

matography on a silicone column at 160° showed no detectable amount of impurities.³²

The second sample of CD₃COOH was prepared by carbonation of the Grignard reagent prepared from 5 g. of CD₃Br (Merck, Canada; 99% deuterated) and 2.5 g. of crystalline magnesium in 45 ml. of dried ether. After hydrolysis with the minimum amount of 25% sulfuric acid, the ether solution was decanted and combined with subsequent ether washings of the magnesium salts. The ether was distilled and the acetic-d₃ acid was fractionated; a middle cut was used for the acidity measurements.

Pivalic-d₉ Acid.—Carbon dioxide was passed over a cooled and stirred solution of the Grignard reagent prepared from 5 g. of *t*-butyl-d₉ chloride (Merck of Canada) and 1.34 g. of crystalline magnesium. After hydrolysis with dilute sulfuric acid, the washed and dried ether solution was distilled giving 1.7 g. of pivalic-d₉ acid in two fractions, b.p. 160–165°. The second fraction was stored in a sublimator and a small amount was sublimed as required for the conductivity measurements.

*Anal.*³³ Calcd. for C₅D₉HO₂: D, 90 atom %. Found: D, 86 atom %.

Ordinary pivalic acid was prepared in the same manner from freshly distilled *t*-butyl chloride. It gave the same results as commercial pivalic acid.

Benzoic Acids.—Reagent grade benzoic acid was sublimed immediately before use in the conductivity measurements.

Deuterium chloride, prepared from D₂O and benzoyl chloride,³⁴

(32) Halevi (ref. 10b) reports that his sample of Merck CD₃COOD contained traces of several contaminants.

(33) Analysis of the Microanalytical Laboratory of the University of California. The deuterium analyses were by density measurement of the combustion water by a drop suspension method. At the time of this work, this method was not accurate for high deuterium content and tended to give low results. The analyses were used only as supplemental evidence for substantial deuterium content of our samples.

was passed through successive portions of a 1 mole % solution of sublimed gallium bromide in benzene until density measurements indicated an isotopic purity of >95%.³⁵ The highest value found for the density of our benzene-d₆ is d_{25}^{25} 0.9438, lit.³⁶ d_{25}^{25} 0.9461.

A sample having d_{25}^{25} 0.940 was brominated with bromine and iron yielding bromobenzene-d₅, b.p. 153–155°, n_D^{25} 1.5564.

*Anal.*³³ Calcd. for C₆D₅Br: D, 100 atom %. Found: D, 90 atom %.

The bromide was converted to the Grignard reagent and carbonated in the usual way. The product benzoic-d₅ acid, m.p. 122–123°, was crystallized from water and was sublimed immediately before use.

*Anal.*³³ Calcd. for C₇D₅HO₂: D, 83 atom %. Found: D, 75 atom %.

Benzoic-2,6-d₂ acid was prepared in a similar manner from bromobenzene-2,6-d₂.³⁷ The product was also crystallized from water and sublimed; m.p. 122.0–122.6°.

*Anal.*³³ Calcd. for C₇D₂H₄O₂: D, 33 atom %. Found: D, 30 atom %.

Conductivity Measurements.—Solutions were made up using distilled water which had been passed through a Penfield mixed-bed demineralizer, model M-8, and aliquots were titrated with standardized sodium hydroxide. Conductivity measurements were made in a cell of conventional design in a thermostat controlled to ±0.01°. Resistance measurements were taken on an Electro-Measurements Inc., impedance bridge, model 250-DA.

(34) H. C. Brown and C. Groot, *J. Am. Chem. Soc.*, **64**, 2223 (1942).

(35) We are indebted to Professor F. R. Jensen for suggesting this method and providing apparatus and details.

(36) L. H. P. Weldon and C. L. Wilson, *J. Chem. Soc.*, 237 (1946).

(37) The preparation of this and other deuterated bromobenzenes will be described in a later paper.

[CONTRIBUTION FROM THE UNION CARBIDE RESEARCH INSTITUTE, TARRYTOWN, N. Y.]

The Protonation of Pyrroles

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Formation of stable α -protonated salts of pyrrole and methylpyrroles in aqueous sulfuric acid is demonstrated by their proton magnetic resonance spectra. The observed rates of deuterium exchange in N-methylpyrrole require, however, that β -protonation of the base occur at the faster rate in concentrated H₂SO₄ solutions. The basicity constant of pyrrole is redetermined as $pK_a = -3.8$, considerably below the currently accepted value, and the variation of the ratio of protonated to unprotonated base with sulfuric acid concentrations, while self-consistent within the methylpyrrole series, differs from previously defined class acidity functions. The basicity constants vary with methyl substitution in a semi-empirically predictable manner.

