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THE REACTION OF METHYL PYRROLE-2-CARBOXYLATE WITH EPOXIDES

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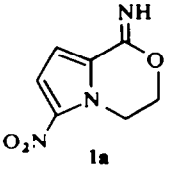
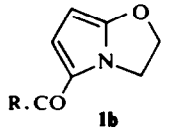
Abstract— Potassium methyl pyrrole-2-carboxylate and styrene oxide are shown to yield *trans*-1-styrylpyrrole-2-carboxylic acid (dry conditions) and 1-(2-hydroxy-2-phenylethyl)pyrrole-2-carboxylic acid (moist conditions). The hydroxy acid yields 1H-3-phenyl-3,4-dihydropyrrolo[2.1-*c*]-[1.4]oxazin-1-one, on treatment with polyphosphoric acid. Vinyl acids were also obtained from the potassium pyrrole ester and ethylene oxide, propylene oxide, and *cis*- and *trans*-stilbene oxide; the latter two compounds yielded stereospecific products. A pyrrolo[2.1-*c*]-[1.4]benzoxazinone was obtained from cyclohexene oxide. The photo chemical isomerization of the *trans*-1-styryl acid and the attempted conversion into lactones is described.

PYRROLE is a weakly acidic compound, p*ka* ≃ 15,[1] and can form alkali metal salts and Grignard reagents. Alkylation of the alkali metal salts may lead to exclusive N-substitution[2-5] but 2-, 3-, and 1,2-di-substituted pyrroles may also be obtained.[6,7] A mechanistic study of the alkylation[7] suggests that N-alkylation is favoured by a polar solvent, a large cation, high solubility of the salt, and a reactive alkylating species.[5] In contrast the alkylation of pyrrole magnesium halides leads almost exclusively to mixtures of 2- and 3-substituted pyrroles.[8] The reactions of pyrroles with epoxides are but little explored. Potassium pyrrole and ethylene oxide yield 1-(2-hydroxyethyl)pyrrole,[9] whereas pyrrole magnesium chloride and this epoxide in ether give a mixture (1 : 3) of 2- and 3-(2-hydroxyethyl)pyrrole.[10] In tetrahydrofuran the 3-hydroxyethylpyrrole is the sole product. Trimethylene oxide reacts similarly but the 2-(3-hydroxypropyl)pyrrole is predominant (4 : 1).[11] In addition it is claimed that 2-cyano-5-nitropyrrole and ethylene oxide produce 1-imino-5-nitro-3,4-dihydropyrrolo[2.1-*c*]-[1.4]oxazine (**1a**),[12] *via* cyclization of the intermediate ethoxide with the nitrile, whereas 2-acyl-5-nitropyrroles and the epoxides yield 5-acyl-2,3-dihydropyrrolo[2.1-*b*]oxazoles (**1b**) by intramolecular nucleophilic substitution of the nitro group.[13]



1a

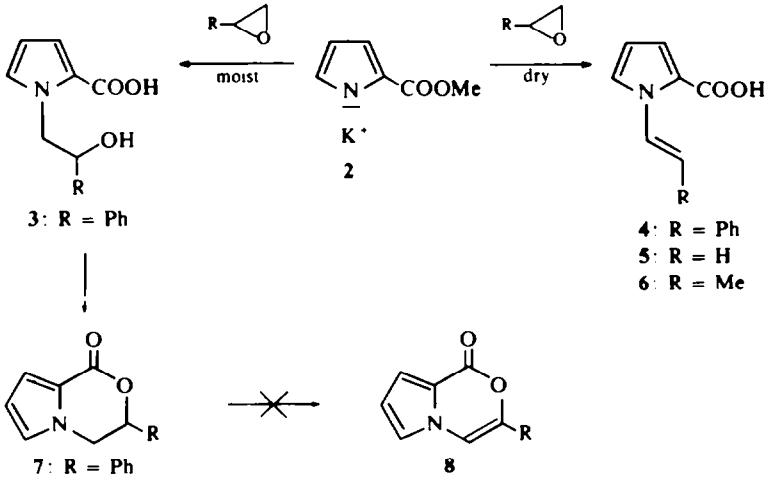


1b

Our interest in cyclic derivatives of β-aminoalcohols has led us to study systems in which the N atom is an integral part of a pyrrole ring. A notional route to this type of compound involved the reaction of potassium methyl pyrrole-2-carboxylate with epoxides to yield pyrrolo-oxazines *via* cyclization of the intermediate alcohol. Few

examples of the pyrrolo[2.1-*c*]-[1.4]oxazine ring-system have been reported[14] and most are saturated derivatives prepared from proline.[15,16]

