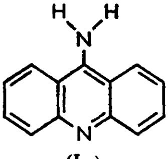
251. The Tautomerism of N-Heteroaromatic Amines.

By S. F. Mason.

The frequencies, extinction coefficients, and band half-widths of the N–H stretching vibration bands of some *N*-heteroaromatic imines, and primary and secondary amines, in dilute carbon tetrachloride solution have been measured in the 3 μ region. The amines give absorption bands lying at higher frequencies by 100—200 cm.$^{-1}$ and some five to ten times more intense than those of the imines, differences which are ascribed to the larger "*s*" character of the N–H bonds in the former compounds. The spectral distinctions are used to show that most of the tetracyclic and all of the tricyclic amines examined, including 5-aminoacridine, exist predominantly as the amino-tautomer, although 5-amino-2 : 3-benzacridine assumes largely the imino-form. The ionisation constant and ultraviolet evidence are reviewed and are shown to support an amino-structure for 5-aminoacridine. The present conclusions are shown to be in accord with the expectations of molecular-orbital theory.

It has been shown by various physical methods [1-7] that the mono- and di-cyclic *N*-heteroaromatic amines exist predominantly in the amino- and not the tautomeric imino-form. In dilute chloroform or carbon tetrachloride solution such amines give two absorption bands in the 3350—3550 cm.$^{-1}$ region [1-5] and another in the 1600—1650 cm.$^{-1}$ region,[1-4] due to the symmetric and the antisymmetric stretching vibrations and the internal deformation mode of the primary amino-group respectively, these bands being readily identified by the deuteration of the amino-group.[4] The ultraviolet spectra of these amines, in general, resemble more closely those of the dimethylamino-analogues with fixed amino-forms than those of the corresponding nuclear *N*-methyl derivatives with fixed imine structures,[4, 6,7] and the ionisation constants of the amines and their nuclear and exocyclic *N*-methyl derivatives show [4,7] that the amino- predominates over the imino-form by a factor of 10^3—10^6. The tautomerism of *N*-heteroaromatic amines has been investigated also by dipole moment measurements, but the results were inconclusive.[3,7,9]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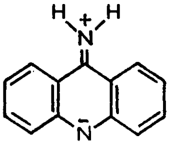
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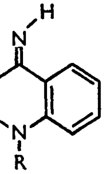
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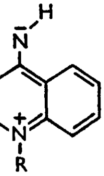
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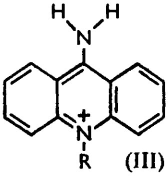
(III)

The structure of the tricyclic amines, notably 5-aminoacridine, has remained uncertain, however. Comparing the ultraviolet spectra of 9-aminoanthracene and 5-aminoacridine, Craig and Short concluded that [10] the latter amine had the amino-structure (I), and Short subsequently found [3] bands at 3435 and 3525 cm.$^{-1}$ in the infrared spectrum of 5-aminoacridine in chloroform, which were assigned respectively to the symmetric and the antisymmetric stretching vibration of the primary amino-group. Working with carbon tetrachloride solutions of 5-aminoacridine, Karyakin and Schablja observed [11] the same

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[1] Angyal and Werner, *J.*, 1952, 2911.
[2] Goulden, *J.*, 1952, 2939.
[3] Short, *J.*, 1952, 4584.
[4] Brown, Hoerger, and Mason, *J.*, 1955, 4035.
[5] Osborn, Schofield, and Short, *J.*, 1956, 4191.
[6] Anderson and Seeger, *J. Amer. Chem. Soc.*, 1949, **71**, 340.
[7] Angyal and Angyal, *J.*, 1952, 1461.
[8] Leis and Curran, *J. Amer. Chem. Soc.*, 1945, **67**, 79.
[9] Pushkarev and Kokoshko, *Doklady Akad. Nauk S.S.S.R.*, 1953, **93**, 77.
[10] Craig and Short, *J.*, 1945, 419.
[11] Karyakin and Schablja, *Doklady Akad. Nauk S.S.S.R.*, 1957, **116**, 969.

