Synthesis of Some 2-Phenylpyrrole Derivatives

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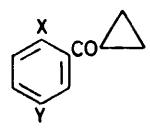
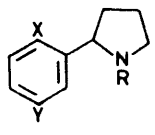
We have made and converted some aryl cyclopropyl ketones (1) into 2-arylpyrrolidines (2) and hence to the 1-pyrrolines (3), the 3-bromo-1-pyrrolines (3d) and to the corresponding 2-arylpyrroles (4). An alternative route *via* the reaction of alkynes with aryloxazolones has been improved.

In particular, substituted 2-(2-methoxyphenyl)pyrroles have been made, also some chloro-analogues (5b, c) of the bromine-containing marine antibiotic, 3,4,5-tribromo-2-(3,5-dibromo-2-hydroxyphenyl)pyrrole (5d).

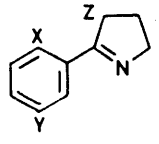
2-ARYLPYRROLIDINES (2)[1] have been made by the reaction of aryl cyclopropyl ketones (1) with formamide. We have been able to aromatize these pyrrolidines and isolate the intermediate pyrrolines (3), thus providing a new route to 2-arylpyrroles (4). In particular, we made 2-phenylpyrrole (4a), shown to be identical with an authentic sample, also pyrroles (4b).



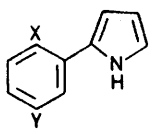
(1) a; X = OH, Y = Hal
b; X = Y = H
c; X = MeO, Y = Hal



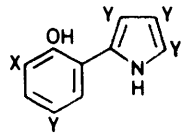
(2) a; R = CHO
b; R = H
c; R = Cl



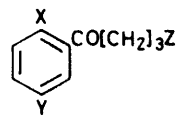
(3) a; X = Y = Z = H
b; X = MeO, Y = Cl, Z = H
c; X = MeO, Y = Br, Z = H
d; Z = Br
e; Z = MeO



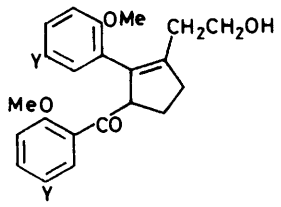
(4) a; X = Y = H
b; X = MeO, Y = Hal
c; X = MeO, Y = Cl
d; X = MeO, Y = Br



(5) a; X = Y = H
b; X = H, Y = Cl
c; X = Y = Cl
d; X = Y = Br



(6) a; Z = Cl
b; X = MeO, Y = Hal, Z = Cl
c; X = HO, Y = Hal, Z = Cl
d; X = MeO, Y = Hal, Z = OH
e; X = Z = OH, Y = Br



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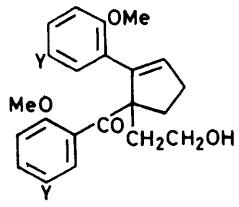

(8)

The cyclopropyl ketones (1) were first prepared by cyclisation of the chloro-ketones (6a) with base.[2] Side reactions were demethylation of the chloro-ketone (6b) to the phenol (6c), hence giving the ketone (1a); hydrolysis of the chloro-ketone (6b) to the hydroxy-ketone (6d); bimolecular condensation and hydrolysis giving the oxo-alcohol (7) or (8), the former structure being more likely, from the chemical shifts in the n.m.r. spectrum. Improved yields of ketones (1) were obtained using cyclopropyl carbonyl chloride.[3]

The 2,4-dihalogenoanisoles did not give aryl ketones by either route, demethylation taking precedence.[4-6]

The cyclopropyl ketones were converted into the formylpyrrolidines (2a) which were hydrolysed to the free amines (2b). Some of our amines contained halogen

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[2] W. J. Close, *J. Amer. Chem. Soc.*, 1957, **79**, 1455.
[3] N. Kishner, *Zhur. fiz-Khim.*, 1911, **43**, 1163.
[4] C. J. Schoot and K. H. Klaassens, *Rec. Trav. chim.*, 1956, **75**, 190.
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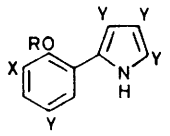
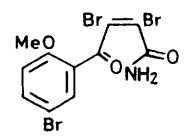
so we avoided catalytic dehydrogenation [7] and achieved aromatization *via* the pyrrolines (3) obtained by several methods, *e.g.* treatment of amides (2a) with *N*-bromosuccinimide in aqueous dioxan. In carbon tetrachloride with peroxide initiator, the pyrrolines were accompanied by some of the bromopyrrolines (3d). The same products were obtained from the free pyrrolidines (2b) but the most satisfactory method [8] was to form the chloroamines (2c) which were treated *in situ* with base to give good yields of the pyrrolines (3a—c).

Dehydrogenating agents such as quinones or selenium [9] were not effective in aromatizing our pyrrolines. We therefore converted them into the bromo-derivatives (3d) which were formed in almost quantitative yield. These compounds were characterized as their picrates since they were themselves unstable but gave the desired pyrroles (4a—d) on treatment with alkali.

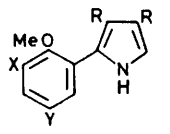
Chlorination of 2-(5-chloro-2-methoxyphenyl)pyrrole (4c) fully substituted then overchlorinated the pyrrole ring before attacking the 3-position of the phenyl ring. Subsequent demethylation of the tetrachloro-ether (9a) gave 3,4,5,5′-tetrachloropseudilin (9b).



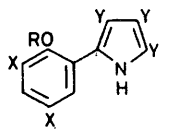
(9) a; R = Me, X = H, Y = Cl
b; R = X = H, Y = Cl
c; R = Me, X = H, Y = Br



(10)



(11) a; R = CO_2Et
b; R = CO_2Et, X = Y = Cl
c; R = CO_2H
d; R = X = Y = H



(12) a; R = Me, X = Cl, Y = H
b; R = Me, X = Y = Cl
c; R = H, X = Y = Cl
d; R = Me, X = Br, Y = H

Bromination of 2-(5-bromo-2-methoxyphenyl)pyrrole (4d) followed the same pattern. The resulting 2-(5-bromo-2-methoxyphenyl)-3,4,5-tribromopyrrole (9c), on storage, underwent photo-oxidation to 2,3-dibromo-4-(5-bromo-2-methoxyphenyl)-4-oxobut-2-enamide (10). This reaction is typical of halogenated 2-(2-methoxyphenyl)pyrroles.

We have improved the synthesis of phenylpyrroles from benzoylglycines. Cyclisation using dicyclohexylcarbodi-imide followed by reaction of the oxazolones with acetylenedicarboxylic ester gives the pyrrole esters (11a). By this route we also made 2-phenylpyrrole and showed it to be identical with the sample obtained by our pyrrolidine route.

In particular, we made the dichloro-ester (11b) and hence the diacid (11c) and the pyrrole (12a). The latter compound on chlorination and demethylation gave the chlorine analogue (12c) of pentabromopseudilin, the marine antibiotic.[10,11]

Preliminary microbiological assays indicate that pentachloropseudilin is more active against *S. aureus* and *Tricophyton* strains than the chloropyrrole antibiotic of *P. aeruginosa*, pyoluteorin.[12]

EXPERIMENTAL

M.p.s were taken on a Kofler hot-stage apparatus and are uncorrected. ^1H N.m.r. spectra were taken on a JEOL Co. C60H spectrometer with JRAI accumulator for solutions in $CDCl_3$ containing 1% tetramethylsilane. I.r. spectra were run in Nujol on a Unicam SP 200 or Perkin-Elmer 237 instrument. U.v. spectra were taken on a Unicam SP 800 spectrometer, 1-cm cells (ethanol). Mass spectra were run on our A.E.I. M.S. 12 instrument or the M.S. 9 (high resolution machine) at the University of Toronto, courtesy of Professor A. G. Harrison (t = probe temp. in °C).

