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Total Synthesis of Pyrrolnitrin. IX.[1] Synthesis of Dialkyl 3-Aryl-2,5-pyrroledicarboxylates and Alkyl β-Aryl-5-methyl-2-pyrrolecarboxylates

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Synthetic methods of dialkyl 3-aryl-2,5-pyrroledicarboxylates (VI) and alkyl β-aryl-5-methyl-2-pyrrolecarboxylates, intermediates to pyrrolnitrin (I), were investigated. VI were prepared by introduction of an ethoxycarbonyl group to ethyl 3-aryl-2-pyrrolecarboxylate (III) and by condensation of arylglyoxals with dimethyl acetyliminodiacetate. Alkyl β-aryl-5-methyl-2-pyrrolecarboxylates were prepared by methylation of alkyl β-aryl-2-pyrrolecarboxylates and by introduction of a methoxycarbonyl group to 2-methyl-3-arylpyrrole.

For the total synthesis of pyrrolnitrin (I),[3] β-arylpyrroles (II) substituted at both α-positions seemed to be favorable intermediates to I.

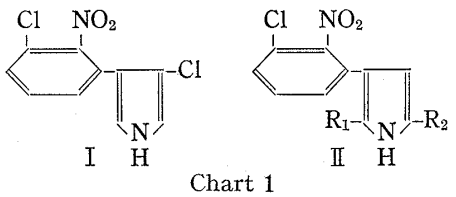

Chart 1

For this purpose alkoxycarbonyl and methyl groups were considered to be suitable protecting substituents in these intermediates.

In the second[4] and third Parts[5] of this series, synthesis of the β-arylpyrrole (II: R_1=$COOC_2H_5$, R_2=CH_3) was reported, and in Part VII[6] synthesis of II (R_1=R_2=CH_3) was described.

In this paper we wish to report on the syntheses of β-arylpyrroles (II: R_1=R_2=COOR, R_1=CH_3, R_2=$COOCH_3$) and the related compounds.

First, synthetic methods of β-arylpyrrole (II: R_1=R_2=COOR) were investigated. Introduction of a formyl group was examined by Vilsmeier reaction to the 5-position of ethyl 3-(2-nitro-3-chlorophenyl)-2-pyrrolecarboxylate (III), which was prepared by a new method of pyrrole ringclosure as reported in Part VIII.[1]

Ethyl 3-(2-nitro-3-chlorophenyl)-5-formyl-2-pyrrolecarboxylate (IV) could be obtained in excellent yield under stronger reaction condition than used for the formylation of ethyl 3-(2-nitro-3-chlorophenyl)-5-methyl-4-pyrrolecarboxylate (VIII).

This difference was consistent with the fact that strong Ehrlich reaction was shown by VIII but it was negative in III. The negative Ehrlich reaction is supposed to show a deficient reactivity to the electrophilic reaction.

The 4-formyl isomer was supposedly difficult to be produced owing to the steric hindrance of 3-(*o*-substituted)-phenyl group, and a little amount of 4-formyl isomer, if any mixed, could be removed by a single recrystallization.

5-Formyl compound (IV) was oxidized to 2-ethoxycarbonyl-3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxylic acid (V) by potassium permanganate or silver oxide. And the following

1) Part VIII: K. Tanaka, K. Kariyone and S. Umino, *Chem. Pharm. Bull.* (Tokyo), **17**, 611 (1969).
2) Location: *1, Kashimacho, Higashiyodogawa-ku, Osaka.*
3) K. Arima, H. Imanaka, M. Kousaka, and A. Fukuta, *Agr. Biol. Chem.*, **28**, 575 (1964).
4) Part II: *Chem. Pharm. Bull.* (Tokyo), **17**, 567 (1969).
5) Part III: *Chem. Pharm. Bull.* (Tokyo), **17**, 576 (1969).
6) Part VII: *Chem. Pharm. Bull.* (Tokyo), **17**, 605 (1969).

