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THE PROTONATION OF N-PHENYLPYRROLES

Y. CHIANG, R. L. HINMAN, S. THEODOROPULOS and E. B. WHIPPLE

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Abstract—The positions of protonation and basicities of a series of N-phenylpyrroles have been determined by NMR and UV spectroscopy. Changes in these properties wrought by methyl substitution and concomitant twisting about the interannular bond are described. Effects on UV spectra of twisting the free bases and conjugate acids around the interannular bond have been analyzed in MO terms. The relationship of the chromophores of the pyrrole conjugate acids are discussed in terms of the simple iminium chormophore and its open-chain conjugated derivatives.

IN PREVIOUS papers effects observed in the protonation of indole,[1a] pyrrole,[1b] and many of their simple alkyl derivatives have been described, with emphasis on positions of protonation and basicities. Observations on the behavior of 2,5-dimethyl-1-phenylpyrrole have also been reported.[2] As an extension of this work we have examined a series of N-phenylpyrroles with the aid of the NMR and UV absorption techniques used in the earlier studies. The UV spectra of the conjugate acids are of added interest as examples of the conjugated iminium chromophore.

1. *Basicities*

Basicities in the pyrrole series can be estimated qualitatively from the acid concentrations required to effect half protonation.[1] For quantitative comparison of basicities some form of numerical pK value is required, either of the relative or thermodynamic type.[1a] Since measurable protonation occurs only in strong acids, the Hammett acidity function concept or one of its variations[3] must be invoked to provide pK values. It has been clearly demonstrated in recent years, however, that the acidity function concept has a number of severe limitations.[1a,3] There is no assurance that this method yields thermodynamic pK values.[1a] Even for relative basicities a troublesome problem is introduced by the many deviations of the slopes of indicator ratio plots at any given acid concentration from the common value expected from the familiar equation $pK_a = H_0 + \log I$, where I = indicator ratio. Thus the average value of $d \log I/d\, C_{acid}$ given in Table 1 ($0{\cdot}86 \pm 0{\cdot}03$) is much higher than that of the H_0 bases ($\sim 0{\cdot}48$)[4] and the alkylindoles ($\sim 0{\cdot}70$),[1a] exceeds slightly the values reported for the alkylpyrroles ($\sim 0{\cdot}77$),[1b] and approaches the average value of H_R' ($\sim 0{\cdot}9$).[5] This trend is in the direction usually associated with decreased solvation of the conjugate acid.[1a,3]

[1a] R. L. Hinman and J. Lang, *J. Amer. Chem. Soc.* **86**, 3796 (1964); [b] Y. Chiang and E. B. Whipple, *Ibid.* **85**, 2763 (1963).

[2] E. B. Whipple, Y. Chiang and R. L. Hinman, *J. Amer. Chem. Soc.* **85**, 26 (1963).

[3] E. M. Arnett, *Progress in Physical Organic Chemistry* (Edited by S. G. Cohen, A. Streitwieser, Jr. and R. W. Taft) Vol. I; p. 223. Interscience, New York (1963).

[4] M. J. Jorgenson and D. R. Hartter, *J. Amer. Chem. Soc.* **85**, 878 (1963).

[5] N. C. Deno, P. I. Groves and G. Saines, *J. Amer. Chem. Soc.* **81**, 5790 (1959); A. J. Kresge and Y. Chiang, *Proc. Chem. Soc.* 81 (1961).

When faced with this problem of comparing basicities among systems which obviously are not equally affected by solvent, one can either rank them according to the strength of acid required to effect a fixed degree of protonation, or compare the extents of protonation in a fixed reference acid (e.g. dilute aqueous solution). The latter method may require long extrapolations of questionable validity, while the former suffers the disadvantage of arbitrariness in the choice of acidity scales. The results of an extensive study of indole basicities proved more self-consistent when based on a single acidity scale despite deviant behavior of the indicator ratio plots,[1a] suggesting that one might better neglect these deviations than extrapolate them over large concentration ranges. Adopting this view, there remains the choice of a uniform measure of acid strength, the particular acidity function chosen for this purpose introducing a scale factor in the relative basicities.[6] Since the values of d log I/d C_{acid} for the N-phenylpyrroles approach those of the H_R' indicators,[5] we have chosen to express the pK_a's in terms of this acidity function.

TABLE 1. BASICITIES OF N-PHENYLPYRROLES

Cpd. No.	Pyrrole	Ratio of conjugate acids $(\beta/\alpha)^a$	Molarity of H_2SO_4 for 50% protonation	$\frac{d \log I^{b,c}}{d C_{H_2SO_4}}$	Acid conc. range (M) over which slope was measured^c	pK_α^d	pK_β^d
1	Pyrrole	0	5·3	0·74	3·6–6·8	4·4^e	
2	1-Methyl	0	4·1	0·76	2·3-5·9	−3·4^e	
3	2,5-Dimethyl	0·42	1·1	0·79	0·7–2·2	−0·8	−1·2
4	1,2,5-Trimethyl	0·56	0·5	—		−0·2	−0·5
5	1-Phenyl	0	6·7	0·83	5·6–8·2	−5·8	
6	1-(2′,6′-Dimethylphenyl)	0	7·3	0·90	6·0–8·6	−6·3	
7	1-(2′,6′-Dimethyl-4′-hydroxyphenyl)	0	6·9	0·90	5·7–8·1	−6·0	
8	2,5-Dimethyl-1-phenyl	0·19	2·7	0·84	1·4–4·1	−2·3	−3·0
9	2,5-Dimethyl-1-(4′-carboxyphenyl)	0·16	3·4	0·82	2·1–4·9	−2·9	−3·7
10	2,5-Dimethyl-1-(2′,6′-dimethylphenyl)	1·9	4·1	0·88	2·8–7·4	−3·9	−3·6
11	2,5-Dimethyl-1-(2′,6′-dimethyl-4′-hydroxyphenyl)	1·3	3·5	0·82	2·1–4·9	−3·3	−3·2

[a] Determined from NMR spectrum of fully protonated pyrrole in sulfuric acid. [b] Slope of indicator ratio plot. [c] See Ref. 1*a* for full explanation. [d] Calculated using H_R'. [e] Taken from Ref. 1*b* and converted to the H_R' scale.

