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A NUCLEAR MAGNETIC RESONANCE STUDY OF THE PROTONATION OF NITROGEN HETEROCYCLIC MOLECULES*

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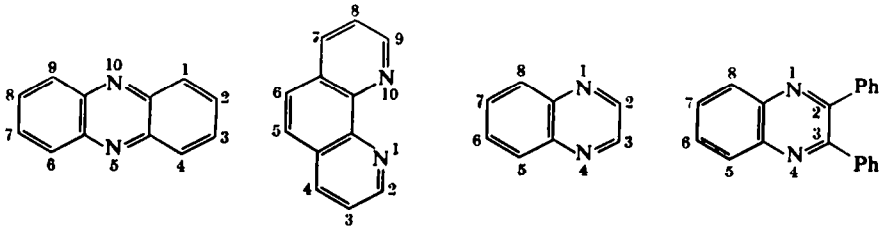
Abstract—The high resolution NMR spectra of quinoxaline, 2,3-diphenylquinoxaline, phenazine and *o*-phenanthroline have been measured in inert (CH_2Cl_2) and proton-donating (CF_3COOH) solvents and have been analyzed by an iterative procedure. Good agreement between observed and calculated spectra is obtained giving accurate values of chemical shifts and coupling constants. The proton signals for all the compounds studied are shifted downfield in CF_3COOH. These downfield shifts are associated with formation of stable mono-cations in acid solution. A qualitative interpretation of the chemical shifts for the bases and their cations has been given in terms of magnetic anisotropy and electric field effects of the neighbouring nitrogen atoms and π-electron charge densities in the rings.

INTRODUCTION

PHENAZINE (I), *o*-phenanthroline (II), quinoxaline (III) and 2,3-diphenylquinoxaline (IV) are members of a series of heterocyclic compounds whose fluorescence, phos-



I II III IV

phorescence and other spectroscopic properties[1–7] are strongly dependent on solvent, concentration and pH. In common with other nitrogen heterocycles the above compounds also show marked activity in many biological systems.[8] It was suggested,[9] on the basis of theoretical considerations, that the unusual properties of these compounds are due to the presence of lone-pair electrons on the nitrogen and their effect upon the π-electron distribution in the ring system.

* Work supported under the auspices of the U.S. Atomic Energy Commission.

[1] W. O. Kermack and J. E. McKail, *Heterocyclic Compounds* Vol. 7; pp. 344. Wiley, New York (1961).
[2] D. E. Pearson, *Heterocyclic Compounds* Vol. 6, pp. 473–661. Wiley, New York (1957).
[3] S. F. Mason, *J. Chem. Soc.* 493 (1962).
[4] R. V. M. White, *Nuclear Magnetic Resonance Spectra* Vol. 2; pp. 103–159. Academic Press, New York (1963).
[5] P. J. Secrest, J. A. Pawley and C. A. Lucchesi, *J. Appl. Spectry.* **13**, 141 (1959).
[6] R. Miller and F. Door, *Z. Elektrochem.* **63**, 1150 (1959).
[7] H. H. Perkampus and A. Roders, *Z. Naturforsch* **15b**, 1 (1960).
[8] B. Pullman and A. Pullman, *Quantum Biochemistry* Wiley, New York (1963).
[9] A. Streitweiser, *Molecular Orbital Theory* pp. 120 and 230. Wiley, New York (1962).

A number of attempts have been made to estimate the π-electron densities in nitrogen heterocycles and their conjugate acids from the chemical shifts of the ring protons.[10,11] However, agreement with densities calculated by SCF methods has been less than satisfactory, indicating that additional factors contribute significantly to the chemical shifts. Gil and Murrell[10] have shown that the agreement is improved considerably in pyridine when contributions due to magnetic anisotropy of the N atom and electric field effects arising from the lone pair electrons are taken into account. Similar calculations have been reported more recently for a series of one and two-ring nitrogen heterocyclic molecules.[11]

It would be worthwhile to extend such correlations to higher heterocycles in order to test further the importance of anisotropy and field effects and to establish the effect of additional rings and N atoms on the π-electron distribution in such systems. In this connection the 2 and 3-ring heterocycles (I to IV) are particularly appropriate because the NMR spectra are relatively simple to analyze.

In earlier studies the spectra for compounds I–III were measured in inert solvents and the parameters obtained by first-order analysis.[12–14] Quite recently, very accurate coupling constants and chemical shifts for phenazine and 2,3-dimethylquinoxaline obtained by "direct" analysis of the AA'BB' spectra were reported.[15] In this work we have re-examined these compounds in CH_2Cl_2 and in a strongly protonating solvent, CF_3COOH, over a range of temperatures and have analysed the spectra by the iterative method.[16] The NMR parameters for the free bases and their conjugate acids are interpreted in terms of the relative importance of the various factors contributing to these parameters.

EXPERIMENTAL

The compounds II and IV were kindly supplied by Dr. F. J. Hopton*; compounds I and III were commercial samples (Aldrich Chemical) as were the solvents CH_2Cl_2 and trifluoracetic acid (TFA). All materials were used without further purification except for TFA which was freshly distilled before use. No impurities were found to be present in the NMR spectra. Spectra were recorded on a Varian A60 spectrometer equipped with a variable-temp controller. Line positions are in c/s relative to 1% internal TMS; line frequencies were checked by the audio side-band method. Coupling constants are also in c/s. Spectra were analysed using NMRIT and NMREN II programs[16] modified for use with a CDC 3600 computer.