TABLE 1.

The positions (ν; cm.$^{-1}$) and the intensities (I; l. mole^{-1} cm.$^{-2}$) of the symmetric and antisymmetric N–H stretching vibration bands of some polycyclic *N*-heteroaromatic primary amines in chloroform and carbon tetrachloride. The intensities (I) are given as the product of the maximum extinction coefficient (l. mole^{-1} cm.$^{-1}$), $E_{\text{max.}} = (1/Cl) \log_{10} (T_0/T)\nu_{\text{max.}}$, and the band half-width. The H–N–H bond angle ($\theta°$), and the charge densities at the positions of the nuclear (q_n) and the exocyclic (q_x) nitrogen atom in the corresponding carbanion, are also given. Values in italics refer to chloroform solution.

	Antisymmetric			Symmetric					
Compound	ν	$E_{\text{max.}}$	I	ν	$E_{\text{max.}}$	I	θ [a]	q_n [b]	q_x [b]
Acridine									
1-NH_2	3498	55	1650	3387	58	1330	118·5°	1·000	1·381
2-NH_2	3497	46	1470	3405	102	2240	113·5	1·118	1·471
3-NH_2	3488	31	990	3400	82	1800	112·4	1·000	1·471
4-NH_2	3477	24	940	3395	37	920	110·8	1·095	1·381
5-NH_2	*3527*	*40*	*1280*	*3436*	*97*	*2520*	113·2	1·286	1·286
5-NH_2-1-Me	3523	42	1140	3433	83	1910	112·9	1·286	1·286
Phenanthridine									
6-NH_2	3499	37	1180	3408	85	1870	113·2	1·082	1·510
9-NH_2	3513	46	1420	3409	80	1680	116·5	1·286	1·446
2-NH_2-9Me	3491	23	810	3403	54	1240	112·4	1·022	1·544
Benzoquinoline									
4′-NH_2-5 : 6-	3482	25	850	3401	40	920	110·5	1·019	1·464
2-NH_2-4-Me-5 : 6-	3512	50	1600	3410	96	2210	116·0	1·195	1·544
3-NH_2-6 : 7-	3484	31	960	3398	71	1630	111·8	1·000	1·471
4-NH_2-6 : 7-	3500	40	1080	3415	72	1660	111·6	1·214	1·381
4-NH_2-7 : 8-	3509	43	1160	3419	77	1620	112·9	1·167	1·464
6-NH_2-7 : 8-	3474	25	850	3393	38	870	110·5	1·000	1·446
1′-NH_2-7 : 8-	3475	25	850	3395	39	970	110·3	1·000	1·464
Benzacridine									
5-NH_2-1 : 2-	3523	40	1120	3432	92	2025	113·2	1·231	1·314
7-NH_2-1 : 2-	3490	28	896	3401	72	1655	112·7	1·000	1·495
8-NH_2-1 : 2-	3497	30	870	3405	83	1825	113·5	1·088	1·480
7-NH_2-2 : 3-	3490	29	956	3401	81	1780	112·7	1·000	1·417
5-NH_2-3 : 4-	3488	42	1050	3405	54	1135	111·0	1·250	1·340
7-NH_2-3 : 4-	3492	25	750	3402	68	1495	113·0	1·000	1·480
8-NH_2-3 : 4-	3498	30	840	3406	88	1850	113·5	1·091	1·495

[a] Calculated by the method of ref. (20). [b] Calculated by the method of ref. 21.

TABLE 2. N-*Heteroaromatic imines and secondary amines* (*for details see Table* 1).