The basicity of pyrrole, which is of theoretical interest in connection with aromaticity in heterocyclic systems and of practical importance to many aspects of its chemistry, has been variously estimated to be in the range -1.7 to $+0.3$ on the pK_a scale.¹ It is commonly felt that side reactions, particularly trimerization,² render the base unamenable to conventional measurements by indicator methods, although results have been obtained for a number of its methyl derivatives.^{3,4} Also, the position of protonation in pyrrole itself has not been clearly established.

Since the trimerization of pyrrole is very likely controlled by a second-order process involving attack by the conjugate acid on the free base,² one would infer that solutions of the salt are stable provided the medium is sufficiently acidic to ensure complete protonation. The failure of earlier workers³ to obtain stable solutions of pyrrole in acid, if due to this cause, would imply that it is a weaker base than expected. One might also argue from what is known about the rate and mechanism of the trimerization² that very dilute solutions ($\sim 10^{-4}$ M) of pyrrole would

react slowly enough to make ultraviolet indicator measurements of the protonation ratio feasible. The fact that the very pronounced change that occurs in the spectra of methylpyrroles^{3,4} was not observed in the most recent measurement of pyrrole¹ is explicable only on the basis that C-protonation was never effected, so that the reported pK_a , at least for C-protonation, would be much too high. Finally, a pK_a of -2.3 was recently reported for the β -protonation of indole.⁵ One intuitively expects pyrrole to be a weaker base than indole for the same reasons that benzene is a weaker base than naphthalene, or that cyclopentadiene is a stronger acid than indene,⁶ although the issue is clouded by the presence of a heteroatom and the availability of several different protonation sites.

1. Structure of Methylpyrrole Salts in Solution.—

The proton magnetic resonance spectra of pyrrole, N-methylpyrrole, and N-phenylpyrrole in 16 M sulfuric acid all show a characteristic pattern of four main envelopes due to protons on the ring carbon atoms, and the intensity ratios of 1:1:1:2 require

(5) R. L. Hinman and J. Lang, Abstracts, 141st National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1961, p. 98Q. The authors are grateful to Dr. Hinman for advanced communication of his detailed results, which are to be published.

(6) R. E. Dessy, Y. Okuzumi, and A. Chen, *J. Am. Chem. Soc.*, **84**, 2899 (1962). See also the discussion in A. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., p. 347.

(1) M. Navqui and Q. Fernando, *J. Org. Chem.*, **25**, 551 (1960).

(2) H. A. Potts and G. F. Smith, *J. Chem. Soc.*, 4018 (1957).

(3) R. J. Abraham, E. Bullock, and S. S. Mitra, *Can. J. Chem.*, **37**, 1859 (1959).

(4) E. B. Whipple, Y. Chiang, and R. L. Hinman, *J. Am. Chem. Soc.*, **85**, 26 (1963).

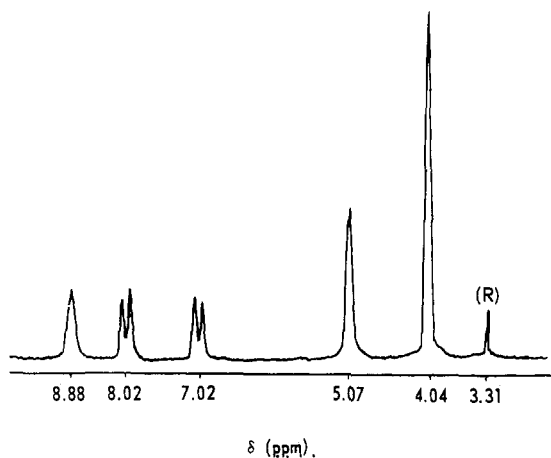


Fig. 1.—Proton magnetic resonance spectrum (60 Mc.) of N-methylpyrrole in 18 *M* sulfuric acid.