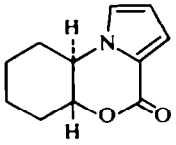
Potassium methyl pyrrole-2-carboxylate (**2**), which was prepared from the pyrrole ester[17] under milder conditions than those previously reported,[2] reacted with styrene oxide in dimethylformamide at room temperature to yield a mixture of *trans*-1-styrylpyrrole-2-carboxylic acid (**4**) and 1-(2-hydroxy-2-phenylethyl)pyrrole-2-carboxylic acid (**3**). No products resulting from abnormal fission of the epoxide[18] were detected by preparative TLC on silica. Repetition of the reaction under reflux conditions yielded more of the more mobile, fluorescent, styryl acid (**4**) but traces of the alcohol (**3**) were always present. The styryl acid (**4**) could, however, be obtained as the sole product, even at room temperature, when the reaction was carried out under scrupulously dry conditions. In contrast, the hydroxy acid (**3**) was the only product of the reaction performed in an atmosphere saturated with water vapour. The configuration of the styryl acid, m.p. 178–9°, was indicated by ^{1}H NMR (CH=CH, J = 14 Hz) and UV spectra and by photochemical isomerization by irradiation at 350 nm to yield *cis*-1-styrylpyrrole-2-carboxylic acid, m.p. 131–3°, (CH=CH, J = 8·5 Hz). 1-(2-Hydroxy-2-phenylethyl)pyrrole-2-carboxylic acid (**3**) was cyclized with polyphosphoric acid to yield 1H-3-phenyl-3,4-dihydropyrrolo[2.1-*c*]-[1.4]oxazin-1-one (**7**). The ^{1}H NMR spectrum of this lactone showed a typical 9 line ABX pattern and the calculated spectral parameters indicated an envelope conformation.[19] Treatment of the lactone (**7**) with potassium methoxide in methanol yielded methyl 1-(2-hydroxy-2-phenylethyl)pyrrole-2-carboxylate. This ester was also obtained from the hydroxy acid (**3**) and diazomethane. Several attempts to dehydrogenate the lactone (**7**), by means of palladised charcoal[20] or DDQ,[21] to yield a fully aromatic pyrrolo-oxazine (**8**), were unsuccessful.



Ethylene oxide and propylene oxide also reacted readily with the potassium pyrrole (**2**) to yield 1-vinyl-(**5**) and 1-(2-methylvinyl)-(**6**) pyrrole-2-carboxylic acid: again the *trans*-olefin (CH=CH, J = 14 Hz) was obtained. Ring-opening reactions of epoxides usually proceed with inversion of configuration[18] and so to test the stereochemistry

of the elimination the potassium pyrrole (**2**) was caused to react with *cis*- and *trans*-stilbene oxide. The reaction was completely stereospecific; the *cis*-epoxide yielded 1-(*trans*-1,2-diphenylvinyl)pyrrole-2-carboxylic acid (**14**), m.p. 193–194°, whereas the *trans*-epoxide gave the *cis*-diphenylvinylpyrrole (**13**), m.p. 164–165°.

The reaction of epoxides with suitable precursors to yield cyclic compounds is well documented[22,23] and carbanions such as that derived from diethyl malonate yield γ-lactones. It is surprising, therefore, that no lactone was produced from potassium methyl pyrrole-2-carboxylate and the above epoxides even under dry conditions. A lactone intermediate which is decomposed before isolation may still, however, be involved in the reaction. The potassium salt of diethyl 3,5-dimethylpyrrole-2,4-dicarboxylate (Knorr's pyrrole) and styrene oxide yielded 3,5-dimethyl-4-ethoxycarbonyl-1-(2-hydroxy-2-phenylethyl)pyrrole-2-carboxylic acid, the reduced nucleophilicity of the anion necessitated the reaction being carried out under reflux. The orientation of the free carboxylic acid group was shown by cyclization with polyphosphoric acid to yield 1*H*-6,8-dimethyl-1-ethoxycarbonyl-3-phenyl-3,4-dihydropyrrolo[2.1-*c*]-[1.4]oxazin-1-one. This reaction, in which only the 2-ester group has been hydrolyzed, suggests the involvement of anchimeric assistance in the hydrolysis, perhaps *via* a lactone in equilibrium with the initially formed oxygen anion.[24] This involvement was further supported by the direct isolation of a lactone, 4*H*-5a, 6,7,8,9,9a-hexahydropyrrolo[2.1-*c*]-[1.4]benzoxazin-4-one (**9**), from the potassium pyrrole (**2**) and cyclohexene oxide. It is worthy of note that this reaction alone of those so far considered yields a product from which elimination is hindered (*cis*-axial, equatorial disposition of H and O atoms).[25]