Compound	ν	$E_{\text{max.}}$	I	q_n [b]	q_x
1-Ethyl-1 : 2-dihydro-2-iminopyridine	3325	9·3	240	1·143	1·571
1-Ethyl-1 : 4-dihydro-4-iminopyridine	3278	~10 [a]	~250 [a]	1·143	1·571
5-Imino-10-methylacridan	3294	6·8	170	1·286	1·286
5-Methylaminoacridine	3443 3463	24 22	1080	1·286	1·286
Acridan	3434	45	1350	—	—
5-Amino-2 : 3-benzacridine	3448	49	1420	1·300	1·208
	3298	7·4	180		

[a] Some decomposition observed. [b] Calculated by the method of ref. 21.

bands at 3440 and 3520 cm.$^{-1}$ and assigned them respectively to the stretching vibrations of the nuclear and the exocyclic N–H groups of the imine structure (II; R = H) which had been proposed earlier [12] from a study of the spectrum of the amine in the overtone region. Similarly Acheson and his co-workers concluded [13] from a comparison of the ultraviolet spectra of 5-imino-10-methylacridan and 5-amino- and 5-dimethylamino-acridine that the imine form (II; R = H) was predominant in methanol or ethyl acetate solution, whilst Sukhomlinov, from the same data and additional spectral comparisons, considered [14] the amine structure (I) to the the main tautomer under these conditions.

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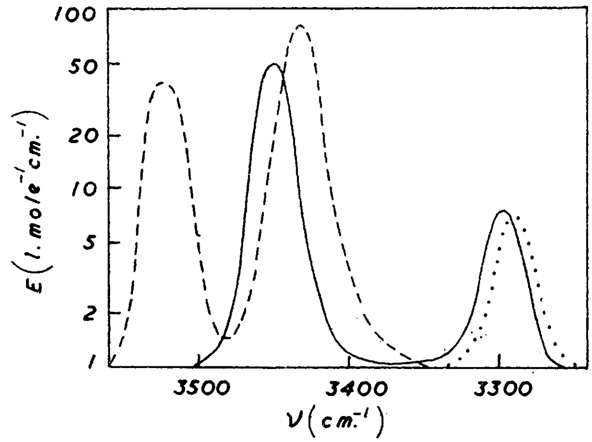
[12] Karyakin, Grigorovski, and Yaroslavskii, *Doklady Akad. Nauk S.S.S.R.*, 1949, **67**, 679.
[13] Acheson, Burstall, Jefford, and Sansom, *J.*, 1954, 3742.
[11] Sukhomlinov, *Zhur. obshchei Khim.*, 1958, **28**, 1038.

In the case of *peri*- and *meso*-amines the investigation of tautomerism by comparing the electronic spectra of an amine and its *N*-methyl derivatives is complicated by the greater steric hindrance to conjugation between the exocyclic nitrogen atom and the aromatic nucleus in the dimethylamino-compound. There is some steric hindrance to conjugation in the *peri*- and *meso*-amines themselves, as is shown by the reduced H–N–H bond angle,[15] and in the corresponding dimethylamino-derivatives the hindrance must be substantial, giving rise to spectral differences independently of any tautomerism. Thus the ultraviolet spectra of the cationic forms of 9-amino- and 9-methylamino-phenanthridine and 9 : 10-dihydro-9-imino-10-methylphenanthridine are similar, but they differ somewhat from that of the cationic form of 9-dimethylaminophenanthridine,[16] a difference which is due to steric hindrance and not tautomerism, as the amino- and imino-form of an *N*-heteroaromatic amine (*e.g.*, I and II; R = H) give a common cation (*e.g.*, III; R = H).

Steric factors do not limit the study of the tautomerism of *N*-heteroaromatic amines by infrared spectroscopy to the same degree, absorption bands due to the vibrations of N–H groups, which may be similarly hindered in different compounds, being compared directly in this method. Hitherto, only the positions of the infrared bands due to N–H vibrations have been used in the investigation of amine tautomerism,[1–5] although the intensities of such bands also indicate the structure of the absorbing group, as the N–H stretching vibration band intensities cover a range [17] of 10^2, the intensity increasing with the " *s* " character of the N–H bond.[18] In order to obtain further information concerning imine–amine tautomerism, the frequencies, extinction coefficients, and band half-widths of the absorption bands due to the N–H stretching vibrations of a number of tri- and tetra-cyclic *N*-heteroaromatic primary and secondary amines and imines have now been measured in carbon tetrachloride (Tables 1 and 2).