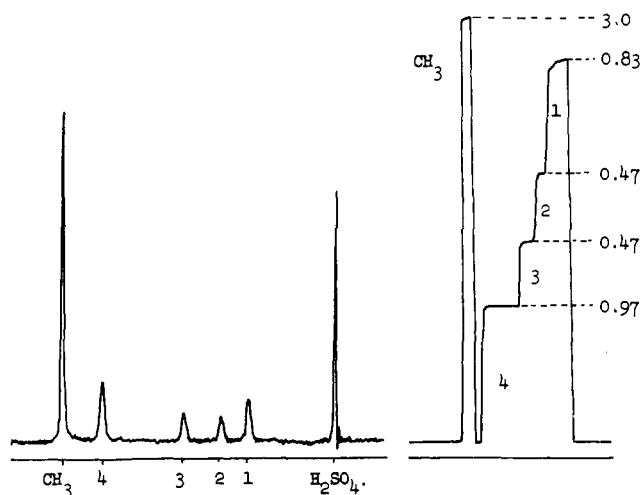
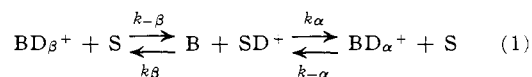


Fig. 2.—N.m.r. spectrum and its integral of N-methylpyrrole in 16 *M* D_2SO_4 10 min. after mixing (increasing external field from right to left).

that an added proton be present on one of these sites. Two of the single protons, with chemical shifts⁷ of about 7.0 and 8.0 p.p.m., show a mutual coupling of 6 c.p.s. while no resolved hyperfine structure occurs in the other lines. However, the line widths of the outermost pair suggest a mutual unresolved coupling of between 2 and 3 c.p.s. which is confirmed by double irradiation experiments. On the basis of these facts alone one might be inclined to assign the β -protonated structure, reasoning that the 6 c.p.s. splitting is about that expected for a single pair of adjacent vinyl protons. The low-field shift of the remaining, uncoupled vinyl proton and its unresolved weak interaction with the methylene group are reasonably explained. However, on dissolving N-methylpyrrole in 16 *M* D_2SO_4 the n.m.r. spectrum after several minutes (Fig. 2) shows ring proton lines with the approximate intensity ratio 1:1/2:1/2:1, and the innermost and outermost pairs appear to maintain their equal intensities during their slow decay. While consistent with a simple exchange involving the symmetrical base as an intermediate, *i.e.*

(7) Chemical shifts are referred in parts per million to internal tetramethylsilane (TMS) with positive sense in the direction of decreasing external field. In aqueous solvents a tetramethylammonium ion (TMA) secondary reference is converted to the TMS standard by adding its shift, $\delta = 3.31$ p.p.m., measured in trifluoroacetic acid. For stable methylpyrrole salts, direct calibration against TMS in trifluoroacetic acid was consistent with the TMA procedure to within 0.01 p.p.m.

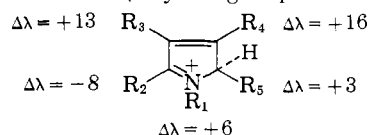


this experiment requires that: (a) regardless of assignment, the faster protonation occurs at the less stable site and (b) the outermost and innermost pairs of ring proton lines in Fig. 1 must be assigned to sites that are equivalent in the base. The assignments deduced from the β -protonated structure are thus inconsistent with the symmetry of the exchange process. Only by assigning the low-field line to 2H(3),⁸ which requires a weak coupling between adjacent 4H(3) and 5H(3) nuclei plus a strong 5H(3)–2H(3) coupling across the ring, could the β -protonated structure be accommodated.

The α -protonated structure requires that the pair of adjacent, coplanar protons 2H(5) and 3H(5) be weakly coupled. A coupling constant of about 6 c.p.s. between protons 3H(5) and 4H(5) is consistently observed in the unambiguously identified α -protonated salt of 2,5-dimethylpyrrole,⁴ and the required cross ring coupling of 2–3 c.p.s. has a clear analogy in the α -protonated salt of 3,4-dimethylpyrrole. Proceeding on the assumption that methyl substitution causes rather small changes in n.m.r. parameters not directly involved, one may on the basis of α -protonation arrive at mutually consistent assignments in the spectra of the fourteen methylpyrrole salts listed in Table I. The chemical shifts fall into nonoverlapping regions, and the coupling constants are consistent throughout. One notes in particular that the vinyl proton coupling in the 2-protonated salt of 3-methylpyrrole is small. Also, in the two cases where spectra of β -protonated salts are identified,⁴ shifts fall outside the ranges established in Table I.

