892. *Hydrogen Bonding and Structural Problems in the Amino-acridines and -quinolines. Infra-red Studies.*

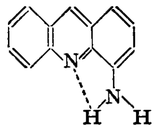
By L. N. SHORT.

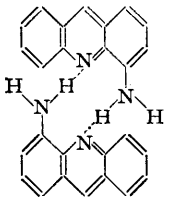
The N–H bond stretching frequencies of the five isomeric monoamino-acridines, 2-, 3-, 4-, 6-, 7-, and 8-aminoquinoline, the monoaminoanthracenes, naphthylamines, and aniline, in dilute solution, have been measured.

The existence of intramolecular hydrogen bonding in 1-aminoacridine and 8-aminoquinoline is demonstrated. All the compounds are shown to exist in the amino-form under the conditions of investigation. The variation in N–H bond stretching frequencies and the corresponding force constants are explained in terms of electromeric interaction between the amino-group and the ring nitrogen atom.

It is shown that electric dipole moments provide an unreliable indication of electromeric displacements in these heterocyclic amines.

ALBERT and GOLDACRE (*J.*, 1943, **454**) have suggested that the physical and chemical properties of 1-aminoacridine may be explained in terms of hydrogen-bond formation, either intramolecular as in (I) or intermolecular to form dimers as in (II). The evidence in favour of this is stated in detail by Albert ("The Acridines," Edward Arnold, 1951, pp. 154, 157) but no conclusive proof is given. Little is known regarding the conditions of the formation of N–H···N bonds. By analogy with O–H···O bonds it is expected that the N–N distance should be about 2·7 Å and the N–H–N angle about 180° (Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, 1940, p. 327). Buswell, Downing, and Rodebush (*J. Amer. Chem. Soc.*, 1940, **62**, 2759) have shown that, for intermolecular hydrogen bonds between nitrogen atoms, there should be a considerable difference in the basicity of the bonded nitrogen atoms. For example, diphenylamine forms N–H···N bonds with the relatively basic nitrogen atom of pyridine, bond formation being revealed by lowering of the N–H bond stretching frequency of diphenylamine from 3460 cm.$^{-1}$ for solution in carbon tetrachloride to 3300 cm.$^{-1}$ for solution in pyridine.


(I)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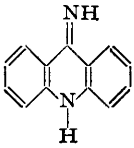
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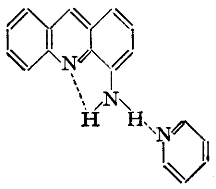
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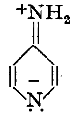
(V)

In 1-aminoacridine and the analogous 8-aminoquinoline the N–N distance is about 2·8 Å but the N–H–N angle is approximately 112°, and intramolecular hydrogen-bond formation would involve a five-membered ring rather than the more usual six-membered ring. The formation of a strong hydrogen bond under these conditions would not be expected although association through intermolecular bonds should be possible. That the ring nitrogen atom is more basic than the amino-nitrogen atom is indicated by the fact that in acid solution it is the former which accepts the first proton (Craig and Short, *J.*, 1945, 419; Turnbull, *J.*, 1945, 441; Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 275).

The chemical properties of 5-aminoacridine are such as to suggest that it readily undergoes tautomerism. Karyakin, Grigorovskiĭ, and Yaroslavskiĭ (*Doklady Akad. Nauk. S.S.S.R.*, 1949, **67**, 679) have concluded, on the basis of ultra-violet spectra in alcoholic solution and infra-red spectra (in the 1—2μ region) of a number of acridine derivatives and binary mixtures of them in the solid state, that 5-aminoacridine is more correctly formulated as the corresponding imine (III). The whole question of such tautomerism in *N*-heterocyclic amines has been discussed by Angyal and Angyal (*J.*, 1952, 1461) who concluded that it occurs to only a slight extent in the cases so far investigated. Should any of the compounds studied in the present investigation exist in the imino-form this should be revealed by the N–H bond stretching frequencies. Instead of the pair of bands at the frequencies characteristic of the amino-group (as shown by the compounds for which tautomerism is impossible, such as 3-aminoacridine, 3-aminoquinoline, and the carbocyclic amines) absorption should occur characteristic of the secondary amine and imine N–H groups.

In attempting to find an explanation of the wide variation in basic strength of the *N*-heterocyclic amines quantum-mechanical methods have been applied by Longuet-Higgins (*J. Chem. Phys.*, 1950, **18**, 275) and by Daudel and Chalvet (*J. Chim. phys.*, 1949, **46**, 332). These authors have shown that the electron density on the ring nitrogen atom depends on the position of the amino-group, which fact indicates the variation in electromeric interaction. It is to be expected that this should lead to variation in the N–H bond stretching force constants since any change in the character of the C–N bond involves a change in the N–H bonds from the p^3 type characteristic of aliphatic amines to hybrid types involving a degree of *s* character. It has been shown by Sutherland and Dennison (*Proc. Roy. Soc.*, 1935, *A*, **148**, 250) that the force constants of the C–H links increase as the proportion of *s* to *p* character in the bond orbitals of the carbon atoms increases, and this should also apply to N–H bonds. The N–H bond stretching force constants of the compounds under investigation might be expected to reveal the presence of this electromeric effect.