N–H *Stretching vibration absorption bands.*



— — — — 5-Aminoacridine in chloroform.
———— 5-Amino-2 : 3-benzacridine in carbon tetrachloride.
. . . . 5-Imino-10-methylacridan in carbon tetrachloride.

A marked distinction is observed between the spectral characteristics of the absorption bands due to the imine and the amine N–H stretching vibration (Tables 1 and 2, Figure). The imines absorb relatively weakly near 3300 cm.$^{-1}$, whilst the amines give bands five to ten times as intense at frequencies higher by 100—200 cm.$^{-1}$ (Tables 1 and 2). The contrasting spectral properties arise mainly from the different hybridisation ratio in the N–H bond of the two clases of compound. The imine group is isoelectronic with the amide

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[15] Elliott and Mason, preceding paper.
[16] Reese, *J.*, 1958, 895.
[17] Russell and Thompson, *J.*, 1955, 483.
[18] Mason, *J.*, 1958, 3619.

anion in one (*e.g.*, IIb) of the two main resonance forms of an *N*-heteroaromatic imine, whilst the N–H group in one (*e.g.*, Ib) of the two principal canonical structures in the corresponding amine is akin to that of pyrrole. The N–H stretching bands of the amide ion lie [19] at 3261 and 3315 cm.$^{-1}$, their intensities being a little smaller than those of the *N*-heteroaromatic imines. The H–N–H bond angle in the amide ion is [19] 104·1°, showing that the low frequencies and the weak intensities of the N–H stretching bands, implying weak N–H bonds of low polarity, are connected with the small " *s* " character of the nitrogen bonding orbitals. The weakness and the low frequency of the imine N–H stretching vibration absorption are probably due to the same cause, as the nitrogen lone-pair orbital which is not in conjugation with the aromatic nucleus may be expected to have a particularly large " *s* " character.

The H–N–H bond angles of the tri- and tetra-cyclic *N*-heteroaromatic amines may be obtained from the frequencies of the symmetric and antisymmetric N–H stretching vibration bands by use of Linnett's valency-force field equations,[20] on the assumption that only the nitrogen and hydrogen atoms of the amino-group move, and that they move along the N–H bond directions, during these vibrations. The calculated H–N–H bond angles (θ) are recorded in Table 1, and they show that the " *s* " character of the N–H bonds of the amines is large, lying, in general, between sp^2 and sp^3. The higher frequencies and intensities of the N–H stretching vibration bands of the *N*-heteroaromatic amines may be ascribed to the larger " *s* " character of the N–H bonds, in conformity with other investigations.[15,18]

The " *s* " character of the N–H bonds in an aromatic amine is determined in part by the hybridisation ratios of the other orbitals of the nitrogen atom, notably, the lone-pair orbital. As the conjugation between the amino-group and the aromatic nucleus increases, the lone-pair orbital becomes more nearly $2p\pi$, and consequently the " *s* " character of the N–H bonds increases. Further, the lone-pair electrons become more completely delocalised over the aromatic nucleus, the smaller is the π-electron charge density on the nitrogen atom. The charge density at the exocyclic atom (q_x) of the carbanion corresponding to the amine provides a semi-quantitative measure of this effect. In a polycyclic *N*-heteroaromatic amine there is additional conjugation due to the polarizing effect of the nuclear nitrogen atom upon the lone-pair electrons of the amino-group (*e.g.*, Ib). The charge density at the position of the nuclear nitrogen atom (q_n) in the carbanion corresponding to the amine affords a semi-quantitative measure of the polarization effect since, in general, the mutual polarizability of a nuclear and the exocyclic atom in a given aryl-methyl carbanion increases with the charge density at the nuclear position (q_n). Values of q_x and q_n for the carbanions corresponding to the amines and imines studied, calculated by Longuet-Higgins's method,[21] are recorded in Tables 1 and 2.