Aryl 3-Chloropropyl Ketones (6).—Anhydrous aluminium chloride (9 g, 0.068 mol) was dissolved in ice-cold nitrobenzene (20 ml) and a mixture of γ-chlorobutyryl chloride (8.3 g, 0.059 mol) and the appropriate benzene derivative (0.054 mol) was added dropwise with stirring during 1 h below 10 °C. The mixture was allowed to warm to room temperature, 3 h, then poured onto crushed ice. The solvent was removed by steam or vacuum distillation and the residue taken up in ether and the solution dried. We thus obtained (i) *3-chloropropyl phenyl ketone* (6a; X = Y = Cl),[13] 95% crude yield, purified by distillation, b.p. 113 °C/2 mmHg; τ 2.55 (2 H, m), 3.0 (3 H, m), 6.8 (2 H, t, J = 6 Hz), 7.4 (2 H, t, J = 6 Hz), and 8.3 (2 H, quint.); *m/e* (%) 184 : 182 (2 : 6, M^+) and 105 (100) (t = 30 °C). (ii) *5-bromo-2-methoxyphenyl 3-chloropropyl ketone* (6b; Hal = Br) purified on silica by column chromatography, eluted with 4 : 1 benzene–ether giving 45% pure *ketone*; $\nu_{max.}$ (film) 1 680 cm^{-1} (CO); τ 2.26 (1 H, d, $J_{4.6}$ = 3 Hz), 2.55 (1 H, q, $J_{3.4}$ = 9 Hz, $J_{4.6}$ = 3 Hz), 3.25 (1 H, d, $J_{3.4}$ = 9 Hz), 6.1 (OCH_3, s), 6.4 (2 H, t, J = 6 Hz), 6.93 (2 H, t, J = 6 Hz), 7.9 (2 H, quint., J = 6 Hz); *m/e* (%) 294 : 292 : 290 (2 : 9 : 7, M^+) and 215 : 213 (100 : 98) (t = 65 °C) (Found: C, 45.4; H, 4.2; Br, 27.0; Cl, 12.4. $C_{11}H_{12}BrClO_2$ requires C, 45.5; H, 4.2; Br, 27.4; Cl, 12.2%).

In an attempt to improve the yield, the reaction mixture was warmed to 50 °C for 2 h prior to being poured onto ice. The product was *5-bromo-2-hydroxyphenyl 3-chloropropyl ketone* (6c; Hal = Br), 51%, m.p. 49 °C (ethanol–water). The *phenol* gave a positive $FeCl_3$ test; $\nu_{max.}$ 1 650 cm^{-1} (CO, H bonded); *m/e* (%) 280 : 278 : 276 (21 : 27 : 7) and 201 : 199 (97 : 100) (Found: C, 43.4; H, 3.6; Br, 29.1; Cl, 12.5. $C_{10}H_{10}BrClO_2$ requires C, 43.3; H, 3.6; Br, 28.8; Cl, 12.8%); (iii) *5-chloro-2-methoxyphenyl 3-chloropropyl ketone* (6b; Hal. = Cl), 9 g crude, cyclized *in situ* as follows.

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[9] E. B. Knott, *J. Chem. Soc.*, 1948, 186.
[10] P. R. Burkholder, R. M. Pfister, and F. H. Leitz, *Appl. Microbiol.*, 1966, **14**, 649.
[11] F. M. Lowell, *J. Amer. Chem. Soc.*, 1966, **88**, 4510.
[12] D. G. Durham, C. G. Hughes, and A. H. Rees, *Canad. J. Chem.*, 1972, **50**, 3223.
[13] J. Dhont and J. P. Wibaut, *Rec. Trav. chim.*, 1943, **62**, 177.

Aryl Cyclopropyl Ketones (1).—*Method A*. The aryl 3-chloropropyl ketone was dissolved in 2.5 volumes of 10% potassium hydroxide in methanol solution. After ½ h with occasional shaking the solvent was removed under reduced pressure and the residue taken up in ether and the solution well washed with water and then dried. We thus obtained (i) *cyclopropyl phenyl ketone* (1b) [14] by distillation, yield 71%.

(ii) *5-Bromo-2-methoxyphenyl cyclopropyl ketone* (1c; Hal = Br) was obtained by evaporation of the ether and crystallization of the residue (88% crude yield) from methanol. The *ketone* had m.p. 66—67 °C, $\nu_{max.}$ 1 655 cm^{-1} (CO); τ 2.45 (1 H, d, $J_{4,6}$ = 3 Hz), 2.6 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 3 Hz), 2.9 (1 H, d, $J_{3,4}$ = 9 Hz), 6.15 (OCH_3, s), 7.36 (1 H, m), 8.95 (4 H, m); *m/e* (%) 256 : 254 (54 : 54, M^+) 215 : 213 (100 : 100) (Found: C, 51.9; H, 4.2; Br, 31.5. $C_{11}H_{11}BrO_2$ requires C, 51.8; H, 4.4; Br, 31.3%.

Column chromatography on silica (5% ether in benzene) gave *5-bromo-2-hydroxyphenyl cyclopropyl ketone* (1a; Hal = Br), m.p. 106—107 °C from aqueous ethanol. This *phenol* gave a positive $FeCl_3$ test and had $\nu_{max.}$ 1 635 cm^{-1} (CO); τ 1.9 (1 H, d, $J_{4,6}$ = 3 Hz), 2.43 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 3 Hz), 3.1 (1 H, d, $J_{3,4}$ = 9 Hz), 7.36 (1 H, m), and 8.76 (4 H, m); *m/e* (%) 242 : 240 (100 : 100, M^+, 161 (100) (*t* = 125 °C) (Found: C, 49.9; H, 3.6; Br, 33.2. $C_{10}H_9BrO_2$ requires C, 49.8; H, 3.8; Br, 33.2%).

The methyl ether (1c) (45%) was eluted using 20% ether in benzene. Pure ether then eluted *2-(5-bromo-2-methoxyphenyl)-3-(5-bromo-2-methoxybenzoyl)-1-(2-hydroxyethyl)-cyclopentene* (7; Y = Br), 16%, m.p. 54—55 °C; $\nu_{max.}$ 3 500, 1 650, and 1 595 cm^{-1}; τ 2.9—3.75 (6 H, m), 4.6 (1 H, t, *J* = 7.5 Hz), 5.6 (2 H, t, *J* = 9 Hz), 6.28 (6 H, OMe's), 6.5 (2 H, t, *J* = 6 Hz), 6.95 (2 H, t, *J* = 9 Hz), 7.9 (2 H, q, *J* = 5 Hz, *J* = 6 H), and 8.35br (1 H, OH); *m/e* (%) 512 : 510 : 508 (16 : 30 : 15, M^+), and 215 : 213 (100 : 100) (Found: C, 51.4; H, 4.35; Br, 31.0. $C_{22}H_{22}Br_2O_4$ requires C, 51.8; H, 4.35; Br, 31.3%).

An oil was next eluted, having $\nu_{max.}$ 3 500 and 1 675 cm^{-1}; τ 2.35 (1 H, d), 2.55 (1 H, q), 3.22 (1 H, d), 6.15 (3 H, OMe), 6.27 (1 H, s), 6.41 (2 H, t), 7.03 (2 H, t), and 8.18 (2 H, quintet); *m/e* (%) 274 : 272 (4 : 5, M^+) and 215 : 213 (95 : 100). These spectra fit structure (6d; Hal = Br) but the compound was not completely characterized.