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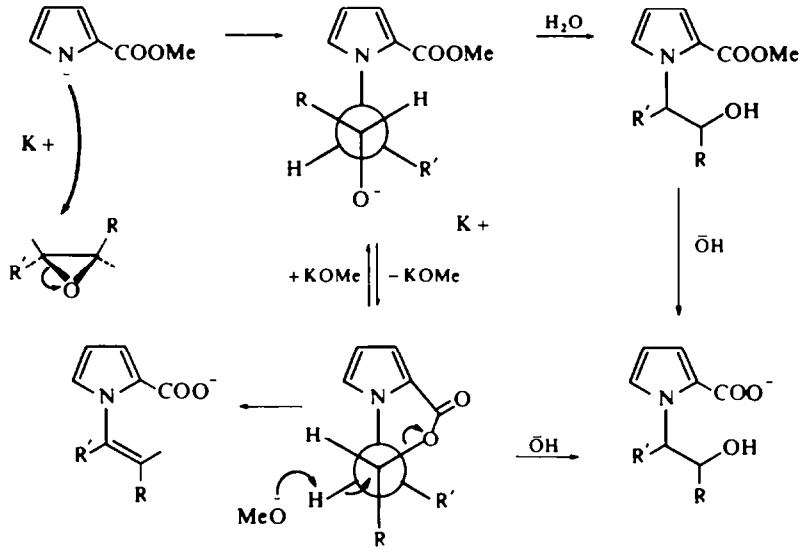
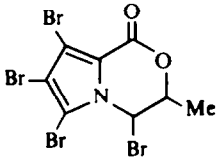
One theoretical pathway leading to the 1-vinylpyrroles is the base-catalyzed elimination of an alcohol ester followed by hydrolysis. However, the presence of moisture, which this scheme necessitates, is known to yield only an alcohol acid, whereas anhydrous conditions lead to elimination. This evidence, together with the hydrolysis of the 2-ester group in Knorr's pyrrole, the isolation of a lactone from cyclohexene oxide, in which elimination is unfavourable, and the facile elimination to yield the 1-vinylpyrroles,[26] lead us to suggest that all of the epoxide reactions proceed *via* a lactone which undergoes hydrolysis (moist conditions) to yield the hydroxy acid or elimination (anhydrous conditions) to yield a vinylpyrrole (scheme).

The cyclization of suitably substituted olefinic acids to give γ- and δ-lactones has been extensively studied and reviewed.[27] Further attempts to obtain pyrroloxazines by the cyclization of the vinylpyrrole acids (**4** and **6**) were largely unsuccessful due to the lability of the 2-carboxylic acid group.[6] Azeotropic distillation of the styryl acid (**4**) with toluene-*p*-sulphonic acid caused decarboxylation to yield *trans*-1-styryl pyrrole, whereas treatment with iodine and base[28] gave *trans*-1-styryl-2-iodopyrrole. The styryl pyrrole (**4**) and bromine[4] yielded *erythro*-1-(1,2-dibromo-2-phenylethyl)-2,3,4,5-tetrabromopyrrole. The methylvinylpyrrole acid (**6**) and bromine



SCHEME 1

however, gave a mixture of the desired lactone (**11**) ($\nu_{C=O}$ 1740 cm^{-1}, Me = 7·8 τ) and the non-eliminated intermediate (**10**) ($\nu_{C=O}$ 1720 cm^{-1}, Me = 8·3 τ) in approximately equal proportions. Lithium chloride in DMF failed to cause dehydrobromination of the mixture.[4]



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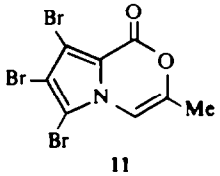

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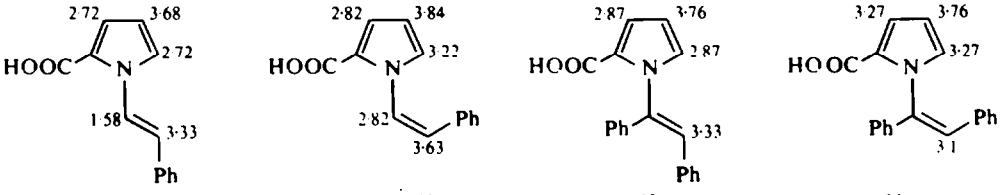
The electronic absorption spectra of the vinylpyrroles (Table 1, 95% ethanol) indicate a significant conjugation of the olefin with the pyrrole ring and may be used to assign the configuration of the geometrical isomers (**4** and **12**) and (**13** and **14**). Thus hypsochromic and hypochromic shifts, similar to those observed with the stilbenes,[32] were observed in the isomerization[33] of the *trans*- to *cis*-1-styrylpyrrole-2-

