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NITROPYRROLES—III*
THE NITRATION OF ACYLPYRROLES

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Abstract—The products and isomer distributions have been determined for the action of nitric acid in acetic anhydride at −15°. Under these conditions the substitution pattern was insensitive to the nature of the acyl group. From 1-acyl- and 2-acyl-pyrroles the products were mixtures containing equimolar amounts of α- and β-nitro derivatives; from 3-acylpyrroles only 4-acyl-2-nitropyrroles were obtained. Structures of the products were conveniently confirmed by their NMR spectra. The relative reactivities of the acylpyrroles are discussed on the basis of a simple HMO treatment, which appears to provide a satisfactory qualitative description if allowance is made for proximity and solvent effects. Oxidation of 2-acetyl-4-and -5-nitropyrroles with dilute nitric acid gave the corresponding furoxans; from 4-acetyl-2-nitropyrrole (2-*nitro*-4-*pyrrolyl*) *glyoxalic acid* was obtained.

ELECTROPHILIC substitution reactions of the 5-membered heteroaromatic rings of pyrrole, furan and thiophen can be characterised[1] as generally fast reactions occurring under mild conditions and leading to preferential attack at the α-position. Both the reactivity of the heteroaromatic ring and the direction of substitution may be modified in the further reaction of mono-substituted derivatives. With electron withdrawing substituents the further substitution reactions proceed less readily in all three ring systems and the proportion of substitution in the β-position may increase significantly. Thus, although the nitration of 2-nitrofuran gives only 2,5-dinitrofuran,[2] from 2-nitrothiophene and 2-nitropyrrole the 2,4-dinitro derivatives[3,4] are the major products. Similarly nitration of 2-acetylfuran[3] gives only 2-acetyl-5-nitrofuran but from 2-acetylthiophen and 2-acetylpyrrole mixtures of the 2,4- and 2,5-isomers are obtained.[3,4] By virtue of their lower accessibility 3-substituted systems have received less attention but typical 3-acylfurans, -thiophenes and -pyrroles are reported to give only the 2-nitro-4-substituted isomers.[5,6] For acylpyrroles although there have been some studies of alkylation and bromination[7] no systematic study of nitration has been reported. Accordingly to establish the influence of acyl substituents the nitration of 1-, 2- and 3-acylpyrroles has been examined using acetyl nitrate generated *in situ* from nitric acid in acetic anhydride.

RESULTS

Acyl pyrroles (I, R = Me, OMe; II, R = H, Me, OH, OMe; III, R = Me, OH, OMe) were prepared by standard routes.

Equimolar solutions of acyl pyrroles and nitric acid in acetic anhydride were allowed to react at −15° for 30 minutes. At the end of this time the solution was allowed to reach room temperature and the products were extracted. By extending the reaction time or by the use of more vigorous conditions higher yields of acylnitropyrroles could be obtained. However the incursion of side reactions particularly under more vigorous conditions makes analysis of the products less reliable. Thus Rinkes[4] reports both nitration and

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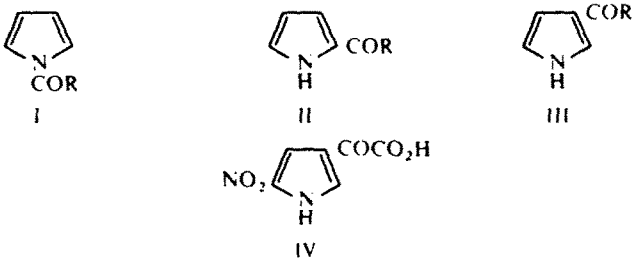
decarboxylation of pyrrole-2-carboxylic acid with 98% nitric acid: under our conditions no decarboxylation was detected.

The yields of nitro compounds under these conditions varied with the location of the acyl substituent from 25% for 1-acyl- to 40–45% for 2-acyl- and 50–60% for 3-acyl-pyrroles. There was no significant variation in yield or in isomer distribution over the range of acyl groups studied.



