

Synthesis of Isothiazolo[2,3-*a*]pyridinium Salts

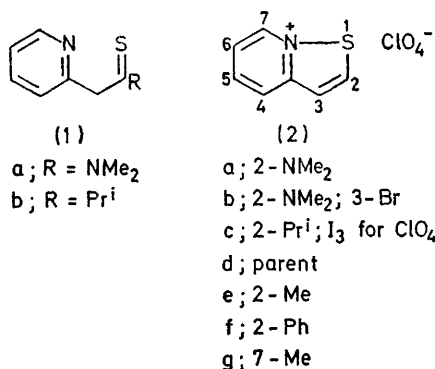
By GRAHAM G. ABBOTT and DEREK LEAVER*

(*Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ*)

Summary Oxidation of 2-(2-pyridyl)thioacetamides, 2-pyridylmethyl thioketones, or 2-(2-benzylthiovinyl)pyridines with bromine yields isothiazolo[2,3-*a*]pyridinium salts.

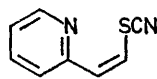
THE failure of a recent attempt¹ to synthesise the isothiazolo-[2,3-*a*]pyridinium ion, by aromatisation of a partially saturated derivative, was attributed to instability of the quaternary isothiazole ring. We have now developed a

general synthesis of isothiazolo[2,3-*a*]pyridinium salts under mild conditions and have confirmed the instability of the system in the presence of nucleophiles. Like many other routes to isothiazoles,² the new method depends on oxidative formation of the S-N bond as a final step.



2-pyridyl CH:CR·SCH₂Ph

(3)



(4)

Oxidation of the thioacetamide (1)^{3†} with hydrogen peroxide, in the presence of perchloric acid, gave the 2-dimethylamino-compound (2a)[‡] and oxidation with bromine gave the corresponding 3-bromo-derivative (2b).

† The n.m.r. spectrum of this compound shows that it exists, to a large extent, as the enethiol tautomer.

‡ Satisfactory analytical results were obtained for all new compounds.

§ Signals can be assigned unambiguously from their multiplicities and by comparison of the spectrum with those of (2e) and (2g).

¹ D. G. Jones and G. Jones, *J. Chem. Soc. (C)*, 1969, 707.

² D. M. McKinnon and E. A. Robak, *Canad. J. Chem.*, 1968, **46**, 1855; N. J. Leonard and G. E. Wilson, *J. Amer. Chem. Soc.*, 1964, **86**, 5307; K. R. H. Wooldridge, *Adv. Heterocyclic Chem.*, 1972, **14**, 1.

³ R. Wegler, E. Kühle, and W. Schäfer in 'Newer Methods of Preparative Organic Chemistry,' vol. 3, eds. W. Foerst and H. Birnbaum, Academic Press, London, 1964, p. 43.

⁴ E. Uhlemann and H. Müller, *J. prakt. Chem.*, 1965, **30**, 163.

⁵ V. Boekelheide and W. G. Gall, *J. Amer. Chem. Soc.*, 1954, **76**, 1832.

⁶ D. Leaver, W. A. H. Robertson, and D. M. McKinnon, *J. Chem. Soc.*, 1962, 5104.

A similar procedure, using iodine as oxidant, converted the thione (1b)⁴ into the 2-isopropyl compound (2c) but this method is not generally convenient because of the lack of efficient routes to thiones of type (1). The isothiazolopyridinium salts (2d—g) were obtained by base-catalysed addition of phenylmethanethiol to 2-ethynylpyridines, followed by oxidation of the resulting crude 2-(2-benzylthiovinyl)pyridines (3) with bromine. The salts were isolated as perchlorates in yields of 25—35% based on the ethynyl compounds, the low yields being attributable to the formation of two geometrically isomeric vinyl compounds (3), only one of which is able to cyclise.

The structures of the isothiazolopyridinium salts follow from their ¹H n.m.r. spectra [e.g. for (2d) in (CD₃)₂SO: τ 0.31 (7-H), 0.83 (2-H), 1.57 (4-H), 1.73 (5-H), 2.21 (6-H), and 2.22 (3-H), $J_{2,3}$ 6.4 Hz]§ and from the u.v. spectrum (in EtOH) of the parent compound [λ_{max} (log ϵ) 212 (3.85), 230 (4.25), 318 (4.07), and 331 nm (4.11)] which is very similar to that of the iso- π -electronic quinolinizinium ion.⁵ The parent compound reacts with sodium cyanide to give *cis*-2-(2-thiocyanovinyl)pyridine (4) but other nucleophiles caused decomposition of the salts and no characterisable products were isolated. Attempts to condense the methyl groups in the salts (2e) and (2g) with *p*-dimethylaminobenzaldehyde failed under conditions which were successful for 3-methyl-1,2-dithiolium salts.⁶

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