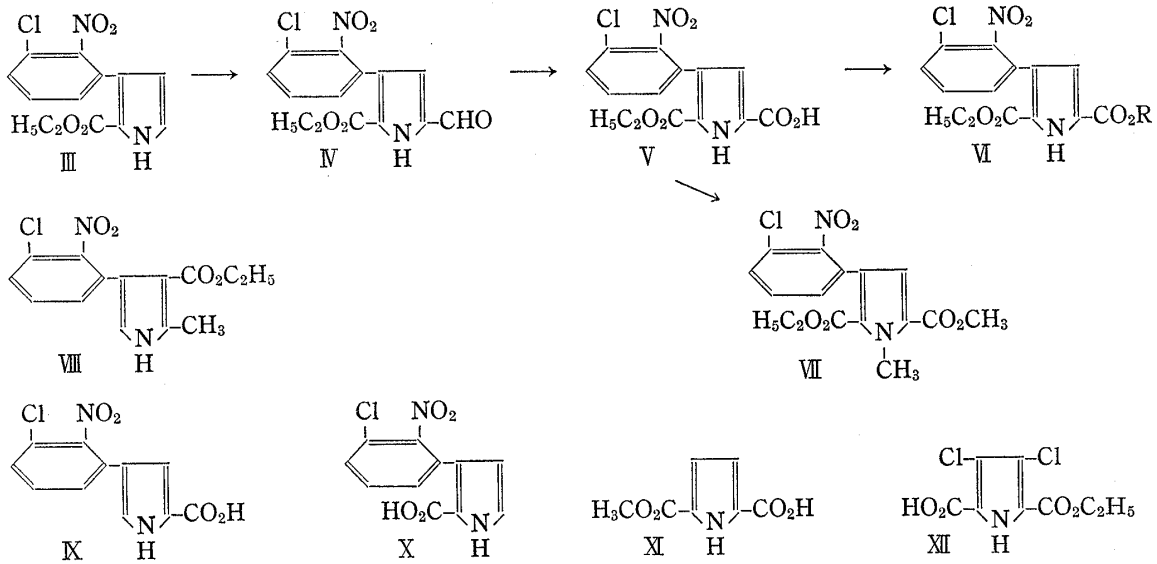

Chart 2

interesting observation was made on an esterification of this half ester (V): treatment of V with etherial solution of diazomethane afforded the N-methylated ester (VII) instead of the expected dicarboxylic ester (V). However, esterification of the pyrrolecarboxylic acids (IX, X) and the halfester (XI) with diazomethane showed no sign of such N-methylation, although similar N-methylation has been reported[7] on esterification of XII with diazomethane.

This unusual N-methylation can be rationalized by considering the activation of an imino group of a pyrrole ring by electron–attracting groups from these data.

The desired diethyl 3-(2-nitro-3-chlorophenyl)-2,5-pyrroledicarboxylate (VI: R=C_2H_5) could be obtained by esterification in boiling ethanol containing hydrogen chloride.

Structure of this dicarboxylic ester (VI: R=C_2H_5) was ascertained by converting this, by chlorination at the 4-position, to known diethyl 3-(2-nitro-3-chlorophenyl)-4-chloro-2,5-pyrroledicarboxylate, which will be reported in Part X.[8]

Further investigation on synthesis of the 2,5-pyrroledicarboxylic ester was tried as in the following way.

Friedman[9] and Dimroth[10] have reported the synthesis of 3,4-diphenyl-2,5-pyrroledicarboxylate (XV) by condensation of benzil (XIII) with dimethyl acetyliminodiacetate (XIV).

An attempt was made to substitute benzil (XIII) by the glyoxal (XVI) in this reaction.

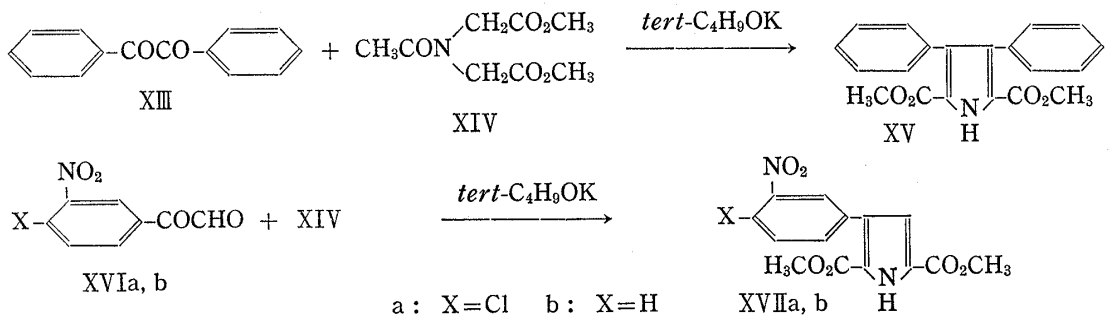

Chart 3

7) P. Hodge and R.W. Rickards, *J. Chem. Soc.*, **1965**, 459.
8) Part X: *Chem. Pharm. Bull.* (Tokyo), **17**, 622 (1969).
9) M. Friedman, *J. Org. Chem.*, **30**, 859 (1965).
10) K. Dimroth and N. Pintschovius, *Ann. Chem.*, **639**, 102 (1961).

