698. *Applications of Proton Resonance Spectroscopy to Structural Problems. Part XXI.*[1] *The Cations of Thiopyridones and Aminopyridines*

By A. R. Katritzky and R. E. Reavill

Proton resonance spectra confirm that thiopyridones form cations by *S*-protonation and that aminopyridines protonate at ring nitrogen.

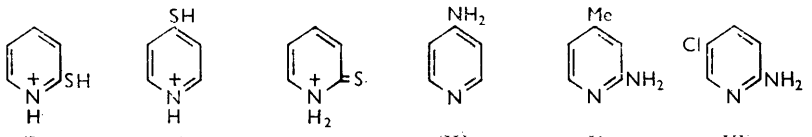
For many years it has been accepted[2] that thiopyridones form *S*-protonated cations (I and II). In view of the controversy over the structure of pyridone cations, now resolved in favour of *O*-protonation,[3] we have measured the proton resonance spectra of 2- and 4-thiopyridone in sulphuric and deuterosulphuric acid. The 6-position proton (τ 1·18) in the 2-thiopyridine cation showed as a triplet (J = 5·5 c./sec.) in sulphuric acid, and a doublet (J = 5·5 c./sec.) in deuterosulphuric acid. The 2- and 3-position protons of 4-thiopyridone showed as a triplet (J = 7·0 c./sec.) at τ 1·63 and a doublet (J = 7·0 c./sec.)

[1] Part XIX, O. Cervinka, A. R. Katritzky, and F. J. Swinbourne, *Coll. Czech. Chem. Comm.*, in the press. The Paper by A. R. Katritzky and B. Wallis, *Chem. and Ind.*, 1964, 2025, is considered to be Part XX.

[2] See, *e.g.*, A. R. Katritzky and J. M. Lagowski, "Heterocyclic Chemistry," Methuen, London, 1960, pp. 93, 97.

[3] A. R. Katritzky and R. A. Y. Jones, *Proc. Chem. Soc.*, 1960, 313; A. R. Katritzky and R. E. Reavill, *J.*, 1963, 753.

at τ 2·13, respectively. In deuterosulphuric acid the triplet collapsed to a doublet. These facts show (cf. ref. 4) that *S*-protonation indeed occurs in 2- and 4-thiopyridone.



That aminopyridines form their first conjugate acids by protonation at ring nitrogen has never seriously been questioned (see, *e.g.*, ref. 2). The proton resonance spectra of three aminopyridines under a variety of conditions (Table) confirm this conclusion, and are also

Parent pyridine	Cation and solvent	2-CH τ	2-CH J	2-CH J'	3-CH τ	3-CH J	NH	NH_2
4-Amino-	Cl^- in SO_2	1·86(4)	6·0	7·5	2·93(2)	7·5	−2·1 *	3·8
	$SbCl_6^-$ in Me_2SO	1·9(2)	7·5	—	3·09(2)	7·5	−3·0	2·0
	Cl^- in Me_2SO	1·69(2)	7·0	—	3·00(2)	7·0	−3·6	1·5

Parent pyridine	Cation and solvent	3-CH τ	3-CH J	5-CH τ	5-CH J	5-CH J'	6-CH τ	6-CH J	NH	NH_2	Me
2-Amino-4-methyl-	Cl^- in SO_2	2·97(2)	1·0	3·12(4)	1·5	6·5	2·20(3)	6·5	−2·8	3·1	7·55
	$SbCl_6^-$ in Me_2SO	3·15(1)	—	3·22(2)	6·5	—	2·2(2)	6·0	−2·8	2·2	—
	Cl^- in Me_2SO	3·04(2)	1·5	3·19(4)	1·5	6·5	2·03(2)	6·0	—	1·7	—

Parent pyridine	Cation and solvent	3-CH τ	3-CH J	3-CH J'	4-CH τ	4-CH J	4-CH J'	6-CH τ	6-CH J	6-CH J'	NH	NH_2
2-Amino-5-chloro-	Cl^- in SO_2	2·81(2)	10·0	—	2·07(4)	2·5	10·0	2·17(1)	—	—	−3·0	2·8
	$SbCl_6^-$ in Me_2SO	2·96(4)	9·0	1·0	2·0(4)	2·0	9·0	1·80(4)	1·0	2·0	—	2·1
	Cl^- in Me_2SO	2·78(4)	9·0	1·0	1·89(4)	2·5	9·0	1·67(4)	1·0	2·0	—	0·5

Peak multiplicities are given in brackets. * Triplet, J = *ca.* 70 c./sec.

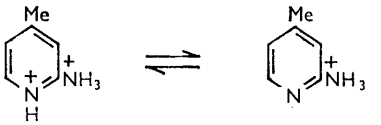
of interest with respect to the lifetime of protonated ring nitrogen. When the lifetime is high, then a distinct peak due to the NH^+ and also the effects of coupling of the NH^+ with adjacent CH are found. For short lifetimes, neither of these phenomena is observed. An intermediate stage where one finds a peak without coupling is possible.