1-*Acylpyrroles*. Nitration of 1-methoxycarbonyl- and 1-acetyl-pyrrole (I, R = Me, OMe) proceeded smoothly under the standard conditions to give mixtures of products which were shown by TLC to contain small amounts of 2- and 3-nitropyrrole. It seemed probable that these had arisen by partial hydrolysis of the acylnitropyrroles during the isolation procedure. To simplify the analysis the whole of the product was subjected to alkaline hydrolysis. The resultant product in each case, after the removal of pyrrole, was a simple mixture containing only 2- and 3-nitropyrrole. GLC and spectroscopic analysis[8] showed the two isomers to be present in equimolar amounts. The proportion of 3-nitropyrrole formed in the nitration of pyrrole[9] is usually not greater than 20%; the increased proportion formed from nitration of 1-acetylpyrrole together with its comparatively simple chromatographic isolation make this a useful route for the preparation of 3-nitropyrrole.

2-*Acylpyrroles*. Nitration of the 2-acylpyrroles (II, R = H, Me, OH, OMe) was shown by TLC to lead in each case to a mixture of two nitro derivatives. Rinkes[4] has analysed the mixture of products from 2-acetylpyrrole by the selective solubility of the 5-nitro derivative in a solution of sodium bicarbonate. Attempts to use this separation quantitatively were unsuccessful. Accordingly the mixture of products was analysed by UV spectroscopy by using the method of Dewar and Urch.[10] Chromatography of the mixture allowed the isolation of the isomeric nitro derivatives samples of which were used to calibrate the UV analyses and to establish the orientation of substituents by NMR spectroscopy.

For pyrrole-2-carboxylic acid it was anticipated that chromatographic separation of the nitro derivatives would be inconvenient and the crude acid product was converted to a mixture of the corresponding methyl esters. Since the acidity of the imino function in these compounds is sufficient to allow diazomethane to form N-Me derivatives,[11] methylation was best accomplished by methanol/sulphuric acid. Preliminary experiments established that conversion to the esters was essentially quantitative. The crude esters were then chromatographed and analysed spectroscopically.

It has been reported[4] that the orientation of nitration is affected by the nature of the 2-acyl substituent. Thus under conditions similar to those used in the present work, methyl pyrrole-2-carboxylate gave approximately equal amounts of the 4- and 5-nitro deriva-

tives but 2-acetylpyrrole gave 64% 4-nitro- and 30% 5-nitro-2-acetylpyrrole. Fournari and Tirouflet[12] found more nearly equal amounts of the two acetylnitropyrroles. In the present work the yields and orientation of substitution in the products were closely similar for all four 2-acylpyrroles. To within experimental error equimolar amounts of the 4- and 5-nitro derivatives were formed in each case; in no case was there evidence for nitration at the 3-position. It is of interest that the 2-aldehyde also gave this distribution of isomers whereas the analogous thiophen-2-aldehyde, reacting in acetic anhydride as 2-diacetoxymethylthiophene[12], nitrates largely in the 5- position.

3-Acylpyrroles. Examination of the products from nitration of 3-acylpyrroles (II, R = Me, OH, OMe) showed that unlike those from the 1- and 2-acylpyrroles only one nitro derivative could be detected. On the basis of the directing effect of the methoxycarbonyl substituent Rinkes[6] had identified the product from the ester as methyl 2-nitropyrrole-4-carboxylate. NMR spectroscopy confirmed this orientation of substituents for all three of the 3-acyl compounds; in no case was there evidence for the formation of 2,3- or 3,4-disubstituted pyrroles.

NMR spectra have been reported for a variety of substituted pyrroles and give clear indication of the location of substituents through the values for chemical shifts and coupling constants.[7, 8, 11, 13] As in benzenoid aromatics introduction of electron withdrawing substituents causes deshielding of the ring protons. The magnitude of this effect varies with the nature, location and proximity of substituents so that it is not always possible to determine the location of substituents directly from the observed chemical shifts. This becomes evident in the case of pyrroles having strongly electron attracting substituents in the 2- and 5- positions when both the 3- and 4-protons are deshielded and absorb at similar frequencies. In contrast the coupling constants for the pyrrole ring protons remain sensibly constant over a wide range of substituents and allow unequivocal assignment of the location of substituents to be made. Spin coupling interactions in