The structures of the methylpyrrole salts are summarized by the rules that α -protonation is preferred, α -methyl groups direct to the opposite α -position, and β -methyl substitution orients protonation to the adjacent α -site. In 2,5-dimethylpyrrole the normal preference for α -protonation is nearly balanced by the combined effects of methyl substitution. In no case has N-protonation in solution been detected.

In contrast to the situation in the base, methyl substitution may cause appreciable shifts in the 241 $m\mu$ electronic absorption band of the salt of pyrrole, and the position of this band appears to be characteristic of the number and positions of substituent methyl groups. Based on the structures deduced from n.m.r., the positions of the observed ultraviolet maxima are predicted within 2 $m\mu$ by the group shifts⁹



2. Relative Protonation Rates.—Although the present study is concerned with the equilibrium behavior of pyrroles in aqueous acids, the deuterium exchange experiment illustrated in Fig. 2 yields an order of protonation rates opposite from that of thermodynamic stability and of protonation rates observed in more weakly acidic solutions, and hence merits further comment. Generally speaking, we observe "normal" order of protonation rates, $r_{\alpha} > r_{\beta}$, for N-methylpyrrole in solvents where the base is predominant in the

(8) The compact notation $nH(m)$ or $nR(m)$ is used to designate protons or methyl groups on ring site n in the pyrrole salt formed by protonation at position m , numbering from the heteroatom.

(9) See H. Booth, A. W. Johnson, E. Markham, and R. Price, *J. Chem. Soc.*, 1587 (1959), for spectral data from pyrroline salts which can serve as models.

TABLE I
 CHEMICAL SHIFTS AND ULTRAVIOLET ABSORPTION MAXIMA IN METHYLPYRROLE SALTS

No.	Parent base ^a	Chemical shifts at ring positions ^b					$\lambda_{\text{max}},^c$ m μ	ϵ_{max}^c
		1	2	3	4	5		
1	Pyrrrole	10.83	9.20	7.35	8.40	5.23	241	3900
2	N-methyl-	(4.07)	8.88	7.02	8.02	5.07	247	4100
3	2-methyl-	...	(2.87)	7.05	8.10	5.03	233	4500
4	4-methyl-	...	8.93	7.03	(2.68)	5.05	258	4800
5	1,2-dimethyl-	(3.82)	(2.72)	6.97	7.88	5.03	240	4500
6	2,3-dimethyl-	...	(2.77)	(2.27)	7.70	4.85	246	...
7	2,4-dimethyl-	10.12	(2.70)	6.72	(2.42)	4.86	249	5200
8	2,5-dimethyl-	...	(2.88)	7.03	8.10	5.16(1.75)	237	...
9	3,4-dimethyl-	...	8.80	(2.18)	(2.39)	4.96	271	5800
10	1,2,5-trimethyl-	(3.70)	(2.70)	6.87	7.83	5.03(1.64)	243	...
11	2,3,4-trimethyl-	...	(2.69)	(2.14)	(2.37)	4.78	262	...
12	2,4,5-trimethyl-	...	(2.68)	6.62	(2.36)	4.83(1.61)	252	5700
13	1,2,4,5-tetramethyl-	(3.67)	(2.65)	6.62	(2.35)	4.80(1.67)	259	5800
14	2,3,4,5-tetramethyl-	10.17	(2.62)	(2.05)	(2.22)	4.80(1.55)	265	(5000)
15	pentamethyl-	(3.63)	(2.53)	(2.07)	(2.20)	4.65(1.57)	269	5600

^a Ring positions are numbered from the heteroatom in the direction corresponding to 5-protonation. ^b P.p.m. to internal tetramethylsilane according to footnote 7 in text. Parentheses enclose methyl group shifts. ^c In aqueous H₂SO₄ over concentration range 2–8 M. No significant variation with solvent was noted.

 TABLE II
 NORMINAL MAGNITUDES OF COUPLING CONSTANTS IN 5-PROTONATED METHYLPYRROLE SALTS

Interacting groups (R = methyl)	J, c.p.s.	Examples (Table I)
5R, 5H	7.5	8, 10, 12, ^a 13, 14, 15
2R, 5H	3.3	3, 5, 6, 7, ^a 8, 10–15
3H, 4H	6	1, 2, 3, 5, 8, 10
2H, 5H	2.5	9
2H, 1H	4.8	9
3H, 4R	1.5	7 ^a , 12 ^a
2R, 1H	1.0	6, 7, 8, 12, 14
2H, 3H	<2	1, 2, 4

