The Major Tautomers of the Pseudobases of 1,5- and 1,8-Naphthyridine Dications

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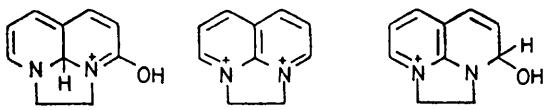
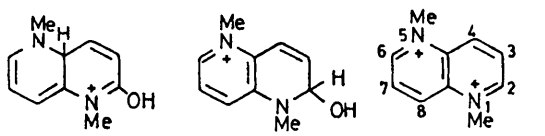
A recent interpretation of the structures of the pseudobases of the 1,5-dimethyl-1.5-naphthyridine and 5.6-dihydroimidazo[1.2.3-*ij*][1.8]naphthyridine dications which involves species bearing bridgehead hydrogen atoms is shown to be in error. The spectral data are consistent with the major pseudobase species being the expected 1,2-dihydro-2-hydroxynaphthyridines.

SUMMERS and his co-workers recently concluded, primarily on the basis of ^{1}H n.m.r. spectral data, that the species (I) is the major tautomer present in aqueous solutions of the pseudobase of the 5,6-dihydroimidazo-[1,2,3-*ij*][1,8]naphthyridine dication (II).[1] This is unexpected in the light of the observation [2-4] that the predominant pseudobases of other 1,8-naphthyridine mono- and di-cations exist as 1,2-dihydro-2-hydroxy-1,8-naphthyridines.† By analogy, the predominant pseudobase species of (II) would have been expected to be (III). Furthermore, these workers [1] also seem to favour tautomer (IV) over the expected tautomer (V) as the predominant pseudobase form of the 1,5-dimethyl-1,5-naphthyridine dication (VI), although they have not unambiguously distinguished between (IV) and (V) on the basis of the available spectral data. I wish to point out that there are several misinterpretations in ref. 1 in the analysis of ^{1}H n.m.r. spectral data, and that, in fact, the data do unambiguously indicate that the



(I) (II) (III)



(IV) (V) (VI)

expected tautomers (III) [mesomeric with (VII)] and (V) are the predominant pseudobase species in aqueous solutions of the dications (II) and (VI), respectively.

† To facilitate comparisons, naphthyridine numbering is used in referring to structures (I)—(III).

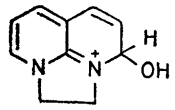
[1] J. E. Dickeson, I. F. Eckhard, R. Fielden, and L. A. Summers, *J.C.S. Perkin I*, 1973, 2885.

[2] J. W. Bunting and W. G. Meathrel, *Canad. J. Chem.*, 1972, **50**, 917.

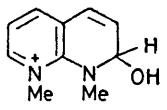
[3] D. J. Pokorny and W. W. Paudler, *Canad. J. Chem.*, 1973, **51**, 576.

[4] J. W. Bunting and W. G. Meathrel, *Canad. J. Chem.*, 1974, **52**, 962.

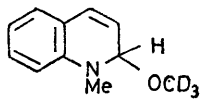
The identification of structures (I) and (IV) by Summers and his co-workers relies upon the assumption that a signal from the bridgehead proton will be observable when salts of the dications (II) and (VI) are dissolved in D_2O buffered with sodium hydrogen carbonate.



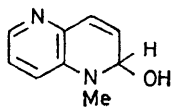
(VII)



(VIII)



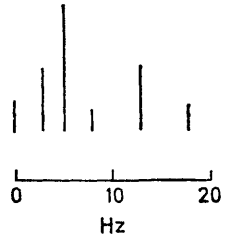
(IX)



(X)

However, since the formation of the species (I) and (IV) requires protonation of the bridgehead carbon atoms, in D_2O solutions (I) and (IV) would exist predominantly as species having a deuterium label on the bridgehead carbons. Thus a ^1H n.m.r. signal will not be observable for the bridgehead hydrogen atoms of (I) and (IV) in D_2O. The presence of a proton on the bridgehead carbon atom in (I) or (IV) would require intramolecular H transfer from C-2 to the bridgehead in each case. Such a migration, without exchange with solvent deuterium, is inherently unlikely in D_2O.

The choice of structure (I) rather than (III) for the predominant pseudobase of (II) was based on the observation of a 'singlet' (δ 6·13) superimposed on a 'quartet' (δ 6·08—6·37). This 'singlet' was assigned to the bridgehead proton although, as discussed above, this position would be labelled with deuterium in D_2O. The complete ^1H n.m.r. spectral assignment given for the ring protons of (I) is indicated in the Table, along with the spectral assignment for the ring protons of the pseudobase (VIII) of the 1,8-dimethyl-1,8-naphthyridine dication.[3] I suggest that the signals assigned to (I) should rather be assigned to (III) as indicated in the Table; for such an assignment there is close agreement between the chemical shifts for all ring protons of (VIII) and (III). Structure (III) was ruled out by Summers and his co-workers [1] on the basis that it contains no ring proton that would give rise to the 'singlet' at δ 6·13. In fact, the signal from H-2 of (III) may appear as an apparent singlet if H-2 and H-3 have similar chemical shifts. In the Figure, a calculated spectrum [5] for H-2 and H-3 of (III) (*i.e.* protons A and B of an ABX system) is presented, based on the following assumptions: $\Delta\delta_{2,3} = 6$ Hz; $J_{2,3} = 5$ Hz; $J_{3,4} = 10$ Hz; $J_{2,4} \simeq 0$.