TABLE 1. NMR SPECTRA OF SOME ACYLPYRROLES

Substituents and chemical shifts for ring protons[a]					Coupling constants[b]					
1	2	3	4	5	J_{23}	J_{24}	J_{25}	J_{34}	J_{35}	J_{45}
H	6·68	6·22	6·22	6·68	2·6	1·4	2·0	3·4	1·4	2·6
$COCH_3$	7·34	6·25	6·25	7·34		$\frac{1}{2}(J_{23} + J_{24}) = 2·4$				
CO_2CH_3	7·34	6·23	6·23	7·34		$\frac{1}{2}(J_{23} + J_{24}) = 2·4$				
H	CHO	7·02	6·33	7·26	—	—	—	3·7	1·4	2·7
H	CHO	8·27	NO_2	7·73	—	—	—	—	1·6	—
H	CHO	7·34	7·24	NO_2	—	—	—	4·5	—	—
H	$COCH_3$	6·89	6·25	7·09	—	—	—	3·8	1·4	2·4
H	$COCH_3$	8·17	NO_2	7·67	—	—	—	—	1·6	—
H	$COCH_3$	7·29	7·22	NO_2	—	—	—	4·3	—	—
H	CO_2CH_3	6·85	6·21	7·06	—	—	—	3·8	1·5	2·5
H	CO_2CH_3	8·13	NO_2	7·44	—	—	—	—	1·8	—
H	CO_2CH_3	7·26	7·06	NO_2	—	—	—	4·3	—	—
H	7·47	CHO	6·69	6·86	—	1·8	1·8	—	—	2·8
H	7·43	$COCH_3$	6·64	6·78	—	1·7	1·7	—	—	2·8
H	7·95	$COCH_3$	7·60	NO_2	—	1·8	—	—	—	—
H	7·43	CO_2CH_3	6·57	6·76	—	1·4	1·9	—	—	2·8
H	7·69	CO_2CH_3	7·37	NO_2	—	1·8	—	—	—	—

[a] δ-values in ppm w.r.t. to TMS for acetone solutions. [b] Hz.

mono and di-substituted pyrroles give rise to complex ABXY and ABX multiplets. These may be simplified by spin decoupling, by studying N-deuteriated pyrroles or by facilitating N-proton exchange. The acidity of acylnitropyrroles is sufficiently great to allow a rapid exchange with acetone as solvent; the resultant spectra (Table 1) allow simple calculation of chemical shifts and coupling constants and confirm the orientation of substituents.

Oxidation of acetylnitropyrroles. The formation of acylfuroxans by the action of dilute nitric acid was demonstrated by Rinkes[4] for 4-nitro- and 5-nitro-2-acetylpyrrole. The IR spectra of the products are entirely in accord with the presence of the furoxan ring.[14] In an attempt to extend this reaction further 4-acetyl-2-nitropyrrole was treated with dilute nitric acid. The IR spectrum of the product differed largely from those of the isomeric furoxans and indicated the presence of a carboxylic acid grouping. The product, which was obtained in good yield, was identified as 2-nitropyrrole-4-glyoxalic acid (IV). The structure was confirmed by oxidation with lead tetra acetate in methanol[15] to methyl 2-nitropyrrole-4-carboxylate.

DISCUSSION

In the absence of precise information on the transition state, substituent effects in aromatic substitution reactions are usually discussed in terms either of the electronic distribution in the ground state of the aromatic substrate or of the stabilities of the appropriate Wheland intermediates. Frequently analysis of ground state polarisation and polarisibility lead to estimates of relative reactivities which are qualitatively similar to those from consideration of the Wheland intermediates. Such agreement corresponds to non-crossing of the energy profiles for competing processes.[16] This condition may not be satisfied for highly polarisible substrates when the nature of the kinetically important transition state and the extent of bonding in it may vary with substituents, reagents and reaction conditions.