^a Confirmed by double irradiation.

equilibrium, e.g., in acetic acid–trifluoroacetic acid mixtures or dioxane–aqueous HCl. On the other hand, the reverse order is again observed[†] with 1,2,5-trimethylpyrrole in strong acids. As mentioned before, the symmetry of the exchange process justifies its description in terms of simple proton transfers of the type in eq. 1, where at equilibrium in strong acids the base is present predominantly in the form BD_α⁺. By increasing the strength of the solvent acid the rate of proton loss, and hence of all subsequent exchanges in BD_α⁺, can be made conveniently slow,¹⁰ enabling one to determine relative magnitudes of the protonation rates r_{α} and r_{β} from measurements of the initial isotope distribution in BD_α⁺. If the base is added to D₂SO₄ under conditions where α -deuteration effectively terminates the exchange, the fraction of deuterium introduced into the β -positions of the salt depends on the fraction $x = r_{\beta}/(r_{\beta} + r_{\alpha})$ entering the β -protonation cycle weighted by the combined probabilities of deuterium introduction and proton loss in this loop. The probability of D⁺ insertion approaches unity in isotopically pure acid, and to this approximation¹¹

(10) In 16 M D₂SO₄, for example, the half-life of a proton in the 5-position is about 40 min.

(11) In practice it is impossible to achieve a completely negligible isotopic ratio since the base, which must be present in substantial (~20%) concentration for accurate n.m.r. area measurements, is a source of protons in solution. In addition to introducing a time variable H⁺/D⁺ ratio, this also raises the possibility of local concentration gradients. Assuming uniformity, the isotope ratio is measurable from the intensity of the solvent line in the n.m.r. spectrum and yields H⁺/D⁺ ratios of 3% by the time initial measurements are conducted on solutions containing 20% by volume of pyrrole in 16 M D₂SO₄ listed as 99.5% isotopically pure. The presence and approximate magnitude of kinetic isotope effects are indicated by the initial area ratio of the protonated and unprotonated α -positions, the value of 1.15 in these experiments giving an isotope effect factor of about 5.

the probability of H-survival in either β -position after a total of n randomly oriented β -exchanges is the binomial expression

$$P_{\beta}^{(n)} = \sum_{j=0}^n \binom{n}{j} \left(\frac{1}{2}\right)^j \left(\frac{1}{2}\right)^{n-j} \xi^j = \left(\frac{\xi+1}{2}\right)^n \quad (2)$$

where

$$\xi = \frac{r_{-\beta}(\text{D})}{r_{-\beta}(\text{D}) + r_{-\beta}(\text{H})} \quad (3)$$

is determined by the kinetic isotope effect in breaking CH bonds.¹² The fraction of β -hydrogen collected in the salt BD_α⁺ on the n th cycle is

$$F_{\beta\text{H}}(n) = (1-x)x^n P_{\beta}^{(n)} \quad (4)$$

Since the equilibrium condition

$$K_{\alpha}/K_{\beta} = k_{-\alpha}k_{\beta}/k_{\alpha}k_{-\beta} \ll 1$$

requires of the rate constants

$$k_{-\beta} \gg \left(\frac{x}{1-x}\right) k_{-\alpha}$$

one is assured that either x is small or n is large during an average lifetime of BD_α⁺; in either event the attainment of acid-base equilibrium gives

$$F \equiv F_{\beta\text{H}}(\infty) = \sum_{n=0}^{\infty} (1-x)x^n \left(\frac{\xi+1}{2}\right)^n = \frac{2(1-x)}{2-x-\xi x} \quad (5)$$

Inserting the reasonable value¹² $\xi = 0.125$ and the experimental value for F of 0.5, one obtains $x = 0.7$ or $k_{\beta} = 2.3k_{\alpha}$ in 16 M sulfuric acid.

3. Base Strengths (pK_a).—Dilute solutions of pyrrole in aqueous sulfuric acid are rather stable: the ultraviolet spectra change only slightly over 10 min. and are not significantly dependent on careful exclusion of air. There is a good isobestic point at 233 m μ (Fig. 3), the absorption bands at both extremes of acidity obey Beer's law, and the spectrum at intermediate acidities is the same whether the equilibrium is approached from the base or the conjugate acid. With respect to the absorption band, the salt closely resembles those previously observed from the methylpyrroles^{3,4} and differs unmistakably from an authentic sample of pyrrole trimer.