Finally an oil was obtained (4%) having $\nu_{max.}$ 3 400 and 1 640 cm^{-1}; τ 2.1 (1 H, d), 2.45 (1 H, q), 3.11 (1 H, d), 6.1 (1 H, s), 6.23 (2 H, t), 6.86 (2 H, t), 8.0 (2 H, quint.), and 8.24 (1 H, s). No molecular ion peak was observed in the mass spectrum but the compound was probably 3-(5-bromo-2-hydroxybenzoyl)propanol (6e) which was not completely characterized.

(iii) *5-Chloro-2-methoxyphenyl cyclopropyl ketone* (1c; Hal = Cl) was isolated from a silica column on elution with 5% ether in light petroleum. The *chloro-ketone* had m.p. 53—54 °C crystallized from aqueous ethanol, $\nu_{max.}$ 1 655 cm^{-1}; τ 2.48 (1 H, d, $J_{4,6}$ = 3 Hz), 2.65 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 3 Hz), 3.13 (1 H, d, $J_{3,4}$ = 9 Hz), 6.1 (3 H, OMe), 7.3 (1 H, m), and 8.85 (4 H, m); *m/e* (%) 212 : 210 (13 : 45, M^+), and 171 : 169 (29 : 100) (*t* = 60 °C) (Found: C, 62.5; H, 5.2; Cl, 16.8. $C_{11}H_{11}ClO_2$ requires 3, 62.9; H, 5.3; Cl, 16.9%).

The forerun contained *5-chloro-2-hydroxyphenyl cyclopropyl ketone* (1a; Hal. = Cl), m.p. 77—78 °C, crystallized from aqueous alcohol. This *phenol* had $\nu_{max.}$ 1 630 cm^{-1}; τ 2.11 (1 H, d, $J_{4,6}$ = 3 Hz), 2.6 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 3 Hz), 3.1 (1 H, d, $J_{3,4}$ = 9 Hz), 7.4 (1 H, m), and 8.8 (4 H, m); *m/e* (%) 198 : 196 (28 : 100, M^+), 157 : 155 (30 : 100) (*t* = 75 °C) (Found: C, 60.8; H, 4.5; Cl, 17.7. $C_{10}H_9ClO_2$ requires C, 61.1; H, 4.6; Cl, 18.0%).

Elution with ether gave *1-(2-hydroxyethyl)-2-(5-chloro-2-methoxyphenyl)-3-(5-chloro-2-methoxybenzoyl)cyclopentene* (7; Y = Cl), m.p. 126—128 °C crystallized from aqueous ethanol, $\nu_{max.}$ 3 750 and 1 645 cm^{-1}; τ 2.98—3.72 (6 H, m), 4.55 (1 H, t, *J* = 7.5 H), 5.56 (2 H, t, *J* = 9 Hz), 6.3 (6 H, OMe's), 6.53 (2 H, t, *J* = 6 Hz), 6.95 (2 H, t, *J* = 9 Hz), 7.98 (2 H, q, *J* = 6 and 7.5 Hz), and 8.2 (1 H, s, exchanged by D_2O); *m/e* (%) 424 : 422 : 420 (2 : 9 : 13, M^+), 171 : 169 (33 : 100) (*t* = 160 °C) (Found: C, 62.9; H, 5.0; Cl, 16.7. $C_{22}H_{22}Cl_2O_4$ requires C, 62.9; H, 5.3; Cl, 16.9%).

Method B. Using cyclopropylcarbonyl chloride instead of 3-chloropropionyl chloride, as above, we obtained from *p*-chloroanisole the ketone (1c; Hal = Cl) in 40% yield. The yield of bromo-analogue was 47%. Substituting dichloroethane for nitrobenzene did not improve the yield of bromo-compound but the yield of chloro-compound went up to 56%.

1-Formyl-2-phenylpyrrolidines (2a).—1-Formyl-2-phenylpyrrolidine, b.p. 145 °C/1 mmHg, was obtained in 46% yield, n_D^{20} = 1.550 9 (lit.,[15] b.p. 160 °C/6 mmHg). We confirmed that the formyl proton appeared as two singlets in the n.m.r. spectrum, τ 1.63 and 1.93 (1 H); *m/e* (%) 175 (100, M^+).

By the same method we obtained *2-(5-chloro-2-methoxyphenyl)-1-formylpyrrolidine* (2a; X = MeO, Y = Cl) eluted in 48% yield from a silica column by 40% ether in light petroleum. Crystallised from benzene–light petroleum, the *formamide* had m.p. 81—83 °C, $\nu_{max.}$ 1 655 (CO) cm^{-1}; τ 1.66 and 1.92 (1 H, 2s), 2.7—3.35 (3 H, m), 4.85 (1 H, m), 6.15 (3 H, OMe), 6.35 (2 H, t), and 7.5—8.3 (4 H, m); *m/e* (%) 241 : 239 (32 : 98, M^+), 212 : 210 : 208 (28 : 100 : 45) (*t* = 50 °C) (Found: C, 60.0; H, 5.9; Cl, 14.6; N, 6.0. $C_{12}H_{14}ClNO_2$ requires C, 60.3; H, 5.9; Cl, 14.8; N, 5.9%).

The *bromide analogue* 66% yield, had m.p. 89—91 °C, $\nu_{max.}$ 1 660 (CO) cm^{-1}; τ 2.76 and 2.0 (1 H, 2s), 2.6—3.4 (3 H, m), 4.9 (1 H, m), 6.13 (s, OMe), 6.4 (2 H, t, *J* = 6 Hz), 7.6—8.4 (4 H, m); *m/e* (%) 285 : 283 (86 : 90, M^+) and 252 : 254 : 256 (34 : 100 : 70) (*t* = 110 °C) (Found: C, 50.6; H, 4.9; Br, 28.2; N, 5.0. $C_{12}H_{14}BrNO_2$ requires C, 50.7; H, 5.0; Br, 28.1; N, 4.9%).

2-Arylpyrrolidines.—The formyl derivatives were refluxed 2—3 h with 5 volumes of 10% sulphuric acid. After addition of sodium hydroxide solution to bring the mixture to pH 7 it was extracted with ether; this solution was dried and evaporated to give the oily pyrrolidines in over 80% yield. We thus obtained the following: (i) *2-phenylpyrrolidine* (2b; X = Y = H), picrate, m.p. 150—151 °C (lit.,[16] m.p. 148—149 °C); (ii) *2-(5-bromo-2-methoxyphenyl)pyrrolidine* (2b; X = MeO, Y = Br), $\nu_{max.}$ (film) 3 325 cm^{-1} (NH); τ 2.41 (1 H, d, $J_{4,6}$ = 2—3 Hz), 2.83 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 2—3 Hz), 3.43 (1 H, d, $J_{3,4}$ = 9 Hz), 5.75br (1 H, t), 6.26 (3 H, OMe), 7.0 (2 H, m), 7.7—9.1 (4 H, m), and 8.03 (1 H, s); *m/e* (%) 257 : 255 (63 : 70, M^+), 70 (100%) (*t* = 35 °C); the *pyrrolidine* was characterised as its *picrate* m.p. 178—180 °C (benzene) (Found: C, 42.1; H, 3.5; Br, 16.8; N, 11.4. $C_{17}H_{17}BrN_4O_8$ requires

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C, 42.1; H, 3.5; Br, 16.5; N, 11.6%); (iii) 2-(5-*chloro*-2-*methoxyphenyl*)*pyrrolidine* (2b; X = MeO, Y = Cl), $\nu_{max.}$ (film) 3 350 cm^{-1} (NH); τ 2.66 (1 H, d, $J_{4,6}$ = 3 Hz), 2.98 (1 H, q, $J_{3,4}$ = 10 Hz, $J_{4,6}$ = 3 Hz), 3.41 (1 H, d, $J_{3,4}$ = 10 Hz), 5.75 (1 H, t, J = 9 Hz), 6.26 (3 H, OMe), 7.0 (2 H, m), and 7.8—8.7 (4 H, m); *m/e* (%) 213 : 211 (26 : 82, M^+) and 185 : 183 (31 : 100) (t = 60 °C); the *pyrrolidine* was characterised as its *picrate*, m.p. 163—165 °C (methanol) (Found: C, 46.3; H, 4.0; Cl, 8.2; N, 12.7. $C_{17}H_{17}ClN_4O_8$ requires C, 46.3; H, 3.9; Cl, 8.1; N, 12.7%).

