The Thermal Deoxygenation of 2-Alkylthiopyridine 1-Oxides

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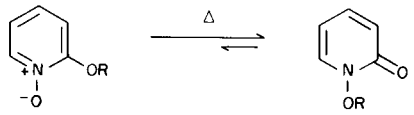
Sir:

Interconversion between substituted pyridine *N*-oxides and isomeric forms is well documented. Mercapto- and hydroxypyridine *N*-oxides **1** exist predominately in the tautomeric form **2** (2,3).

1 **2**

X = O, S

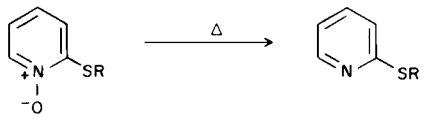
The thermal rearrangement of 2-alkoxypyridine 1-oxides **3** to the 1-alkoxypyridones **4** proceeds in high yield and is thought to occur *via* an intermolecular displacement reaction and ion pair formation (4,5).



3 **4**

Rearrangements of the corresponding alkylthiopyridine 1-oxides remain unreported. Attempts to effect rearrangement of 2-benzylthiopyridine 1-oxide to the analogous 1-benzyloxypyridine-2-thione in the presence of boron trifluoride failed (2).

In connection with our work on the transition metal complexes of pyridine 1-oxide derivatives, we have examined the thermal reactions of alkylthiopyridine 1-oxides **5**. We wish to report that in marked contrast to the oxygen derivatives **3**, at elevated temperatures **5** undergoes essentially quantitative deoxygenation to the corresponding pyridines **6**,



5 **6**

Syntheses of alkylthiopyridine 1-oxides in the literature utilize mercaptide displacements of halopyridine 1-oxides (2,6). In this study, the thioethers were obtained by direct alkylation of the readily available sodium salt of 2-mercaptopyridine 1-oxide in acetone. Thermal reaction was then effected by heating the alkylthiopyridine 1-oxides **5** in an oil bath above the melting point (150-190°). At periodic intervals, aliquots were withdrawn, quenched, and the extent of reaction monitored by nuclear magnetic resonance spectroscopy. After the reactions were judged complete a pure sample of the product was isolated by short path vacuum distillation. The nmr data for the compounds studied is shown in Table I. The absorptions given represent the chemical shifts of the alkyl hydrogens immediately adjacent to sulfur.

TABLE I

NMR Spectral Data
(Italicized hydrogens shown in ppm relative to TMS)

Alkyl Group	**5**	**6**	$\Delta\nu$	Solvent
a, -C*H*$_2$C$_6$H$_5$	4.13	4.41	.28	$CDCl_3$
	4.41	4.53	.12	CF_3CO_2H
b, -C*H*$_3$	2.73	2.83	.10	CF_3CO_2H
c, -CH$_2$CH$_3$	3.23	3.35	.12	CF_3CO_2H
d, -C*H*CH$_2$CH$_3$ (CH$_3$)	3.22	3.80	.58	$CDCl_3$

As indicated, the absorption of the alkyl hydrogens exhibited a downfield shift as the reaction progressed. The magnitude of difference in the chemical shift values ($\Delta\nu$) was not sufficient to indicate transfer of the alkyl moiety to the electronegative oxygen but rather was in accord with the proximity of the pyridine ring and increased deshielding due to the loss of the *N*-oxide function.

Confirmation of the deoxygenation pathway was provided by elemental analysis, mass spectroscopy, and synthesis (7). As an example, reaction of 2-benzylthiopyridine 1-oxide (**5a**) at 184° was judged by nmr to be complete after an hour. Distillation under reduced pressure gave a liquid b.p. 118°, 0.2 mm, n_D^{22} 1.610 (lit. (8), b.p. 153-154°, 4 mm, n_D^{22} 1.628). Elemental analysis

calculated for $C_{12}H_{11}NS$ gave: C, 71.63; H, 5.47; N, 6.90. Found: C, 71.63; H, 5.63; N, 6.73. The mass spectrum showed a molecular ion of m/e 201. Treatment of **5a** with phosphorus pentachloride, a known deoxygenating agent of aromatic *N*-oxides (9), gave a compound identical to **6a**.

It has been reported that alkylthiopyridines may rearrange to *N*-alkyl-2-thiopyridones in the presence of a catalyst, while the conversion of alkoxypyridines to the corresponding pyridones occurs more readily (10). Under the reaction conditions utilized in the present study, **6** does not appear to rearrange. For example, *N*-methyl-2-thiopyridone shows a reported methyl resonance centered on 4.00 ppm (9) in contrast to the observed 2.83 ppm absorption of **6b**. In addition, the ultraviolet spectra of **6** [λ max (methanol) (log ε) = 254 (4.00), 294 (3.69) nm, for **6a**] are similar to those reported for 2-substituted pyridines (11).

The deoxygenation of pyridine *N*-oxides is known to be catalyzed by the presence of sulfur compounds (12), although upon heating **5**, no intermediate sulfoxides were detected. The reaction appears to be accelerated by the presence of radical initiators such as benzoyl peroxide, suggesting that a radical chain mechanism may be involved. It has been reported that pyridine *N*-oxide itself gives some pyridine if heated at 220°. At that temperature 4-ethoxypyridine *N*-oxide also is reduced, while 4-nitropyridine *N*-oxide is thermally stable (13).

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