RESULTS

Quinoxaline and 2,3-diphenylquinoxaline. A summary of the parameters obtained from the analysis of the AA'BB' type spectra of quinoxaline and its protonated form and 2,3-diphenylquinoxaline is given in Table 1. Fig. 1A shows the fit between observed and calculated spectra of the unprotonated form while Fig. 1B shows the fit

* Department of Chemistry, Bristol University; now at Ontario Research Foundation, Toronto, Canada.

[10] V. M. S. Gil and J. N. Murrell, *Trans Farad. Soc.* **60**, 248 (1964).
[11] A. H. Gawer and B. P. Dailey, *J. Chem. Phys.* **42**, 2658 (1965).
[12] E. F. G. Herington and I. J. Lawrenson, *Spectrochim. Acta* **21**, 1010 (1965).
[13] E. Van der Donckt, R. H. Martin and F. Geerts-Errard, *Tetrahedron* **20**, 1495 (1964).
[14] J. D. Miller and R. H. Prince, *J. Chem. Soc.* 3185 (1965).
[15] T. K. Lim, A. Taurins and M. A. Whitehead, *Canad. J. Chem.* **44**, 1211 (1966).
[16] J. D. Swalen and C. A. Reilly, *J. Chem. Phys.* **37**, 21 (1962).

TABLE 1

Quinoxaline Temp	Solvent‡	M†	$\tau_{6,7}$*	$\tau_{5,8}$	$\tau_{2,3}$	$J_{6,7}$	$J_{7,8}$	$J_{5,7}$	$J_{6,8}$	$J_{5,6}$	$J_{5,8}$	Center of gravity of AA′ BB′	$\Delta\tau$	τ_{OH}
	50% CH_2Cl_2/													
−27°	50% CF_3COOH	0·4	512·7	521·6	580	4·16	9·34	2·53	2·53	9·34	0·71	517·1	8·9	689
36°	50% CF_3COOH	0·4	503·4	514·6	569	5·65	8·30	1·49	1·49	8·30	0·64	509·0	11·2	651
36°	CF_3COOH	0·4	507·4	518·6	571	5·64	8·37	1·55	1·55	8·37	0·58	513·0	11·2	656
36°	CH_2Cl_2	0·4	467·4	486·7	526	6·59	8·25	1·41	1·41	8·25	0·38	477·0	19·4	—
2,3-*diphenylquinoxaline*														
36	CH_2Cl_2	~0·4	467·3	489·7	—	6·98	8·84	1·42	1·42	8·84	0·13	478·5	22·4	—

* Errors in Tables 1 and 2 are: $\tau_{1,2,3,4}$: ±0·05 c/s; J_{13} etc.: <0·3, >0·05 c/s; others: ±0·5 c/s.
All shifts are relative to internal TMS as reference.

† Moles per liter.

‡ Solvent concentrations are in volume percent.

obtained for the protonated form of quinoxaline. The spectrum of 2,3-diphenylquinoxaline is similar to that shown in Fig. 1A. The spectrum of protonated 2,3-diphenylquinoxaline was sufficiently broadened at the concentration studied ~0·4M to preclude an accurate determination of the coupling constants. However, the proton chemical shifts are $\tau_6 = \tau_7 = 467{\cdot}3$ and $\tau_5 = \tau_8 = 489{\cdot}7$ c/s relative to TMS giving $\Delta(AA'-BB') = 22{\cdot}4$ c/s. The two Ph groups, in CH_2Cl_2 as solvent, give rise to a

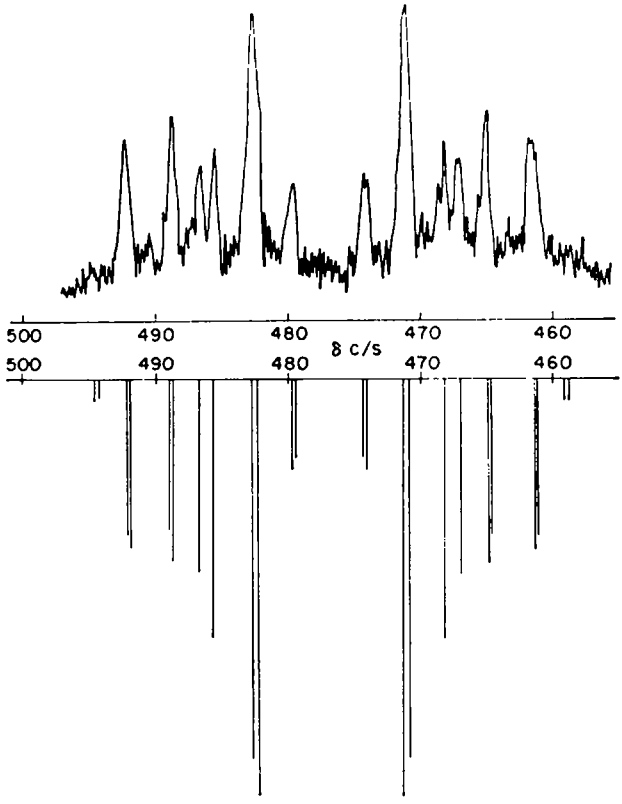


FIG. 1A. Spectra of 0·4M quinoxaline in CH_2Cl_2 at 36°. Upper trace, observed spectrum; lower trace, calculated spectrum.

multiple splitting pattern spread over a width of approximately 24 c/s and centered at 444 c/s downfield from TMS. In the protonated species this pattern collapses to a single line (half-width ~0·8 c/s) with a small low-field shoulder, centered at 452·2 c/s downfield from TMS. The spectrum of the 5, 6, 7, 8 protons is similarly collapsed in the protonating solvent and is centered at 502·6 c/s downfield of TMS. Also included in Table 1 are the chemical shifts and coupling constants for quinoxaline in a 1:1 solution of CH_2Cl_2 and TFA at −27° and 36°.