2-*Phenylpyrroline*.—*Method A*. 2-Phenylpyrrolidine (3 g) in 25% aqueous acetic acid (50 ml), at 0 °C, was treated with 6% sodium hypochlorite solution (25 ml) during 2 h with stirring. Ether extraction and evaporation of the solvent left an oil which was taken up in ethanol (25 ml) and cooled below 20 °C. A solution of 5% potassium hydroxide in ethanol (25 ml) was added slowly and the mixture was left overnight. Evaporation of the reaction solution under reduced pressure gave a residue which was taken up in ether and the extract dried ($MgSO_4$). Evaporation of the ether left the pyrroline (2.1 g, 71%) as an oil, $\nu_{max.}$ (film) 1 615 cm^{-1} (C=N); $\lambda_{max.}$ 243 nm; τ 2.26 (2 H, m), 2.71 (3 H, m), 6.03 (2 H, m), 7.16 (2 H, m), and 8.1 (2 H, quint.); *m/e* (%) 145 (50, M^+), 117 (100) (t = 140 °C). The pyrroline gave a picrate, m.p. 196 °C (ethanol), (lit.,[17] m.p. 198 °C).

Method B. In this methylene chloride and *N*-bromosuccinimide (1 equiv.) at 20 °C overnight were used. Work-up included a neutralization step (sodium hydrogen carbonate solution) and resulted in a product resolved on a thin layer of silica (2 : 1 ether in benzene) to give 2-phenylpyrroline (45%) at R_F 0.3 and a product at R_F 0.4 later shown to be 3-bromo-2-phenylpyrroline (3d; X = Y = H) (6%).

Method C. 1-Formyl-2-phenylpyrrolidine was refluxed under nitrogen for 2 h with *N*-bromosuccinimide (2 equiv.) in 60% aqueous dioxan (75 ml). Work-up as above gave 2-phenylpyrroline (17%) identical with the product of method A.

Method D followed method C but in carbon tetrachloride at reflux for 15 h in the presence of a few drops of conc. hydrogen peroxide. Work-up as under method B gave 3-bromo-2-phenylpyrroline (3d; X = Y = H) as a major product.

2-(5-*Bromo*-2-*methoxyphenyl*)*pyrroline* (3c).—By method A, the corresponding pyrrolidine (2b; X = MeO, Y = Br) was converted into the *pyrroline* (48%), m.p. 84 °C (light petroleum), $\nu_{max.}$ 1 605 cm^{-1}; $\lambda_{max.}$ 242 and 305 nm; τ 2.1 (1 H, d, $J_{4,6}$ = 3 Hz), 2.7 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 3 Hz), 3.33 (1 H, d, $J_{3,4}$ = 9 Hz), 6.18 (2 H, m), 6.25 (OMe), 7.13 (2 H, t), and 8.15 (2 H, quint.); *m/e* (%) 255 : 253 (26 : 27, M^+) and 118 (100) (t = 55 °C); the *picrate* had m.p. 177—179° (ethanol) (Found: C, 42.4; H, 3.1; Br, 16.6; N, 11.3. $C_{17}H_{15}BrN_4O_8$ requires C, 42.3; H, 3.1; Br, 16.5; N, 11.6%).

2-(5-*Chloro*-2-*methoxyphenyl*)*pyrroline* (3b).—As described above, the pyrrolidine (2b; X = MeO, Y = Cl) was converted into the pyrroline (86%), m.p. 51—52 °C (light petroleum), $\nu_{max.}$ 1 605 cm^{-1}; $\lambda_{max.}$ 242 and 305 nm; τ 2.3 (1 H, d, $J_{4,6}$ = 3 Hz), 2.76 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 3 Hz), 3.25 (1 H, d, $J_{3,4}$ = 9 Hz), 6.08 (2 H, m), 6.2 (OMe), 7.05 (2 H, m), and 8.05 (2 H, quint.); *m/e* (%) 211 : 209 (32 : 100, M^+) (t = 65 °C); an *immediate* microanalysis was performed (Found: C, 63.3; H, 6.0: Cl, 16.6: N, 6.3. $C_{11}H_{12}ClNO$ requires C, 63.0: H, 5.8: Cl, 16.9: N, 6.7%). The *picrate* had m.p. 153—155° (methanol) (Found: C, 46.5; H, 3.6; Cl, 8.1; N, 12.5. $C_{17}H_{15}ClN_4O_8$ requires C, 46.5; H, 3.5; Cl, 8.1; N, 12.8%).

3-*Bromo*-2-*phenylpyrrolines* (3d).—The pyrroline (15 mmol) in carbon tetrachloride (50 ml) was stirred overnight with *N*-bromosuccinimide (16 mmol). After the insoluble succinimide had been filtered off, the filtrate was evaporated to give the bromopyrroline in over 90% yield. We thus made the following: (i) 3-*bromo*-2-*phenylpyrroline*, an oil, $\nu_{max.}$ 1 610 cm^{-1}; $\lambda_{max.}$ 252 nm; τ 2.05 (2 H, m), 2.6 (3 H, m), 4.76 (1 H, m), 5.6 (2 H, m), and 7.53 (2 H, m); *m/e* (%) 225 : 223 (21 : 20, M^+) and 117 (100); the *picrate* had m.p. 160—162 °C (benzene) (Found: C, 42.3; H, 2.9; Br, 17.7; N, 12.2. $C_{16}H_{13}BrN_4O_7$ requires C, 42.4; H, 2.9; Br, 17.6; N, 12.4%); (ii) 3-*bromo*-2-(5-*Bromo*-2-*methoxyphenyl*)-*pyrroline* (3d; X = MeO, Y = Br), m.p. 92—94 °C (petroleum), $\nu_{max.}$ 1 590 cm^{-1}; τ 2.02 (1 H, d, $J_{4,6}$ = 3 Hz), 2.61 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 3 Hz), 3.27 (1 H, d, $J_{3,4}$ = 9 Hz), 4.5br (1 H, t), 6.02 (2 H, m), 6.13 (OMe), and 7.53 (2 H, m); *m/e* (%) 335 : 333 : 331 (17 : 34 : 18, M^+), 254 : 252 (100 : 100) (t = 30 °C); the *picrate* had m.p. 135—137 °C (benzene) (Found: C, 36.5; H, 2.5; Br, 28.0; N, 10.0. $C_{17}H_{14}Br_2N_4O_8$ requires C, 36.3; H, 2.5; Br, 28.5; N, 10.0%); (iii) 3-*bromo*-2-(5-*chloro*-2-*methoxyphenyl*)*pyrroline* (3d; X = MeO, Y = Cl), m.p. 65 °C (decomp), $\nu_{max.}$ 1 595 cm^{-1}; $\lambda_{max.}$ 247 and 309 nm; τ 2.21 (2 H, d), 2.70 (1 H, q), 3.18 (1 H, d), 4.44br (1 H, t), 5.98 (2 H, m), 6.15 (OMe), and 7.52 (2 H, m); *m/e* (%) 291 : 289 : 287 (5 : 20 : 16, M^+) and 210 : 208 (35 : 100); the *picrate* had m.p. 139—141 °C (aqueous alcohol) (Found: C, 39.7; H, 2.8; Br, 15.4; Cl, 6.8; N, 10.8. $C_{17}H_{14}BrClN_4O_8$ requires C, 39.4; H, 2.7; Br, 15.4; Cl, 6.9; N, 10.8%).