By assuming, as has been verified in the case of 1-phenyl-2,5-dimethylpyrrole,[2] that equilibria for α- and β-protonation follow the same acidity function, and using the protonation ratios determined (at much higher concentration) by NMR, values for both pK_α and pK_β were calculated where applicable in Table 1. It was determined earlier[2] by NMR that addition of an N-phenyl group to 2,5-dimethylpyrrole decreased the ratio of β- to α-protonation from 0·42 to 0·19. It has since been found (Table 1) that when four methyl groups are introduced in the 2,5,2′- and 6′-positions of 1-phenylpyrrole, the β-protonated conjugate acid predominates. This result appears to be a consequence of increased steric hinderance in the α-protonated salt compared to the β-isomer in which the methyl group repulsions are more successfully minimized

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[6] A. J. Kresge, G. W. Barry, R. R. Charles and Y. Chiang, *J. Amer. Chem. Soc.* **84**, 4343 (1962). A linear relation among indicator acidity functions is implicit in the method of data analysis introduced in this paper. See reference 1a for further discussion on this point.

by orienting the rings at a dihedral angle of 90°. Since in this conformation β-protonation of the base causes no apparent change in steric hindrance, one might, ignoring a possible difference in solvation, attribute the entire change in protonation ratio to steric hindrance in the α-protonated salt and estimate its magnitude from the difference in logarithms of the protonation ratios which amount to 1·0 pK_a unit, or 1·3 kcal/mole^{-1}.

Apart from this, the basicities in Table 1 can be considered in terms of three effects used to explain basicity differences among the anilines:[7] steric inhibition of solvation, steric inhibition of resonance, and inductive effects. The positive charge in the pyrroleninium ions is localized to a considerable extent (>50%) on nitrogen,[1b] and solvation is probably concentrated in this vicinity with the solvent molecules approaching out of the plane of the pyrrole ring. It is this approach which is most effectively hindered by *ortho*-methyl groups on the N-phenyl ring. It is, moreover, reasonable to expect that a change in solvation alters the acidity function[1a] and in particular that when the heteroatom is effectively shielded from the solvent the pyrroles might resemble the hydrocarbon bases.[5] With one exception (compound 11) the slopes of the indicator ratio plots in Table 1 do parallel the expected steric hindrance to solvation at the nitrogen atom, and the most shielded bases approach the H_R' acidity function[6] rather closely. Without N-phenyl substitution the slopes are in the range 0·74–0·79, N-phenyl groups increase the slopes to the range 0·82–0·84, while ortho substitution causes a further increase to the range 0·88–0·90.

A decrease in basicity of 0·6 pK unit accompanying *ortho*-dimethylation which is found in comparison of β-protonation of 2,5-dimethyl- and 2,5,2′,6′-tetramethyl-1-phenylpyrrole can be attributed almost entirely to inhibition of solvation since interannular conjugation is essentially eliminated by the α-methyl groups on 2,5-dimethyl-1-phenylpyrrole.[8] A corresponding depression of about 0·5 pK_a unit occurs for α- protonation on adding *ortho*-methyl groups to 1-phenylpyrrole. Interannular conjugation must be essentially eliminated in this case too, since steric hinderance is greater for a six-membered ring than a five-membered ring substituted in this way.[9] Since the entire change in basicity wrought by *ortho*-dimethylation is attributable to solvation effects, one is led to infer that interannular conjugation in N-phenylpyrrole has no significant effect on its base strength. Dipole moment measurements show that interannular conjugation does affect the charge distribution in N-phenylpyrrole,[8] and its effect on the resonance energy has been estimated to be as large as 6 kcal/mole^{-1}.[10] Failure to observe effects of this magnitude in the base strengths implies the presence of a largely compensating interannular resonance energy in the conjugate acids. This conclusion is substantiated by the molecular-orbital delocalization energies listed in Table 2. The added stabilization associated with an increase in the interannular resonance integral from 0·0 to 1·0β is 0·32β for the salts, compared to a value of 0·29β similarly calculated for the free base. The pK_a is affected by the difference in stabilization energies, which is seen to be much smaller than the interannular stabilization of either the base or its conjugate acid.

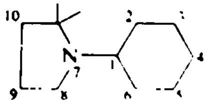
[7a] B. M. Wepster, *Rec. Trav. Chim.* 76, 357 (1957); [b] J. Burgers, M. A. Hoefnagel, P. E. Verkade, H. Visser and B. M. Wepster, *Ibid.* 77, 491 (1958).

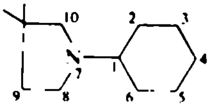
[8] H. Koford, L. E. Sutton and J. Jackson, *J. Chem. Soc.* 1467 (1952).

[9] L. L. Ingraham, *Steric Effects in Organic Chemistry* p. 481. (Edited by M. L. Newman) Wiley, New York (1956).

[10] V. Schomaker and L. Pauling, *J. Amer. Chem. Soc.* 61, 1778 (1939).

TABLE 2. π-ORBITAL ENERGIES AND CHARGES IN N-PHENYLPYRROLE FOR VARIOUS INTERANNULAR RESONANCE INTEGRALS[a]





			$k = 0$	$k = 0{\cdot}5\beta$	$k = 1{\cdot}0\beta$	$k = 0$	$k = 0{\cdot}5\beta$	$k = 1{\cdot}0\beta$
Total energy[b]			15·750	15·830	16·068	15·664	15·743	15·978
	H_B		1·067	0·987	0·843	1·067	1·073	1·082
Orbital energies[b]	H_N		1·236	1·281	1·338	0·906	0·877	0·809
	V_N		−0·133	−0·131	−0·124	−0·210	−0·205	−0·192
Orbital charges (α-positions)	H_B	C_8	0·000	0·000	00·08	0·000	0·091	0·230
		C_{10}		—	-	0·000	0·000	0·001
	V_N	C_8	0·440	0·433	0·414	0·006	0·006	0·004
		C_{10}	--	—	-	0·726	0·712	0·678
	H_N	C_8	0·085	0·101	0·136	0·371	0·287	0·165
		C_{10}	—	—	—	0·118	0·133	0·174
Orbital charges (*ortho*-positions)	H_B		0·063	0·071	0·096	0·063	0·051	0·034
	V_N		0·000	0·006	0·022	0·000	0·008	0·029
	H_N		0·000	0·002	0·001	0·000	0·018	0·005

[a] Huckel approximation with $h_N = 2{\cdot}0\beta$, $k_{C-N} = 1{\cdot}0$, and AIP = $0{\cdot}1h$. See A. Streitweiser, *Molecular Orbital Theory for Organic Chemists.* Wiley New York (1961); [b] Energies in units of the carbon–carbon exchange integral, β.

Wepster has argued[7] that N-phenyl groups lower the basicity constants of amines by both inductive and resonance effects, each amounting to about 2·7 logarithmic units. In N-phenylpyrroles the latter effect is cancelled by stabilization of the conjugate acid, and inductive effects are expected to be diminished by delocalization of charge. Neglecting the smaller differences in electron density on nitrogen in the bases, the evidence[1b] that the positive charge in the pyrroleninium salt is only ~50 % localized on the nitrogen atom suggests that the inductive effect of phenyl substituents will be only half as effective in pyrroles as in amines. The observed base weakening effect of ~1·5 logarithmic units (Table 1 and Ref. 2) thus compares reasonably with Wepster's result.

