973. *Infrared Absorption of Substituents in Heterocyclic Systems. Part IX.* Amine–Imine Tautomerism by Infrared Spectroscopy*

By N. BACON, A. J. BOULTON, R. T. C. BROWNLEE, A. R. KATRITZKY, and R. D. TOPSOM

The infrared partial deuteration criterion is used to confirm the predominance of the amino-form for certain amides, sulphonamides, and 9-aminoacridine. The existence of 3-methyl-6-azacytosine in the imino-form is confirmed.

AMINO-GROUPS show two N–H stretching modes in the 3500-cm.$^{-1}$ region as a result of coupling; the two bands correspond to NH_2 symmetric and asymmetric stretching vibrations. Two of us pointed out some years ago[1] that two bands in this region could be confirmed as NH_2 modes by examination of the spectra of partially deuterated specimens.

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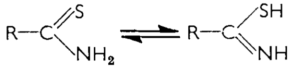
* Part VIII, A. R. Katritzky and B. J. Ridgewell, *Spectrochim. Acta*, 1964, **20**, 589.

[1] A. J. Boulton and A. R. Katritzky, *Tetrahedron*, 1961, **12**, 51.

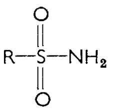
In the NHD group, coupling between N–H and N–D is weak, and the N–H stretch shows up at a frequency *between* those of the symmetric and asymmetric NH_2 stretching modes. If the original bands had been due to hydrogen attached to different nitrogen atoms, partial deuteration would not give rise to such an intermediate frequency. A similar criterion was suggested independently by Moritz [2] and this method has been used by Bauer [3] and by Hambly [4] (cf. also ref. 5). We have now applied it to some cases of potential amine–imine tautomerism.

Thioamides.—Most authors have concluded that thioamides exist essentially completely in the form (I) (cf. refs. 6*a* and *b*); however, reports continued to appear [7-9] of the presence of greater or lesser amounts of imino-form (II) under various conditions. We therefore examined the spectra of thioacetamide, phenylthioacetamide, and thiobenzamide in the NH-stretching region and those of partially deuterated samples in the NH- and ND-stretching regions. Dichloroethane was used as solvent to minimise solute association. The results (Table 1) show clearly that the thioamides all exist predominantly as such.

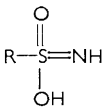


(I) (II)

Sulphonamides.—Sandell [10] alleged that partition coefficients between water and chloroform or ether showed that primary sulphonamides (III) exist partly or wholly in the imino-form (IV). This conclusion has already been strongly criticised,[11,12] and the results of our partial deuteration experiments (Table 2) indicate convincingly that the three sulphonamides investigated exist in the amino-form in dichloroethane solution.



(III)



(IV)

9-Aminoacridine.—There has been considerable controversy as to the relative importance of the amino- (V) and imino-structure (VI) for 9-aminoacridine. Chemical evidence in favour of each formulation for amino-heterocycles in general has been summarised by Angyal and Angyal [13] who conclude that the chemical evidence is indecisive. Dipole-moment studies likewise proved inconclusive.[14,15] The similarity of the ultraviolet spectrum to that of 9-aminoanthracene was taken [16] to support the amino-formulation, but this opinion has been criticised [17] and two groups [17,18] have deduced the predominance of the imino-form from ultraviolet comparisons. This work has in turn been criticised [19]

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[2] A. G. Moritz, *Spectrochim. Acta*, 1960, **16**, 1176; 1962, **18**, 671.

[3] C. L. Bell, C. N. V. Nambury, and L. Bauer, *J. Org. Chem.*, 1964, **29**, 2873.

[4] A. N. Hambly and B. V. O'Grady, *Chem. and Ind.*, 1962, 459.

[5] P. J. Krueger, *Canad. J. Chem.*, 1964, **42**, 201.

[6] (*a*) P. May, *J.*, 1913, **103**, 2272; (*b*) M. G. Ettlinger, *J. Amer. Chem. Soc.*, 1950, **72**, 4699.