2-*Phenylpyrrole*.—The bromopyrroline (3d; X = Y = H) (1 g, 45 mmol) in methanol (10 ml) was refluxed for ½ h with a solution of sodium hydroxide (0.2 g) in methanol (40 ml). The solvent was removed and the product taken up in ether. The ether solution was washed with water, dried ($MgSO_4$), and evaporated to give 2-phenylpyrrole (4a) (475 mg, 74%), m.p. 128 °C (lit.,[18] m.p. 129 °C), undepressed when mixed with a sample prepared below by another route.

When the reaction was done at 20 °C and the product purified on a thin layer of silica using ether–light petroleum (3 : 2), a second product at R_F 0.3 was found; this, an oil (30 mg, 18%) had $\nu_{max.}$ 1 615 cm^{-1}; $\lambda_{max.}$ 242 nm; τ 2.15 (2 H, m), 2.7 (3 H, m), 5.15 (1 H, m), 6.05 (2 H, m), 6.76 (3 H, s), and 8.0 (2 H, m); *m/e* (%) 175 (17, M^+), 117 (52), 104 (35), 77 (35), 72 (100), 71 (30), 57 (35), 51 (30), and 41 (15) (t = 70 °C). These results are consistent with the compound being 3-*methoxy*-2-*phenylpyrroline* (3e; X = Y = H). The methoxy-compound was analysed as its *picrate*, m.p. 149—152° (benzene) (Found: C, 50.4; H, 3.9; N, 14.0. $C_{17}H_{16}N_4O_8$ requires C, 50.5; H, 4.0; N, 13.9%).

2-(5-*Halogeno*-2-*methoxyphenyl*)*pyrrole* (4b).—By the method above, the bromopyrroline (3d; X = MeO, Y = Br) (1.6 g) was converted into the oily *pyrrole* (4d) and purified by chromatography (0.96 g), $\nu_{max.}$ 3 600 cm^{-1}; $\lambda_{max.}$ 242, 292, and 319 nm; τ 2.26 (1 H, d, $J_{4,6}$ = 3 Hz), 2.85 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 3 Hz), 3.27 (1 H, d, $J_{3,4}$ = 9 Hz), 3.16 (1 H, m), 3.42 (1 H, m), 3.72 (1 H, m), and 6.13 (OMe); *m/e* (%) 253 : 251 (90 : 100, M^+) (t = 70 °C) (Found: C, 52.6; H, 4.0; Br, 31.2; N, 5.6. $C_{11}H_{10}BrNO$ requires C, 52.4; H, 4.0; Br, 31.7; N, 5.6%).

Similarly the chloropyrroline (3d; X = MeO, Y = Cl)

[17] See ref. 16, p. 517.

[18] A. Pictet and P. Crepieux, *Chem. Ber.*, 1895, **29**, 1904.

(0.5 g) gave the oily *pyrrole* (4c) (0.35 g, pure); $\nu_{max.}$ 3 525 cm^{-1}; $\lambda_{max.}$ 241, 290, and 318 nm; τ 0.33br (1 H, s) 2.46 (1 H, d, $J_{4.6}$ = 2.5 Hz), 2.97 (1 H, q, $J_{3,4}$ = 9 Hz, $J_{4.6}$ = 2.5 Hz), 3.25 (1 H, d, $J_{3,4}$ = 9 Hz), 3.23 (1 H, m), 3.45 (1 H, m), 3.75 (1 H, m), and 6.13 (OMe); *m/e* (%) 209 : 207 (28 : 100, M^+) (t = 100 °C) (Found: Cl, 17.1. $C_{11}H_{10}ClNO$ requires Cl, 17.1%). The compound was not very stable so it was chlorinated, below.

2-(5-*Chloro*-2-*methoxyphenyl*)-3,4,5-*trichloropyrrole* (9a).—The chloropyrrole (4c) (100 mg) in carbon tetrachloride (10 ml) was treated with sulphuryl chloride (200 mg) at 0 °C with stirring overnight. The product was purified on a thin layer of silica to give the *tetrachloro-compound* (9a) (100 mg), m.p. 117—119 °C (light petroleum), $\nu_{max.}$ 3 450 cm^{-1}; $\lambda_{max.}$ 281 and 307 nm; τ 0.6br (1 H, s), 2.05 (1 H, s), 2.82 (1 H, q), 3.15 (1 H, d), and 6.08 (OMe); *m/e* (%) 317 : 315 : 313 : 311 : 309 (1 : 11 : 49 : 100 : 78, M^+) (t = 130 °C) (Found: C, 42.3; H, 2.2; Cl, 46.2; N, 4.4. $C_{11}H_7Cl_4NO$ requires C, 42.5; H, 2.3; Cl, 45.6; N, 4.5%).

2-(5-*Chloro*-2-*hydroxyphenyl*)-3,4,5-*trichloropyrrole* (5b).—To the pyrrole ether (9a) (30 mg) in methylene chloride (5 ml) at 60 °C was added 12% boron trichloride in methylene chloride (0.5 ml). After 24 h the solution was washed with water and chromatographed on silica to give the *phenol* (5b) as an oil, $\lambda_{max.}$ 279, 286, 312 (OH^-) 280, 288, and 388 nm; *m/e* (%) 301 : 299 : 297 : 295 (10 : 32 : 68 : 54, M^+) (Found: Cl, 48.0. $C_{10}H_5Cl_4NO$ requires Cl, 47.8%).

Aroylglycines.—The appropriate salicylic acids, obtained commercially, were methylated to the ester ethers [19] and hydrolysed to the known acids.[20] These were converted into the aroylglycines [21] to give the following new compounds: 2-*methoxybenzoylglycine* (59% calc. on the acid), *m/e* (%) 209 (5, M^+) and 135 (100) (t = 110 °C), anhydrous, m.p. 113—114 °C (benzene) (Found: C, 57.75; H, 5.3; N, 6.7. $C_{10}H_{11}NO_4$ requires C, 57.4; H, 5.3; N, 6.7%), monohydrate, m.p. 50—60 °C (decomp.) (water) (Found: C, 53.1; H, 5.8; N, 6.2. $C_{10}H_{11}NO_4 \cdot H_2O$ requires C, 52.9; H, 5.8; N, 6.2%); 5-*bromo*-2-*methoxybenzoylglycine* m.p. 162—164 °C (aqueous ethanol), *m/e* (%) 289 : 287 (14 : 14, M^+), 215 : 213 (95 : 100) (t = 110 °C) (Found: C, 41.7; H, 3.6; Br, 27.8; N, 4.9. $C_{10}H_{10}BrNO_4$ requires C, 41.6, H, 3.5; Br, 27.7; N, 4.9%); 5-*chloro*-2-*methoxybenzoylglycine*, m.p. 166—168 °C (aqueous ethanol), *m/e* (%) 245 : 243 (4 : 11, M^+), 171 : 169 (28 : 100) (t = 105 °C) (Found: C, 49.3; H, 4.3; Cl, 14.4; N, 5.6. $C_{10}H_{10}ClNO_4$ requires C, 49.3; H, 4.1; Cl, 14.0; N, 5.8%); 3,5-*dibromo*-2-*methoxybenzoylglycine*, m.p. 204—206 °C (aqueous dioxan), *m/e* (%) 369 : 367 : 365 (6 : 11 : 6, M^+), and 76 (100) (t = 115 °C) (Found: C, 32.9; H, 2.5; Br, 43.3; N, 4.0. $C_{10}H_9Br_2NO_4$ requires C, 32.7; H, 2.4; Br, 43.5; N, 3.8%); 3,5-*dichloro*-2-*methoxybenzoylglycine*, m.p. 182—184 °C (benzene), *m/e* (%) 281 : 279 : 277 (1 : 7 : 11, M^+), 207 : 205 : 203 (10 : 65 : 100) (t = 110 °C) (Found: C, 43.1; H, 3.2; Cl, 25.5; N, 5.1. $C_{10}H_9Cl_2NO_4$ requires C, 43.2; H, 3.3; Cl, 25.5; N, 5.0%).