2. *Ultraviolet spectra*

N-Phenylpyrroles. N-phenylpyrrole has an intense UV absorption at 248 mμ (Fig. 1) which is not present in pyrrole or its methyl derivatives (Table 3).[11] It has been shown previously[12] that twisting along the N-phenyl bond caused by introduction of methyl groups in the 2- and 5-positions is accompanied by a marked decrease in intensity of the 248 mμ band. Thus the UV absorption spectrum of 2,5-dimethyl-1-phenylpyrrole is similar to that of 1-benzylpyrrole but differs from that of 1-phenylpyrrole.[12] The spectra of the four bases shown in Fig. 1 extend these observations and show that *ortho*-methyl groups in the phenyl ring are more effective in suppressing

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[11] R. L. Hinman and S. Theodoropulos, *J. Org. Chem.* **28**, 3052 (1963).

[12] J. Davoll, *J. Chem. Soc.* 3802 (1953).

TABLE 3. UV SPECTRA OF N-PHENYLPYRROLES[a]

Entry	Pyrrole	Free base (95% EtOH) $\lambda_{max}(m\mu)$	Free base (95% EtOH) ϵ_{max}	Conjugate acids λ^{α}_{max}	Conjugate acids ϵ^{α}_{max}	Conjugate acids $\lambda^{\sim 270\ m\mu^{k}}_{max}$	Conjugate acids $\epsilon^{\sim 270\ m\mu^{k}}_{max}$	$C^{b}_{H_2SO_4}$
1	Pyrrole	208	7300	241	7900			7·6
2	1-Methyl	210[c]	5800	247	4100			7·2
3	2,5-Dimethyl	209[c]	7700	237	4100[d]	275	2500[d]	2·5
4	1,2,5-Trimethyl	211[c]	8300	243	4850[d]	280[e]	2600[d]	3·0
5	1-Phenyl	248	11, 300	239, 244	2400, 3200			12·0
				315	5500			
6	1-(4′-Nitrophenyl)	225, 330	12, 200, 15, 500	213 sh	7350			18·0
				242	4310			
				311	14,300			
7	1-(2′,6′-Dimethylphenyl)	207 sh, 230 sh	15, 400, 3500	207	7700			12·0
				250	5440			
				287	840			
8	1-(2′,6′-Dimethyl-4′-hydroxyphenyl)	275	930	214	6700			12·6
				250	6050			
9	2,5-Dimethyl-1-phenyl	230 sh	5230	239[f]	5700[d]	270[f]	28,000[g]	4·5
10	2,5-Dimethyl-1-(4′-carboxyphenyl)	215, 251	13, 100, 7200	227[h]	10,400[d]	272	48,200[i]	6·5
11	2,5-Dimethyl-1-(2′,6′-dimethylphenyl)	207	13,100	206	8550			
				252	8700[d]	(270)[j]	(3100)[d,j]	9·4
12	2,5-Dimethyl-1-(2′,6′-dimethyl-4′-hydroxyphenyl	272, 278	1000, 930	215	7000			9·4
				250	6300[d]	(270)[j]	(3100)[d,j]	

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[a] Measured on 10^{-4}–10^{-5} M sols of pyrroles. [b] Molarity of sulfuric acid in which spectra were measured. [c] In water. [d] Corrected for β/α ratio (Table 1). [e] Inflection; see Ref. 7. [f] Tail absorption to 330 mμ, probably from peak at 315 mμ of α-protonated isomer—see text. [g] Observed value after correction for β/α ratio. Subtracting absorption of α-protonated isomer at this wavelength (using absorption of N-phenylpyrrole as model) reduces value to ~18000. [h] Band due to p-ammonio-benzoic acid portion obscures peak from α-protonated isomer. [i] Observed value after correction for β/α ratio. Allowance for absorption of α-isomer reduces value to ~36000. [j] No peak observed, presumably due to interannular twist. [k] Ascribed to β-isomeric salt in alkylpyrroles, but to coincidental superposition of a mixture of absorption bands in N-phenylpyrroles (see text).

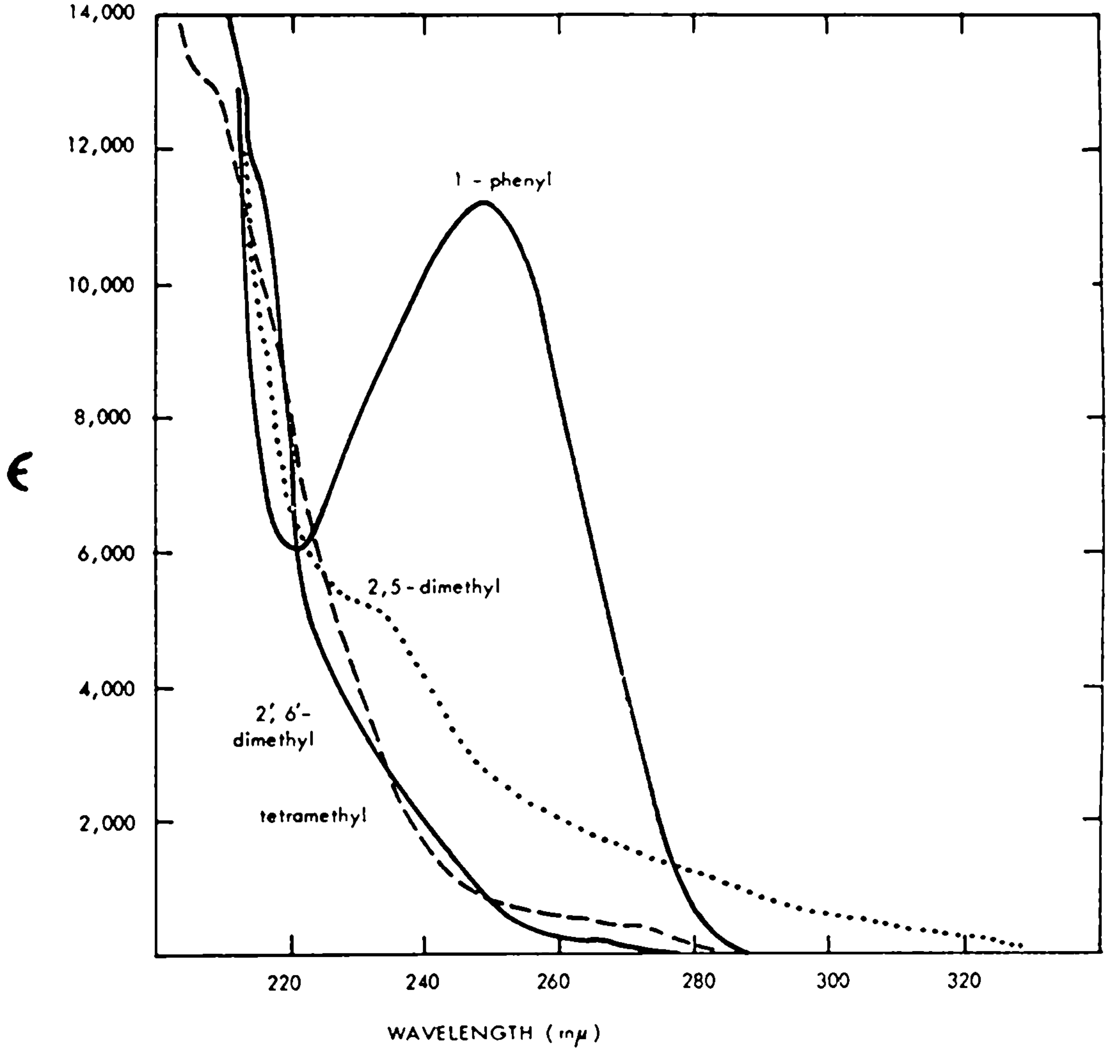


FIG. 1. UV spectra of 1-phenylpyrrole and its methyl derivatives in water.

