Tetrahedron Letters No. 37, pp 3337 - 3338, 1976. Pergamon Press. Printed in Great Britain.

A NEW SYNTHESIS OF PYRIMIDINE 1-OXIDES[1,2]

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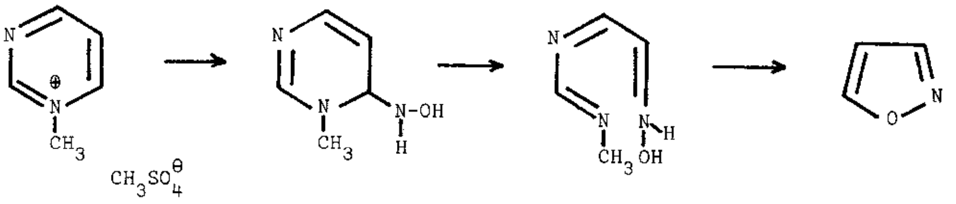
(Received in UK 20 July 1976; accepted for publication 20 July 1976)

In our current research on the behaviour of diazines with nucleophiles, it was recently found that pyrimidines, 1-methylpyrimidinium methosulfate (1) and pyrimidine 1-oxides are converted into isoxazoles (4) by the action of hydroxylamine[3]. The mechanism for the conversion of 1 into isoxazole (4) occurs via the intermediates 2 and 3 (see scheme below). The first step common to these reactions is an addition of the nucleophile at C(6). Ring-opening by fission of the C-N bond in (2) gives (3), which cyclises into (4) by a nucleophilic attack of the oxygen lone pair on C(4). Subsequent aromatisation occurs by loss of N-methylformamidine.



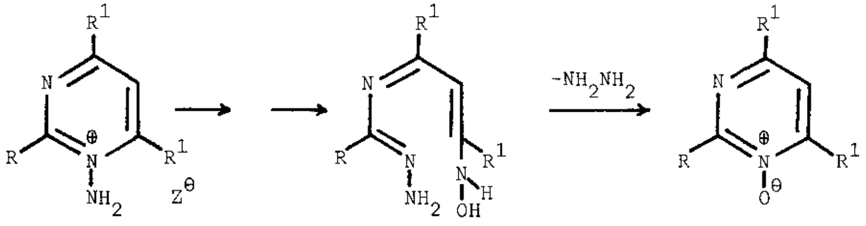
1 2 3 4

In principle the nitrogen lone pair of the hydroxylamino group in an open-chain compound like (3) is also able to perform the cyclisation leading to a heteroaromatic N-oxide. For example pyrylium salts can easily be converted into either isoxazoles or pyridine N-oxides[4]. 3-Aza-pyrylium salts however, failed to give pyrimidine N-oxides[5], isoxazoles being formed instead.

We wish to report now on a new, non-oxidative conversion of pyrimidine N-oxides, observed on treatment of 1-aminopyrimidinium mesitylenesulfonates (5)[6] ($Z^{\ominus} = {}^{\ominus}OSO_2C_6H_2(CH_3)_3$) with hydroxylamine.

Reaction of 3 x 10^{-3} mol of 5 in water with a fivefold molar amount of NH_2OH . HCl for 15 min gave a solution, which was neutralized with K_2CO_3 and extracted with ether. After drying and distilling off the solvent the pyrimidine N-oxides (7) were isolated in moderate to high yields (7a: R=H, R^1=CH_3, 85%; 7b: R=R^1=CH_3, 90%; 7c: R=H, R^1=C_6H_5, 35%).

We assume that the intermediate 6 is formed from 5 by the same mechanism as reported above, after which ring closure yields the pyrimidine 1-oxides (7). No trace of a corresponding isoxazole could be detected.



In the cases of 7a and 7b this new method gives yields, which are higher than the ones obtained in the direct oxidation of pyrimidines, moreover this non-oxidative method opens up the possibility of synthesizing pyrimidine 1-oxides with substituents which are sensitive for oxidation.

Acknowledgement

We are indebted to Dr.P.Smit and Mr.A.van Veldhuizen for measuring ^1H-NMR and IR spectra and to Mr.K.van Dijk for technical assistance.

This investigation has been carried out under the auspices of the Netherlands Foundation for Chemical Research (SON) and with financial aid from the Netherlands Organisation for the Advancement of Pure Research (ZWO).

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7. The ^1H-NMR, IR spectra and melting points were identical with those of the authentic compounds.