The downfield shifts of the individual quinoxaline protons on protonation i.e. $\Delta\tau = [\tau_{base} - \tau_{protonated\ base}]$ are:

Solvent	$\Delta\tau_{6,7}$	$\Delta\tau_{5,8}$	$\Delta\tau_{2,3}$*
CH_2Cl_2	0	0	0
CH_2Cl_2–CF_3COOH 1:1	−36·0	−27·9	−43·0
CF_3COOH	−40·0	−31·9	−45·0

* Chemical shift differences are in c/s.

TABLE 2

Phenazine Temp	Solvent	M	$\tau_{2,3}$	$\tau_{1,4}$	$J_{2,3}$	$J_{1,2}$	$J_{2,4}$	$J_{1,3}$	$J_{3,4}$	$J_{1,4}$	Center of gravity of AA′ BB′	$\Delta\tau$ (AA′ BB′)
−27°	2% CF_3COOH/ 98% CH_2Cl_2	0·4	479·4	500·6	6·15	8·28	1·26	1·26	8·28	0·44	489·5	20·2
36°	2% CF_3COOH/ 98% CH_2Cl_2	0·4	475·4	498·6	6·57	8·58	1·27	1·27	8·58	0·26	486·2	23·2
36°	5% CF_3COOH/ 95% CH_2Cl_2	0·4	487·1	508·9	5·73	8·48	1·40	1·40	8·48	0·13	498·0	21·8
36°	CH_2Cl_2	0·4	468·7	491·3	6·28	8·51	1·46	1·46	8·51	0·40	480·5	22·6
36°	CF_3COOH	0·037	502·7	518·1	6·97	9·27	1·29	1·29	9·27	0·53	510·4	15·4

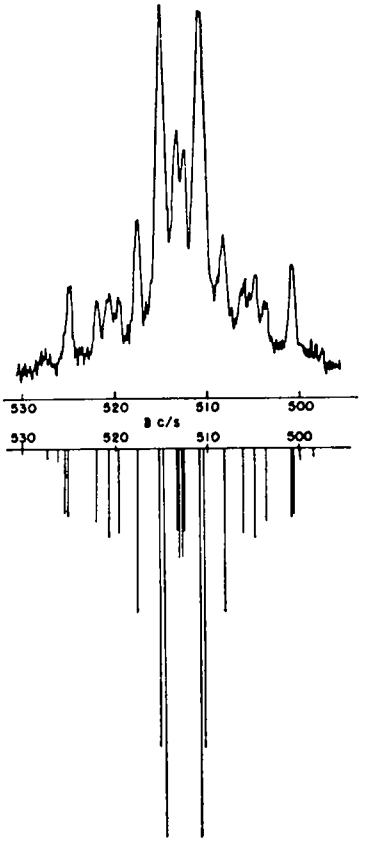


FIG. 1B Spectra of 0·4M quinoxaline in TFA at 36°. Upper trace, observed spectrum; lower trace, calculated spectrum.

Phenazine. The spectra for phenazine in CH_2Cl_2 and dilute (2%) TFA solution are essentially the same as those in Figs. 1A, 1B. However, increasing the acid concentration has a much more marked effect upon the line-widths than in the case of quinoxaline, which even in pure TFA gives a well-resolved spectrum. Fig. 2A shows the broadened spectrum of 0·4M phenazine in a 5% TFA-95% CH_2Cl_2 solution. In a 1:1 TFA–CH_2Cl_2 solution (Fig. 2B) the fine structure is completely absent and the spectrum of the AA'BB' protons is a broad unresolved band of half-width ~18 c/s centered at 498 c/s downfield from TMS. Upon further addition of acid the broad band increases in half width ($\Delta\tau_{1/2} = 22$ c/s for a 0·3M solution in 100% TFA) and also moves to lower field (centered at 510 c/s for a 0·3M solution in 100% TFA). At low concentration of phenazine a resolvable fine structure reappears and the spectrum for the protonated species is fully resolved in 0·037M solution (Fig. 2C). The results of the AA'BB' analyses carried out under varying conditions of solvent and temperature are shown in Table 2. In addition the downfield shifts of the individual phenazine protons on protonation are as follows:

Solvent	$\Delta\tau_{2,3}$ c/s	$\Delta\tau_{1,4}$ c/s
CH_2Cl_2	0	0
2% CF_3COOH-98% CH_2Cl_2	−6·7	−7·3
5% CF_3COOH-95% CH_2Cl_2	−18·4	−19·6