TABLE 1

Compound	λ_{max} nm	ε_{max}
Pyrrole-2-carboxylic acid	254	11,300
trans-1-(2-Methylvinyl)pyrrole-2-carboxylic acid (**6**)	267	12,100
trans-1-Styrylpyrrole-2-carboxylic acid (**4**)	302	20,900
cis-1-Styrylpyrrole-2-carboxylic acid (**12**)	270	12,900
2-Styrylpyrrole[31]	333	31,200
1-(*cis*-1,2-Diphenylvinyl)pyrrole-2-carboxylic acid (**13**)	292	9,800
1-(*trans*-1,2-Diphenylvinyl)pyrrole-2-carboxylic acid (**14**)	299	25,000

carboxylic acid. The situation is more complex in the case of the diphenylvinylpyrrole acids but the UV spectrum of the *trans*-isomer is surprisingly similar to that of *trans*-stilbene,[32] which suggests that the pyrrole ring plays little part in the conjugation. The similarity of the UV spectrum of *trans*-stilbene and those of tri- and tetraphenylethylene is well documented.[34,35] The *cis*-diphenylvinylpyrrole acid was found to exhibit hypsochromic and hypochromic shifts due to the greater distortion from planarity of the more strongly conjugating groups in this isomer.



4 **12** **13** **14**

FIG 1

The NMR spectra of these geometrical isomers (Fig, τ values shown), which indicate a general deshielding of the pyrrole protons in the isomer containing the more conjugated pyrrole ring (**4** and **13**), further confirm the above configurational assignments. The comparison of position of the 2-vinyl protons in the diphenylvinylpyrrole acids (**13** and **14**) with *cis*- and *trans*-stilbene (τ = 3·45 and 2·9 respectively)[36] and between **4** and **13** is worthy of note.

The mass spectra of 1-(2-hydroxy-2-phenylethyl)pyrrole-2-carboxylic acid (**3**) and the derived lactone (**7**) showed small molecular ion peaks[37] and a principal decompoisiton pathway initiated by loss of benzaldehyde and then CO_2 or CO. The hydroxyacid (**3**) also underwent cyclodehydration in the mass spectrometer to show fragments characteristic of the lactone. The styryl pyrrole (**4**) showed a more intense molecular ion than either the hydroxy acid or the isomeric lactone and decomposition occurred principally by loss of CO_2 and H, to yield the base peak at *m/e* 168. A similar fragmentation pathway was observed with 1-(2-methylvinyl)pyrrole-2-carboxylic acid (**6**) although a small ·OH loss (9%) was also present. In contrast the 1-vinylpyrrole acid (**5**) showed the molecular ion as the base peak and underwent decomposition by loss of ·OH (*m/e* 120) and CO_2 and H (*m/e* 94, 93).

EXPERIMENTAL

NMR spectra were measured in $CDCl_3$ soln using a Varian A60-A spectrometer with TMS as internal standard. IR spectra were measured with a Unicam SP200 and UV spectra with a Unicam SP800 spectrophotometer. Mass spectra were obtained using an A.E.I. MS9 instrument with direct introduction of the samples into the heated inlet system.

General method for the reaction of methyl pyrrole-2-carboxylate with epoxides. Potassium metal (0·16 g, 0·004 mole), cut under petrol was added in small portions to methyl pyrrole-2-carboxylate[17,38,39] (0·5 g, 0·004 mole) in DMF (5 cm³) with external cooling. When all the K had dissolved (10–15 min) to form **2** the epoxide (0·004 mole) was added and the mixture was stirred, usually under reflux, for the stated time (2–18 hr). The cooled mixture was washed with ether and then was added slowly to 0·5N HCl (20 cm³) to precipitate the product which was collected after refrigeration (1 hr).

1-(2-*Hydroxy*-2-*phenylethyl*)*pyrrole*-2-*carboxylic acid* (3)

The potassium pyrrole and styrene oxide (0·48 g) stirred together at room temp for 18 hr in an atmosphere saturated with water vapour yielded the *hydroxy pyrrole* (0·4 g, 50%), colourless prisms, m.p. 161–163°, from acetone–petrol. (Found: C, 67·7; H, 5·6; N, 6·2. $C_{13}H_{13}NO_3$ requires: C, 67·5; H, 5·6; N, 6·1%): ν_{max} (Nujol): 3400 (OH), 2700 (COO—H), 1670 cm^{-1} (C=O); τ (acetone): 2·65 (5H, m, *Ph*), 3·05 (2H, d, J = 3·4 Hz, 3-H and 5-H), 3·94 (1H, t, J = 3·4 Hz, 4-H), 4·17 (1H, broad exchangeable S, OH), 4·96 (1H, q, J = 3·6 and 8·5 Hz, CH_2—CH), 5·25 (1H, q, J = 3·6 and 13 Hz, CHH—CH), 5·79 (1H, q, J = 8·5 and 13 Hz, CHH—CH). *m/e* (I%): 231 (5, M^+), 213 (21, M-H_2O), 187 (13), 169 (6, M—CO_2—H_2O), 168 (10, 169-H), 125 (87, M-PhCHO), 108 (18), 107 (100, 213-PhCHO), 106 (20), 105 (16), 94 (13), 91 (13), 81 (68, 125-CO_2), 80 (58), 79 (92, 107-CO), 78 (24), 77 (50), 66 (9), 65 (10), 63 (9), 54 (10), 53 (37), 52 (34, 79-HCN), 51 (42), 50 (16), 44 (42), 41 (10), 39 (40). m* 167 (169 → 168), 123·5 (231 → 169), 58·3 (107 → 79), 53·6 (213 → 107), 34·2 (79 → 52).

