Study of the Wallach Rearrangement in the Phenylazoxypyridine Series. Differing Reactivity of α- and β-Azoxy Isomers

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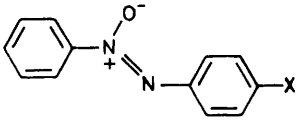
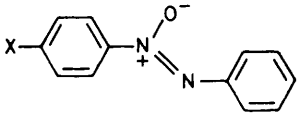
The rearrangement of 4-(phenyl-β-azoxy)pyridine to 4-hydroxyphenylazopyridine has been investigated in H_2SO_4 media under conditions where the α-azoxy isomer is virtually unreactive; a mechanism involving a tricationic reaction intermediate is proposed.

In studies of the acid catalysed Wallach rearrangement of azoxyarenes,[1] much information about mechanism has been deduced from structural changes in the azoxyarene, and from the kinetic form of the acid catalysis.[2] Thus isomeric α- and β-azoxybenzenes (**1**) and (**2**), while generally giving rise to the same rearrangement product (4-X-4′-hydroxyazobenzene), have been found to exhibit relative rates varying from *ca.* 1 : 1 (X=Br) to 90 : 1 (X=NO_2).[3] The isomeric α- and β-2-phenylazoxynaphthalenes have been shown, on the basis of kinetic evidence, to rearrange by different mechanisms while giving rise to a common product, 2-phenylazo-1-naphthol.[4]

In an extension of our studies of the Wallach rearrangement into the heterocyclic series, we have begun investigation



(1)



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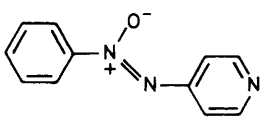

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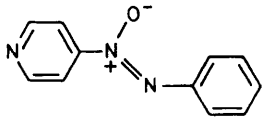
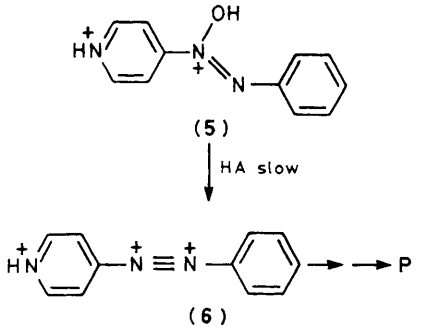


(4)

Table 1. Kinetic data for rearrangement of 4-(phenyl-β-azoxy)-pyridine (**4**) in aqueous H_2SO_4 at 50 °C.

H_2SO_4 wt. %	$\frac{[SH_2^{2+}]^a}{[SH^+] + [SH_2^{2+}]}$	$10^4 k_{obs}$ /s^{-1}
97.17	0.756	0.229
98.46	0.881	1.52
98.91	0.901	2.68
99.17	0.020	5.14
99.47	0.944	9.45
99.62	0.958	23.5
99.74	0.973	80.2
99.82	0.976	85.5
99.88	0.982	168
99.91	0.986	270

[a] Calculated from the relationship $pK_a = H_0 + \log [SH_2^{2+}]/[SH^+]$ where SH^+ denotes the substrate protonated on the pyridine nitrogen while SH_2^{2+} is the species protonated on the azoxy N–O function as well.



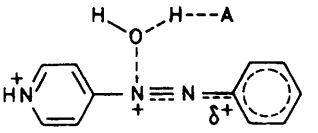
Scheme 1

of phenylazoxypyridines and report here the first kinetic and product studies pertaining to such systems. Contrary to previous findings, we have isolated both isomers 4-(phenyl-α-azoxy)pyridine (**3**) and 4-(phenyl-β-azoxy)pyridine (**4**) in the oxidation of 4-phenylazopyridine.[5]

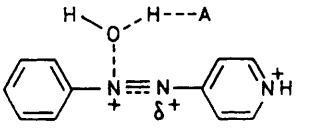
Unexpectedly, we have found that (**3**) does not undergo detectable rearrangement† under conditions where (**4**) reacts readily to give 4-hydroxyphenylazopyridine (95—100% H_2SO_4). A similar reactivity difference has been found for the corresponding α- and β-phenylazoxypyridine *N*-oxides. This difference in reactivity enables one to separate cleanly the α-isomers from the mixture of α- and β-azoxy compounds obtained on oxidation of phenylazopyridines. These results may lead to a facile chemical method for the evaluation of regioselectivity in the oxidation of phenylazopyridines, contrasting with the azobenzene series.[6]

The rate of rearrangement of (**4**) was conveniently followed spectrophotometrically in the 97—99.9% H_2SO_4 region at 50 °C. The results are given in Table 1. The pK_a for N–O protonation of (**4**) has been determined to be −9.58 (H_0 for half protonation)[7] from which it follows that N–O as well as pyridine ring protonation of (**4**) is extensive over the whole acid region studied. Thus on increasing the acid concentration from 97.17 to 99.91% H_2SO_4 the extent of protonation increases from 76 to 99%, while the rate of rearrangement increases more than 1000-fold over this range. This marked increase in rate in acid media in which the substrate is extensively diprotonated indicates that a third proton transfer step is required for reaction to occur. The results suggest a mechanism involving a tricationic intermediate (**6**) formed through rate determining proton transfer[8] to (**5**), followed by attack of nucleophile (HSO_4^-) on the phenyl ring to give product (Scheme 1).

† No reaction could be detected for (**3**) in *ca.* 99% H_2SO_4 at 50 °C over 24 h whereas (**4**) reacts rapidly under these conditions (Table 1).



(**7**)



(**8**)

In the transition state (**7**) of the slow step the developing positive charge on nitrogen can be delocalized onto the benzene ring; this, however, is not possible in the corresponding transition state structure (**8**) derived from (**3**) resulting in destabilization.

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