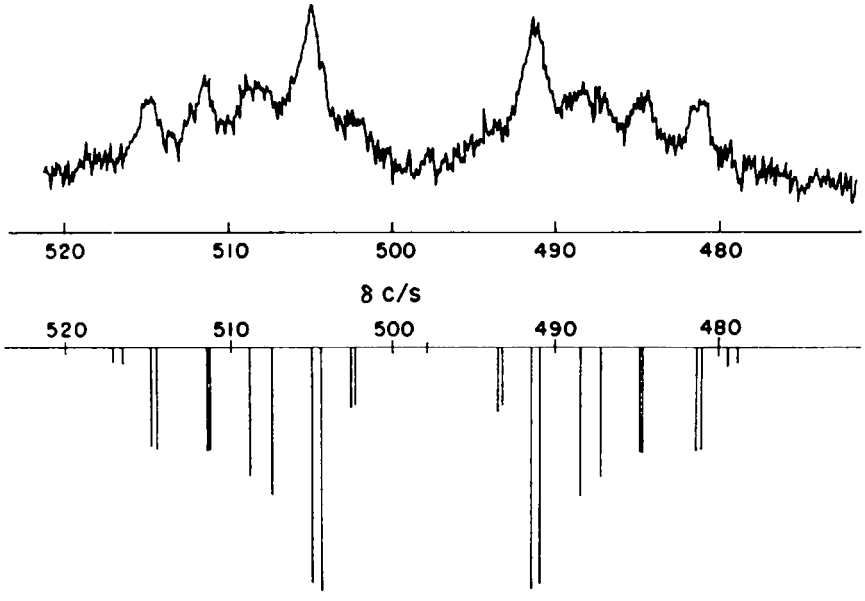


FIG. 2A Spectra at 0·4M phenazine in 5% TFA-95% CH_2Cl_2 at 36°. Upper trace, observed spectrum; lower trace, calculated spectrum.

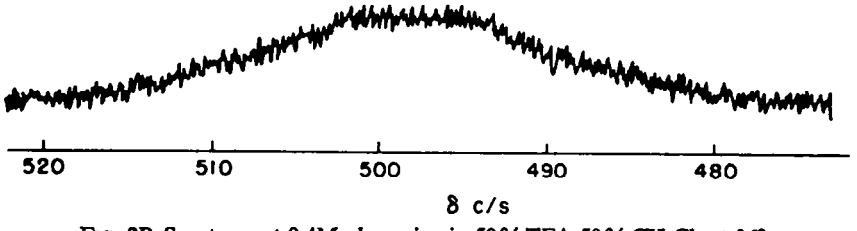


FIG. 2B Spectrum at 0·4M phenazine in 50% TFA-50% CH_2Cl_2 at 36°.

TABLE 3

Phenanthroline Solvent	M	τ_2	τ_3	τ_4	τ_5	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$
CH_2Cl_2	0·4	559·5	468·7	509·8	477·0	4·8	1·7	8·5
85% CH_2Cl_2– 15% CF_3COOH	0·4	561·2	498·6	547·3	502·3	5·2	1·7	8·7
CF_3COOH	0·4	574·2	512·6	566·8	515·2	5·2	1·5	8·5

Error in τ is $\pm$0·1 c/s
Error in J is $\pm$0·2 c/s

o-Phenanthroline. *o*-phenanthroline gives rise to essentially first order ABC spectra in CH_2Cl_2 and TFA solvents. These spectra consist of three sets of quartets for the protons α, β, and γ to the hetero-atom and a single peak for protons in position 5,6. The results are given in Table 3.

The spectrum in TFA shows considerable broadening of all protons, e.g., the half-width of the 5,6 protons is 2·2 c/s compared to that in CH_2Cl_2 solvent of 0·70 c/s. The magnitude of the latter line-width indicates long-range coupling with protons in the

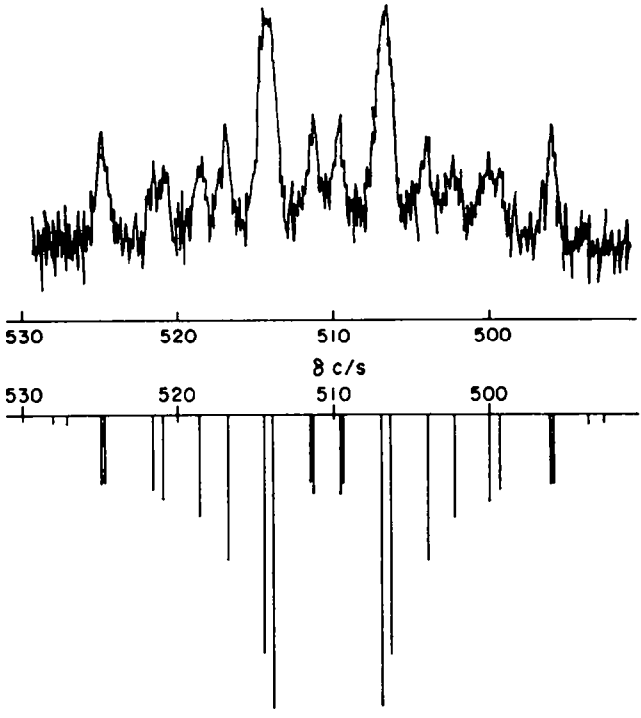


FIG. 2C Spectra of 0·037M phenazine in TFA. Upper trace, observed spectrum; lower trace, calculated spectrum.

adjacent rings. The total spread of the spectrum ($\tau_2 - \tau_3$) is considerably reduced on protonation, being 90·8 c/s in CH_2Cl_2 solvent (Fig. 3), 62·6 c/s in 85% CH_2Cl_2-15% TFA (Fig. 4) and 61·6 c/s in pure TFA.