After some examination of reaction conditions, dimethyl 3-aryl-2,5-pyrroledicarboxylates (XVIIa,b) were obtained by condensation of glyoxals (XVIa,b) with dimethyl acetyliminodiacetate (XIV) in the presence of potassium *tert*-buthoxide in *tert*-butanol at −30°.

However, yields were poor in these reactions accompanied with production of a large quantity of tarry materials owing to the unusual instability of glyoxals (XVIa,b) under this reaction condition.

Then we turned to the investigation of a synthetic method of β-arylpyrroles (II), in which R_1 and R_2 were methyl and alkoxycarbonyl groups.

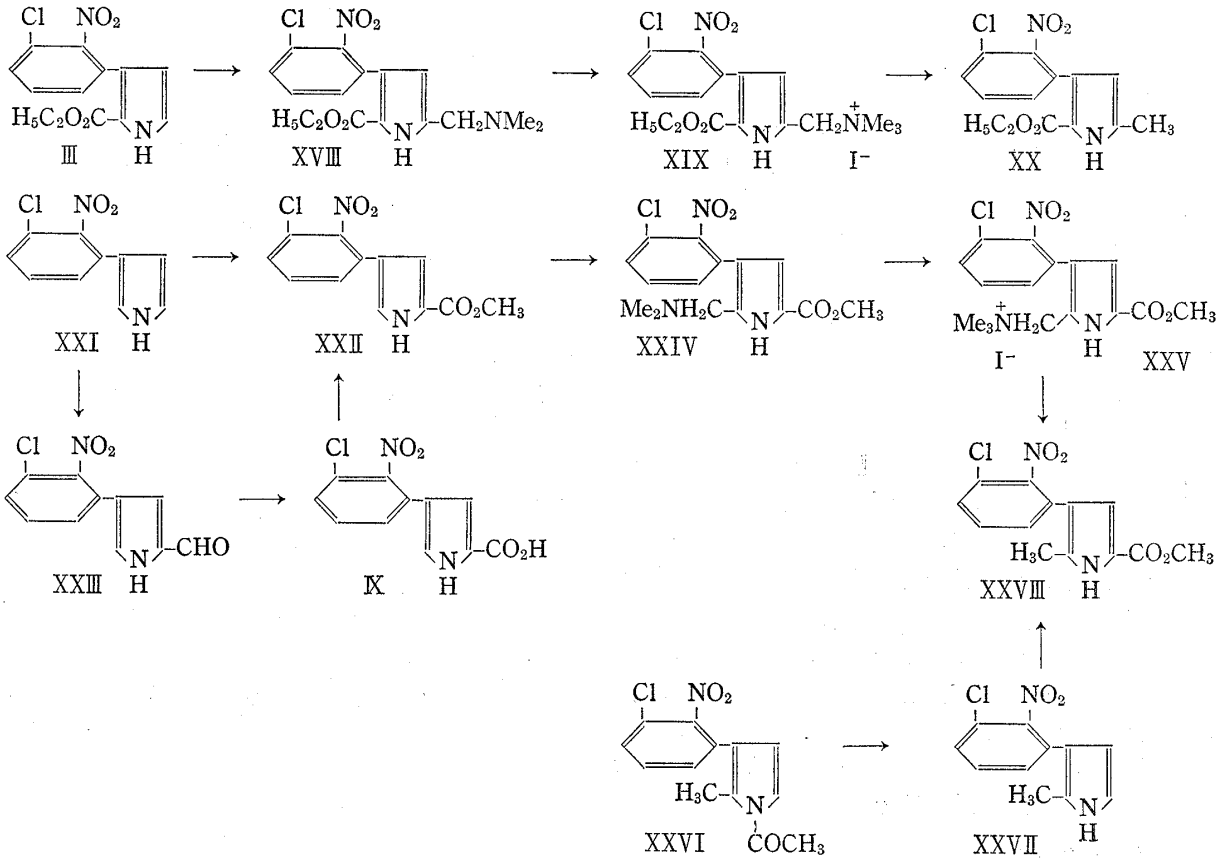

Chart 4

3-(2-Nitro-3-chlorophenyl)pyrrole (XXI), prepared by a new method of pyrrole ring-closure in Part VIII,[1] was treated with phosgene followed by methanol to give methyl 3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxylate (XXII), which was found to be contaminated with an isomer, methyl 3-(2-nitro-3-chlorophenyl)-2-pyrrolecarboxylate (methyl ester of X), by the nuclear magnetic resonance (NMR).