This restriction may well apply to discussion of the reactions of pyrrole itself but should be less evident in the behaviour of the acylpyrroles. Nevertheless intuitive assessment of the relative perturbations derived from substituents on the ground states and intermediates can be misleading. To provide a more satisfactory qualitative basis for discussion simple HMO calculations were performed for the species concerned in the nitration of pyrrole and the acylpyrroles. The results (Table 2) from unsophisticated calculation using largely arbitrary parameters are necessarily imprecise and are not expected to yield even approximately correct quantitative values. However the relative changes in charge distribution and π-electron energies arising from perturbation of the

TABLE 2. LOCALIZATION ENERGIES AND π-ELECTRON DENSITIES FOR ACYLPYRROLES

Ring position	π-Electron density (q)				Localization energy (L) (β)				Total π-energy (β)
	2	3	4	5	2	3	4	5	
Pyrrole	1·035	1·106	1·106	1·035	1·933	2·298	2·298	1·933	8·253
1-Acylpyrrole	1·032	1·089	1·089	1·032	1·912	2·319	2·319	1·912	11·826
2-Acylpyrrole	1·061	0·965	1·092	0·903	–	2·474	2·369	2·147	12·049
3-Acylpyrrole	0·885	1·098	1·089	1·021	2·016	--	2·497	1·987	12·000

parent structures are likely to be more reliable and provide a useful guide to substituent effects.

This may be conveniently demonstrated by the correlation between the calculated charge densities and the NMR chemical shifts for the adjacent ring protons. The importance of π-electron density in determining ring proton chemical shifts in aromatic systems is well established though the effects cannot usually be separated from effects due to ring currents and magnetic anisotropy.[17] For the spectra of an isolectronic series of geometrically isomeric compounds measured in a common solvent other effects should be minimised. The observed chemical shifts for pyrrole and acylpyrroles give a satisfactory correlation with the calculated charge densities* (Fig 1). Only for the 2-

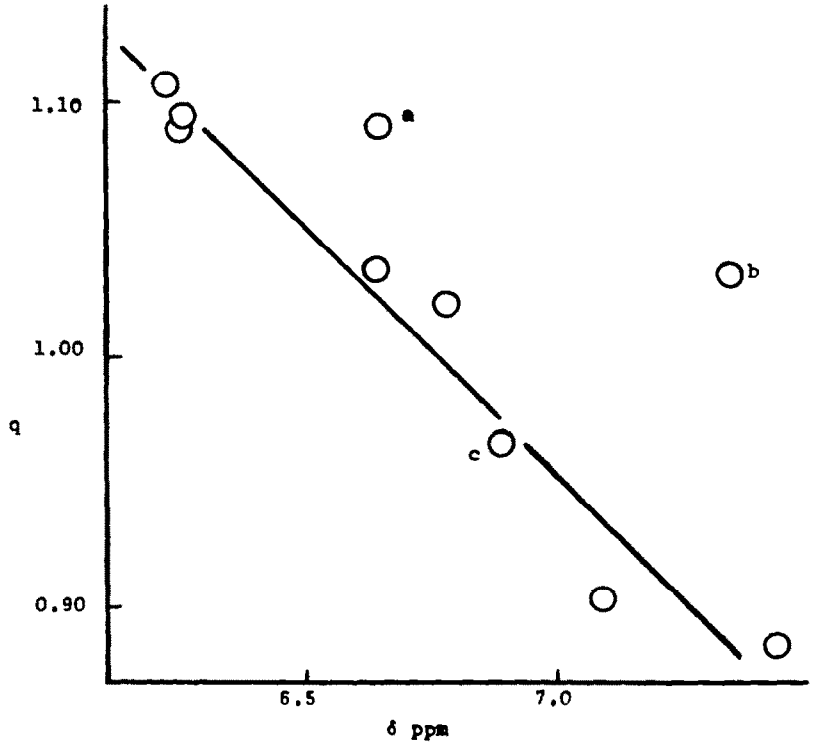


FIG 1. Plot of π-electron density, q, calculated for ring carbon atoms of pyrrole and acylpyrroles *vs* observed chemical shifts, δ, for attached protons.
(a 3-acylpyrrole-4-H; b 1-acylpyrrole-2-H; c 2-acylpyrrole-3-H)

proton in 1-acylpyrroles and the 4-proton in 3-acylpyrroles is there any marked discrepancy. These may well arise from the anistropy of the carbonyl group, indicating a preferred configuration for 3-acylpyrroles, while the absence of any effect for 2-acylpyrroles is expected from its preferred N-*syn*-configuration.[18]

* The insensitivity of the spectra and reactivities to the nature of the acyl group allows a general treatment for a carbonyl substituent to be used satisfactorily for all acylpyrroles.