the 248 $m\mu$ band than are methyl groups at the α-positions of the pyrrole ring, a result in accord with other observations on steric inhibition of resonance.[9]

Similar behavior has been observed for the closely corresponding C-band in *ortho*-substituted N,N-dimethylanilines,[7b] which can be associated with the primary band of substituted benzenes.[13] From these correlations, the band at λ_{max} 248 $m\mu$ in N-phenylpyrrole can be assigned to a $\pi \rightarrow \pi^*$ transition of a substituted benzene. Its similarity to N,N-dimethylaniline is reasonable[14] in view of the fact that the ionization potentials of pyrrole (8·97 eV) and dimethylamine (8·93) are quite similar.[15]

[13] L. Doub and J. M. Vanderbelt, *J. Amer. Chem. Soc.* **69**, 2714 (1947).

[14] F. A. Matsen, *Technique of Organic Chemistry* (Edited by A. Weissberger) Vol IX. Interscience, New York (1956).

[15] I. Omura, H. Baba and K. Higasi, *J. Phys. Soc. Japan* **10**, 317 (1955); J. Collin, *Canad. J. Chem.* **37**, 1053 (1959).

As a related observation the UV spectra of N-phenylpyrrole, N-phenylpyrrolidine, and N,N-divinylaniline[16] all have the principal absorption band near 250 mμ with similar intensity ($\varepsilon = 12{,}000$–$15{,}000$).

Weaker bands which appear in the spectra of the substituted N-phenylpyrroles can generally be accounted for by considering the molecule as a polysubstituted benzene. Thus, the 275 nμ band in the spectra of compounds 8 and 12 of Table 3 is undoubledly the secondary band[13] of phenol.

Conjugate acids. The conjugate acid of 1-phenylpyrrole has a maximum in the 240 mμ region, but of much lower intensity than that of the free base, and a new band is present at 315 mμ (ε 5550). Since the band head at lower wavelength has about the

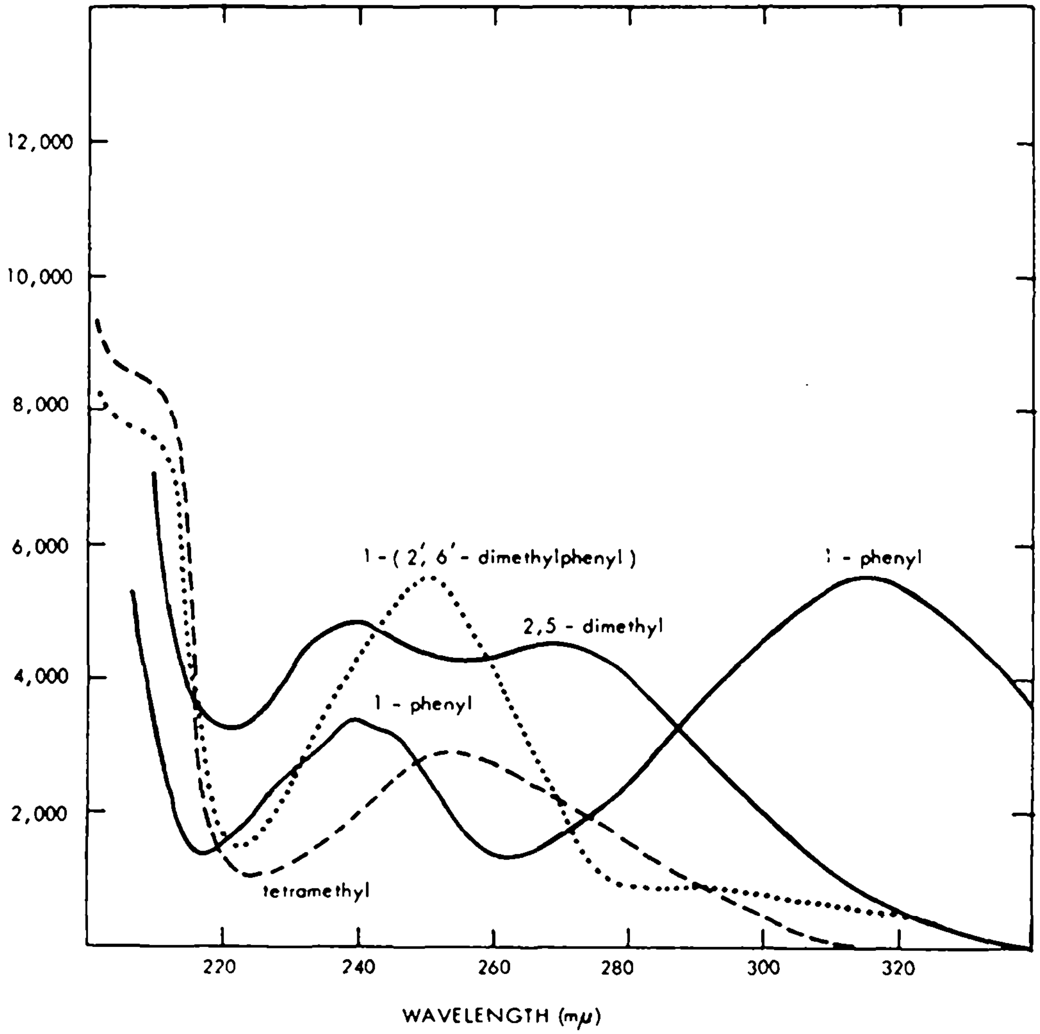
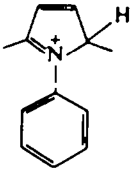


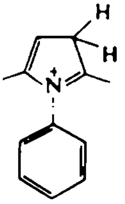
FIG. 2. UV spectra of 1-phenylpyrrole conjugate acids in sulfuric acid. Intensities are derived from observed absorptions, not corrected for relative amounts of α- and β-conjugated acids.