Pure XXII was obtained by the following sequence of reactions: formylation of the pyrrole (XXI) by Vilsmeier reaction gave 3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxaldehyde (XXIII), and XXIII was oxidized with silver oxide to 3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxylic acid (IX), which was converted to a pure ester (XXII) with an etherial solution of diazomethane.

In Vilsmeier reaction of XXI, formation of 3-(2-nitro-3-chlorophenyl)-2-pyrrolecarboxaldehyde, isomeric with XXIII, was not observed. The difference between this reaction and that using phosgene in the formation of the isomer is explained from comparing the bulkiness of intermediates in both reactions.

Then introduction of the methyl group was examined, using Mannich reaction, to methyl 3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxylate (XXII), and to ethyl 3-(2-nitro-3-chlorophenyl)-2-pyrrolecarboxylate (III) described before.

As in the case of Vilsmeier reaction of III, Mannich bases, XVIII and XXIV, could be obtained under much stronger reaction conditions than that used for VIII.

These Mannich bases, XVIII and XXIV, when treated with methyl iodide in ethanol, gave the corresponding methiodides, XIX and XXV, which were reduced with sodium borohydride to ethyl 3-(2-nitro-3-chlorophenyl)-5-methyl-2-pyrrolecarboxylate (XX)[11] and methyl 2-methyl-3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxylate (XXVIII) respectively.

XXVIII could be also prepared by an alternate route as in the following way: hydrolysis of 1-acetyl-2-methyl-3-(2-nitro-3-chlorophenyl)pyrrole (XXVI), prepared as described in Part VIII,[1] afforded 2-methyl-3-(2-nitro-3-chlorophenyl)pyrrole (XXVII), which was treated with phosgene followed by methanol to produce XXVIII in good yield.

Conversion of pyrroles (II), prepared in this paper, to pyrrolnitrin (I) will be described in Part X.[8]

Experimental[12]

Ethyl 3-(2-Nitro-3-chlorophenyl)-5-formyl-2-pyrrolecarboxylate (IV)——$POCl_3$ (4 g) was mixed with dimethylformamide (6 g) and the resulting solution was stirred at 60° for 10 min. To this solution was added powdered ethyl 3-(2-nitro-3-chlorophenyl)-2-pyrrolecarboxylate (III) (1 g) and the mixture was stirred at 95° for 4 hr. After cooling, $AcONa \cdot 3H_2O$ (36 g) and ice (48 g) were added and the mixture was stirred on a warm water bath for 30 min. The precipitated solid was filtered and dissolved in AcOEt. The AcOEt solution was washed with aqueous $NaHCO_3$ and H_2O, dried and evaporated to give a brown solid (1 g). Recrystallization from AcOEt-*n*-hexane yielded IV (0.7 g), mp 139—141°. Further recrystallization raised the melting point to 144—145°. *Anal.* Calcd. for $C_{14}H_{11}O_5N_2Cl$: C, 52.10; H, 3.44; N, 8.68; Cl, 10.99. Found: C, 51.81; H, 3.52; N, 8.79; Cl, 11.02. IR (nujol) cm^{-1}: 3250 (NH), 1707, 1678 ($COOC_2H_5$, CHO), 1531., 1362 (NO_2).

2-Ethoxycarbonyl-3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxylic Acid (V)——i) With $KMnO_4$: To a cooled suspension of (IV) (0.7 g) and NaOH (0.25 g) in H_2O (40 ml) was added with stirring a solution of $KMnO_4$ (0.34 g) in H_2O (10 ml) over a period of 2 hr. Stirring was continued overnight in an ice-H_2O bath and precipitated MnO_2 was filtered off. The filtrate was acidified with HCl and extracted with AcOEt. The AcOEt solution was extracted several times with chilled aqueous NaOH and H_2O. From the AcOEt solution, the starting material (IV) (0.12 g) was recovered. The alkaline extracts and washings were combined, acidified with HCl and extracted with AcOEt. The AcOEt extracts were washed with H_2O, dried and evaporated to give a crude V (0.55 g), mp 260° (decomp.). This crude V was shown by IR to contain a small amount of 3-(2-nitro-3-chlorophenyl)-2,5-pyrroledicarboxylic acid.

ii) With Ag_2O in Aqueous NaOH: To a cooled suspension of IV (0.5 g) in abs. EtOH (7 ml) was added with stirring Ag_2O (prepared from 0.53 g of $AgNO_3$) in an ice-H_2O bath, followed by dropwise addition of NaOH (0.25 g) dissolved in H_2O (10 ml). Stirring was continued at this temperature for 2 ½ hr and then at room temperature for 13 hr. The suspension was filtered and the solid was washed with H_2O. The filtrate and washings were combined, acidified with HCl and extracted with AcOEt. The AcOEt extracts were worked up in the similar manner as in i), to give V (0.45 g), mp 275° (decomp.). Recrystallization from AcOH yielded colorless crystals, mp 290° (decomp.). IR (nujol) cm^{-1}: 3240 (NH), 1706, 1674 ($COOC_2H_5$, COOH), 1531, 1365 (NO_2).