trans-1-*Styrylpyrrole*-2-*carboxylic acid* (4)

The potassium pyrrole and styrene oxide (0·48 g) stirred together at room temp for 18 hr in a dry atmosphere under N_2 yielded the *styrylpyrrole* (0·17 g, 21%), cream platelets, m.p. 178–179° from chloroform–petrol. When no precautions were taken to eliminate moisture the styrylpyrrole was again the main product but 3 was always present (*ca.* 3:1) and could not be eliminated by a period of reflux. This mixture was separated by preparative TLC on silica with AcOH (0·5%)—methanol (2%)—benzene (97·5%), the styryl acid being the more mobile, fluorescent compound. (Found: C, 73·4; H, 5·2; N, 6·2. $C_{13}H_{11}NO_2$ requires: C, 73·2; H, 5·2; N, 6·6%): ν_{max} (KBr): 2650 (OH), 1670 (C=O), 1640 (C=C), 950 cm^{-1} (*trans*-CH=CH); *m/e* (I%): 214 (6), 213 (38, M^+), 212 (11, M—H), 169 (47, M—CO_2), 168 (100, M—H—CO_2), 167 (47, 168-H), 166 (10), 141 (11, 167-C_2H_2), 140 (4, 167-HCN), 115 (11), 102 (17), 94 (27, M—OH—PhC≡CH), 91 (10), 77 (27), 51 (23), 39 (17): m* = 211 (213 → 212), 166 (168 → 167), 134 (213 → 169), 132·5 (213 → 168), 41·5 (213 → 94).

cis-1-*Styrylpyrrole*-2-*carboxylic acid* (12)

trans-1-Styrylpyrrole-2-carboxylic acid (0·15 g, 0·0007 mole) in benzene (100 cm^3) was irradiated for 6 hr with a "Camag" Universal UV lamp TL-900/U at 350 nm through a glass filter to yield the cis-*styrylpyrrole acid* (0·12 g, 80%) straw-coloured prisms, m.p. 131–133° (chloroform–petrol). (Found: C, 73·1; H, 5·2; N, 6·6%): ν_{max} (KBr): 2650 (OH), 1670 (C=O), 700 cm^{-1} (*cis* CH=CH).

1H-3-*Phenyl*-3,4-*dihydropyrrolo*[2.1-c]-[1.4]*oxazin*-1-*one* (7)

Compound 3 (0·56 g) was stirred into polyphosphoric acid (5 g) and the mixture was left at room temp for 18 hr. Ice-cold water (20 cm^3) was added and the yellow oil was extracted with ether, dried ($MgSO_4$) and passed through a bed (3 cm) of neutral alumina. Evaporation of the eluate yielded the *lactone* (0·4 g, 86%), colourless plates, m.p. 111–112° from chloroform–petrol. (Found: C, 73·3; H, 5·2; N, 6·4. $C_{13}H_{11}NO_2$ requires: C, 73·2; H, 5·2; N, 6·6%); ν_{max} (KBr): 1710 (C=O), 1090 cm^{-1} (C—O). τ ($CDCl_3$): 2·51 (5H, *s*, *Ph*), 2·83 (1H, q, J = 1·5 and 4Hz, 8-H), 3·05 (1H, q, J = 1·5 and 2·5 Hz, 6-H), 3·64 (1H, q, J = 2·5 and 4 Hz, 7-H), 4·32 (1H, q, $|J_{3,4} + J_{3,4'}|$ = 14Hz, 3-H), 5·7 (2H, m, $J_{4,4'}$ = 13 Hz, 4-H2); *m/e* (I%): 213 (17, M^+), 169 (3; M—CO_2), 168 (9, 169-H), 167 (11, 168-H), 108 (10), 107 (100, M-PhCHO), 91 (10), 79 (73, 107-CO), 78 (15), 77 (20), 52 (18, 79-HCN), 51 (15), 39 (11). m* = 167 (169 → 168), 166 (168 → 167), 58·3 (107 → 79); 53·6 (213 → 107), 34·2 (79 → 52): *m/e* 107 = 107·036960 (C_6H_5NO): *m/e* 79 = 79·042312 (C_5H_5N).

This lactone was not dehydrogenated when heated under reflux with (i) Pd-C in toluene for 18 hr or (ii) 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in dioxan for 4 days.