The π-electron distribution in this simple HMO model for pyrrole without the use of auxiliary inductive parameters[19] gives a negative charge on the β-positions of the ring greater than that on the α-positions. On acyl substitution the charge density at all unsubstituted ring carbon atoms is reduced though the greater charge density is still found at the β-positions with the exception of the 3-position in 2-acylpyrrole. To assess substituent effects it is appropriate to consider the relative changes in charge density at each position. Thus the greater reduction in charge at the β-position in 1-acylpyrroles should correspond to a greater selectivity for α-substitution than is found in pyrrole itself. Similarly for 2- and 3-acylpyrroles the relative changes in π-electron density would suggest increased preference for 4- and 5-substitution respectively.

The total π-electron energy for acylpyrroles is increased by the presence of the two additional electrons in the carbonyl group. Subtraction of the energies for the π-electrons separately in the carbonyl group (3·236β) and the pyrrole ring from that calculated for the HMO models of acylpyrroles gives the additional conjugation energies for the acylpyrroles. In accord with expectation this is least for the 1-acyl- (0·337β) and greatest for the 2-acyl-isomer (0·560β). Similar comparisons of the additional conjugation energies for the Wheland intermediates show that these are all lower than for the related aromatic systems with the exception of the intermediate leading to 1-acyl-2-nitropyrrole. In consequence, with this exception the localisation energies for substitution into the acylpyrroles are greater than for the corresponding positions for pyrrole. Again, comparison with the localisation energies for pyrrole suggests an increased proportion of α-substitution in 1- and 3-acylpyrroles and an increased proportion of β-substitution for 2-acylpyrroles.

For pyrrole itself, where acetyl nitrate preferentially attacks the α-position, the localisation energies give the better qualitative agreement with experiment though the difference (L_α-L_β) is considerably greater than estimates of the difference in activation energies for attack at the α- and β-positions.[9] However, when they are used relatively for the 2- and 3-acylpyrroles, the changes in both parameters q and L are in general agreement and in accord with the experimental evidence *viz* they indicate for 2-acylpyrroles an increased tendency to 4-substitution; and for 3-acylpyrroles preferential substitution at the 5- position. In the case of 1-acyl-pyrroles both parameters predict predominantly α-substitution though they differ in ascribing this to β-deactivation (q) and α-activation (L). Here the models are at variance with the experimental results which show both positions to be of similar reactivity.

The discrepancy shown for 1-acylpyrroles can obviously be ascribed to the neglect of steric factors in HMO calculations. On the assumption of steric hindrance to substitution at positions adjacent to the acyl group the results can be qualitatively reconciled. It is fortuitous that for the other acyl-pyrroles factors originating in the π electron system also disfavour substitution at positions adjacent to the acyl group and no other proximity effects are apparent in the isomer distribution. A further major discrepancy is however evident in the apparent relative reactivities of the acylpyrroles. The observed yields indicate an order of reactivity 3- > 2- > 1-acylpyrroles whereas, even allowing for proximity effects, the calculated localisation energies suggest the order 1- > 3- > 2-acylpyrrole. The range of reactivity shown experimentally is small as are the differences in the calculated localisation energies and it may be that minor factors not originating in the π-electron system become significant. In particular the possibility of increased hydrogen bonding of solvent to the N—H group may provide additional stabilisation for

the transition states for 2- and 3-acylpyrroles.* The effects of solvent in these and related reactions is at present under investigation.

TABLE 3. UV SPECTRA[a] OF SOME SUBSTITUTED PYRROLES

Substituents	λ_{max}[b] log ε (nm)	λ_{max} log ε (nm)
2-NO_2	231 (3·61)	335 (4·23)
3-NO_2	268 (3·86)	315 (3·73)
2-CHO	[252] (3·79)	289 (4·24)
2-CHO 4-NO_2	247 (4·02)	299 (3·79)
2-CHO 5-NO_2	242 (3·85)	333 (4·04)
2-$COCH_3$	[250] (3·70)	287 (4·21)
2-$COCH_3$ 4-NO_2	247 (4·10)	303 (3·88)
2-$COCH_3$ 5-NO_2	241 (4·08)	330 (4·17)
2-CO_2CH_3	[235] (3·70)	265 (4·15)
2-CO_2CH_3 4-NO_2	236 (4·25)	301 (3·78)
2-CO_2CH_3 5-NO_2	228 (4·10)	325 (4·10)
3-$COCH_3$	243 (3·97)	[270] (3·66)
4-$COCH_3$ 2-NO_2	226 (4·06)	323 (3·95)
3-CO_2CH_3	225 (3·91)	[247] (3·76)
4-CO_2CH_3 2-NO_2	-- --	321 (4·08)

[a] Solution in methanol

[b] Points of inflexion are shown in square brackets.