[7] A. Hantzsch, *Ber.*, 1931, **64***B*, 661.

[8] G. Hopkins and L. Hunter, *J.*, 1942, 638.

[9] A. J. Speziale and L. R. Smith, *J. Org. Chem.*, 1963, **28**, 3492.

[10] K. B. Sandell, *Monatsh.*, 1961, **92**, 1066.

[11] W. Walter and H.-L. Weidemann, *Monatsh.*, 1962, **93**, 1235.

[12] O. Exner, *Coll. Czech. Chem. Comm.*, 1964, **29**, 1337.

[13] S. J. Angyal and C. L. Angyal, *J.*, 1952, 1461.

[14] L. N. Short, *J.*, 1952, 4584.

[15] Z. V. Pushkareva and Z. Y. Kokoshko, *Doklady Akad. Nauk S.S.S.R.*, 1953, **93**, 77.

[16] D. P. Craig and L. N. Short, *J.*, 1945, 419.

[17] R. M. Acheson, M. L. Burstall, C. W. Jefford, and B. F. Sansom, *J.*, 1954, 3742.

[18] A. V. Karyakin, A. M. Grigorovskii, and N. G. Yaroslovskii, *Doklady Akad. Nauk S.S.S.R.*, 1949, **67**, 679.

[19] A. Albert, *Chem. Soc. Special Publ.*, No. **3**, 1955, 130.

(but cf. ref. 20), and later ultraviolet work interpreted[21] in favour of the amino-form. Infrared spectra from the overtone region was early[18] held to demonstrate the imino-form; two bands in the NH-stretching region were assigned first to an amino-group[14] and later by others[22] to the two separate NH-modes of the imino-form. In a definitive Paper,[23] Mason showed that detailed consideration of the infrared intensities as well as frequencies in the ν_{NH} region strongly supported the amino-formulation, and that the ultraviolet spectra and basicities could also be most satisfactorily interpreted on the amino-formulation. However, the authors of a recent Paper[24] still consider that the matter is controversial and state that " the properties seem to favour the imino-structure " after referring to some of the preceding work. To remove all doubt as to the correct structure we examined the infrared spectra of 9-aminoacridine, before and after partial deuteration, in several solvents. For carbon tetrachloride, chloroform, and tetrachloroethane solutions, the results (Table 3) show conclusively that the amino-form predominates. For dioxan and pyridine solutions, strong hydrogen-bonding precluded application of the criterion to the ν_{NH} stretching modes, but in these solvents the NH_2-scissors mode[25] was found at 1656 and 1676 cm.$^{-1}$, respectively, and was reduced in intensity on partial deuteration, as expected.

TABLE 1

Infrared spectra (peaks in cm.$^{-1}$) of deuterated thioamides[a]

Compound	$NH_2\nu_{as}$	$NHD\nu_{NH}$	$NH_2\nu_{sym}$	$ND_2\nu_{as}$	$NHD\nu_{ND}$	$ND_2\nu_{sym}$
Thioacetamide	3490	3430	3375	2615	2535	2460
Phenylthioacetamide	3480	3420	3365	2600	2520	2445
Thiobenzamide	3495	3430	3375	2610	2525	2450

[a] In dichloroethane solution. An additional, concentration-dependent, band appears at *ca.* 3200 cm.$^{-1}$, assigned to ν_{NH} of the hydrogen-bonded dimers.

TABLE 2

Infrared spectra (peaks in cm.$^{-1}$) of deuterated sulphonamides[a]

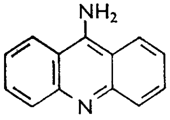
Compound	$NH_2\nu_{as}$	$NHD\nu_{NH}$	$NH_2\nu_{sym}$	$ND_2\nu_{as}$	$NHD\nu_{ND}$	$ND_2\nu_{sym}$
Methanesulphonamide ...	3445	3395	3345	2570	2505	2445
Benzenesulphonamide ...	3455	3395	3350	2580	2510	2455
p-Toluenesulphonamide ...	3440	3385	3340	2565	2495	2440

[a] In dichloroethane solution.