In general, the H–N–H bond angle, and thus the " *s* " character of the N–H bonds, becomes larger in the series of polycyclic *N*-heteroaromatic amines as q_n increases and q_x decreases (Table 1), though the trend is overlaid by steric and hydrogen-bonding effects. Comparable pairs of amines free from such effects show, however, the increase of θ with q_n (compounds 2 and 3, 18 and 23, 19 and 22, Table 1). Intramolecular hydrogen-bonding opens up the H–N–H bond angle, *peri*-bonding (compound 1) being more effective in this respect than *ortho*-bonding [18] (compounds 8 and 11). Steric hindrance between the amino-group and *peri*- or *meso*-C–H groups reduces the H–N–H bond angle (cf. compounds 3 and 4, 2 and 6, 12 and 13, 17 and 19), both by the direct compression of the angle and by the partial inhibition of conjugation between the amino-group and the nucleus.[15] However, the H–N–H bond angle suggests that the delocalisation of the lone-pair electrons of the amino-group over the aromatic nucleus remains substantial even in the grossly hindered 5-amino-3 : 4-benzacridine (IV).

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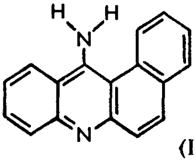
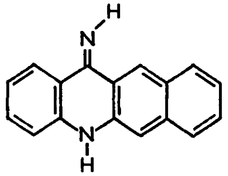
[19] Mason, *J. Phys. Chem.*, 1957, **61**, 384.
[20] Linnett, *Trans. Faraday Soc.*, 1945, **41**, 223.
[21] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265.

The observed intensities of the N–H stretching vibration bands give further information concerning the structure of the amino-group in the polycyclic *N*-heteroaromatic amines. The intensity of an absorption band in the infrared region is proportional to the square of the change of dipole moment with the vibration responsible for the absorption. To a good approximation,[18] only the change of the N–H bond moment with bond length contributes to the transition moment of the antisymmetric stretching vibration absorption in aromatic primary amines, but there is an additional contribution from the variation in the π-electron component of the permanent dipole of the amine to that of the symmetric stretching vibration.[15] Accordingly, the intensity of the antisymmetric stretching vibration band of the polycyclic *N*-heteroaromatic amine should increase with the " *s* " character of the N–H bonds,[18] whilst that of the symmetric bands should show the additional effect of the variation of conjugation with the vibration.[15]



(IV)



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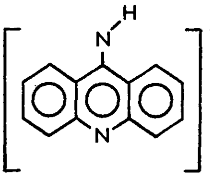


(VI)

It is found (Table 1) that the intensities of the antisymmetric stretching vibration bands of the amines studied increase with the H–N–H bond angle, as expected, apart from the *meso*-amines (compounds 5, 6, 17, and 21) where the intensity is large in relation to the angle, suggesting that the angle is sterically compressed.[15] The intensities of the symmetric stretching vibration bands vary more widely (Table 1), indicating that they depend on factors other than the N–H bond dipole gradient. Comparable pairs of unhindered amines show that the intensity of the symmetric band is larger the greater the conjugation between the nitrogen atoms of the nucleus and the amino-group (compounds 2 and 3, 18 and 23, 19 and 22, Table 1). Steric hindrance appears partly to inhibit the variation of conjugation with the symmetric vibration (cf. compounds 3 and 4, 2 and 6, 12 and 13) in the *peri*- and *meso*-amines, and perhaps to suppress the variation entirely in the grossly hindered 5-amino-3 : 4-benzacridine (IV) which has a symmetric band not much more than half as intense as those of the other *meso*-amines (compounds 5, 6, and 17). The N–H stretching vibration band of 5-methylaminoacridine, which has a double peak, is less intense than either of those of 5-aminoacridine (Tables 1 and 2), owing to the greater hindrance introduced with the methyl group. The double peak probably arises from the two conformations of 5-methylaminoacridine, one with the methyl group and the hydrogen atom of the MeNH group on the opposite sides of the plane of the acridine ring, and the other with the methyl group and hydrogen atom on the same side, though it is possible that the two bands are due to the two tautomeric forms.