A semilogarithmic plot of the indicator ratio $I = [\text{BH}^+]/[\text{B}]$, determined from the absorbance at 240 m μ , is reasonably linear against the Hammett acidity function,¹³ H_0 , but has a slope of 1.62; plots against

(12) F. Westheimer, *Chem. Rev.*, **61**, 265 (1961).

(13) L. A. Flexer, L. P. Hammett, and A. Dingwall, *J. Am. Chem. Soc.*, **57**, 2103 (1935); M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957).

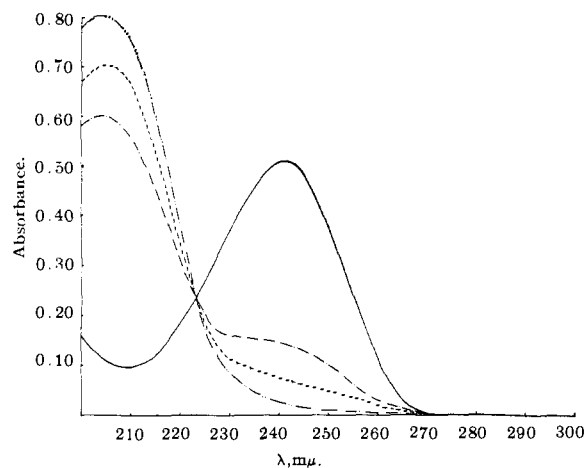


Fig. 3.—Ultraviolet absorption spectra of $1.3 \times 10^{-4} M$ solutions of pyrrole in: (1) water, (2) $4.0 M H_2SO_4$, (3) $4.7 M H_2SO_4$, and (4) $7.6 M H_2SO_4$ in order of decreasing absorbance at $200 m\mu$.

the other previously defined acidity functions for arylolefins¹⁴ or methylindoles⁵ also fail to give unit slopes. However, the overlapping indicator ratio plots of the series of substituted pyrroles in Fig. 4 are closely parallel, permitting a repetition of the original procedure¹³ wherein one assumes the displacement between parallel titration curves to be due to differences in basicity constants and relates the series of bases stepwise to a zero point defined in terms of an aqueous solution reference state. The results so obtained using the experimental procedure described previously⁴ are given in Table III.

TABLE III
pK_a's FOR α-PROTONATION OF METHYL-SUBSTITUTED PYRROLES

Compound, pyrrole	Wave length used, mμ	λ_B	λ_{BH^+}	Half-protonation point (M of H ₂ SO ₄)	Mean slope ^a	pK _a
2,4-Dimethyl-	260	270	3700	0.0081		2.55 ^b
2,3,5-Trimethyl-	260	360	3800	.009		2.00 ^b
3,4-Dimethyl-	260	94	3700	.164		0.66 ^c
1,2,5-Trimethyl-	242	90	3000	.54		-0.24 ^{c,e}
2-Methyl-	240	480	3400	.70	0.79	-0.21 ^c
2,5-Dimethyl-	237	160	2900	1.10	.79	-0.71 ^{c,e}
3-Methyl-	257	84	4800	1.50	.79	-1.00 ^c
1-Methyl-	248	130	4100	4.14	.76	-2.90 ^d
Pyrrole	240	170	3900	5.34	.74	-3.80 ^d

^a $d \log I/d C_{H_2SO_4}$ above $1 M H_2SO_4$. ^b $pK_a = pH + \log I$.
^c $pK_{BH^+} = \lim_{C_a \rightarrow 0} \left[\log \left(\frac{[BH^+]}{[B]} \right) - \log [H^+] \right]$. ^d pK_a is evaluated by the relation $pK_{CH^+} - pK_{BH^+} = \log \left(\frac{[CH^+]}{[C]} \right) - \log \left(\frac{[BH^+]}{[B]} \right)$ for compounds with parallel titration curves. ^e Corrected for β-protonation (see ref. 4).

In keeping with the chemical properties mentioned in the Introduction, the pK_a of pyrrole is found to be over two units below the range of previous estimates.¹⁵ The discrepancy with the latest value of -0.27^1 is due to the measurement of different changes in the ultraviolet spectrum. It seems clear both that the

(14) N. Deno, P. Groves, and E. Jaimes, *J. Am. Chem. Soc.*, **81**, 5790 (1959).