Methyl 1-(2-*hydroxy*-2-*phenylethyl*)*pyrrole*-2-*carboxylate*

(i) Compound 3 (0·14 g, 0·0006 moles) was added slowly to an ethereal soln (0–5°) of diazomethane (0·42 g, 0·01 mole) and the mixture was allowed to evaporate overnight at room temp to yield the *ester* (0·11 g, 74%), colourless prisms, m.p. 93–94° (chloroform–petrol).

(ii) KOMe (from K 0·02 g, 0·0005 mole) in dry MeOH (2 cm^3) was added to 7 (0·1 g, 0·0005 mole) in DMF (3 cm^3) and the mixture was stirred at room temp under N_2 for 18 hr to yield the ester. (Found: C, 67·9; H, 6·1; N, 5·6. $C_{14}H_{15}NO_3$ requires: C, 68·5; H, 6·1; N, 5·7%): ν_{max} (KBr): 3500 (OH), 1675 cm^{-1} (C=O). τ ($CDCl_3$): 2·65 (5H, br, *Ph*), 3·04 (1H, q, J = 2 and 3·8 Hz, 3-H) 3·28 (1H, t, J = 2 Hz, 5-H), 3·94 (1H, q, J = 2 and 3·8 Hz, 4-H) 5·0 (1H, q, J = 4 and 8 Hz CHH—CH), 5·3 (1H, q, J = 4 and 14 Hz, CHH—CH), 5·83 (1H, q, J = 8 and 14 Hz, CHH—CH), 6·2 (3H, s, *Me*).

3,5-Dimethyl-4 ethoxycarbonyl-1-(2-hydroxy-2-phenylethyl)pyrrole-2-carboxylic acid

Potassium diethyl 3,5-dimethylpyrrole-2,4-dicarboxylate (0·01 mole) (from Knorrs' pyrrole, 2·39 g) in DMF (10 cm^3), and styrene oxide (2·4 g, 0·02 mole) heated together under reflux for 4 hr yielded a yellow oil after acidification. Extraction with ether and evaporation of the dried ($MgSO_4$) soln yielded the *pyrrole acid ester* (1·9 g, 57°,), colourless needles, m.p. 153–154° from chloroform–petrol. (Found: M^+, 331·141616. $C_{18}H_{21}NO_5$ requires: M^+, 331·141962); ν_{max} (Nujol): 2650 (OH), 1700 and 1670 cm^{-1} (C=O); τ (acetone): 2·65 (5H, m, *Ph*), 5·05 (1H, m, CH_2–CH), 5·4–6·0 (4H, m, CH_2–CH and CH_3–CH_2), 7·48 (6H, s, 3-*Me* and 5-*Me*), 8·73 (3H, t, CH_3–CH_2).

1H-6,8-Dimethyl-7-ethoxycarbonyl-3-phenyl-3,4-dihydropyrrolo[2,1-c]-[1,4]oxazin-1-one

The pyrrole acid ester (0·4 g) and polyphosphoric acid (4 g) at room temp for 6 hr and elution of the product through a neutral alumina column with chloroform yielded the *lactone* (0·12 g, 32%), colourless microprisms, m.p. 180–181° from chloroform–petrol. (Found: C, 69·3; H, 6·2; N, 4·3. $C_{18}H_{19}NO_4$ requires: C, 69·0; H, 6·1; N, 4·5%); ν_{max} (Nujol): 1700 cm^{-1} (C=O); τ ($CDCl_3$): 2·6 (5H, s, *Ph*), 4·46 (1H, q, J = 4 and 10 Hz, 3-H), 5·5–6·2 (4H, *m*, 4-H_2 and CH_3–CH_2), 7·45 (6H, s, 6-*Me* and 8-*Me*), 8·65 (3H, t, CH_3–CH_2).

trans-1-(2-*Methylvinyl*)*pyrrole-2-carboxylic acid* (**6**)

The potassium pyrrole (0·02 mole) and propylene oxide (2·3 g, 0·04 mole) heated under reflux for 2 hr and stirred at room temp for 18 hr yielded the *methylvinylpyrrole acid* (1·57 g, 52%) colourless needles, m.p. 152–153 from chloroform–petrol. (Found: C, 63·6; H, 6·1; N, 9·3. $C_8H_9NO_2$ requires: C, 63·6; H, 6·0; N, 9·3%); ν_{max} (Nujol): 2650 (OH), 1680 (C=O) 950 cm^{-1} (*trans*-CH=CH); τ ($CDCl_3$): −0·58 (1H, broad exchangeable singlet, OH), 2·42 (1H, m, J = 1·6 and 14 Hz, NCH=CH), 2·8 (2H, d, J = 3·5 Hz, 3-H and 5-H) 3·76 (1H, t, J = 3·5 Hz, 4-H), 4·16 (1H, m, J = 7 and 14 Hz, CH_3–CH=), 8·15 (3H, q, J = 1·6 and 7 Hz, CH_3–CH=); *m/e* (I%): 152 (8), 151 (57, M^+), 150 (5, M−H), 134 (9, M–OH), 108 (5), 107 (35, M−CO_2), 106 (100, M−CO_2H), 105 (10), 104 (14), 94 (18), 80 (19), 79 (44), 78 (17), 77 (20), 68 (5), 67 (13), 66 (12), 65 (10), 54 (7), 53 (11), 52 (11), 51 (15), 50 (10), 44 (26), 41 (25); m* 74·5 (151 → 106), 59 (106 → 79).

