 h. After being cooled to room temperature, the solution was diluted with dichloromethane and washed twice with 2 N HCl, once with water, and then once with brine. After drying over Na_2SO_4, the solvent was removed under vacuum. The yellow fragrant oil was chromatographed on a 2 × 50 cm silica gel column, and the desired pyrrole was eluted from the column with 70:30 cyclohexane/ethyl acetate. The solvent was removed under high vacuum, leaving a pale-yellow oil (80 mg, 61%). ^1H NMR ($CDCl_3$): δ 2.05 (s, 3 H, ring methyl), 3.79 and 3.86 (each s, 3 H, NMe and OCH_3), 6.56 (s, 1 H, α-H), 6.74 (s, 1 H, β-H). LR mass spectrum: *m/e* 153 (92), 122 (100), 94 (27).

Mercurated Methyl 1,4-Dimethylpyrrole-2-carboxylate Chloride Salt (35). The foregoing pyrrole **34** (80 mg, 0.53 mmol) in freshly distilled tetrahydrofuran (15 mL) was added slowly to a solution of mercury(II) acetate (168 mg, 0.53 mmol) in dry methanol (15 mL), and the mixture was stirred at room temperature for 6.5 h. The mixture was diluted with dichloromethane in a separatory funnel and shaken vigorously for 10 min with a saturated aqueous solution of sodium chloride. The layers were separated, and the organic layer was shaken once again with brine. The organic layer was separated, dried over Na_2SO_4, and evaporated under vacuum. Addition of dichloromethane to the white solid resulted in the dissolution of only a portion of the material. The solvent was separated from the insoluble material, and the resulting white solid was washed with more dichloromethane. The white solid (29 mg) was not soluble in any organic solvents, and LR mass spectroscopy indicated it was most likely bis-mercurated. The solvent was stripped from the material that remained in solution, and recrystallization of the resulting yellow-white powder from dichloromethane/petroleum ether afforded the title monomercurated pyrrole as white crystals (57 mg, 15% yield), mp >300 °C. ^1H NMR ($CDCl_3$): δ 2.16 (s, 3 H, ring methyl), 3.80 and 3.97 (each s, 3 H, NMe and OCH_3), 6.83 (s, 1 H, β-H); no α-proton was detected by NMR spectroscopy.

Deuterated Methyl 1,4-Dimethylpyrrole-2-carboxylate (36). To a cooled solution (0 °C) of MeOD (1 mL) and $NaBD_4$ (25 mg) was added the foregoing pyrrole **35** in dimethyl sulfoxide (3 mL). After 15 min the solution was diluted with dichloromethane, washed three times with water and once with brine, and then dried over Na_2SO_4, and the solvent was removed under vacuum. ^1H NMR ($CDCl_3$): δ 2.05 (s, 3 H, ring methyl), 3.79 and 3.85 (each s, 3 H, NMe and OCH_3), 6.73 (s, 0.94 H, β-H), 6.56 (s, 0.10 H, α-H).

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