EXPERIMENTAL AND RESULTS

The spectra of dilute solutions (0·2M or less) of the isomeric monoaminoacridines and monoaminoquinolines were measured in the region of the N–H bond stretching frequencies, carbon tetrachloride, chloroform, dioxan, and pyridine being used as solvents where possible. For reference the spectra of the monoaminoanthracenes, the naphthylamines, and aniline were also measured, carbon tetrachloride or chloroform being used as solvent. A Perkin-Elmer Spectrometer (Model 12C) was used with a lithium fluoride prism.

1-, 2-, 3-, and 4-Aminoacridine, 4-, 6-, 7-, and 8-aminoquinoline, and 1-, 2-, and 9-aminoanthracene were supplied by Professor A. Albert of the Australian National University. 2- and 3-aminoquinoline were supplied by Dr. C. Culvenor of the Dyson Perrins Laboratory, Oxford. The remaining compounds were commercial samples. All materials were recrystallized and then had the published melting points. The solvents were dried and distilled.

The N–H bond stretching frequencies of the compounds studied are shown in Tables 1 and 2;

TABLE 1.

Compound	ν_s	ν_a	ν_s	ν_a	ν_s	ν_a	ν_s	ν_a
	in CCl_4		in $CHCl_3$		in dioxan		in pyridine	
1-Aminoacridine	3387	3497	3390	3494	3360	3472	3307	3449
2-Aminoacridine	3406	3494	3411	3502	3243	3361	3199	3337
3-Aminoacridine	—	—	3400	3494	3241	3367	3206	3337
4-Aminoacridine	3394	3474	3399	3477	3260	3363	3218	3351
5-Aminoacridine	—	—	3435	3525	3270	3377	3206	3366
2-Aminoquinoline	—	—	3413	3517	—	—	—	—
3-Aminoquinoline	—	—	3402	3472	—	—	3204	3333
4-Aminoquinoline	—	—	3425	3513	—	—	3203	3350
6-Aminoquinoline	—	—	3402	3488	—	—	3210	3338
7-Aminoquinoline	—	—	3407	3496	—	—	3207	3337
8-Aminoquinoline	—	—	3389	3493	—	—	3313	3452
*2-Aminopyridine	3411	3509	—	—	—	—	—	—
*3-Aminopyridine	3396	3482	—	—	—	—	—	—
*4-Aminopyridine	3413	3508	—	—	—	—	—	—

* From Goulden, *J.*, 1952, 2939.

TABLE 2.

Compound	ν_s	ν_a	ν_s	ν_a
	in CCl_4		in $CHCl_3$	
1-Aminoanthracene	3394	3472	—	—
2-Aminoanthracene	3396	3484	3397	3485
9-Aminoanthracene	—	—	3408	3482

Compound	ν_s	ν_a
	in CCl_4	
α-Naphthylamine	3396	3476
β-Naphthylamine	3399	3485
Aniline	3397	3480

TABLE 3.

Compound	N–H force constant × 10^{-5}, dyne/cm., for solution in CCl_4	$CHCl_3$	Pyridine §	Extra electron density on ring nitrogen Q †	q ‡
1-Aminoacridine	6·56	6·56	6·32	0	0
2-Aminoacridine	6·59	6·62	5·92	0·041	0·118
3-Aminoacridine	—	6·58	5·93	0	0
4-Aminoacridine	6·53	6·55	5·98	0·030	0·095
5-Aminoacridine	—	6·71	5·98	0·078	0·286
2-Aminoquinoline	—	6·65	—	0·068	0·235
3-Aminoquinoline	—	6·54	5·92	0	0
4-Aminoquinoline	—	6·67	5·95	0·060	0·200
6-Aminoquinoline	—	6·57	5·94	0	0
7-Aminoquinoline	—	6·60	5·93	0·037	0·059
8-Aminoquinoline	—	6·56	6·34	0	0
1-Aminoanthracene	6·53	—	—	—	—
2-Aminoanthracene	6·55	6·56	—	—	—
9-Aminoanthracene	—	6·57	—	—	—
α-Naphthylamine	6·54	—	—	—	—
β-Naphthylamine	6·56	—	—	—	—
Aniline	6·55	—	—	—	—
*2-Aminopyridine	6·63	—	—	0·064	0·143
*3-Aminopyridine	6·55	—	—	0	0
*4-Aminopyridine	6·63	—	—	0·064	0·143

* Calculated from frequencies reported by Goulden (*J.*, 1952, 2939).
† From Daudel and Chalvet (*J. Chim. phys.*, 1949, **46**, 332).
‡ From Longuet-Higgins (*J. Chem. Phys.*, 1950, **18**, 275).
§ These force constants will be valid only if two equivalent N–H···N bonds are formed by each amino-group.