The characteristics of the infrared absorption bands studied show that all of the tricyclic *N*-heteroaromatic amines, including 5-aminoacridine, and most of the tetracyclic compounds, exist predominantly in the amino-form (*e.g.*, I) in carbon tetrachloride solution. Even in the most hindered amine studied (IV) and in the amines which are both weakly conjugated and partially hindered (compounds 15 and 16) the N–H stretching vibration bands are some five times as intense and 100—200 cm.$^{-1}$ higher in frequency than those of the *N*-heteroaromatic imines. The tetracyclic compound, 5-amino-2 : 3-benzacridine, exists predominantly in the imino-form (V), however. Of the two N–H stretching vibration bands of 5-amino-2 : 3-benzacridine, the one at 3448 cm.$^{-1}$ falls into the intensity and frequency range typical of the amino N–H group, and the other at 3298 cm.$^{-1}$ into the range characteristic of the imine N–H group. The former band is similar to the single absorption of acridan, and it is due to the nuclear N–H group of (V), whilst the latter resembles that of 5-imino-10-methylacridan, being due to the exocyclic N–H group of (V) (Table 2, Figure).

These findings are in accord with the expectations of molecular-orbital theory. The amino- or the imino-form of a given *N*-heteroaromatic amine may be obtained by the addition of a proton to the exocyclic or the nuclear nitrogen atom, respectively, of the corresponding anion (*e.g.*, VI). A σ N–H bond is formed in both cases, so that the π-electron energy change resulting from the protonation of a nitrogen atom of the anion determines which of the two tautomers is predominantly formed. According to first-order perturbation theory, the π-electron energy change, ΔE, resulting from the protonation of the anion (*e.g.*, VI) is given by

$$\Delta E = q_r \Delta\alpha_N \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $\Delta\alpha_N$ is the increment in the Coulomb integral of a nitrogen atom when it is protonated, and q_r is the charge density of the corresponding carbanion q_x or q_n, depending upon the particular nitrogen atom protonated.

In the series of amines studied 5-amino-2 : 3-benzacridine is unique in that the corresponding carbanion has a charge distribution with $q_n > q_x$ (Table 2). Thus, by eqn. (1), the imine form (V) should be the stable tautomer, as found. In the carbanions corresponding to the remaining amines, apart from 5-aminoacridine, $q_x > q_n$, so that the amino-form should be the predominant tautomer in these amines. In the case of 5-amino-acridine, where $q_x = q_n$, recourse must be made to second-order perturbation theory, according to which the π-electron energy change resulting from the protonation of an amine anion (*e.g.*, VI) is given by

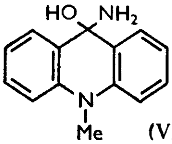
$$\Delta E = q_r \Delta\alpha_N + \pi_{r\cdot r} \Delta\alpha_N{}^2/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $\pi_{r\cdot r}$ is the self-polarizability of the atom r in the corresponding carbanion. The self-polarizabilities of the positions in the 9-anthrylmethyl anion occupied by nitrogen atoms in 5-aminoacridine, calculated by Coulson and Longuet-Higgins's method,[22] are 0·724 and 0·466 β^{-1} for the exocyclic and the nuclear position respectively, β being the carbon–carbon resonance integral. Thus the amino- and the imino-form of 5-amino-acridine should be equally stable in the first order, but the amino-tautomer should be the predominant form in the second order of approximation.