Reaction of the Half Ester (V) with CH_2N_2——To a suspension of V (0.1 g) in ether was added dropwise a large excess of ethereal solution of CH_2N_2, and the solution was allowed to stand overnight. Excess CH_2N_2 was decomposed with AcOH. The solution was washed with aqueous $NaHCO_3$, dried and evaporated to give a colorless solid (0.09 g), mp 134—140°. Recrystallization from EtOH yielded colorless crystals, mp 144—145°, which was assigned to be N-methylated compound (VII) by IR and NMR. *Anal.* Calcd. for $C_{16}H_{15}O_6N_2Cl$: C, 52.39; H, 4.13; N, 7.64; Cl, 9.67. Found: C, 52.51; H, 4.21; N, 7.59; Cl, 9.92. IR (nujol) cm^{-1}: 1727, 1702 ($COOC_2H_5$, $COOCH_3$), 1532, 1371 (NO_2). NMR ($CDCl_3$) ppm: 0.95 (3H, triplet, OCH_2-$C\underline{H}_3$), 3.97 (3H, singlet, $COOCH_3$), 4.20 (2H, quartet, $COOC\underline{H}_2CH_3$), 4.39 (3H, singlet, NCH_3).

Diethyl 3-(2-Nitro-3-chlorophenyl)-2,5-pyrroledicarboxylate (VI: $R=C_2H_5$)——A stream of dry HCl was passed through a boiling solution of V (0.5 g) in abs. EtOH (50 ml) for 11 hr. Most of EtOH was removed *in vacuo*, H_2O was added and the mixture was extracted with AcOEt. The AcOEt extracts were washed with dil. aqueous NaOH and H_2O, dried and evaporated to dryness. Recrystallization from EtOH gave

11) This was identified with a sample prepared in Part II.

12) All melting points are uncorrected. The infrared spectra were recorded on a Hitachi EPI S2. The nuclear magnetic resonance spectra were measured with a Varian A-60 spectrometer using tetramethylsilane as an internal standard.

colorless crystals (VI: R=C_2H_5) (0.4 g), mp 127—128°. Further recrystallization raised the melting point to 131—132°. *Anal.* Calcd. for $C_{16}H_{15}O_6N_2Cl$: C, 52.39; H, 4.13; N, 7.64; Cl, 9.67. Found: C, 52.23; H, 4.42; N, 7.77; Cl, 9.83. IR (nujol) cm^{-1}: 3290 (NH), 1720, 1691 ($COOC_2H_5$), 1534, 1371 (NO_2).

3-Nitro-4-chlorophenylglyoxal (XVIa)——To a warm solution of SeO_2 (1.1 g) and H_2O (0.2 ml) in dioxane (6 ml) was added with stirring 3-nitro-4-chloroacetophenone (2 g) in one portion at 55°. Stirring was continued at 120° (bath temp.) for 4 hr. After cooling, precipitated Se was filtered off and the filtrate was evaporated *in vacuo*. The residue was distilled under *vacuum* giving a yellow oil (XVIa) (1.9 g), bp 130—132°, (0.7 mmHg), which solidified on standing. *Anal.* Calcd. for $C_8H_4O_4NCl$: C, 44.98; H, 1.89; N, 6.56. Found: C, 44.47; H, 2.55; N, 6.50.

Dimethyl 3-(3-Nitro-4-chlorophenyl)-2,5-pyrroledicarboxylate (XVIIa)——A solution prepared from metallic potassium (1 g) and abs. *tert*-BuOH (30 ml) was diluted with abs. ether (20 ml) and cooled to −30° in a MeOH–dry-ice bath. To this was added dropwise with stirring a solution of XVIa (1.5 g) and dimethyl acetyliminodiacetate (XIV) (2.1 g) in abs. tetrahydrofuran (15 ml) at −30° during 1½ hr. Stirring was continued at −30——20° for 4 hr and then the reaction mixture was allowed to stand overnight at this temperature. After most solvents were removed *in vacuo*, H_2O was added and the mixture was extracted with ether. The ether extracts were washed with H_2O, dried and evaporated to give a pale brown solid (0.4 g). This was purified by trituration in hot *n*-hexane and by recrystallization from MeOH to give colorless crystals (XVIIa) (0.05 g), mp 181—182°. *Anal.* Calcd. for $C_{14}H_{11}O_6N_2Cl$: C, 49.46; H, 3.06; N, 8.54; Cl, 10.54. Found: C, 49.64; H, 3.28; N, 8.27; Cl, 10.47. IR (nujol) cm^{-1}: 3300 (NH), 1705 ($COOCH_3$), 1526, 1352 (NO_2).