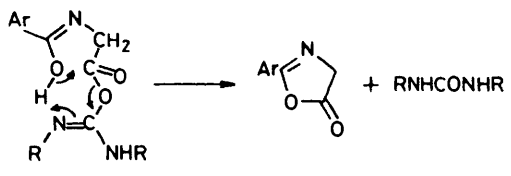
2-*Phenyl*-Δ^2-*oxazolin*-5-*one*.—Benzoylglycine (1 g, 5.6 mmol) and *NN'*-dicyclohexylcarbodi-imide * (1.15 g. 5.6 mmol) were heated for 2 h on a steam-bath in toluene (40 ml). Filtration to remove the urea followed by evaporation of the solvent gave the product in 97% yield. This yield and 83% for the 4-methyl derivative [22] were better than those recorded using acetic anhydride.[23,24] We similarly obtained the following aryloxazolines: 3,5-dibromo-2-methoxyphenyl (95%) and 3,5-dichloro-2-methoxyphenyl (83%). Though chromatographically pure and giving good mass spectra, they remained oily so were used immediately.

Diethyl 2-*Arylpyrrole*-3,4-*dicarboxylates*.—By the literature method [25] we prepared the compounds below. Yields are generally lower when there is no substituent at the 5-position of the pyrrole ring. (i) *Diethyl* 2-(2-*methoxyphenyl*)-*pyrrole*-3,4-*dicarboxylate* (11a; X = Y = H), an oil (56%), $\lambda_{max.}$ (log ε) 274 nm (4.07) and 293 nm (4.02); τ 0.17br (1 H, s), 2.55—3.3 (4 H, m), 5.8 (4 H, q), 2.76 (1 H, d), 6.26 (OMe), and 8.75 (6 H, sextet); *m/e* (%) 317 (20, M^+) (t = 80 °C) (Found: C, 64.5; H, 6.1; N, 4.3. $C_{17}H_{19}NO_5$ requires C, 64.3; H, 6.0; N, 4.4%).

This *ester* was characterized as its 5-*chloro-derivative*, m.p. 121—125 °C (ether–light petroleum), $\lambda_{max.}$ (log ε) 274 (3.9) and 296 nm (3.85); τ 0.7br (1 H, s), 2.5—3.25 (4 H, m), 5.75 (4 H, octet), 6.15 (OMe), and 8.76 (6 H, sextet); *m/e* (%) 353 : 351 (37 : 100, M^+) (t = 95 °C) (Found: C, 58.0; H, 5.3; Cl, 10.1; N, 3.9. $C_{17}H_{18}ClNO_5$ requires C, 58.0; H, 5.2; Cl, 10.1; N, 4.0%). (ii) *Diethyl* 2-(3,5-*dibromo*-2-*methoxyphenyl*)*pyrrole*-3,4-*dicarboxylate* (11a; X = Y = Br) (14%), m.p. 136—138 °C (ether), $\lambda_{max.}$ (log ε) 284 nm (4.0); τ −0.15br (1 H, s), 2.42 (1 H, d, J = 3 Hz), 2.55 (1 H, d, J = 3 Hz), 2.72 (1 H, d), 5.8 (4 H, q), 6.52 (OMe), and 8.73 (6 H, q); *m/e* (%) 477 : 475 : 473 (52 : 100 : 55, M^+) (t = 130 °C) (Found: C, 42.8; H, 3.7; Br, 33.6; N, 2.9. $C_{17}H_{17}Br_2NO_5$ requires C, 43.0; H, 3.6; Br, 33.6; C, 3.0%).

The *ester* was characterized as its 5-*bromo-derivative*, m.p. 81—82 °C (benzene–hexane), $\lambda_{max.}$ (log ε) 285 nm (3.96); τ 0.13br (1 H, s), 2.42 (1 H, d, J = 3 Hz), 2.53 (1 H, d, J = 3 Hz), 5.77 (4 H, octet), 6.42 (OMe), and 8.72 (6 H, quartet); *m/e* (%) 557 : 555 : 553 : 551 (40 : 100 : 100 : 38, M^+) (t = 90 °C) (Found: C, 42.9; H, 3.6; Br, 38.3; N, 2.2. $C_{17}H_{16}Br_3NO_5 \cdot C_6H_6$ requires C, 43.6; H, 3.5; Br, 37.9; N, 2.2%). (iii) *Diethyl* 2-(3,5-*dichloro*-2-*methoxyphenyl*)*pyrrole*-3,4-*dicarboxylate* (11b) (34%), m.p. 110—112 °C (ether–light petroleum), $\lambda_{max.}$ (log ε) 283 nm (4.0); τ 0.02br (1 H, s), 2.62 (1 H, d), 2.71 (2 H, s), 5.78 (4 H, q), 6.57 (OMe), and 8.72 (6 H, sextet); *m/e* (%) 389 : 387 : 385 (15 : 73 : 100, M^+) (t = 100 °C) (Found: C, 52.9; H, 4.5; Cl, 18.3; N, 3.6. $C_{17}H_{17}Cl_2NO_5$ requires C, 52.9; H, 4.4; Cl, 18.4; N, 3.6%).

* The mechanism of this reaction probably involves the initial formation of an acylated intermediate which undergoes an internal cyclisation of the tautomeric imidol species *via* a six-centred transition state.



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The *ester* was characterized as its *5-chloro-derivative* m.p. 82—83 °C (ether–light petroleum), $\lambda_{max.}$ (log ε) 284 nm (3.83); τ 0.15br (1 H, s), 2.68 (2 H, s), 5.75 (4 H, octet), 6.38 (OMe), and 8.72 (6 H, sextet); *m/e* (%) 425 : 423 : 421 : 419 (4 : 32 : 97 : 100 M^+) (*t* = 85 °C) (Found: C, 48.6; H, 3.9; Cl, 25.1; N, 3.2. $C_{17}H_{16}Cl_3NO_5$ requires C, 48.5; H, 3.8; Cl, 25.3; N, 3.3%). (iv) *Diethyl* 2-(*5-bromo-2-methoxyphenyl*)*pyrrole-3,4-dicarboxylate* (11a; X = H, Y = Br) (33%), m.p. 126—128 °C (benzene–light petroleum), $\lambda_{max.}$ (log ε) 275 (4.04) and 305 nm (3.96); τ 0.1br (1 H, s), 2.58 (1 H, d), 8.73 (6 H, sextet), 2.70 (1 H, q), 2.81 (1 H, d), 3.33 (1 H, d), 5.81 (4 H, octet), and 6.3 (OMe); *m/e* (%) 397 : 395 (98 : 100, M^+) (*t* = 100 °C) (Found: C, 51.7; H, 4.7; Br, 20.5; N, 3.3 $C_{17}H_{18}BrNO_5$ requires C, 51.5; H, 4.6; Br, 20.2; N, 3.5%).