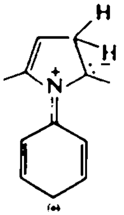
same wavelength and intensity as that of pyrrole conjugate acid and its simple methyl derivatives, it presumably arises from the pyrrole portion of the molecule. The absorption at longer wavelength probably involves a longer conjugated system extending over both rings. Structures involving considerable charge separation can be written similar to IIIc and would of course be expected to be more important in the excited state than in the ground state.

Support for this assignment is found in the spectra of the conjugate acids of the substituted N-phenylpyrroles. When methyl groups are introduced adjacent to the nitrogen, the max at 315 mμ vanishes, but absorption is still moderately intense. As substitution is increased, the intensity of absorption at 315 mμ decreases in the same order as that observed for the free bases (Table 4). Since the absorption intensity at 315 mμ of protonated 2,5-dimethyl- and 1,2,5-trimethylpyrrole (ε^{315} 20 and 0, respectively) is markedly weaker, absorption of the protonated phenylpyrroles in this region can be ascribed to the α-protonated-1-phenyl-pyrrole chromophore, which exemplifies, like the free bases, a typical case of steric inhibition of resonance[9] when the phenyl ring is forced out of the plane of the pyrrole ring. For the 2′,6′-dimethyl derivative (entry 7, Table 3) the maximum at 250 mμ is ascribed to the protonated pyrrole ring, shifted bathochromically by the *m*-xylyl system. The corresponding 4′-hydroxy derivative (entry 8 in Table 2) has a similar spectrum with an additional maximum at 214 mμ, undoubtedly due to the *p*-ammoniophenol chromophore, since $p\text{-}\overset{+}{N}H_3C_6H_4OH$ in water has a maximum at 218·5 mμ (ε_{max} 6200).[15]

The spectrum of protonated 2,5-dimethyl-1-phenylpyrrole differs from that of the other dimethyl derivative (entry 7, Table 3) in having two max at 239 and 270 mμ. Assuming that these arise respectively from the α- and β-protonated species (IIIa and IIIb), as suggested in an earlier report,[8] the intensities can be corrected for the amount of each isomer present in the mixture, as determined by NMR. The intensities thus obtained are $\varepsilon_{\alpha}^{239}$ 5700 and 18,000 $\leq \varepsilon_{\beta}^{270} \leq$ 28,000.[17] This pronounced enhancement by the N-phenyl group of absorption in the 270 mμ region, which was not described in the earlier report,[8] also appears in the *p*-carboxy derivative (Table 3, entry 10). In this case the band of the α-protonated species is obscured by the increased intensity of the 272 mμ band.[18] This unexpectedly large perturbation prompts more careful analysis of the absorption near 270 mμ, which leaves much more doubt than before as to the identity of the responsible chromophoric group.


IIIa


IIIb


IIIc

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[16] E. Y. C. Chang and C. C. Price, *J. Amer. Chem. Soc.* **83**, 4650 (1961).

[17] Uncertain because intensity of tail absorption of α-peak is unknown.

[18] The max at 227 mμ is probably due to the $p\text{-}\overset{+}{N}\text{-}C_6H_4CO_2H$ chromophore, since $p\text{-}\overset{+}{N}H_3C_6H_4CO_2H$ absorbs at 227 mμ (ε_{max} 12300).[16]

When four methyl groups restrict coplanarity as in entries 11 and 12 of Table 3, absorption in the 270 mμ region decreases to values approaching those of the β-conjugate acids of simple methylpyrroles, suggesting that interannular resonance interactions are involved in the less-twisted salts. Support for this view is found in the *p*-hydroxy derivative (entry 12). Although this substituent would be expected to aid the development of charge-separated structures such as IIIc, the spectrum of 12 is is almost identical to that of 11. It is not clear from these results, however, whether the increased absorption near 270 mμ is due to a perturbation of the simple β-pyrroleninium chromophore or to the coincidence of a new band from the N-phenylimminium chromophore, or to a combination of these and other effects.

TABLE 4. INTENSITY OF UV ABSORPTION OF N-PHENYLPYRROLES AT 315 Mμ

Pyrrole	ε Observed	ε corrected for % of α-isomer present
1-Phenyl	5550 (ε_{max})	5550
2,5-Dimethyl-1-phenyl	1000	1200
2,5-Dimethyl-1-(4-carboxyphenyl)	930	1070
1-(2′,6′-Dimethylphenyl)	600	600
2,5-Dimethyl-1-(2′,6′-dimethylphenyl)	90	270
2,5-Dimethyl-1-(2′,6′-dimethyl-4′-hydroxyphenyl)	250	580

This question is considered more explicitly in terms of a molecular orbital description along lines proposed by Nagakura for substituted benzenes.[19] In this approach the longest wavelength bands in the N-phenylpyrroleninium salts are assigned to the transfer of an electron from an upper filled[20] benzene π-orbital, H_B, to the lowest vacant π^* orbital, V_S, of the protonated pyrrole substituent. The 250 mμ band in the free base would then correspond to charge transfer in the opposite direction; i.e., $H_S \rightarrow V_B$. The pyrroleninium bands are, according to this notation, designated $H_S \rightarrow V_S$. The energy levels calculated from a simple Huckel treatment are diagrammed in Fig. 3. Protonation in the pyrrole ring lowers the V_S with respect to the H_S orbitals and lowers both relative to the benzene levels. The $H_S \rightarrow V_B$ band in the base thus shifts to higher frequency, while both the $H_B \rightarrow V_S$ and $H_S \rightarrow V_B$ transitions undergo bathochromic shifts into the observed region of the spectrum. The H_S level in the α-protonated salt falls below the H_B level, while the H_S and H_B orbital energies in the β-protonated salts are rather close. The V_S orbital is slightly lower in the α-protonated salt. These results are generally consistent with the spectra.

Methyl substitution affects the spectra, both directly through inductive electron release, and indirectly through steric inhibition of interannular conjugation. These effects can be observed clearly only in the case of the α-protonated salts. Substitution in the α-positions of either ring should decrease the intensity of the charge transfer

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[19] S. Nagakura and J. Tanaka, *J. Chem. Phys.* **22**, 236 (1954).

[20] The relative energies of the two uppermost benzenoid π-orbitals is not certain. One has a node on the carbon atom bearing the substituent, and is in this approximation unaffected by interannular conjugation. Any $H_B \rightarrow V_S$ transition originating from this orbital should have very low intensity. The relative energy of the other H_B orbital, from which the observed transition originates, depends on a balance between inductive and resonance effects by the substituent (Fig. 3).

bands because of hinderance to coplanarity.[21] However, the shape of the hindering potential is different for α-protonated N-phenylpyrroles than it is for the bases and their β-protonated salts. One can in general expect that blocking groups are less effective toward preventing a coplanar arrangement when the hindering potential approximates a threefold rather than a twofold barrier, so that the hypochromic effect of 2,5- or 2′,6′-methyl groups would be reduced in the α-protonated salts. It seems doubtful, therefore, that the excess absorption near 270 mμ by the salts of 1-phenyl-2,5-dimethylpyrrole would be due to charge transfer bands from the ~18% of β-protonated isomer present, since this band should be more effectively damped than that from the α-protonated isomer, whose absorption near 315 mμ is comparatively weak.