Methyl trans-1-(2-*methylvinyl*)*pyrrole-2-carboxylate*

Compound **6** (1·01 g, 0·007 mole), MeI (1·9 g, 0·014 mole) and K_2CO_3 (6 g) in acetone (20 cm^3) were heated under reflux for 4 hr. The cooled mixture was filtered and the filtrate evaporated to yield an oil which was dissolved in chloroform and washed with water. Evaporation of the dried ($MgSO_4$) soln yielded the *ester* (1·4 g, 100%) as a pale yellow oil. Chromatography showed the product to consist of one component. (Found: M^+ 165·076847. $C_9H_{11}NO_2$ requires: M^+, 165·078973); ν_{max} (Thin Film): 1710 cm^{-1} (C=O); τ (CCl_4): 2·3 (1H, q, J = 1·7 and 14 Hz, NCH=CH), 2·93 (1H, t, J = 2 and 2·5 Hz, 5-H), 3·1 (1H, q, J = 2 and 4 Hz, 3-H), 3·9 (1H, t, J = 2·5 and 4 Hz, 4-H), 4·3 (1H, m, J = 7 and 14 Hz, CH_3–CH=); 6·27 (3H, s, CH_3O), 8·2 (3H, q, J = 1·7 and 7 Hz, CH_3–CH=).

1-*Vinylpyrrole-2-carboxylic acid* (**5**)

The potassium pyrrole (0·01 mole) and ethylene oxide (3·5 g, 0·08 mole) were heated at 100° in a sealed tube for 6 hr to yield the *vinylpyrrole acid* (0·28 g, 20%), colourless needles, m.p. 137–138° from chloroform–petrol. (Found: C, 61·4; H, 5·3; N, 10·2. $C_7H_7NO_2$ requires: C, 61·3; H, 5·1; N, 10·2%); ν_{max} (KBr): 2700 (OH), 1680 (C=O), 980 cm^{-1} (CH=CH_2); τ ($CDCl_3$): −2·11 (1H, broad exchangeable s, OH), 2·09 (1H, q, J = 9 and 16 Hz, CH_2=CH), 2·77 (2H, m, 3-H and 5-H), 3·74 (1H, t, 4-H); 4·82 (1H, q, J = 0·3 and 16 Hz, (CHH=CH), 5·14 (1H, q, J = 0·3 and 9 Hz, CHH=CH); *m/e* (I%): 137 (100, M^+), 136 (8, M−H), 120 (29, M−OH), 109 (5), 108 (7), 95 (5), 94 (27, M−CO_2), 93 (28, M−CO_2H), 92 (21), 91 (12), 81 (5), 80 (11), 77 (6), 67 (12), 66 (29), 65 (42), 64 (15), 63 (8), 55 (6), 54 (10), 53 (7), 52 (8), 51 (10), 50 (10), 45 (10), 44 (8), 41 (10).

1-(trans-1,2-*Diphenylvinyl*)*pyrrole-2-carboxylic acid* (**14**)

The potassium pyrrole and *cis*-stilbene oxide[40] (0·78 g, 0·004 mole) heated under reflux for 6 hr yielded the *vinylpyrrole acid* (0·25 g, 21%), colourless prisms, m.p. 193–194° from chloroform–petrol. (Found: C, 78·8; H, 5·2; N, 4·8. $C_{19}H_{15}NO_2$ requires: C, 78·9; H, 5·2; N, 4·8%); ν_{max} (Nujol): 2650 (OH), 1680 cm^{-1} (C=O).

1-(cis-1,2-*Diphenylvinyl*)*pyrrole-2-carboxylic acid* (**13**)

The potassium pyrrole (0·02 mole) and *trans*-stilbene oxide (3·92 g, 0·02 mole) heated under reflux for 8 hr and elution of the acid-insoluble product from 3 cm acidic alumina column (Et_2O) yielded the *vinyl-*

pyrrole acid (2·3 g, 40%), colourless prisms, m.p. 164–165° from chloroform–petrol. (Found: C, 78·8; H, 5·2; N, 5·0. $C_{19}H_{15}NO_2$ requires: C, 78·9; H, 5·2; N, 4·8%): ν_{max} (KBr): 2650 (OH), 1670 cm^{-1} (C=O).