The *ester* was characterized as its *5-bromo-derivative* (68%), m.p. 159—161 °C (ether), $\lambda_{max.}$ (log ε) 275 (3.94) and 305 nm (3.84); τ 0.44br (1 H, s), 2.51 (1 H, d), 2.66 (1 H, q), 3.25 (1 H, d), 5.74 (4 H, q), 6.2 (OMe), and 8.7 (6 H, sextet); *m/e* (%) 477 : 475 : 473 (54 : 100 : 54, M^+) (*t* = 150 °C) (Found: C, 43.0; H, 3.6; Br, 33.7; N, 3.0. $C_{17}H_{17}Br_2NO_5$ requires C, 43.0; H, 3.6; Br, 33.6; N, 3.0%). (v) *Diethyl* 2-(*5-chloro-2-methoxyphenyl*)*pyrrole-3,4-dicarboxylate* (11a; X = H, Y = Cl) (53%), m.p. 119—121 °C (benzene–light petroleum), $\lambda_{max.}$ (log ε) 273 (4.03) and 304 nm (3.96); τ 0.03br (1 H, s), 2.72 (1 H, d), 2.74 (1 H, s), 2.87 (1 H, q), 3.27 (1 H, d), 5.7 (4 H, octet), 6.3 (OMe), and 8.73 (6 H, sextet); *m/e* (%) 353 : 351 (39 : 100, M^+) (*t* = 110 °C) (Found: C, 58.6; H, 4.7; Cl, 10.2; N, 4.0%. $C_{17}H_{18}ClNO_5$ requires C, 58.0; H, 5.2; Cl, 10.1; N, 4.0%).

The *ester* gave the *5-chloro-derivative* (82%), m.p. 153—155 °C (benzene), $\lambda_{max.}$ (log ε) 274 (3.91) and 304 nm (3.84); τ 0.35br (1 H, s), 2.66 (1 H, d), 2.82 (1 H, q), 3.25 (1 H, d), 5.75 (4 H, q), 6.21 (OMe), and 8.71 (6 H, sextet); *m/e* (%) 389 : 387 : 385, M^+) (*t* = 125 °C) (Found: C, 52.9; H, 4.5; Cl, 18.0; N, 3.7. $C_{17}H_{17}Cl_2NO_5$ requires C, 52.9; H, 4.4; Cl, 18.4; N, 3.6%).

Synthesis of Pyrroles from Isolated Oxazolinones.—The freshly prepared oxazolinones above were heated at about 140 °C with a slight excess of diethyl acetylenedicarboxylate for ½ h under nitrogen. The crude product was purified on a silica column, with 5% ethyl acetate in benzene as eluant. We thus obtained the following: (i) *diethyl 5-methyl-2-phenylpyrroledicarboxylate* (82%) (lit.,[25] 72% for dimethyl ester, by *in situ* synthesis of oxazolinone), m.p. 98—100 °C (benzene–light petroleum), $\lambda_{max.}$ (log ε) 283 nm (4.2); τ 0.46br (1 H, s), 2.78 (5 H, m), 5.83 (4 H, octet), 7.65 (OMe), and 8.76 (6 H, sextet); *m/e* (%) 301 (85, M^+) and 255 (100) (*t* = 100 °C) (Found: C, 67.8; H, 6.3; N, 4.7. $C_{17}H_{19}NO_4$ requires C, 67.8; H, 6.3; N, 4.7%); (ii) *diethyl 2-phenylpyrrole-3,4-dicarboxylate* (33%), m.p. 129—131 °C (benzene–light petroleum), $\lambda_{max.}$ (log ε) 277 nm (4.11); τ 0.26br (1 H, s), 2.75 (5 H, s), 2.93 (1 H, d), 5.81 (4 H, q), and 8.76 (6 H, sextet); *m/e* (%) 287 (100, M^+) (*t* = 120 °C) (Found: C, 67.0; H, 5.9; N, 4.8. $C_{16}H_{17}NO_4$ requires C, 66.9; H, 6.0; N, 4.9%). This *ester* was characterized as its *5-bromo-derivatives* (98%), m.p. 124—126 °C (benzene–light petroleum); $\lambda_{max.}$ (log ε) 276 nm (4.13); τ 0.56br (1 H, s), 2.62 (5 H, s), 5.74 (4 H, octet), and 8.74 (6 H, quartet); *m/e* (%) 367 : 365 (100 : 100, M^+) (*t* = 115 °C) (Found: C, 52.9; H, 4.3; Br, 21.8; N, 3.9. $C_{16}H_{16}BrNO_4$ requires C, 52.5; H, 4.5; Br, 21.8; N, 3.8%); also as its *5-chloro-derivative* (79%), m.p. 110—111 °C (benzene–light petroleum), $\lambda_{max.}$ (log ε) 275 nm (4.12); τ 0.71br (1 H, s), 2.63 (5 H, s), 5.72 (4 H, octet), and 8.71 (6 H, quartet); *m/e* (%) 323 : 321 (29 : 100, M^+) (*t* = 120 °C) (Found: C, 59.5; H, 5.0; Cl, 10.9; N, 4.3. $C_{16}H_{16}ClNO_4$ requires C, 59.7; H, 5.1; Cl, 11.0; N, 4.4%); (iii) *diethyl* 2-(*3,5-dibromo-2-methoxyphenyl*)*pyrrole-3,4-dicarboxylate* (11a; X = Y = Br) (19%), compared with the acetic anhydride route (14%), described above.

Hydrolysis and Decarboxylation of Pyrrole-3,4-diesters.—The diester (10 mmol) was refluxed 4 h in 50% aqueous alcohol (100 ml) with sodium hydroxide (23 mmol). After cooling, the alcohol was removed at the pump and the residue extracted with ether. The aqueous solution was acidified with dilute mineral acid and again extracted with ether. Evaporation of the dried ($MgSO_4$) solution gave crude *diacids* which were purified by chromatography and crystallization. The diacids were not very stable and underwent slow spontaneous decarboxylation. They gave unsatisfactory microanalyses and rarely gave molecular ions in the mass spectrometer. The following dicarboxylic acids were obtained. (i) *2-Phenylpyrrole-3,4-dicarboxylic acid*, m.p. 228—230 °C (ethanol–water), $\lambda_{max.}$ (log ε) 285 nm (4.0) (OH^-) and 286 (4.19); *m/e* (%) 231 (3, M^+), 187 (100), and 44 (100) (*t* = 140 °C). The *diacid* was treated with diazomethane in methanol and characterized as its *dimethyl ester*, m.p. 103—105 °C (ether); $\lambda_{max.}$ (log ε) 278 nm (4.11); τ 0.08br (1 H, s), 2.73 (5 H, s), 2.84 (1 H, s), and 6.25 (6 H, s); *m/e* (%) 259 (70, M^+) and 228 (100) (*t* = 105 °C) (Found: C, 64.6; H, 5.1; N, 5.6. $C_{15}H_{13}NO_4$ requires C, 64.9; H, 5.1; N, 5.4%). (ii) 2-(*2-Methoxyphenyl*)*pyrrole-3,4-dicarboxylic acid* (11c: X = Y = H), m.p. 143 °C (decomp.) (acetic acid), $\lambda_{max.}$ (log ε) 280 (4.05) (OH^-), 283 (4.39), and 301 nm (4.39). The *diacid* was characterized as its *dimethyl ester*, m.p. 116—118 °C (ether), $\lambda_{max.}$ (log ε) 274 (4.02) and 294 nm (2.75); τ 0.21b (1 H, s), 2.75 (1 H, s), 2.63—3.36 (4 H, m), and 6.26 (9 H, s); *m/e* (%) 289 (100, M^+) (*t* = 100 °C) (Found: C, 62.1; H, 5.3; N, 5.1. $C_{15}H_{15}NO_5$ requires C, 62.3; H, 5.2; N, 4.8%). (iii) 2-(*3,5-Dibromo-2-methoxyphenyl*)*pyrrole-3,4-dicarboxylic acid* (11c; X = Y = Br) (83%), m.p. 220 °C (decomp.) (acetone–light petroleum), $\lambda_{max.}$ (log ε) 275 nm (3.89); *m/e* (%) 421 : 419 : 417 (5 : 11 : 5, M^+) (*t* = 160 °C). (iv) 2-(*3,5-Dichloro-2-methoxyphenyl*)*pyrrole-3,4-dicarboxylic acid* (11c; X = Y = Cl) (88%), m.p. 110 °C (decomp.) (ether–light petroleum), $\lambda_{max.}$ (log. ε) 275 nm (3.62); *m/e* (%) 333 : 331 : 329 (2 : 14 : 20, M^+) (*t* = 150 °C).