Table 1 also includes some figures for the monoaminopyridines determined by Goulden (*J.*, 1952, 2939). In Table 3 are given the N–H bond stretching force constants calculated by using Linnett's formulæ (*Trans. Faraday Soc.*, 1945, **41**, 223) :

$$\nu_s^2 = k(R_1 + 2R_2 \cos^2\theta)/4\pi^2\mathbf{c}^2 \qquad \nu_a^2 = k(R_1 + 2R_2 \sin^2\theta)/4\pi^2\mathbf{c}^2$$

(where ν_s and ν_a = the symmetric and the asymmetric N–H stretching frequencies, respectively, in cm.$^{-1}$; k = N–H bond stretching force constant; $1/R_1$ = mass of hydrogen atom; $1/R_2$ = mass of nitrogen atom; 2θ = H–N–H angle; and $\mathbf{c}$ = velocity of light).

In calculating the force constant from the observed frequencies θ is eliminated from the formulæ. The formulæ are only valid when the two N–H bonds of the amine group are equivalent. The uncertainty in the measured frequencies should not produce an error greater than 0·02 × 10^5 dyne/cm. in the calculated force constants.

DISCUSSION

The N–H bond stretching frequencies of the carbocyclic amines, given in Table 2, show very good agreement, the corresponding force constant being 6·55(± 0·02) × 10^5 dyne cm.$^{-1}$. The presence of a nitrogen atom in one of the rings leads to significant variation in the frequencies and force constants, but in no case is the change produced sufficient to suggest that tautomerism has occurred. Goulden (*loc. cit.*) reported the N–H bond stretching frequencies of 2-methylaminopyridine (3450 cm.$^{-1}$) and 1 : 2-dihydro-2-imino-1-methylpyridine (3323 cm.$^{-1}$) in carbon tetrachloride solution, and these figures indicate the regions in which absorption should occur, corresponding to secondary amine and imine N–H bond stretching vibrations, respectively, if any of the compounds undergoes tautomerism. These results support the conclusion reached from a comparison of the ultra-violet absorption spectra of 5-aminoacridine and 9-aminoanthracene (Craig and Short, *J.*, 1945, 419). The close resemblance between the spectra of these two compounds indicates that 5-aminoacridine exists in the amino-form unless 9-aminoanthracene itself undergoes tautomerism. That this is not so (at least in chloroform solution) is shown by the infra-red results in Table 2. Consideration of the ultra-violet and infra-red spectra leads to the conclusion that the equilibrium between the two tautomers strongly favours the amino-form, there being no detectable absorption corresponding to the imino-form. However, this does not preclude the possibility that in other solvents the imino-form might be favoured.

The two compounds for which intramolecular hydrogen bonding has been suggested, *viz.*, 1-aminoacridine and 8-aminoquinoline, give N–H bond stretching frequencies in chloroform solution which are only slightly lower than those of the remaining isomerides. The frequencies for 1-aminoacridine were found to be independent of concentration over the range 0·008—0·2M, indicating the absence of intermolecular association, as in (II). The considerable lowering of frequency usually associated with hydrogen-bond formation does not occur. It must be remembered, however, that the effect on the spectrum of the formation of a single hydrogen bond by an amino-group, as in (I), is not known. It may well be that a bond of significant strength can be formed which will have little effect on the N–H bond stretching frequencies particularly when the N–H–N angle is closer to 90° than to 180°.

In dioxan and pyridine solution the N–H bond stretching frequencies were much lower than in carbon tetrachloride or chloroform solution, the lowering being due to association with the solvent through the formation of hydrogen bonds of the type N–H···O and N–H···N, respectively. This formation of N–H···O bonds with the oxygen of dioxan is contrary to the suggestion of Buswell, Downing, and Rodebush (*J. Amer. Chem. Soc.*, 1940, **62**, 2759) that such bonds are only formed with semipolar oxygen atoms. In general the lowering in pyridine is about 150 cm.$^{-1}$, but for 1-aminoacridine and 8-aminoquinoline it is only about 50 cm.$^{-1}$. This is what would be expected if the amino-groups of these compounds are intramolecularly bonded, in which case the observed lowering would be due to the formation of a single hydrogen bond to a solvent molecule as in (IV).