Dimethyl 3-(3-Nitrophenyl)-2,5-pyrroledicarboxylate (XVIIb)——To a stirred solution prepared from potassium (2 g), abs. *tert*-BuOH (60 ml) and abs. ether (40 ml), was added dropwise a solution of *m*-nitrophenylglyoxal (XVI b) (3 g) and XIV (5 g) in abs. tetrahydrofuran (30 ml) at −30° during 1½ hr. The reaction mixture was worked up in the similar manner as in the preparation of XVIIa. Twice recrystallizations of the crude product from MeOH yielded colorless crystals (XVIIb) (0.15 g), mp 182—185°. *Anal.* Calcd. for $C_{14}H_{12}O_6N_2$: C, 55.26; H, 3.98; N, 9.21. Found: C, 55.26; H, 4.13; N, 9.19. IR (nujol) cm^{-1}: 3260 (NH), 1705 ($COOCH_3$), 1523, 1345 (NO_2).

Ethyl 3-(2-Nitro-3-chlorophenyl)-5-dimethy aminomethyl-2-pyrrolecarboxylate (XVIII)——A mixture of ethyl 3-(2-nitro-3-chlorphenyl)-2-pyrrolecarboxylate (III) (0.6 g), 36% formalin (0.8 ml), $Me_2NH \cdot HCl$ (0.7 g) and AcONa (0.7 g) in glacial AcOH (12 ml) was stirred at 95° (bath temp.) for 17 hr. After most AcOH was removed *in vacuo*, H_2O was added, the mixture was made strongly alkaline with powdered K_2CO_3 and extracted with AcOEt. The AcOEt extracts were washed with H_2O, dried and evaporated to give a pale yellow solid (0.7 g). Recrystallization from benzene-*n*-hexane yielded colorless crystals (XVIII) (0.55 g), mp 150—151°. Further recrystallization raised the melting point to 154—156°. *Anal.* Calcd. for $C_{16}H_{18}O_4N_3Cl$: C, 54.62; H, 5.17; N, 11.95; Cl, 10.08. Found: C, 54.91; H, 5.10; N, 11.87; Cl, 10.10. IR (nujol) cm^{-1}: 3270 (NH), 1685 ($COOC_2H_5$), 1532, 1366 (NO_2).

Ethyl 3-(2-Nitro-3-chlorophenyl)-5-methyl-2-pyrrolecarboxylate (XX)——A solution of the Mannich base (XVIII) (0.4 g) and CH_3I (1 ml) in abs. MeOH (2 ml) was allowed to stand overnight, and evaporated to dryness to give a colorless solid (0.55 g). Twice recrystallizations of a part of this solid from EtOH gave colorless crystals of the methiodide (XIX), mp 228—230° (decomp.). *Anal.* Calcd. for $C_{17}H_{21}O_4N_3ClI$: C, 41.35; H, 4.30; N, 8.51. Found: C, 41.56; H, 4.32; N, 8.64.

To a stirred solution of the crude XIX (0.45 g) in abs. EtOH (10 ml) was added $NaNH_4$ (0.1 g) at 50—60° (bath temp.), and stirring was continued at this temperature for 30 min. After cooling, the reaction solution was diluted with H_2O, acidified with HCl and the mixture was extracted with ether. The ether extracts were washed with H_2O, dried and evaporated to give a colorless solid (XX) (0.25 g), mp 217—219°. Recrystallization from benzene yielded colorless crystals, mp 219—221°, which showed no mixed melting point depression with a sample prepared in Part II[4]. *Anal.* Calcd. for $C_{14}H_{13}O_4N_2Cl$: C, 54.46; H, 4.25; N, 9.08; Cl, 11.48. Found: C, 54.38; H, 4.37; N, 9.23; Cl, 11.55.