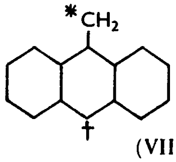
In aqueous solution, as in non-polar solvents, it is probable that the amino-form of 5-aminoacridine is the more stable tautomer. In water 5-aminoacridine has a pK_a value of [23] 9·99, and that of 5-imino-10-methylacridan is [24] 11·01, so that the amino-tautomer predominates over the imine by a factor of approximately 10. The pK_a value for 5-imino-10-methylacridan (II; R = Me) is reported [24] to be that for the equilibrium between the cation (III; R = Me) and the carbinol base (VII) in aqueous solution. However, the light-absorption characteristics in the visible region of the species in equilibrium are very similar,[24] and those species are, therefore, the cation (III; R = Me) and the imine (II; R = Me), which have similar spectra in the visible,[13,14] as the band of longest wavelength in the electronic spectrum of the carbinol base (VII) would be that of the diphenylamine chromophore in the ultraviolet region at [25] 290 mμ. Moreover; both of the species in equilibrium fluoresce in the visible region,[13,24] but diphenylamine has no visible fluorescence. The imine (II; R = Me) is hygroscopic, but water is combined only as solvent of crystallisation as the solid hydrate is yellow, and undergoes little colour change on dehydration, which is readily effected.[26] Similarly the ionisation constant reported [24] for 2-amino-10-methylacridinium bromide in water (pK_a = 11·85) probably governs the equilibrium between the cation and the corresponding imine. The pK_a value of 2-amino-acridine in water is [23] 8·04, so that the amino-tautomer predominates over the imine by a factor of approximately 6 × 10^3 in aqueous solution.

[22] Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, **191**, *A*, 39.
[23] Albert, Goldacre, and Phillips, *J.*, 1948, 2240.
[24] Goldacre and Phillips, *J.*, 1949, 1724.
[25] Jaffe, *J. Chem. Phys.*, 1954, **22**, 1430.
[26] Albert and Ritchie, *J.*, 1943, 458.

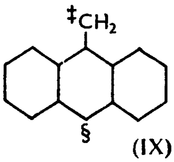
The electronic spectra of 5-aminoacridine and its *N*-methyl derivatives are consistent with the conclusion that the amine tautomer predominates in aqueous and methanol solution, but not with the view that the imine form is more stable. The salient features of the visible spectra are[10,13,14,27,28] that 5-imino-10-methylacridan and the cation of 5-aminoacridine absorb at slightly shorter wavelengths ($\lambda_{\text{max.}}$ 400 mμ) than the neutral molecule of 5-aminoacridine ($\lambda_{\text{max.}}$ 408 mμ) but with nearly the same intensity ($\varepsilon_{\text{max.}}$ $\sim 10^4$), whilst 5-dimethylaminoacridine absorbs at longer wavelengths ($\lambda_{\text{max.}}$ 420 mμ) with a lower intensity ($\varepsilon_{\text{max.}}$ $5{\cdot}6 \times 10^3$). In alternant systems the methyl group invariably gives rise to a bathochromic shift of the electronic spectrum, so that if 5-aminoacridine existed mainly in the imine form, 5-imino-10-methylacridan would absorb at longer wavelengths than the parent substance, which is not observed.



(VII)



(VIII)



(IX)

Charges: * 0·286, † 0·286, ‡ 0·231, § 0·045.