EXPERIMENTAL

Nitration of methylpyrrole-2-carboxylate. A soln of methyl pyrrole-2-carboxylate[20] (4 g) in Ac_2O (24 g) was treated with a cold soln of 70% HNO_3 (3 g) in Ac_2O (15 g). After 30 min at −15° the mixture was allowed to warm to room temp, poured onto ice and extracted into ether (2 × 100 ml). The residue, after removal of solvent, was chromatographed on silica gel using 10% chloroform in benzene giving methyl 4-nitropyrrole-2-carboxylate, m.p. 196°, (from MeOH-light petroleum, b.p. 100–120°) and methyl 5-nitropyrrole-2-carboxylate, m.p. 183° (from MeOH-light petroleum, b.p. 100–120°); the total yield of nitro esters was 2·6 g.

The identity of methyl 4-nitropyrrole-2-carboxylate was confirmed by methylation of 4-nitropyrrole-2-carboxylic acid obtained from condensation of nitromalondialdehyde and glycine ester hydrochloride.[21] The acid (0·22 g) was boiled under reflux for 12 hr with MeOH (2 ml) and H_2SO_4 (0·2 ml); extraction of the product into ether (2 × 150 ml) gave the ester, m.p. 198° (from water) which was spectroscopically and chromatographically identical with the nitration product.

Similarly, 2-formylpyrrole[22] (10 g) gave a mixture of nitroproducts (4·8 g) which was resolved chromatographically giving 2-formyl-4-nitropyrrole, m.p. 139–141° (from light-petroleum, b.p. 100–120°) and 2-formyl-5-nitropyrrole, m.p. 183° (from light petroleum, b.p. 100–120°); and 2-acetylpyrrole[23] (7 g) gave a mixture (4·5 g) of 2-acetyl-4-nitropyrrole, m.p. 195–6° (from light petroleum, b.p. 100–120°) and 2-acetyl-5-nitropyrrole, m.p. 156° (from light petroleum b.p. 100–120°).

Nitration of pyrrole-2-carboxylic acid. Pyrrole-2-carboxylic acid[20] (5 g) was nitrated in the usual way. The mixture of crude nitro acids was boiled under reflux for 12 hr with MeOH (24 ml) and H_2SO_4 (2·5 ml) and the resultant esters were extracted into ether (2 × 100 ml). The mixture of nitro esters (2·75 g) was chromatographed over silica gel giving methyl 4-nitro-pyrrole-2-carboxylate, m.p. 196°, and methyl 5-nitropyrrole-2-carboxylate, m.p. 183°, identical in all respects with the nitration products from methyl pyrrole-2-carboxylate.

* Variation in hydrogen bonding is largely a function of δ-electron distribution. Consequently although the π-electron density on nitrogen does not uniformly decrease in the Wheland intermediates from the acylpyrroles, the inductive effects of the positively charged α-positions will lead to an increase in the strength of the N—H... solvent bond.

Nitration of 1-acetylpyrrole. A soln of 1-acetylpyrrole[24] (5 g) in Ac_2O (30 g) was treated with 70% HNO_3 (4·5 g) in Ac_2O in the usual way. The crude product in MeOH (20 ml) was boiled under reflux for 6 hr with 20% NaOH aq (50 ml). Removal of the solvents left a brown oil which was filtered through a short column of silica gel using benzene, giving a mixture (1·0 g) of nitropyrroles as a pale yellow coloured solid.

A similar mixture (1·5 g) was obtained from methyl pyrrole-1-carboxylate[25] (5 g). Chromatography of the mixture on silica gel using benzene gave 2-nitropyrrole, m.p. 65° and 3-nitropyrrole, m.p. 101°, identical with authentic samples.