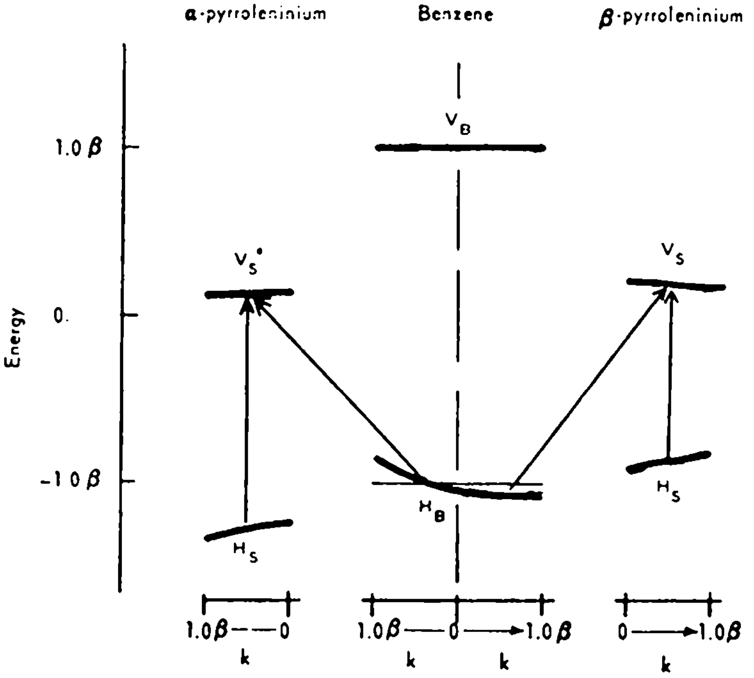

FIG. 3. Variation of uppermost filled and lowermost vacant benzenoid and substituent π-orbitals with interannular resonance integral, k.

Interannular conjugation also affects the energy levels, so that steric inhibition can lead to frequency shifts. In Fig. 3, the H_B and H_S levels appear particularly sensitive, in such a way that steric hindrance should lead to a hypsochromic shift of the $H_B \rightarrow V_S$ band and a bathochromic shift of the $H_S \rightarrow V_S$ pyrroleninium band. The latter shift is observed, free of complication by hypochromic effects and/or inductive shifts when ortho-methyl groups are introduced into either 1-phenylpyrrole or its 2,5-dimethyl homolog. In each case the absorption shifts to longer wavelengths by 10 mμ and intensifies slightly. The charge transfer bands behave in a more complicated way, since the methyl groups directly affect either the H_B or V_S levels, depending upon the ring in which they are placed. Methyl groups are generally considered to be

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[21] H. H. Jaffé and M. Orchin, *Theory and Applications of Ultraviolet Spectroscopy* Chap. 16. Wiley, New York (1962).

electron-releasing, so that their inductive effect would be to raise all energy levels by amounts proportional in first-order to the orbital charge density on the substituted atom.[22] The generalization can hence be made that methyl substitution in the pyrroleninium ring raises the V_S levels, producing a hypsochromic shift in the $H_B \rightarrow V_S$ band, while methyl substitution in the benzene ring raises the H_B levels to give a bathochromic shift. The latter opposes the shift expected (Fig. 3) from damping of interannular conjugation, so that the net shift from ortho methyl substitution in the the phenyl ring may be small. The two effects combine in the event of α-substitution in the pyrroleninium ring, however, raising the V_S level by inductive release and lowering the H_B level by causing the position of the minimum in the rotational barrier. A strong hypsochromic shift of the charge transfer band from the α-protonated salt thus seems to offer the most plausible explanation of the strong absorption near 270 mμ from acidic solutions of 1-phenyl-2,5-dimethylpyrrole. The $H_B \rightarrow V_S$ transition from the $\sim$18% β-protonated salt may also occur in this region, although for reasons stated earlier its intensity should be damped by steric hindrance to a greater degree than the α-protonated isomer. The normal pyrroleninium absorption of the β-protonated salt also contributes substantially to the total absorption near 270 mμ.

Methyl substituents in the pyrrole ring will also cause inductive shifts of the $H_S \rightarrow V_S$ transition[16] although here both the molecular orbitals involved are affected. The displacements should tend to be smaller than for the $H_B \rightarrow V_S$ bands, since the H_S level will shift in the same direction as the V_S level. The orbital charge density on the α-carbon of the α-protonated salts is greater in the V_S orbital, so that a hypsochromic shift is predicted and does occur in simpler systems.[16] In the N-phenylpyrroles it is largely compensated by a shift in the H_S level due to damping of interannular conjugation, as was observed independently when methyl groups were introduced onto the benzene ring.

MO calculations similar to those illustrated in Fig. 3 further predict that the V_S level in the simple iminium chromophore is about the same as that of the β-pyrroleninium ring, leading to the conclusion that the $\sim$270 mμ band in β-protonated indoles (line 10, Table 4) is also due to an $H_B \rightarrow V_S$ band uncomplicated by $H_S \rightarrow V_S$ absorption. Despite the fact that in the indole salts the chromophore is coplanar with the benzene ring, the intensity of the charge transfer absorption appears to be much reduced from the value derived from 1-phenyl-2,5-dimethylpyrrole by attributing its 280 mμ absorption entirely to the β-protonated salt. There is no apparent reason why either the $H_B \rightarrow V_S$ or $H_S \rightarrow V_S$ absorptions should be enhanced in the β-protonated N-phenylpyrroleninium salts. The degree of methyl substitution is similar in both cases. A hyperchromic effect due to cross conjugation with the iminium chromophore would not seem likely on comparing entries 6 and 5 in Table 5. The intensities are entirely consistent however, with the assumption that the α-protonated salt of 1-phenyl-2,5-dimethylpyrrole absorbs strongly near 280 mμ. A similar $H_B \rightarrow V_S$ band appears in indolenine salts, and is observed to shift to shorter wavelength in indolenines.[23] This reflects a simple shift of the V_S levels on protonating the iminium substituent in the plane of the molecule.

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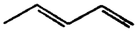
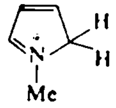
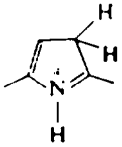
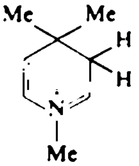
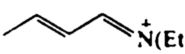
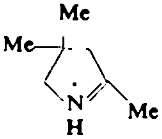
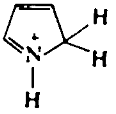
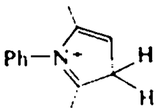
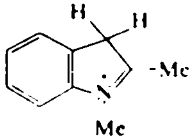
[22] C. A. Coulson and H. C. Lonquet-Higgins, *Proc. Roy. Soc.* A **191**, 39 (1947).