4H-5a,6,7,8,9,9a-*Hexahydropyrrolo*[2,1-c]-[1,4]*benzoxazin*-4-*one* (**9**)

The potassium pyrrole and cyclohexene oxide (0·39 g, 0·004 mole) heated under reflux in a N_2 atmosphere for 2 hr yielded the *lactone* (0·44 g, 58%), cream platelets, m.p. 128–129° from chloroform–petrol. (Found: C, 69·3; H, 6·7; N, 7·5. $C_{11}H_{13}NO_2$ requires: C, 69·1; H, 6·8; N, 7·3%): ν_{max} (Nujol): 1700 cm^{-1} (C=O): τ (CCl_4): 3·15 (2H, m, 1-H and 3-H), 3·84 (1H, q, J = 2·5 and 4 Hz, 2-H), 6·06 (2H, m, 5a-H and 9a-H), 8·13 (8H, m, 6-H_2, 7-H_2, 8-H_2, and 9-H_2).

Attempted cyclization reactions

(i) A soln of I_2 (0·127 g, 0·0005 mole) and KI (0·25 g) in water (5 cm^3) was added slowly over 45 min to *trans*-1-styrylpyrrole-2-carboxylic acid (0·106 g, 0·0005 mole) in $NaHCO_3$ aq (5 cm^3, 0·5N) and the mixture was stirred for 1 hr. Elution of the ppt through neutral and then basic alumina columns with cyclohexene yielded *trans*-1-styryl-2-iodopyrrole (0·03 g, 20%) colourless prisms, m.p. 109–110° from 30–40° petrol; ν_{max} (KBr): 1650 (C=C), 950 cm^{-1} (*trans* CH=CH); τ ($CDCl_3$): 2·57 (1H, d, J = 14 Hz, N—CH=), 2·64 (5H, br, *Ph*), 2·78 (1H, t, 5-H), 3·39 (1H, d, J = 14 Hz, Ph-CH=), 3·53 (1H, q, 3-H), 3·7 (1H, t, 4-H); m/e = 295 (M^+); m^* = 95·7 (295 → 168, M-I).

(ii) *trans*-1-Styrylpyrrole-2-carboxylic acid (0·1 g), toluene-*p*-sulphonic acid (0·01 g) and benzene (10 cm^3) were heated together with azeotropic distillation for 1 hr. Evaporation and elution of the product from a neutral alumina column with ether yielded *trans*-1-styrylpyrrole: ν_{max} (thin film): 1645 (C=C), 950 cm^{-1} (*trans* CH=CH); τ ($CDCl_3$); 2·77 (6H, *Ph* and NCH=), 3·14 (2H, t, J = 2 Hz, 2-H and 5-H), 3·5 (1H, d, J = 14 Hz, PhCH=), 3·85 (2H, t, J = 2 Hz, 3-H and 4-H).

(iii) Br_2 (1·2 g, 0·0075 mole) in chloroform (5 cm^3) was added slowly to *trans*-1-styrylpyrrole-2-carboxylic acid (0·31 g, 0·0015 mole) in chloroform (10 cm^3). K_2CO_3 (0·9 g) was added and the mixture was stirred at room temp for 24 hr. Evaporation of the filtrate and elution from a neutral alumina column with cyclohexane yielded erythro-1-(1,2-*dibromo*-2-*phenylethyl*)-2,3,4,5-*tetrabromopyrrole* (0·15 g, 16%), colourless prisms, m.p. 209–210° from chloroform–petrol. (Found: C, 22·6; H, 1·3; Br, 73·9; N, 2·3. $C_{12}H_7Br_6N$ requires: C, 22·3; H, 1·1; Br, 74·4; N, 2·2%): ν_{max} (KBr): 1290 cm^{-1} τ ($CDCl_3$): 2·52 (5H, br, *Ph*), 3·08 (1H, d, J = 11·5 Hz, N—CHBr), 3·76 (1H, d, J = 11·5 Hz, Ph-CHBr).

(iv) Br_2 (0·425 g, 0·0024 mole) in AcOH (2 cm^3) was added slowly to *trans*-1-(2-methylvinyl) pyrrole-2-carboxylic acid (0·1 g, 0·0006 mole) in AcOH (5 cm^3) and the mixture was heated under reflux for 4 hr. The cooled mixture was poured into water, and neutralized with 10% $NaHCO_3$ aq to yield a gummy solid. Elution of this product from a neutral alumina column with ether yielded a mixture (1:1) of **10** and **11**. Variation in reaction conditions, attempted dehydrobromination of the mixture with LiCl-DMF,[4] or TLC failed to yield a pure product; ν_{max} (KBr): 1740 and 1720 cm^{-1} (C=O); τ ($CDCl_3$): 2·8 (1H, s, N—CH=), 3·18 (1H, d, J = 2 Hz, N—CHBr), 5·1 (1H, m, J = 2 and 7 Hz, CH_3—CH), 7·83 (3H, s, CH_3—C=) 8·53 (3H, d, J = 7 Hz, CH_3—CH).

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