The downfield shifts on protonation are $\Delta\tau_{2,9} = -14{\cdot}7$ c/s, $\Delta\tau_{3,8} = -43{\cdot}9$ c/s, $\Delta\tau_{4,7} = -57{\cdot}0$ c/s and $\Delta\tau_{5,6} = -38{\cdot}2$ c/s.

A comparison of the relative separations of the 2,3,4, and 5 protons in the protonated and unprotonated forms gives the shifts in Table 4.

TABLE 4

Solvent	$(\tau_2-\tau_3)$	$(\tau_2-\tau_4)$	$(\tau_3-\tau_5)$	$(\tau_3-\tau_4)$	$(\tau_2-\tau_5)$	$(\tau_4-\tau_5)$
CH_2Cl_2	90·8	49·7	82·5	—41·1	−11·3	32·8
15% CF_3COOH/85% CH_2Cl_2	62·6	13·9	58·9	−48·7	−3·7	45·0
CF_3COOH	61·6	7·4	59·0	−54·2	−2·6	51·6

DISCUSSION

Quinoxaline. The parameters for quinoxaline lie in the range generally observed for naphthalene-type derivatives.[17–19] For quinoxaline in CH_2Cl_2, $J_{5,6}$ is greater than $J_{6,7}$ while the meta coupling $J_{5,7}$ is about 1 c/s larger than the cross-ring coupling $J_{5,8}$. No evidence of a coupling between the protons in neighboring rings is noted. The

[17] J. A. Pople, W. G. Schneider and H. J. Bernstein, *Canad. J. Chem.* **35**, 1060 (1957).
[18] T. Schaefer, *Canad. J. Chem.* **39**, 1864 (1961).
[19] J. W. Emsley, J. Feeney and L. H. Sutcliffe, *High-Resolution Nuclear Magnetic Resonance Spectroscopy* Vol. 1; pp. 399–423. Pergamon Press (1965).

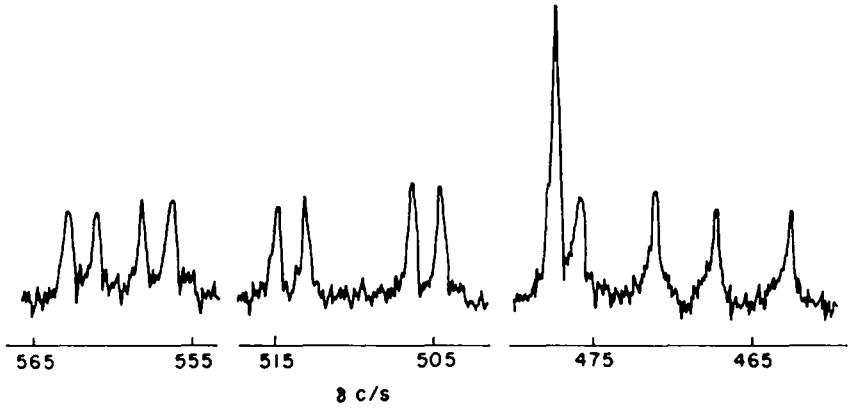


FIG. 3 Spectrum of 0·4M *o*-phenanthroline in CH_2Cl_2 at 36°.

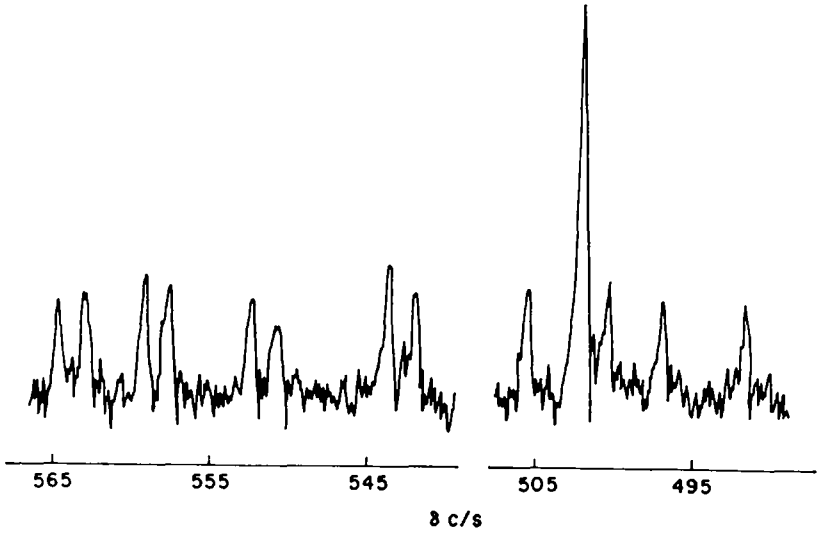


FIG. 4 Spectrum of 0·4M *o*-phenanthroline in 15% TFA-85% CH_2Cl_2 36°.

coupling constants for quinoxaline are not significantly different from the accurate values reported for 2,3-dimethyl quinoxaline.[15]