As hydrochlorides in sulphur dioxide solution, 4-aminopyridine (IV) (pK 9·17),[5] 2-amino-4-methylpyridine (V) (pK 7·48),[6] and 2-amino-5-chloropyridine (VI) (pK 4·14; in 1 : 1 ethanol–water; found by potentiometric titration) all show peaks attributable to the NH^+, but only the two stronger bases show splitting of the α-CH by the NH^+. As hexachloroantimonates in dimethyl suphoxide only the two stronger bases (IV) and (V) show the NH^+ peaks, and as chlorides in dimethyl sulphoxide only the strongest base (IV) shows an NH^+ peak: under these conditions none of the bases has effective coupling between α-CH and NH^+.

In 100% sulphuric acid the two stronger bases (IV and V) showed NH^+ peaks and NH^+–CH coupling, but the chloro-amine showed neither of these phenomena. However, the spectra in sulphuric acid are not strictly comparable with those previously mentioned, as the amines will exist in strong sulphuric acid principally in the form of dications (2nd pK of 2-aminopyridine −7·6, of 4-aminopyridine −6·3)[7]. Examination of 2-amino-4-methylpyridine (V) in progressively more dilute sulphuric acid showed that the triplet of the

[4] E. Spinner, *J.*, 1962, 3127.
[5] A. Albert, R. Goldacre, and J. Phillips, *J.*, 1948, 2240.
[6] F. Fastier, *Austral. J. Exptl. Biol. Med. Sci.*, 1958, **36**, 491.
[7] M. Bender and Y. Chow, *J. Amer. Chem. Soc.*, 1959, **81**, 3929.

6-position proton coalesced to a doublet in 95% acid—when the NH^+ was still clearly visible. In 90% acid the NH^+ peak was so broadened by exchange to be undiscernible.



(VII) (VIII)

These exchange processes probably occur by routes of type (VII ⇌ VIII). Spectra in deuterosulphuric acid were in agreement with the above interpretations.

Experimental

Amines were recrystallised before measurement and had m. p.s in agreement with literature values.

Hexachloroantimonates. These were prepared in concentrated hydrochloric acid by using equimolecular quantities of the amine and of antimony pentachloride and were crystallised from hydrochloric acid to constant m. p.: **4-*amino*-**, m. p. 230—231° (Found: C, 14·3; H, 1·8; N, 6·6. $C_5H_7Cl_6N_2Sb$ requires C, 14·0; H, 1·6; N, 6·5%), **4-*methyl*-2-*amino*-**, m. p. 137—137·5° (Found: C, 16·5; H, 2·0; N, 6·3. $C_6H_9Cl_6N_2Sb$ requires C, 16·3; H, 2·0; N, 6·3%), **5-*methyl*-2-*amino*-**, m. p. 173—174° (Found: C, 16·4; H, 2·1; N, 6·5%) and **5-*chloro*-2-*amino*-*pyridine***, m. p. 220—225° (decomp.) (Found: C, 13·3; H, 1·4; N, 6·0. $C_5H_6Cl_7N_2Sb$ requires C, 13·0; H, 1·3; N, 6·0%).

Hydrochlorides. These were prepared by dissolving the base in concentrated hydrochloric acid, evaporating to dryness at 12 mm. pressure and crystallising from methanol to constant m. p.: 4-amino-, m. p. 173—174° (lit.,[8] m. p. 240°) (Found: C, 45·8; H, 5·5; N. 21·4. Calc. for $C_5H_7ClN_2$: C, 46·0; H, 5·4; N, 21·4%), 4-methyl-2-amino-, m. p. 180—181·5° (lit.,[9] m. p. 176—177°) (Found: C, 50·0; H, 6·6; N, 19·8. Calc. for $C_6H_9ClN_2$: C, 49·8; H, 6·4; N, 19·4%), **5-*methyl*-2-*amino*-**, m. p. 192—194° (Found: C, 49·9; H, 6·3; N, 19·8%), and **5-*chloro*-2-*amino*-*pyridine***, m. p. 196—197° (Found: C, 36·7; H, 3·7; N, 17·0. $C_5H_6Cl_2N_2$ requires C, 36·4; H, 3·6; N, 17·3%). Spinner has stated that he prepared some of these hydrochlorides, but gives no m. p.s or analyses.[10]

Nuclear magnetic resonance spectra were measured with sample spinning at 40 Mc./sec. on a Perkin-Elmer permanent magnet spectrometer. Molar solutions were used except for the work in liquid sulphur dioxide. Tetramethylsilane was used as an internal standard in all solutions except for concentrated sulphuric or deuterosulphuric acid (cf. ref. 11) where Me_4N^+ = 6·80 τ was utilised.

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The School of Chemical Sciences, The University of East Anglia,
Norwich. [*Received, December 3rd*, 1965.]

[8] Heilbron and Bunbury, " Dictionary of Organic Chemistry."
[9] O. Seide, *Ber.*, 1924, **57**, 792.
[10] E. Spinner, *J.*, 1962, 3119.
[11] R. E. Reavill, *J.*, 1964, 519.