(15) The magnitude of the difference in pK_a's involves the choice of acidity scales. Navqui and Fernando (ref. 1) assumed the H_0 function to apply, whereas the stepwise procedure used in Table III amounts to the definition of an explicit acidity function for methylpyrroles, which, in aqueous H₂SO₄, is between H_0 and $H_{R'}$, and closer to the latter.

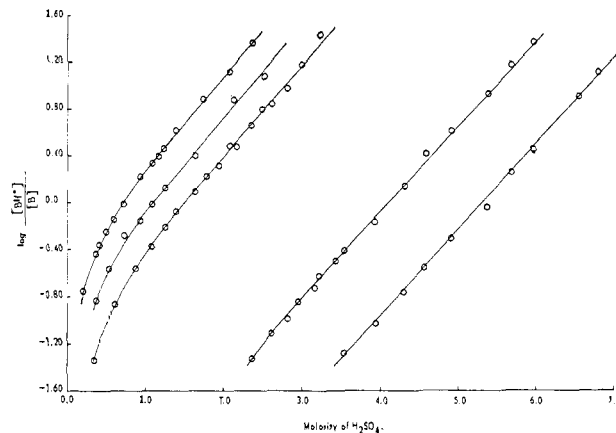


Fig. 4.—Indicator ratio plots of (left to right): 2-methylpyrrole, 2,5-dimethylpyrrole, 3-methylpyrrole, 1-methylpyrrole, and pyrrole in aqueous sulfuric acid.

241 $m\mu$ band utilized in the present work is correctly identified with the α-protonated salt and that α-protonation is the only significant reaction in concentrated acids. The presence of a simple isobestic point further argues that the equilibrium is uncomplicated in dilute acid. The slight spectral change previously measured has not been clearly identified with any simple acid-base reaction.¹⁶

A smaller, but significant, difference exists between the result in Table III for 2,4-dimethylpyrrole and the value of 1.9 ± 0.14 reported by Abraham, *et. al.*³ In this case the ultraviolet bands observed are the same, although there appears to be a twofold discrepancy in the extinction coefficient of the salt,¹⁷ and the base is sufficiently strong to remove any ambiguity in the acidity function. However, the use of buffer solutions in the earlier work does constitute a difference in reference states. The result in Table III was also obtained in perchloric acid, where a second ionization of the solvent acid does not enter, and was reconfirmed using the absorbance at $210 m\mu$, which is largely due to the free base.

The pK_a's in Table III yield roughly constant differences $\Delta_m(pK_j)$ corresponding to the effects of methyl substitution at ring sites m on the affinity toward protonation at position j .¹⁸ In two instances independent verification of the substituent effects derived from ultraviolet indicator measurements is possible. Both 3-methylpyrrole and 2,3,5-trimethylpyrrole should undergo 2- and 5-protonation in the ratio

$$\frac{[BH_2^+]}{[BH_5^+]} = \frac{1-x}{x} = 10^{\Delta_3(pK_2) - \Delta_5(pK_5)} \approx 12$$

so that the less stable salt should be detectable by n.m.r. From the ranges of chemical shift in Table I, one would expect weak 4H(5) and 3R(5) lines to be resolved from the stronger peaks from the 2-protonated salt. In both cases these lines are found, have the expected chemical shift, and by area ratio yield a consistent value of $x \approx 0.06$. In agreement with the assumption that C-protonation is described by a consistent acidity function, this fraction does not vary significantly with changes in concentration of the

(16) We have not unambiguously eliminated the possibility that N-protonation may occur in weak acids without appreciably changing the ultraviolet spectrum of the base and follows an acidity function (e.g., H_0) of slope less than 1.62. We do not consider this likely although rapid N-protonation may affect the rate situation described in section 2 of this paper.

(17) E. Bullock, *Can. J. Chem.*, **36**, 1686 (1958).

(18) The correction for equivalent sites in symmetrical bases has not been included here. The corrected $\Delta_m(pK_j)$ vary more, tending to decrease with increasing substitution.

solvent acid. Similar experiments have shown that α - and β -protonation also have parallel solvent effects.⁴