The chemical shifts in CH_2Cl_2 are similar to those reported by Gawer and Dailey. Upfield shifts of 7·8 c/s, 6·0 c/s and 11·9 c/s are noted for the 2,3, 5,8 and 6,7 protons respectively in cyclohexane solvent, as compared to CH_2Cl_2. This solvent dependence can be partially attributed to the higher concentration (10 mole %) used by Gawer and Dailey. A concentration effect has been observed in both solvents used in the present work, e.g. in TFA doubling the concentration of quinoxaline for 0·4M to 0·8M produces an upfield shift of up to 3 c/s for all protons. Similar concentration and solvent effects have been reported for 2,2′ bipyridyl[20] in a variety of inert and proton-donating solvents and have been attributed, in the case of proton-donating solvents, to the formation weak 1:1 hydrogen-bonded complexes. The chemical

[20] S. Castellano, H. Günther and S. Ebersole, *J. Phys. Chem.* **69**, 4166 (1965).

shifts for the 2,3 protons are at lower field than the α proton shifts in pyridine reflecting the additional deshielding influence of the second nitrogen atom and the ring current of the benzocyclic ring.

2,3-*Diphenylquinoxaline.* A comparison of the chemical shifts for 2,3-diphenylquinoxaline, $\tau_{6,7} = 467{\cdot}3$ c/s and $\tau_{5,8} = 489{\cdot}7$ c/s, with the corresponding values for quinoxaline shows that apart from a slight downfield shift for $\tau_{5,8}$ in III the values are practically the same in both compounds. The slight downfield shift of the 5,8 protons in 2,3-diphenylquinoxaline is due to a ring current effect of the phenyl substituents. The coupling constants $J_{6,7}$ and $J_{5,6}$ are slightly larger in 2,3-diphenylquinoxaline than in quinoxaline and phenazine in CH_2Cl_2 solvent.

Phenazine. The chemical shifts for phenazine $\tau_{2,3} = 468{\cdot}7$ c/s and $\tau_{1,4} = 491{\cdot}3$ c/s in CH_2Cl_2 differ somewhat from the quoted values of 440·4 c/s and 489·6 c/s for a saturated solution of phenazine in $CDCl_3$.[12] The difference can be attributed in part to a concentration effect;[12] a further deshielding could arise from a H-bonding interaction between $CDCl_3$ and the nitrogen atoms although this would tend to deshield protons in the 4 position more than those at 2,3. The relative shift between the 2,3 and 1,4 protons in CH_2Cl_2 is 22·6 c/s in agreement with the reported value of 23·9 c/s in dioxan.[15] Comparison of the shifts with those for quinoxaline shows that the protons for phenazine are shifted slightly to low field ($\sim$3 c/s), reflecting the additional intramolecular ring current effect in phenazine. The coupling constants obtained by the iterative procedure used in the present work are in good agreement with the values obtained by the more rigorous analysis of Lim.[15]

o-*Phenanthroline.* The parameters obtained for II by the iterative procedure are in reasonable agreement with the values reported earlier.[13,14] The latter workers reported chemical shifts in CCl_4 relative to TMS of $\tau_2 = 547{\cdot}5$ c/s, $\tau_3 = 452{\cdot}5$ c/s, $\tau_4 = 489{\cdot}0$ c/s and $\tau_5 = 461{\cdot}8$ c/s. These shifts are at higher field ($\sim$12–20 c/s) than the corresponding shifts in CH_2Cl_2 and reflect the effects of concentration and possible H-bonding interactions acting in the latter solvent. Such interactions are probable in all of these solutions since *o*-phenanthroline is known to be extremely hygroscopic with hydrogen bonding with the H_2O occurring at the nitrogen atom.[21]

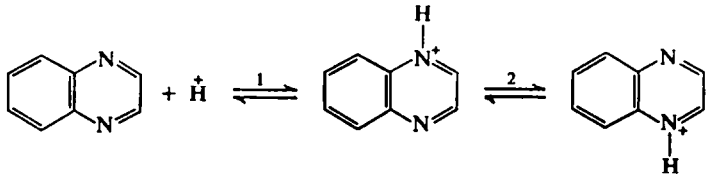
The coupling constants reported for II in CCl_4 are comparable to the values in CH_2Cl_2. A comparison of $J_{2,3}$ with the corresponding coupling constant $J_{2,3}$ in the carbon analogue, phenanthrene, shows that the latter is $\sim$2·5 c/s larger (no major differences are noted in the other J's). A possible explanation of the decrease of $J_{2,3}$ and other ortho couplings in N-heterocyclic molecules is the effect of the somewhat greater electronegativity of the N atom which would tend to draw σ and π-electron density from the region of the adjacent atoms and hence decrease the J's.

The spectra for *o*-phenanthroline complexes with transition metal ions have been reported in H_2O and DMSO[14] and apart from the chemical shifts, the parameters do not differ significantly from those for *o*-phenanthroline. A large upfield shift was noted for α and β protons in *o*-phenanthroline in its metal complexes and was attributed to a non-bonded interaction between the protons and the metal ion. Changes of the solvent did not alter either the chemical shifts or the coupling constants for the complexes.