The crude diacids were heated in glycerol or digol (10 volumes) at 170—250 °C for ½—1 h. The mixture was poured into water, extracted with ether, and purified on thin layers of silica. Addition of 1 mol equiv. of sodium hydroxide or of powdered soda glass, made little difference to the yields of the following pyrroles: (i) *2-phenylpyrrole* (4a), identical with the sample prepared above, $\lambda_{max.}$ 243 nm, τ 2.26 (2 H, m) 2.71 (3 H, m), 6.03 (2 H, m), 7.16 (2 H, m), and 8.1 (2 H, quint.); *m/e* (%) 145 (50, M^+), 117 (100), 104 (15), and 77 (20) (*t* = 140 °C); (ii) 2-(*2-methoxyphenyl*)*pyrrole* (11d) (22%) an oil, $\lambda_{max.}$ 284 and 306 nm; τ 2.3—3.3 (4 H, m), 3.18 (1 H, m), 3.4 (1 H, m), 3.71 (1 H, m), and 6.09 (OMe); *m/e* (%) 173 (100, M^+) (Found: C, 76.1; H, 6.7; N, 7.6. $C_{11}H_{11}NO$ requires C, 76.3; H, 6.4; N, 8.1%); (iii) 2-(*3,5-dibromo-2-methoxyphenyl*)*pyrrole* (12d), m.p. 106 °C (light petroleum), undepressed by an authentic sample,[26] $\lambda_{max.}$ 301 nm; *m/e* (%) 333 : 331 : 329

[26] S. Hanessian and J. S. Kaltenbronn, *J. Amer. Chem. Soc.*, 1966, **88**, 4509.

(50 : 100 : 52, M^+) (t = 45 °C); (iv) 2-(3,5-*dichloro*-2-*methoxyphenyl*)*pyrrole* (12a), m.p. 107—108 °C (light petroleum), $\lambda_{max.}$ 300 nm; τ 0.2br (1 H, s), 2.66 (1 H, d), 2.93 (1 H, d), 3.25 (1 H, m), 3.56 (1 H, m), 3.9 (1 H, m), and 6.28 (OMe); *m/e* 245 : 243 : 241 (9 : 70 : 100, M^+) (t = 70 °C) (Found: Cl, 28.6. $C_{11}H_9Cl_2NO$ requires Cl, 29.3%).

Chlorination of 2-(3,5-*Dichloro*-2-*methoxyphenyl*)*pyrrole* (12a).—The pyrrole (50 mg) in carbon tetrachloride (3 ml) was treated with sulphuryl chloride (140 mg) for 2 h at 20 °C. The solvent was removed at the pump and the residue purified on a thin layer of silica (10% ether in light petroleum) giving 3,4,5-*trichloro*-2-(3,5-*dichloro*-2-*methoxyphenyl*)*pyrrole* (12b), m.p. 118—121 °C, $\nu_{max.}$ 3 450, 1 495, 1 420, 1 370, 1 235, 1 130, 975, and 885 cm^{-1}; $\lambda_{max.}$ 288 nm; *m/e* (%) 351 : 349 : 347 : 345 : 343 (2 : 22 : 65 : 100 : 64, M^+) (t = 100 °C). This compound was demethylated, as described below, since it was not very stable. Thus, it underwent ready oxidation to a compound considered by analogy with the amide (10), to be 2,3-dichloro-4-(3,5-dichloro-2-methoxyphenyl)-4-oxobut-2-enamide, *m/e* (%) 349 : 347 : 345 : 343 : 341 (1 : 11 : 47 : 100 : 80, M^+).

Preparation and Photo-oxidation of 3,4,5-*Tribromo*-2-(5-*bromo*-2-*methoxyphenyl*)*pyrrole* (9c).—The pyrrole (4d) (100 mg) in chloroform (15 ml) was treated with bromine (190 mg) in chloroform (10 ml) at 0 °C for 2 h. After removal of the solvent at the pump, the product (190 mg) purified on a thin layer of silica, had m.p. 127—129 °C (ether). $\nu_{max.}$ 3 500, 1 495, 1 240, 1 030, 970, and 805 cm^{-1}; $\lambda_{max.}$ 282 and 307 nm; τ 0.7br (1 H, s), 2.0 (1 H, d), 2.65 (1 H, q), 3.22 (1 H, d), and 6.12 (OMe); *m/e* (%) 493 : 491 : 489 : 487 : 485 (17 : 65 : 100 : 70 : 20, M^+) (t = 100 °C). The *tetrabromo-compound* (9c) readily absorbed oxygen to give a new compound, m.p. 192—194 °C (benzene), $\nu_{max.}$ 3 450, 1 725, 1 695, 1 270, 1 105, 1 050, 1 020, 990, 920, and 820 cm^{-1}; *m/e* (%) 445 : 443 : 441 : 439 (28 : 85 : 88 : 29, M^+), 428 : 426 : 424 : 422 (3 : 10 : 10 : 3), and 364 : 362 : 360 (50 : 100 : 50) (Found: C, 29.8; H, 2.0; Br, 53.4. $C_{11}H_{18}Br_3NO_4$ requires C, 30.3; H, 1.9; Br, 53.6%). This compound is probably 2,3-*dibromo*-4-(5-*bromo*-2-*methoxyphenyl*)-4-*oxobut*-2-*enamide* (10).

3,4,5-*Trichloro*-2-(3,5-*dichloro*-2-*hydroxyphenyl*)*pyrrole* (5c).—The methyl ether (12b) (20 mg) in dichloromethane (0.5 ml) was treated overnight with 12% boron trichloride in methylene chloride (0.5 ml). The solution was washed with water, dried, and purified on a thin layer of silica (10% ether in light petroleum). The *phenol* (5c) had m.p. 126—130 °C (ether–light petroleum), $\lambda_{max.}$ 284 and 309 nm; *m/e* (%) 337 : 335 : 333 : 331 : 329 (3 : 21 : 64 : 100 : 62, M^+), 302 : 300 : 298 : 296 : 294 (1 : 7 : 32 : 66 : 52), 263 : 261 : 260 : 259 (10 : 12 : 20 : 19), and 273 : 271 : 269 : 267 (5 : 25 : 55 : 47) (Found: 328.875 0. $C_{10}H_4{}^{35}Cl_5NO$ requires 328.873 6. Found: 332.869 0. $C_{10}H_4{}^{37}Cl_{\frac{1}{2}}{}^{35}Cl_3NO$ requires 332.868 7).

We thank the National Research Council of Canada, Trent and Carleton Universities for financial support (to D. G. D.).

[8/447 *Received*, 13*th March*, 1978]