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BROMINATION OF PYRIDINE-N-OXIDE

H.C. van der Plas, H.J. den Hertog, M. van Ammers and Miss B. Haase
Laboratory of Organic Chemistry of the Agricultural University,
Wageningen, The Netherlands

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The reactivity of pyridine-N-oxide towards electrophilic reagents has been investigated extensively. It has been found that when pyridine-N-oxide is heated with a mixture of fuming nitric acid and sulphuric acid at 90° for 1 h 4-nitropyridine-N-oxide is formed in a high yield[1]. The mercuration also proceeds smoothly: heating of the N-oxide with mercuric acetate in acetic acid solution for 2 hrs at 130° produces a reaction mixture containing derivatives substituted in positions 2 and 6[2]. Sulphonation only occurs under extreme conditions; it leads to the formation of pyridine-3-sulphonic acid[3]. The halogenation, however, has not yet been accomplished, as far as we know.

Several years ago we have found that pyridine-N-oxide was not brominated when it was heated with bromine for several hours above

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[1] a. E. Ochiai, K. Arima and M. Ishikawa, J. Pharm. Soc. Japan **63**, 79 (1943); Chem. Abstr. **45**, 5151 (1951).
b. H.J. den Hertog and J. Overhoff, Rec. Trav. Chim. **69**, 468 (1950).

[2] M. van Ammers and H.J. den Hertog, Rec. Trav. Chim. **77**, 340 (1958).

[3] a. H.S. Mosher and F.J. Welch, J. Am. Chem. Soc. **77**, 2902 (1955).
b. M. van Ammers and H.J. den Hertog, Rec. Trav. Chim. **78**, 586 (1959).

100° in the presence of various metallic bromides as a catalyst[4]. We now treated the N-oxide with bromine at more elevated temperatures using sulphuric acid as a solvent in order to prevent deoxydation. Even when pyridine-N-oxide was heated with an excess of bromine in sulphuric acid for 20 hrs at 200°, no reaction occurred. Application of a method of bromination given by Derbyshire and Waters i.e. the use of a mixture of bromine, 90% aqueous sulphuric acid and silver sulphate which contains a high concentration of bromine cations, proved to be successful. The rate of the bromination according to this procedure at 150° is still very low, but when the heating is carried out at 200° for 20 hrs a mixture of bromopyridine-N-oxides is formed in a yield of about 10%.

The composition of the reaction product was established by reducing the N-oxides with iron powder and acetic acid and separating the bromopyridines formed by gas chromatography over a column filled up with 20% tritolylphosphate on chromosorb, using hydrogen as a carrier gas. It appeared that a mixture of 2- and 4-bromopyridine-N-oxide was formed in a ratio of about 1 : 2.

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[4] Cf. also the paper cited in note 3a.

[5] Cf. D.H. Derbyshire and W.A. Waters, J. Chem. Soc. 1950, 573.