Protonation effects. Downfield shifts are noted for all of the protons in the compounds studied in the strongly protonating solvent, CF_3COOH. The deshielding can

[21] I. R. Beattie and M. Webster, *J. Phys. Chem.* **66**, 115 (1962).

be attributed to formation of the corresponding conjugate acids with proton addition occurring at the nitrogen in each case. In view of the low pK_a values for phenazine and quinoxaline, i.e., 1·23 and ~0·8[22] it is unlikely that any significant amounts of the dication are formed, even in the most concentrated TFA solutions at room temperature. From the symmetrical appearance of the spectra in acid solution it can be concluded that a rapid equilibration is occurring among the mono-cation, the free base and tautomers of the cation as represented by V and VI for quinoxaline.



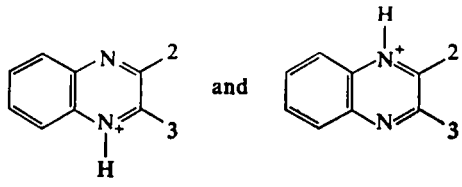
V VI

A much more complicated spectrum of the ABCD type rather than the observed AA'BB' would have been expected if the lifetime of the mono-cation was sufficiently greater than the exchange rates represented by reactions 1 and 2.

A qualitative indication of the extent of protonation is provided by the chemical shift-concentration curves in binary CH_2Cl_2–CF_3COOH solutions cf. Tables 1–3. These show that the largest incremental shift change occurs at low acid concentrations (<0·2 mole fraction) as would be expected on the basis of monocation formation at approximately stoichiometric amounts of acid and base. Little shift change is observed at high acid concentrations, >0·5 mole fraction, indicating that protonation of the bases is essentially complete at these concentrations. The small downfield shift noted upon dilution of quinoxaline in TFA may be associated with the larger excess of acid required for complete protonation of the somewhat weaker base, pK_a ~0·80.

The protonation shifts for the 5 and 6 protons in quinoxaline and 2 and 1 protons in phenazine vary in the same order, i.e. $\Delta\tau_5 = -0{\cdot}532$ ppm $< \Delta\tau_6 = -0{\cdot}677$ ppm as observed for pyridine where the deshielding varies as $\alpha < \beta < \gamma$. However, the magnitude of the deshielding is roughly the same for the 1 and 2 protons in phenazine and 5 and 6 protons in quinoxaline cations whereas the shift change for the β proton is approximately four times as great as for the α proton in pyridinium. The difference between the mono- and bi-cyclo compounds arises because the primary factors which give rise to the shieldings in the nitrogen ring i.e. electric field, magnetic anisotropy and π-electron density shifts do not contribute as effectively to the shieldings in adjacent rings. Somewhat surprising is the much larger deshielding of the α(2, 3) protons in the quinoxaline cation (−0·715 ppm) compared to the α protons in pyridinium (−0·250 ppm). In the former compound however, the observed shift for the α protons actually represents a weighted average between the shifts in two different monocations, where in VII the 3 proton is α to the N—H^+ and in VIII is located β to the N—H^+. In the presence of fast exchange δ_{obs} will be given by, $\delta_{obs} = 0{\cdot}5\delta_\alpha + 0{\cdot}5\delta_\beta$, and if δ_α and δ_β are assumed to be the same as in pyridine then the calculated value for δ_{obs}, −0·66 ppm is in reasonable agreement with the actual value −0·71 ppm.

[22] A. Albert, *Physical Methods in Heterocyclic Chemistry* Vol. 1; Chap. 1, pp. 76–77. Academic Press, New York (1963).



VII VIII

The surprisingly sharp collapse of the signals for the phenyl groups in 2,3-diphenylquinoxaline which occurs in acid solution i.e. $\Delta\tau_{1/2} = 24$ c/s (CH_2Cl_2) to $\Delta\tau_{1/2} = 0{\cdot}8$ c/s in TFA, is similar to the changes which have been observed in other carbocyclic compounds upon protonation[23] and is presumably indicative of a more uniform distribution of the π-electron density in the benzene ring when the 2,3-diphenylquinoxaline is in the cation form.

For *o*-phenanthroline the shifts to low field in TFA vary in the same order as for pyridine i.e. $4 > 3 > 2$. However, the magnitudes of the deshieldings are less in the phenanthroline cation reflecting the effect of the additional ring upon the π-electron deficiency.

The line-widths for all of the compounds show an initial increase at low acid concentrations and then sharpen slightly at high acid concentration. The changes are most pronounced for phenazine where a single broad structureless band, $\Delta\tau_{1/2} = 18$ c/s, is observed in 1:1 CF_3COOH–CH_2Cl_2 solutions. Similar changes have been observed for pyridine in TFA[24] and have been attributed to a slow exchange of the proton between the acid and pyridine, i.e. step I. In the present systems the situation is more complicated because of the additional possibility of intra and/or intermolecular exchange of the proton between the two ring nitrogens, step 2. A meaningful quantitative analysis of the line-width changes in terms of a specific exchange reaction is therefore not feasible for the present data although it is likely that at the acid-base concentrations used the dominant exchange reaction is step 1 and the corresponding exchange rate is slowest for the phenazine cation.