3-(2-Nitro-3-chlorophenyl)-5-pyrrolecarboxaldehyde (XXIII)——3-(2-nitro-3-chlorophenyl)pyrrole (XXI) (0.5 g) was added to a warm solution of $POCl_3$ (1.1 g) in dimethylformamide (3.3 ml). The reaction mixture was stirred at room temperature for 1 hr, at 40° for 1 hr and then at 60° for 2 hr. After cooling, a mixture of $AcONa \cdot 3H_2O$ (9 g) and ice (12 g) was added, and the reaction mixture was warmed at 60° for 30 min. The reaction mixture was warmed at 60° for 30 min. The precipitated solid was filtered, washed wtih H_2O and dissolved in AcOEt. The AcOEt solution was washed with aqueous $NaHCO_3$, dried and evaporated, leaving a yellow solid (0.56 g). After trituration with hot benzene and filtration, yellow crystals (XXIII) (0.4 g), mp 223—225°, was obtained. Further recrystallization raised the melting point to 224—225°. *Anal.* Calcd. for $C_{11}H_{17}O_3N_2Cl$: C, 52.70; H, 2.82; N, 11.18; Cl, 14.15. Found: C, 52.79; H, 2.52; N, 11.44; Cl, 14.13. IR (nujol) cm^{-1}: 3250 (NH), 1653 (CHO), 1532, 1378 (NO_2).

3-(2-Nitro-3-chlorophenyl)-5-pyrrolecarboxylic Acid (IX)——To a stirred suspension of XXIII (1.05 g) in abs. EtOH (20 ml) was added under ice-cooling Ag_2O (prepared from 1.5 g of $AgNO_3$), followed by dropwise addition of NaOH (0.72 g) dissolved in H_2O (6 ml). Stirring was continued at room temperature for 24 hr and precipitated Ag and unreacted Ag_2O were filtered off. The filtrate was diluted with H_2O, acidified with HCl and extracted with AcOEt. Acidic materials were extracted with dil. aqueous NaOH, acidified with

HCl and extracted with AcOEt. The AcOEt extracts were washed with H_2O, dried and evaporated to give a crude IX (0.83 g), mp 277°. A part of this was recrystallized from AcOEt to yield pale yellow crystals, mp 286° (decomp.). *Anal.* Calcd. for $C_{11}H_7O_4N_2Cl$: C, 49.54; H, 2.65; N, 10.51; Cl, 13.30. Found: C, 49.73; H, 2.84; N, 10.78; Cl, 13.08. IR (nujol) cm^{-1}: 3370 (NH), 1677 (COOH), 1538, 1380 (NO_2).

Methyl 3-(2-Nitro-3-chlorophenyl)-5-pyrrolecarboxylate (XXII)——i) From 3-(2-Nitro-3-chlorophenyl)-pyrrole (XXI): To a solution of phosgene (4 g) in dry benzene (20 ml), was added XXI (0.5 g) and dimethylaniline (0.5 g). The solution was stirred and refluxed for 1½ hr. Then the reaction mixture was treated with abs. MeOH (10 ml), and stirred at 50° for ½ hr. Most of the solvents were removed *in vacuo* and the residue was dissolved in ether. The ether solution was washed with dil. HCl, aqueous $NaHCO_3$ and H_2O, dried and evaporated to give a yellow oil (0.6 g). This was chromatographed on a silicagel column using benzene as eluent and at first, the starting material (XXI) (0.1 g) was obtained, followed by colorless crystals (0.4 g), mp 141—150°. Recrystallization of this from benzene did not make mp sharp. Judging from mp, IR and NMR, this product was assumed to be a mixture of XXII and the methyl ester of X, in which XXII predominated. *Anal.* Calcd. for $C_{12}H_9O_4N_2Cl$: C, 51.34; H, 3.24; N, 9.98; Cl, 12.63. Found: C, 51.40; H, 3.26; N, 9.94; Cl, 12.87. IR (nujol) cm^{-1}: 3230 (NH), 1668 ($COOCH_3$), 1530, 1367 (NO_2). NMR ($CDCl_3$) ppm: 3.80 (singlet, $COOCH_3$), 3.98 (singlet, $COOCH_3$).

ii) From 3-(2-Nitro-3-chlorophenyl)-5-pyrrolecarboxylic Acid (IX): To a suspension of crude IX (0.25 g) in ether was added dropwise a solution of excess CH_2N_2 in ether. After standing overnight, excess CH_2N_2 was decomposed and the resulting solution was washed with aqueous $NaHCO_3$ and H_2O, dried and evaporated to give a colorless solid (0.25 g), mp 150—152°. Recrystallization from CCl_4 yielded colorless crystals (XXII) (0.2 g), mp 155—156°. Further recrystallization raised the melting point to 156—158°. *Anal.* Calcd. for $C_{12}H_9O_4N_2Cl$: C, 51.34; H, 3.24; N, 9.98; Cl, 12.63. Found: C, 51.55; H, 3.27; N, 9.86; Cl, 12.81. IR (nujol) cm^{-1}: 3330 (NH), 1690 ($COOCH_3$), 1542, 1375 (NO_2).