The visible absorption of 5-aminoacridine and its *N*-methyl derivatives is due to the promotion of an electron from the highest occupied to the lowest unoccupied molecular orbital of the π-electron system. The highest occupied π-orbital, which is filled with the lone-pair electrons of the exocyclic nitrogen atom, is derived from the non-bonding molecular orbital of the corresponding carbanion, which has the charge distribution (VIII). The lowest unoccupied π-orbital of the 9-anthrylmethyl anion has an energy of 0·683 β and the charge distribution (IX). On the substitution of nitrogen atoms into the carbanion the energy of the orbital is lowered by an amount depending upon the charge density at the position of substitution and the Coulomb integral increment of the nitrogen atom (*e.g.*, eqn. 1). In the amino-tautomer the exocyclic nitrogen atom is partly positively charged (*e.g.*, Ib) so that it has a larger Coulomb-integral increment than the nuclear nitrogen atom, whilst the reverse is true in the imino-tautomer (*e.g.*, IIb). The lowest unoccupied π-orbital in the amine tautomer is thus lower in energy than that of the imine form, as the charge density in (IX) is larger at the exocyclic than the nuclear position. The highest occupied π-orbital has the same energy in both tautomers, since there is the same charge density at the position of both nitrogen atoms in (VIII). Hence the amine tautomer should absorb at longer wavelengths than the imine form, as is found, in spite of the probable bathochromic effect of the methyl group in 5-imino-10-methylacridan.

The blue shift of the visible absorption of 5-aminoacridine on cation formation, a phenomenon which is quite unusual in the series of *N*-heteroaromatic amines,[4,5,10] can be similarly explained. When the nuclear nitrogen atom of 5-aminoacridine is protonated the energy of the highest occupied level is lowered more than that of the lowest unoccupied level, as the charge density at the nuclear position in (VIII) is larger than that in (IX) and the electronic transition energy is increased.

In 5-dimethylaminoacridine the steric hindrance between the methyl and *peri*-C–H groups has the effect that the nodal plane of the *p*-component in the lone-pair hybrid orbital of the amino-group nitrogen atom is twisted out of the plane of the acridine nucleus. The twist partially localises the lone-pair electrons upon the nitrogen atom of the amino-group, whilst the π-orbitals of the nucleus become less akin to those of the 9-anthrylmethyl anion and resemble more those of anthracene. The lowest unoccupied orbital of anthracene has a lower energy (0·414 β) than that of the 9-anthrylmethyl anion and a larger charge density (0·193 *e*) at the position corresponding to that of the nitrogen atom in acridine.

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[27] King, Gilchrist, and Tarnoky, *Biochem. J.*, 1946, **40**, 706.

[28] Turnbull, *J.*, 1945, 444.

The lowest unoccupied π-orbital in 5-aminoacridine has a higher energy than that of the dimethylamino-analogue, therefore, and the latter may be expected to absorb at longer wavelengths, and with a reduced intensity, since the partial localisation of the lone-pair electrons upon the dimethylamino-group results in a poor overlap between the electron distributions of the highest occupied and the lowest unoccupied orbitals.

EXPERIMENTAL

Materials.—1-Ethyl-1 : 2-dihydro-2- and 1-ethyl-1 : 4-dihydro-4-iminopyridine were prepared by Anderson and Seeger's method.[6] The remaining compounds were as in Albert, Goldacre, and Phillips [23] and in Albert and Ritchie,[26] and they were recrystallised to the m. p.s quoted.[23, 26]

Infrared Spectra.—These were measured with a Perkin-Elmer model 12C spectrometer with a lithium fluoride prism and a quartz filter, and a Mervyn N.P.L. grating spectrometer using an *F*-centre filter for the 3μ region. The amines were examined in the range M/1000 to M/250, and the imines in the range M/250 to M/50, in carbon tetrachloride in a 5 cm. cell. 5-Aminoacridine was insufficiently soluble in carbon tetrachloride to allow the measurement of the intensity of the N–H stretching vibration absorptions with any precision, and it was examined in the region of M/100 in chloroform solution in a 1 cm. cell. The frequencies of the bands were reproducible to within 1 and 2 cm.$^{-1}$ with the prism and the grating instruments respectively, and the intensities to within about 5% with both spectrometers. The two instruments differed by up to 5 cm.$^{-1}$ in the measurement of frequency and up to 10% in the determination of intensities in the present work.

The author is indebted to Professor A. Albert for the provision of compounds, to the Australian National University for a Research Fellowship, and to the Royal Society for the loan of an infrared spectrometer.

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[*Received, September* 13*th*, 1958.]