π-Electron densities in the cations and free bases. The factors which influence the chemical shifts of protons in aromatic compounds have been summarized in a number of recent papers.[10,11,20,25] For the N-heterocyclic compounds and their conjugate acids the effects which predominate[10,11,20] are (i) the magnetic anisotropy of the N atom, (ii) the diamagnetic anisotropy of the π-electron system including adjacent rings, (iii) the electric field associated with the N (and $\overset{+}{N}$—H) atom and (iv) the π-electron densities of the directly-bonded carbon atoms. The chemical shifts of protons in pyridine and the pyridinium cation have been interpreted semi-quantitatively by Gil and Murrell[10] in terms of effects (i), (iii), and (iv). When the observed shifts for pyridine have been corrected for effects (i) and (iii) a good correlation is obtained between calculated π-electron densities and the values derived from the corrected shifts. A similar correlation between "corrected" chemical shifts and π-electron densities for the pyridinium cation was less satisfactory. Nevertheless, the downfield shifts can be rationalized qualitatively in terms of a decrease in the charge densities at the individual carbon atoms occurring as a result of proton addition at the nitrogen lone pair.

[23] S. S. Danyluk and W. G. Schneider, *Canad. J. Chem.* **40**, 1777 (1962).
[24] W. G. Schneider and I. C. Smith, *Canad. J. Chem.* **39**, 1158 (1961).
[25] B. P. Dailey, A. Gawer and W. C. Niekam, *Disc. Faraday Soc.* **34**, 18 (1962).

A detailed quantitative analysis of the shift contribution expected from effects (i)–(iii) for mono- and bi-cyclic nitrogen heterocyclic molecules with both one and two nitrogen atoms per ring has been given more recently.[11] Although a rough correlation between corrected proton shifts and calculated charge densities was observed for a series of compounds, including quinoxaline, Gawer and Dailey[11] concluded that the corrected shifts were not reliable enough to warrant any quantitative estimates of π charge densities. In the present work the charge densities for the three ring heterocycles phenazine and *o*-phenanthroline and the two-ring heterocycle quinoxaline have been estimated by the same procedure as followed by Gil and Murrell[10] and Gawer and Dailey.[11] A summary of the charge densities along with the pertinent shift corrections for anisotropy and electric field effects due to the nitrogen is given in Table 5.* Numerical agreement of the charge densities for quinoxaline in Table 5 with the values reported by Gawer and Dailey is not particularly good and reflects the somewhat different values of the anisotropy and electric field corrections calculated in this work. However, the trend in decreasing charge densities, is the same in both cases i.e. $q_5 < q_1 < q_3$, and is in agreement with the calculated order.[26] No comparable calculations of π densities by the SCF method are available as yet for phenazine

TABLE 5

		δ obs* Relative to hydrocarbon	Anisotropy of Nitrogen	Electric Field	δ corrected	q†
Quinoxaline	1	−0·51	−0·02	0	−0·49	+0·061
	3	−0·45	−0·11	0	−0·34	+0·042
	5	−1·48	−0·33(α) −0·01(β)	−0·40	−0·74	+0·091
Phenazine	1	−0·31‡	−0·02	0	−0·29	+0·036
	3	−0·21	−0·11	0	−0·10	+0·012
o-Phenanthroline	1	−1·72§	−0·33	−0·40	−0·99	+0·122
	2	−0·24	−0·01	−0·18	−0·05	+0·006
	3	−0·65	0	−0·15	−0·50	+0·062
	4	−0·25	0	0.	−0·25	+0·031

* All shift values are in ppm.

† Gawer and Dailey's expression of $\delta = 8{\cdot}08q$ was used to evaluate q.

‡ Shift values for anthracene were from Jonathan *et al.*[27]

§ Shift values used for phenanthrene were from Fahey and Graham.[28]

and *o*-phenanthroline. It can be noted, however, that for the phenanthroline the charge densities estimated from corrected shifts vary in the same order, $q_1 > q_3 > q_2$, as observed for pyridine. Little difference in charge densities would be expected between the hetero-rings of these two molecules since the presence of an additional benzocyclic ring does not significantly alter the properties of the hetero-ring, cf. pK_A of pyridine is 5·23 and of quinoline is 4·87.[22]

It should be possible, in principle, to calculate π-electron densities for the N-heterocyclic cations of I to IV from corrected chemical shifts in much the same manner

* The ring currents are assumed to be the same in the heterocycles and their carbon analogues.

[26] O. W. Adams and P. G. Lykos, quoted in Ref. 11.

[27] N. Jonathan, S. Gordon and B. P. Dailey, *J. Chem. Phys.* **36**, 2443 (1962).

[28] R. C. Fahey and G. C. Graham, *J. Phys. Chem.* **69**, 4417 (1965).

as for the parent bases. In practice, however, the presence of a positive charge on the molecule leads to a number of complications[25] which make any quantitative correlations of shifts and charge densities impractical. Qualitatively, the downfield shifts which occur for the protons in the cations can be ascribed to a delocalization of the charge deficiency throughout all of the rings in the molecule. The similarity in magnitude of the shift changes observed for the α and β protons in quinoxaline and in phenazine indicates that the charge deficiency is distributed more or less uniformly in the benzocyclic rings in the cations. This is evidently not the case for *o*-phenanthroline where a much larger change in charge density occurs at the γ protons than at α protons. A rough estimate of the charge deficiency in a given ring can be made from the total shift change observed for the protons in the ring.[23,24] On this basis for quinoxaline, roughly 30–40% of the positive charge is estimated to be in the benzocyclic ring according to the observed shift change. A similar distribution is also indicated for the other cation.

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