Methyl 2-Dimethylaminomethyl-3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxylate (XXIV)——A mixture of XXII (1.55 g), $Me_2NH \cdot HCl$ (2.8 g), AcONa (2.4 g) and 36% formalin (2.8 ml) in glacial AcOH (30 ml) was stirred for 3 hr and then allowed to stand at 95° (bath temp.) for 40 hr. The reaction mixture was worked up in the similar manner as in the preparation of (XVIII) to give a crude solid (XXIV) (1.3 g). Recrystallization from AcOEt–*n*-hexane yielded colorless crystals (1 g), mp 165°. Further recrystallization from benzene raised the melting point to 169—170°. *Anal.* Calcd. for $C_{15}H_{16}O_4N_3Cl$: C, 53.33; H, 4.78; N, 12.44. Found: C, 53.54; H, 4.91; N, 12.59. IR (nujol) cm^{-1}: 3320 (NH), 1706 ($COOCH_3$), 1538, 1372 (NO_2).

2-Methyl-3-(2-nitro-3-chlorophenyl)pyrrole (XXVII)——A solution of 1-acetyl-2-methyl-3-(2-nitro-3-chlorophenyl)pyrrole (XXVI) (0.75 g) and NaOH (1 g) in H_2O (10 ml) and 95% EtOH (30 ml) was refluxed for 1 hr. The reaction mixture was diluted with H_2O and extracted with ether. The ether extracts were dried and evaporated to give a yellow solid (0.6 g). Recrystallization from CCl_4–*n*-hexane yielded yellowish crystals (XXVII) (0.4 g), mp 102.5—103°. *Anal.* Calcd. for $C_{11}H_9O_2N_2Cl$: C, 55.82; H, 3.84; N, 11.84; Cl, 14.98. Found: C, 56.02; H, 3.78; N, 11.75; Cl, 15.02. IR (nujol) cm^{-1}: 3460 (NH), 1540, 1373 (NO_2).

Methyl 2-Methyl-3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxylate (XXVIII)——i) From Methyl 2-dimethylaminomethyl-3-(2-nitro-3-chlorophenyl)-5-pyrrolecarboxylate (XXIV): A solution of XXIV (0.35 g) and CH_3I (2 ml) in abs. EtOH (3 ml) was allowed to stand overnight. The solution was diluted with abs. ether and precipitated crystals were collected to give XXV (0.45 g), mp 210—214°. Recrystallization from EtOH raised the melting point to 231° (decomp.). *Anal.* Calcd. for $C_{16}H_{19}O_4N_3ClI$: C, 40.05; H, 4.00; N, 8.76. Found: C, 39.96; H, 4.10; N, 8.69. XXV (0.4 g) was dissolved in abs. EtOH (40 ml) and the solution was stirred and warmed to 60°. Then $NaBH_4$ (0.05 g) was added to this solution, and stirring was continued at 50—60° for 1½ hr. Most of EtOH was removed *in vacuo*, and dil. HCl was added to the residue and the mixture was extracted with ether. The extracts were washed with H_2O, dried and evaporated to leave a colorless solid (XXVIII) (0.28 g). Recrystallization from benzene yielded colorless crystals (0.24 g), mp 186—187°. Further recrystallization raised the melting point to 187.5—188.5°. *Anal.* Calcd. for $C_{13}H_{11}O_4N_2Cl$: C, 52.98; H, 3.77; N, 9.51. Found: C, 52.81; H, 3.70; N, 9.58.

ii) From 2-Methyl-3-(2-nitro-3-chlorophenyl)pyrrole (XXVII): Dry $COCl_2$ was bubbled gently through a solution of XXVII (0.1 g) and dimethylaniline (0.1 g) in abs. benzene (17 ml) for 10 min. The solution was refluxed with stirring for 1.5 hr, and then abs. MeOH (5 ml) and dimethylaniline (0.1 g) was added. After stirring and refluxing were continued for an hr, most of MeOH was removed *in vacuo* and the residue was dissolved in ether. The ether solution was washed with dil. HCl, aqueous $NaHCO_3$ and H_2O, and evaporated to dryness. Recrystallization of the residue from benzene–*n*-hexane yielded pale yellow crystals (XXVIII) (0.1 g), mp 191—192°, which showed no mixed melting point depression with a sample from i).