

TAUTOMERIC EQUILIBRIA OF MERCAPTOPYRIDINES IN THE GAS PHASE;
AN ION CYCLOTRON RESONANCE STUDY¹

Carla B. Theissing and Nico M. M. Nibbering

Laboratory for Organic Chemistry, University of Amsterdam,
Nieuwe Achtergracht 129, Amsterdam, The Netherlands

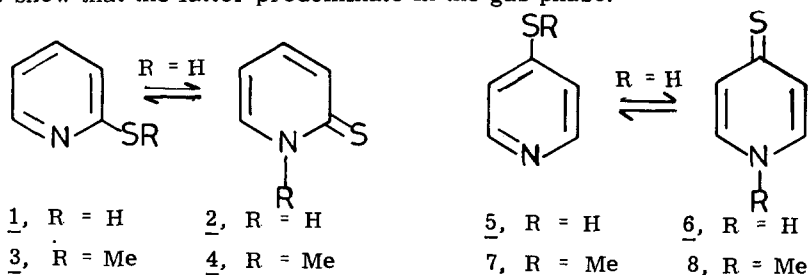
Michael J. Cook, Samia El-Abbady and Alan R. Katritzky

School of Chemical Sciences, University of East Anglia, Norwich NR4 7TJ, England.

(Received in France 24 March 1977; received in UK for publication 12 April 1977)

The use of pK_a values for evaluating tautomeric equilibrium constants in aqueous media is well documented² and recently, it has been shown that the ion cyclotron resonance technique (ICR) can extend the approach to the gas phase.³ The difference in gas phase basicities of 2-hydroxypyridine and 2-pyridone was estimated using ICR and agreed well with the enthalpy difference obtained by Beak *et al* from UV and IR data.⁴

We now wish to report an extension of this study to 2 and 4-mercaptopyridine \rightleftharpoons pyridithione. It is well known that both thiones are strongly favoured over the mercapto forms in solution⁵ but recent UV, IR,⁴ mass spectrometry⁶ and photoelectron spectroscopy⁷ studies show that the latter predominate in the gas phase.



The gas phase basicities (GB) of the tautomeric compounds (1 \rightleftharpoons 2) and (5 \rightleftharpoons 6), and the fixed derivatives 2- and 4-methylthiopyridine (3 and 7) and 1-methyl-2- and 4-pyridithione (4 and 8) were determined using ICR⁸ (Table). Compounds were introduced via a direct insertion probe (probe temperature 50-80^o; cell temperature 100^o), and each compared with at least four standards. With one exception the assigned GB is that of the reference base for which proton transfer has been observed with negative (dk/dE_{ion}) in both directions (see ref. 9).

The effect of N-methylation on the basicity of 2 will differ from the effect of S-methylation on the basicity of 1. The former can be estimated as 4 kcal mole⁻¹ from the GBs of N,N-dimethylthiobenzamide (10) and N-methylthiobenzamide (9) where protonation is expected to occur, as in 2 and 4, at sulphur. Thus we evaluate the GB of tautomer 2 as 219.4 kcal mole⁻¹. The S-methylation effect however cannot be determined because of the lack of suitable model compounds.

TABLE. RELATIVE GAS PHASE BASICITIES (KCAL MOLE⁻¹)⁸

Compound	Gas phase basicity ^a	Reference base
<u>1</u> ⇌ <u>2</u>	217.0	dimethylamine
<u>3</u>	217.4	cyclohexylamine
<u>4</u>	223.4	3,5-dimethylpyridine
<u>5</u> ⇌ <u>6</u>	220.3	3-methylpyridine
<u>7</u>	223.4	3,5-dimethylpyridine
<u>8</u>	228.5-230.4	triethylamine - tripropylamine ^b
<u>9</u>	217.6	pyridine
<u>10</u>	221.6	trimethylamine

^a Based upon PA(NH₃) = 201.0 + 2 kcal mole⁻¹ (see ref. 9a). ^b Negative double resonance signal for only one direction.

Tautomeric equilibria are biased in favour of the least basic tautomer and the lower basicity of the mobile compound (1⇌2) relative to the estimated basicity of 2 demonstrates that tautomer 1 is significantly more stable. Indeed it is reasonable to take 217.0 kcal mole⁻¹ as the GB of 1: combining the values of 217.0 and 219.4 kcal mole⁻¹ gives K₁₀₀ = 0.04, a value in good agreement with K < 0.1 reported by Beak.⁴

This approach cannot be used for the equilibrium 5⇌6 because the lack of suitable models precludes estimation of either the S- or N-methylation effects. However the sequence of basicity found for the 2-series, viz N-Me model > S-Me model > mobile system, is obtained again for the 4-series and we conclude that 5 is the predominant tautomer in the gas phase, in agreement with results of other studies.^{4,6,7}

These results demonstrate that ICR is a potentially valuable tool for measuring tautomeric equilibrium constants in the gas phase but suffers a little at the present time from insufficient data to estimate heteroatom alkylation effects.

Acknowledgement The authors wish to thank the Netherlands Organization for Pure Research (SON/ZWO) for the grant to purchase the ICR spectrometer. We thank Prof. A. Maquestiau (Mons) and Prof. G. Pfister-Guillouzo (Pau) for helpful comments.

REFERENCES

- (1) Part XXI of the series 'Tautomeric Pyridines'. Part XX, see Ref 7.
- (2) J. Elguero, C. Marzin, A. R. Katritzky, and P. Linda, The Tautomerism of Heterocycles, Supplement No. 1 to Adv. Heterocyclic Chem., 1976.
- (3) M. J. Cook, A. R. Katritzky, M. Taagepera, T. D. Singh and R. W. Taft, J. Am. Chem. Soc. **98**, 6048 (1976).
- (4) P. Beak, F. S. Fry, Jr., J. Lee and F. Steele, J. Am. Chem. Soc. **98**, 171 (1976).
- (5) A. R. Katritzky, Chimia **24**, 134 (1970).
- (6) (a) T. Grønneberg and K. Undheim, Org. Mass Spectrom. **6**, 823 (1972); (b) A. Maquestiau, Y. van Haverbeke, C. de Meyer, A. R. Katritzky and J. Frank, Bull. Soc. Chim. Belge **84**, 465 (1975).
- (7) M. J. Cook, S. El-Abbady, A. R. Katritzky, C. Guimon and G. Pfister-Guillouzo, J. Chem. Soc. Perkin II, submitted for publication.
- (8) (a) J. L. Beauchamp and S. E. Buttrill, Jr., J. Chem. Phys. **48**, 1783 (1968); (b) J. I. Brauman and L. K. Blair, J. Am. Chem. Soc. **92**, 5986 (1970).
- (9) (a) J. F. Wolf, R. H. Staley, I. Koppel, M. Taagepera, R. T. McIver, Jr., J. L. Beauchamp and R. W. Taft, J. Am. Chem. Soc., submitted for publication; (b) D. H. Aue, H. M. Webb, M. T. Bowers, C. L. Liotta, C. J. Alexander and H. P. Hopkins, Jr., J. Am. Chem. Soc. **98**, 854 (1976).