Calculated spectrum for the protons A and B of an ABX system with $\Delta\delta_{AB}$ 6 Hz; J_{AB} 5 Hz; J_{BX} 10 Hz; J_{AX} *ca.* 0

(These coupling constants are typical of 1,2-dihydroquinolines.[2,4]) This multiplet could easily be misinterpreted in an experimental spectrum as a singlet superimposed on a quartet, and although the value of 6 Hz for $\Delta\delta_{2,3}$ is a somewhat arbitrary choice it does lead to a calculated width of 18 Hz (*i.e.* 0·3 p.p.m. at 60 MHz) for this multiplet, which is in good agreement with the experimentally observed 0·29 p.p.m. (δ 6·08—6·37). Furthermore, a precedent for such a multiplet from the overlap of H-2 and H-3 signals is available: the H-2 and H-3 signals for (IX) in 3M-$NaOCD_3$–CD_3OD occur as a multiplet centred at δ 5·70.[2]

The greatest discrepancy in chemical shifts in the Table between corresponding protons of (III) and (VIII) occurs for H-2 (δ *ca.* 6·13 and 5·63, respectively). However, the spectrum reported [3] for (VIII) was run in 0·5N-NaOD–D_2O and under these conditions (VIII) will be mainly present as its alkoxide ion [4] (*i.e.* a zwitterion), which will result in an upfield shift for the H-2 signal of *ca.* 0·2 p.p.m. relative to the same proton in (VIII).[2] Furthermore, in (III) the charge at N-8 is transmitted to C-2 through both the ethylene bridge and the naphthyridine ring system, and this would be expected to result in a downfield shift for the signal of H-2 in (III) relative to (VIII). The expected multiplicity for the signals from the ring protons in (III) is consistent with that reported in ref. 1, provided that multiplets which are reported as triplets are in fact pairs of overlapping doublets.

While noting that (IV) and (V) cannot be unambiguously distinguished by the splitting observed in the ^1H n.m.r. spectrum of the pseudobase of (VI) [*cf.* H-3, H-4, H-4a of (IV) with H-2, H-3, H-4 of (V)], Summers and his co-workers seem to favour the unusual tautomer (IV) on the basis of the observed long-wavelength u.v. maximum at 377 nm. (We have recently reported [4]

^1H N.m.r. spectra of the pseudobases of naphthyridine dications

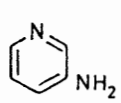
Cation	Chemical shift (δ) H-2	H-3	H-4	H-5	H-6	H-7	H-8a
(I) [a,b]		7·82—8·10	7·82—8·10	6·90—7·16	6·08—6·37	6·90—7·16	6·13
(III) [b]	6·13	6·08—6·37	6·90—7·16	7·82—8·10	6·90—7·16	7·82—8·10	
(VIII) [c]	5·63	6·33	6·65	7·77	7·05	7·89	

[a] As assigned in ref. 1. [b] 1,8-Naphthyridine numbering used to facilitate comparisons. [c] From ref. 3.

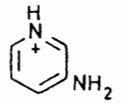
[5] D. J. Pasto and C. R. Johnson, 'Organic Structure Determination,' Prentice-Hall, Englewood Cliffs, New Jersey, 1969, p. 203.

374 nm for this same species.) This represents a significant bathochromic shift from 342 nm, which is the long-wavelength maximum in the spectrum of the pseudobase (X) of the corresponding 1-methyl-1,5-naphthyridine cation.[2] This shift is then suggested[1] to be more consistent with the more highly conjugated structure (IV).

As pointed out earlier, there can be no ambiguity between the ^1H n.m.r. spectra of (IV) and (V) in D_2O since the bridgehead carbon atom in (IV) would bear a deuterium label. Furthermore, the difference in the absorption spectra of (X) and (V) is consistent with the bathochromic shift of 27 nm observed[6] between the neutral molecule (XI) (288 nm) and the cation (XII) (315 nm) of 3-aminopyridine, which may be considered as partial models for (X) and (V), respectively. Protonation of 2-vinylpyridine [an alternative partial model for (X)] also results in a bathochromic shift (9 nm);[7] thus the observed bathochromic shift of 32 nm between (X) and (V) is to be expected on the basis of the individual substituent effects of the 2-vinyl and 3-amino-groups upon the spectra of pyridine cations.



(XI)



(XII)

To summarize, the 1,2-dihydroquinoline derivatives (III) and (V) are the major tautomers present in aqueous solutions of the pseudobases of the cations (II) and (VI), respectively. This conclusion is required by the observed spectral data, and is also consistent with the expected greater stability of (III) and (V), which each retain the Kekulé stabilization of one of the pyridinium rings, relative to (I) and (IV) which require a complete disruption of the aromatic character of the parent dications. Similar theoretical considerations suggest that (VII) will only be a minor contributor to the resonance hybrid of (III) and (VII).

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[6] S. F. Mason, *J. Chem. Soc.*, 1960, 219.
[7] G. Favini, *Gazzetta*, 1963, **93**, 635.