Nitration of methyl pyrrole-3-carboxylate. A soln of the ester[26] (0·3 g) in Ac_2O (5 ml) was treated in the usual way with 70% HNO_3 (0·25 g) in Ac_2O (3 ml). The crude product, showing the presence of only one nitro compound on TLC, was filtered through a short column of silica gel using 40% benzene in chloroform to give methyl 2-nitropyrrole-4-carboxylate (0·22 g), m.p. 201–203° (from light petroleum, b.p. 100–120°). (Found: C, 42·5; H, 3·8; N, 16·5. $C_6H_6N_2O_4$ requires: C, 42·4; H, 3·5; N, 16·5%).

Similarly 3-acetylpyrrole[23] (5 g) gave 4-acetyl-2-nitropyrrole (2·9 g), m.p. 197–198·5° (from water). (Found: C, 47·2; H, 4·1; N, 18·0. $C_6H_6N_2O_3$ requires: C, 46·8; H, 3·9; N, 18·2%).

Pyrrole-3-carboxylic acid[26] (1 g) was nitrated in the usual way and the crude product was boiled under reflux for 12 hr with MeOH (2 ml) and HSO_4 (0·2 ml) to give methyl 2-nitropyrrole-4-carboxylate (0·93 g) m.p. 204–5° (from water), mixed with the nitration product from methyl pyrrole-3-carboxylate, m.p. 202–4°; the IR spectra of both samples were identical. TLC showed the formation of only one isomer.

Action of nitric acid on acetylnitropyrroles

(i) 2-Acetyl-4-nitropyrrole (2 g) was boiled under reflux for 2 hr with 25% HNO_3 (40 ml) giving 3,4-di-(4′-nitro-2′-pyrroloyl)-furoxan[4], m.p. 216°. Similarly 2-acetyl-5-nitropyrrole gave 3,4-di-(5′-nitro-2′-pyrroloyl)-furoxan[4], m.p. 174–6°.

(ii) 4-Acetyl-2-nitropyrrole (2 g) treated similarly gave (2-nitro-4-pyrroloyl)-glyoxalic acid, m.p. 164–6° (from water). (Found: C, 38·6; H, 3·0; N, 15·0. $C_6H_4N_2O_5$ requires: 38·7; H, 3·2; N, 15·0%). Treatment of the keto acid with an excess of ethereal diazomethane gave methyl (1-methyl-2-nitro-4-pyrrolyl)-glyoxalate, m.p. 166–8° (from light petroleum b.p. 100–120°). (Found: C, 45·3; H, 4·0. $C_8H_8N_2O_5$ requires: C, 45·3; H, 3·8%).

A soln of the keto acid (0·2 g) in dry MeOH (5 ml) and benzene (10 ml) was treated at 45° for 1 hr with lead tetra-acetate (0·5 g) in benzene (20 ml). The soln was filtered and the filtrate combined with ether washings (2 × 25 ml) of the ppt. The combined organic soln was washed with 10% $NaHCO_3$ aq dried, and evaporated leaving methyl 2-nitropyrrole-4-carboxylate (0·1 g) m.p. 202–3°, identical in all respects to the previous samples.

Analytical methods. NMR spectra (Table 1) were measured for acetone soln using a Varian A60-A spectrometer, UV spectra (Table 3) were recorded on a Unicam SP800 spectrometer. TLC refers to silica gel with either chloroform or ether/benzene as solvent. GLC for nitroyrroles was with a silicone gum column.

To determine isomer ratios each acylpyrrole was nitrated in the ususal way and the total nitration products isolated under standard conditions. The UV spectra were recorded, analysed according to the method of Dewar and Urch[10] and finally matched by comparison with synthetic mixtures of authentic compounds. The results appear to be accurate to *ca* ±2%.

HMO calculations were performed with Coulomb integrals for nitrogen and oxygen set at $(\alpha + 1{\cdot}58\beta)$ and $(\alpha + \beta)$ respectively; and with resonance integrals for C—N and C—O bonds at $0{\cdot}8\beta$ and β respectively.[27] No auxiliary inductive parameter[IV] was used for the α-carbon atoms. Variation in the Coulomb integral for nitrogen alters the absolute values of q and L but does not lead to any significant change in qualitative predictions of relative reactivities.

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