A similar case of intramolecular hydrogen bonding has been reported by Hathway and Flett (*Trans. Faraday Soc.*, 1949, **45**, 818) as occurring in 1-amino-2-nitro- and 2-amino-1-nitro-naphthalene. It is noteworthy that the hydrogen bonding is not revealed by any marked lowering of the N–H bond stretching frequencies although it is of sufficient strength to produce very significant changes in the properties of the compounds.

The results given in Table 3 show that the N–H bond stretching force constants for solutions in non-associating solvents are approximately parallel to the calculated values of the extra electron density on the ring nitrogen atom. Although the different methods employed yield numerically different results the authors agree on the order of the compounds with respect to electron density on the ring nitrogen atom, and a high value is associated with a high force constant. It seems reasonable to conclude that the variation in the N–H bond stretching force constants within the several series of isomerides is due to differences in the degree of electromeric interaction between the amino-group and the ring nitrogen atom. The force constant of 4-aminoacridine is lower than expected but as the corresponding quinoline derivative was not available it cannot be stated whether the low value is characteristic of this position of substitution.

Leis and Curran (*J. Amer. Chem. Soc.*, 1945, **67**, 79) pointed out that electromeric interaction between the two nitrogen atoms in *N*-heteroaromatic amines should be revealed by electric dipole-moment measurements. An estimate of the moment to be expected in the absence of such interaction can be obtained by the vector addition of the moments of the corresponding carbocyclic amine and the heterocyclic base, and the amount by which the observed moment exceeds this estimate is an indication of the extent to which dipolar forms contribute to the resonance hybrid. Assuming that the dipole-moment vector of aniline lies in the direction of the C–N bond, and using the moments of aniline and pyridine determined in dioxan solution, they estimated that the dipole moment of 4-aminopyridine should be 4·12 D. The difference between this figure and the measured moment (4·36 D) is taken as indicating a considerable contribution of the dipolar form (V) to the structure of this compound. This procedure is open to two objections. First, the moments used were determined in dioxan solution and, as shown by Kumler and Halverstadt (*J. Amer. Chem. Soc.*, 1941, **63**, 2182), this solvent has a marked effect on the dipole moments of certain amines. The figures given in Table 4 show that while this effect is large (0·3—0·4 D) for the amines investigated it is negligible in the case of pyridine. As has been shown above, the amines form hydrogen bonds with dioxan and this fact may provide the explanation of the dipole-moment results. If instead of the figures for the dipole moments determined in dioxan solution those for benzene solutions are used, the estimated moment of 4-aminopyridine becomes 3·74 D compared with the actual value of 3·79 D.

TABLE 4.

Compound	μ, in dioxan	μ, in benzene	Compound	μ, in dioxan	μ, in benzene
Pyridine	2·22 [1]	2·20 [1]	Diphenylylamine	2·07 [2]	1·74 [8]
Aniline	1·90 [2]	1·54 [3]	*p*-Nitroaniline ...	6·68 [4]	6·32 [5]
4-Aminoquinoline	4·38 [6]	3·97 [7]	4-Aminopyridine	4·36 [1]	3·79 [8]

[1] Leis and Curran, *J. Amer. Chem. Soc.*, 1945, **67**, 79. [2] Kumler and Halverstadt, *J. Amer. Chem. Soc.*, 1941, **63**, 2182. [3] Cowley and Partington, *J.*, 1938, 1598. [4] Kumler and Porter, *J. Amer. Chem. Soc.*, 1934, **56**, 2549. [5] Le Fèvre and Le Fèvre, *J.*, 1936, 1130. [6] Angyal and Angyal, *J.*, 1952, 1461. [7] Edgerley, personal communication. [8] Goethals, *Rec. Trav. chim.*, 1935, **54**, 299.

The second objection relates to the direction assumed for the aniline dipole-moment vector. Cowley and Partington (*J.*, 1938, 1598) suggested that in aniline the dipole-moment vector makes an angle of about 70° with the plane of the benzene ring. This being assumed, the calculated value for 4-aminopyridine becomes 3·09 D and the difference between the measured and calculated values is increased to 0·7 D. The significance of these results must be questioned, however, since the same assumptions give unreasonable values for 2-aminopyridine (calculated, 2·46 D; measured, 2·17 D) and 3-aminopyridine [calculated, 2·89 D; measured, 3·19 D (Goethals, *Rec. Trav. chim.*, 1935, **54**, 299)].

Little reliance can therefore be placed on the results obtained for 5-aminoacridine although there is a large difference between the calculated moment obtained by the addition of the aniline moment (1·54 D) and that of acridine [1·95 D, in benzene solution (Bergmann, Engel, and Meyer, *Ber.*, 1932, **65**, *B*, 446)] and the actual moment [4·14 D (Edgerley, personal communication].

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