[23] R. L. Hinman and E. B. Whipple, *J. Amer. Chem. Soc.* **84**, 2534 (1962).

TABLE 5. COMPARISON OF THE IMMONIUM CHROMAPHORE WITH HYDROCARBON ANALOGS

Entry	Compound	λ_{max}	ϵ_{max}	Solvent[a]	Ref.
1		224	25,500	H	*b*
2	Cyclopentadiene	239	3400	H	*c*
3		241	3900	S	8
4		275	2500	S	8
5		274	2300	A	*d*
6		250	10,700	A	*e*
7		<210		C	24
8		247	4100	S	8
9		~270	see text	S	*f*
10		230 237 272-275	4550 4250 5600	S	1*a*
11	PhCH:CHMe	251	17,300	E	*g*
12	*cis*-PhC(Me):CHMe	243	12,100	H	*h*

[a] H = hexane; S = sulfuric acid; E = ethanol; A = acetonitrile; C = dil hydrochloric acid.

[b] K. B. Alberman, R. N. Hazeldine and F. B. Kipping, *J. Chem. Soc.* 3284 (1952)

[c] L. W. Pickett, N. J. Hoeflich and T. Lin, *J. Amer. Chem. Soc.* 63, 1073 (1941).

[d] F. M. Kosower and T. S. Sorensen, *J. Org. Chem.* 27, 3764 (1962).

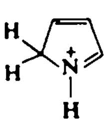
[e] G. Opitz, H. Hellmann and H. W. Schubert, *Liebigs Ann.* 623, 117 (1959).

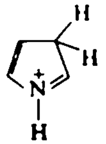
[f] Present work.

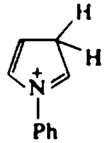
[g] C. G. Overberger and D. Tanner, *J. Amer. Chem. Soc.* 77, 369 (1955).

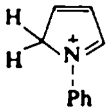
[h] D. J. Cram. *Ibid.* 71, 3953 (1949).

Qualitative comparison of the four chromophoric systems (IVa–d) discussed in this paper with the formally related chromophores in hydrocarbon systems reveals some interesting relationships. All of the pyrrole conjugate acids contain the imnium group. The most readily observed absorption maximum of this group would probably arise from a $\pi \rightarrow \pi^*$ transition, and would be expected to have position and intensity similar to those of the $\pi \rightarrow \pi^*$ transitions of olefins and carbonyl groups (i.e., below 200 mμ). In support of this hypothesis, acidified solutions of 2,4,4-trimethyl-1-pyrroline[24a] (entry 7, Table 5) have maxima below 210 mμ, as does an ethanolic solution of the iminium salt 2,3,5,6,7,8-hexahydro-1H-indolizinium perchlorate.[24b,c] Conjugation of the iminium group with an olefinic double bond yields open-chain analogs of the pyrrole α-conjugate acids, with absorption maxima in about the same region as the latter (entries 6 and 8, Table 5). It is noteworthy that the absorption maximum is positioned at considerably longer wavelengths than those of the analogous 1,3-dienes and α,β-unsaturated ketones. With the hydrocarbon diene a pronounced bathochromic shift accompanies cyclization (entries 1 and 2, Table 5), though with


IVa


IVb


IVc


IVd

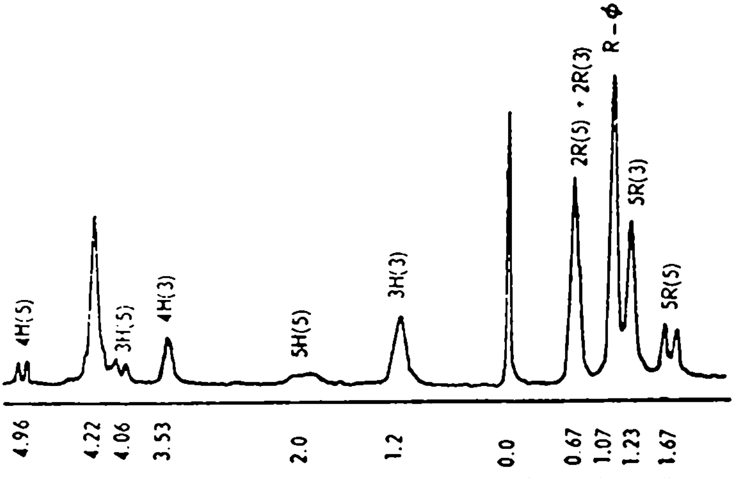


FIG. 4. NMR spectrum at 60 mc of 2,5-dimethyl-1-(2′,6′-dimethylphenyl) pyrrole in 17M sulfuric acid relative to tetramethylammonium chloride as internal standard. The notation nH (k) or nR (k) indicates the assignment to protons (H) or methyl groups (R) at ring position n in the salt protonated at position k.

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[24] [a] R. Bonnett, *J. Chem. Soc.* 2313 (1965), and personal communication; [b] R. A. Johnson, The Upjohn Company, personal communication; [c] It has been reported that the iminium chromophore absorbs with moderate intensity near 220 mμ [G. Opitz, H. Hellmann, and H. W. Schubert, *Ann.* 623, 117 (1959)]. For the reasons discussed above, this assignment seems of doubtful validity. The use of acetonitrile as the solvent near its spectral cut-off point may have given erroneous results.

both the dienes and the eneiminium salts a decrease in absorption intensity accompanies cyclization.

It is instructive to attempt to apply reasoning derived from hydrocarbon dienes and related series to the chromophores of the pyrrole conjugate acids. From consideration of the length of the chromophoric system the relative positions of absorption max of IVa–d would be predicted to be IVd > IVc > IVa–b. The observed facts bear out the predictions insofar as IVd $\gg$ IVa with IVc falling somewhere between, although its exact position, as discussed above, is not known with certainty. The relative positions of IVa and IVb cannot be anticipated or explained by any of the well-known simple generalizations. The terminally charged conjugate acid IVa has about the same absorption maximum as cyclopentadiene but the internally charged isomer absorbs much farther toward the red (entries 2, 3 and 4 and 5). A comparison of β-protonated indoles (and perhaps N-phenylpyrroles) with the corresponding hydrocarbons (entries 9, 10, 11, 12) also shows that when the conjugated iminium chromophore bears the positive charge on an internal atom, absorption occurs at longer wavelengths than for the hydrocarbon.