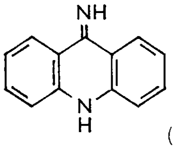
TABLE 3

Infrared spectra (peaks in cm^{-1}) of deuterated 9-aminoacridine

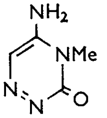
Solvent	$NH_2\nu_{as}$	$NHD\nu_{NH}$	$NH_2\nu_{sym}$	$ND_2\nu_{as}$	$NHD\nu_{ND}$	$ND_2\nu_{sym}$
CCl_4	3527	3488	3442	—	—	—
$CHCl_3$	3526	3480	3440	2744	2682	2640
$(CHCl_2)_2$	3523	3488	3438	2740	2684	2638



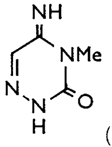
(V)



(VI)



(VII)



(VIII)

3-*Methyl*-6-*azacytosine*.—Gut and his co-workers[26] concluded from spectral data that this derivative existed in the unusual imino-form (VIII) rather than as structure (VII). This conclusion has now been confirmed. In chloroform solution peaks were found at

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[20] R. M. Acheson, " Chemistry of Heterocyclic Compounds," Interscience, New York, 1956, vol. 9, pp. 90 and 291.

[21] A. K. Sukhomlinov, *Zhur. obshchei Khim.*, 1958, **28**, 1038.

[22] A. V. Karyakin and A. V. Shablya, *Doklady Akad. Nauk S.S.S.R.*, 1957, **116**, 969.

[23] S. F. Mason, *J.*, 1959, 1281.

[24] P. Kristian, K. Autos, D. Vlochova, and R. Zahradník, *Coll. Czech. Chem. Comm.*, 1963, **28**, 1651.

[25] D. J. Brown, E. Hoerger, and S. F. Mason, *J.*, 1955, 4035.

[26] J. Gut, J. Jonas, and J. Pitha, *Coll. Czech. Chem. Comm.*, 1964, **29**, 1394.

3430 and 3308 cm.$^{-1}$; after partial deuteration, these two peaks were still found, but with reduced intensity, and new ν_{ND} bands had appeared at 2678 and 2562 cm.$^{-1}$. No peak was found between the two original ν_{NH} bands.

EXPERIMENTAL

The thioamides, sulphonamides, and aminoacridine were all either commercial samples or prepared by standard methods. The 3-methyl-6-azacytosine was kindly supplied by Dr. J. Gut of the Institute of Organic Chemistry and Biochemistry of the Czechoslovak Academy of Sciences. Solvents were dried by passing them through a column of dry alumina, followed by distillation.

The general procedure for deuteration was as follows. The compound to be investigated was refluxed for 10—20 min. with deuterium oxide (1 ml.). The solvent was evaporated off and then finally removed by repeated azeotropic distillation with dried benzene (10 ml.). The last traces of benzene were removed *in vacuo*. Usually such an azeotropically dried product contained sufficient unchanged protium to give spectra as required. 5-Aminoacridine was deuterated by boiling the base with deuterium oxide for 10 hr., in the presence of sodium deuteroxide. 3-Methyl-6-azacytosine (5 mg.) was deuterated by standing overnight in a mixture of deuterium oxide (1 ml.) and ethanol (0·1 ml.).

Spectra were taken of solutions as indicated in the Tables, on a Perkin-Elmer model 237 grating instrument. 1-mm. Sodium chloride cells, and 1- and 4-cm. Supracil cells, were used, both types having adequate transmission characteristics in the region of the spectrum investigated.

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THE SCHOOL OF CHEMICAL SCIENCES,
THE UNIVERSITY OF EAST ANGLIA, NORWICH.

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