4. Discussion.—The orientation of protonation in pyrrole and indole can be rationalized either intuitively⁴ or by simple molecular orbital arguments based either on initial charge distributions¹⁹ or on π -electron localization energies,²⁰ which are more closely related in principle to the relative equilibrium constants.²¹ The orientations by methyl groups can be included in each argument by simple inductive models, although Hückel calculations tend to underestimate the promotion of δ -protonation by 3-methyl groups and do not readily accommodate the ultraviolet shifts. Within the molecular orbital framework, and in terms only of first-order changes in π -electron energy, the increment $\Delta_m(pK_j)$ is proportional to the difference in π -electron density localized on atom m , between the base and its j -protonated conjugate acid.²² This can in turn be related to the displacement in chemical shift²³ $\delta_m^{(j)}$, of a proton attached to atom m on protonation at position j .²⁴ Thus one arrives at an approximate proportionality

$$\Delta_m(pK_j) = k\delta_m^{(j)}$$

In pyrrole, δ -protonation causes chemical shifts of $\delta_2^{(5)} = 2.58$, $\delta_3^{(5)} = 1.30$, and $\delta_4^{(5)} = 2.35$ which are representative of the methylpyrrole series,²⁵ and these together with the respective $\Delta_m(pK_\delta)$ values in Table IV yield $k = 1.3$, constant to within $\pm 10\%$. A comparable value $k = 1.2$ is derived from the β -protonation of methylindoles. The required value of the simple inductive parameter h_{Me} is obtained in units of the exchange integral, β , from

$$k = \beta h_{Me} / 2.3RTa_m$$

where $a_m \cong 10$ p.p.m. per electronic charge is an empirical constant^{23b} independently relating vinyl proton shifts to adjacent π -electron charge. While of correct

(19) G. W. Wheland and L. Pauling, *J. Am. Chem. Soc.*, **57**, 2086 (1935). For reference to many subsequent calculations, see A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., New York, N. Y., 1961.

(20) R. D. Brown, *Australian J. Chem.*, **8**, 100 (1955).

(21) For a simple description of the salts in terms of heteroatom electronegativity ($h\dot{N}$) and inductive parameters ($0.1h\dot{N}$), the best over-all correspondence with the relative stabilities and π -electron distributions (chemical shifts) occurs around $h\dot{N} = 1.0$.

(22) C. A. Coulson and H. C. Longuet-Higgins, *Proc. Roy. Soc. (London)*, **A191**, 39 (1947).

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(24) One neglects here differences in corrections normally applied for ring currents in the base and different solvent effects or long range polarizations in the ion. However, these differences tend in the same direction and probably cancel in large degree. An estimated ring current shift of 0.5 p.p.m. in pyrrole is about equal, for example, to the shift of the vinyl protons on N-protonation of Δ^3 -pyrrolines.

(25) A detailed listing of the chemical shifts will be included in a subsequent paper (R. L. Hinman and S. Theodoropoulos) describing the synthesis and properties of these pyrrole bases.

sign, the magnitude of $\beta h_{Me} \cong 0.8$ e.v. seems large, as is the case with other estimates derived from acid-base equilibrium constants.²⁶

TABLE IV
 $\Delta_m(pK_j)$ VALUES FOR METHYL SUBSTITUTION IN PYRROLE

m	j			
	2	3	4	5
1	0.7	0.8	0.8	0.7
2	-0.6	(3.6)	(1.4)	3.6
3	2.8	(-0.7)	(1.2)	1.7
4	1.7	(1.2)	(-0.7)	2.8
5	3.6	(1.4)	(3.6)	-0.6

The approximate additivity of substituent effects plus evidence that all C-protonations of methylpyrroles depend consistently on the solvent acid suggests that the basicity constants at all the ring carbon atoms in the nineteen methylpyrroles can be semi-empirically estimated. By addition of rows in Table IV appropriate to the substitution and taking as reference points the indicated pK_a 's for α - and β -protonation in pyrrole, a set of predicted basicity constants is obtained for any particular case. The increments involving β -protonation are for the most part intuitive estimates and are parenthetically enclosed to emphasize this point. The value $\Delta_3(pK_\delta) = 1.2 = \Delta_4(pK_3)$ is based, for example, on the proton resonance shift $\delta_3^{(5)} = 0.9$ p.p.m. observed on β -protonation of 2,5-dimethylpyrrole and 1,2,5-trimethylpyrrole.⁴ Considerations involved in the other cases include comparison between methylpyrroles and methylindoles,⁵ protonation shifts of substituent methyl groups,²⁷ and failure to observe directly β -protonation in selected examples. The pK_a for β -protonation in pyrrole is based on these estimates and the measured value in 2,5-dimethylpyrrole.⁴ Its value is consistent with the fact that β -oriented products of electrophilic substitution in pyrrole occur to the extent of a few per cent.

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