EXPERIMENTAL[25]

Synthesis of N-*phenylpyrroles*. Pyrroles unsubstituted in the hetero ring were prepared by variations of the classical pyrrole synthesis from ammonia and mucic acid. Members of the 2,5-dimethylpyrrole series were prepared from the appropriate amine and acetonylactone, as described previously.[11] Details of specific preparations which are of special interest follow.

1-(p-*Nitrophenyl*) *pyrroles*. Although an unsuccessful attempt to prepare this compound by the reaction of mucic acid and *p*-nitroaniline has been reported,[26,27] we have found the following procedure useful. A mixture of 6·9 g (0·05 mole) *p*-nitroanline, 12 g (0·06 mole) mucic acid, and 10 g desiccant-grade aluminum oxide were placed in a 300 ml steel autoclave with 75 ml benzene. The vigorously stirred reaction mixture was maintained under N at 250° for 3 hr. The cooled mixture was filtered and the benzene removed *in vacuo*. By crystallization of the residue from MeOH, 3·1 g (40%) of white crystals was obtained, m.p. 179–180° (lit.[26] m.p. 181°). The product analyzed correctly for 1-(*p*-nitrophenyl) pyrrole.

By mixing the same quantities of reactants with 150 ml decahydronaphthalene and refluxing until the theoretical amount of water had been removed by azeotropic distillation, the desired product was obtained in 20% yield. No reaction occurred when ethylene glycol or bis-(2-ethoxylethyl) ether were substituted for decahydronaphthalene.

1-(2′,6′-*Dimethylphenyl*) *pyrrole*. This synthesis was carried out in an autoclave in a manner similar to the prep above, using 0·1 mole 2,6-dimethylaniline, 0·11 mole mucic acid, and 50 ml benzene. After removal of the solvent the residue was steam-distilled, the distillate was extracted with ether and the ether was removed under red. press. After crystallization from MeOH the white crystals weighed 11·9 g (68%) and melted at 47–48°. (Found: C, 84·05, H, 7·87; N, 8·05. Calc. for $C_{12}H_{13}N$: C, 84·16; H, 7·65; N, 8·18%.)

No reaction occurred in other attempts to effect the reaction of mucic acid and the aniline, by refluxing in the aniline as solvent, by refluxing in decahydronaphthalene or by heating at 250° in glycerol.

[25] M.ps and b.ps are uncorrected. Methods for determining NMR and UV spectra in acidic media have been described in earlier papers.[1,2]

[26] J. Dhont and J. P. Wibaut, *Rec. Trav. Chim.* **62**, 177 (1943).

[27] 1-(*p*-Nitrophenylpyrrole was prepared previously[10] by nitration of 1-phenylpyrrole in a sulfuric–nitric acid mixture. When nitric acid and acetic anhydride were used, nitration of the pyrrole ring took place. Nitration in sulfuric acid undoubtedly involves the protonated pyrrole and is related to the studies of Noland (e.g. W. E. Noland, L. R. Smith, and O. C. Johnson, *J. Org. Chem.* **28**, 2262 (1963)) on nitration of indoles. The conjugated eneimmonium group of N-phenylpyrrole conjugate acid is para-directing as is the simpler immonium system of the 3-protonated indoles (cf. K. Brown and A. R. Katritzky, *Tetrahedron Letters* 803 (1964)).

3,5-*Dimethyl-4-aminophenol.* Sulfanilic acid (19·1 g, 0·1 mole) and anhyd Na_2CO_3 (5·3 g, 0·05 mole) were dissolved in 200 ml water by boiling. To the cooled soln, 7·6 g $NaNO_2$ was added and this soln was poured in turn into a beaker containing 100 g ice and 20 ml conc HCl. The resulting white slurry was added with stirring to a soln of 12·2 g (0·1 mole) 3,5-dimethylphenol in 100 ml 10% NaOH. To the resulting dark red mixture, heated to 70°, 50 g of solid sodium hydrosulfite was added in 3 portions. The resulting yellow solution was stirred for 30 min, cooled to 15° and filtered. The pale yellow product weighed 9·5 g (69%) and melted at 181–182 °(lit.[28] m.p. 180·5–181·5°). The product can be recrystallized from acetone if necessary.

1-(2′,6′-*Dimethyl-4′-hydroxyphenyl) pyrrole.* The procedure was similar to that used for 1-(*p*-nitrophenylpyrrole). From 6·8 g (0·05 mole) 3,5-dimethyl-4-aminophenol, 13 g (0·123 mole) mucic acid, 10 g aluminum oxide and 75 ml benzene was obtained after 2 hr at 275°, 3 g (32%) of tan solid, m.p. 75°, b.p. (3 mm) 142°. For best results the product was distilled under red. press. and then crystallized from n-hexane. (Found: C, 76·76; H, 7·06; H, 7·30. Calc. for $C_{12}H_{13}NO$: C, 76·97; H, 6·99; N, 7·48%.)

No reaction occurred when reaction in high-boiling solvents without pressure was attempted.

2,5-*Dimethyl*-1-(2′,6′-*dimethyl-4′-hydroxyphenyl) pyrrole.* A soln of 6·8 g (0·05 mole) 3,5-dimethyl-4-aminophenol and 8 g acetonylacetone in 100 ml of toluene was refluxed until the theoretical quantity of water had been collected by azeotropic distillation. The cooled reaction mixture was filtered, the solvent was removed under red. press. and the residue was distilled, b.p. (3 mm) 140–150°. Crystallization of the distillate from a large volume of *n*-hexane gave 5·2 g (48%) white needles, m.p. 127–128°. (Found : C, 78·20; H, 8·05; N, 6·77. Calc. for $C_{14}H_{17}NO$: C, 78·10; H, 7·95; N, 6·50%.)

2,5-Dimethyl-1-(2′,6′-dimethylphenyl) pyrrole and 2,5-dimethyl-1-(4′-carboxyphenyl) pyrrole were prepared by a similar procedure.[29]

Conjugate acids of 2,5-*dimethyl*-1-(2′,6′-*dimethylphenyl) pyrrole.* The NMR spectrum of 1-phenyl-2,5,2′,6′-tetramethylpyrrole in 17M H_2SO_4 is shown in Fig. 4, where the assignments are indicated. As was observed previously for 1,2,5-trimethylpyrrole,[8] the β-protonated salt undergoes faster proton exchange so that one may selectively time-average its pyrrole ring methyl group lines by diluting the solvent acid, thus confirming the assignments in Fig. 4. In trifluoroacetic acid, for example, the lines assigned to 2R(3) and 5R(3) in Fig. 4 merge to a single line due to the exchange reactions, line appears at 2·32 ppm due to both η-methyl groups in the system:

while the lines assigned to 3H(3) and 4H(3) are absent.

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[28] E. Bamberger and A. Rising, *Liebigs Ann.* **316**, 292 (1901).

[29] S. J. Hazlewood, G. K. Hughes and F. Lions, *J. Proc. Royal Soc. N. S. Wales* **71**, 92 (1937).