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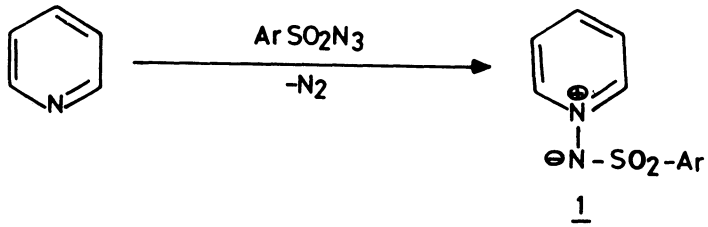
THE REACTION OF PYRIDINE N-OXIDE AND ITS BENZOANALOGUES WITH ARENESULFONYL AZIDES: NOVEL SYNTHESIS OF TETRAZOLOAZINES

K. SREENIVAS REDDY, D. S. IYENGAR,* and U. T. BHALERAO

Regional Research Laboratory, Hyderabad-500 007, India

Pyridine N-Oxide reacts with arenesulfonyl azides under thermal conditions, to form tetrazolo[1,5-a]pyridine. The condensed pyridine N-Oxides also behaved similarly, giving the respective tetrazoloazines. These reaction results indicate a novel azido transfer from arenesulfonyl azides and provide an alternative route to tetrazoloazines.

The reaction of pyridine and its benzoanalogues with arenesulfonyl azides was studied by Abromavitch and Takaya,[1] who reported the formation of N-sulfonyliminopyridinium ylide (1) and sulfonylaminopyridine. These results were explained by invoking a direct trapping of the electrophilic nitrene intermediate or a concerted attack of the pyridine nitrogen lone pair on the azide function with elimination of nitrogen. It is conceivable that blocking the lone pair of the ring nitrogen by a suitable functionality such as an N-oxide would suppress ylid formation and lead to insertion products. However, the reaction between pyridine N-oxide (2) and the arenesulfonyl azides (3 or 4) followed a different course, giving tetrazolo[1,5-a]pyridine (5). The unusual nature of this reaction which provides a novel synthesis of tetrazoloazines necessitated this communication.



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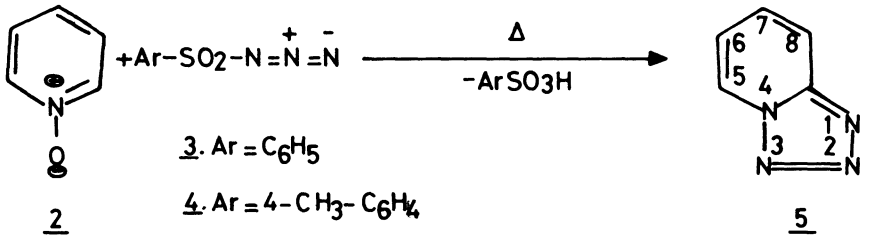
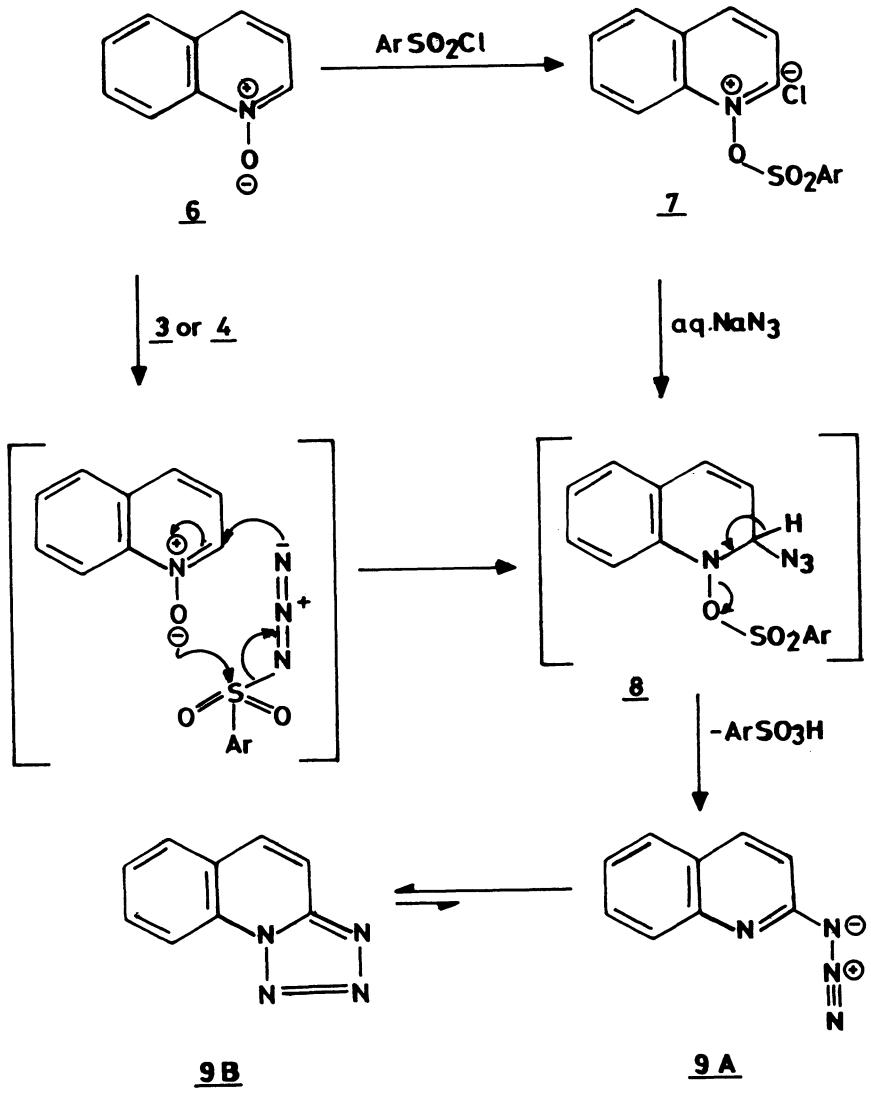


Thermolysis[2] of 3 or 4 in pyridine N-oxide yields the tetrazolopyridine (5) as the major product (40%). The reaction also proceeded smoothly by heating the reactants in acetonitrile with a catalytic quantity of copper powder. The structural evidence for 5 comes from its high resolution mass analysis, IR and ^{1}H-NMR data. Molecular ion m/e 120.0437 ($C_5H_4N_4$= 120.0430), IR: $CHCl_3$, 1620, 1480, 1360, 1330, 1210, 1130, 1080, and 1000 cm^{-1}; ^{1}H-NMR: ($CDCl_3$), (δ) 8.33 (1H, 5-H), 7.58-8.00 (m, 2H, 6 and 7-H) and 7.33 (m, 1H, 8-H). The structure (5) has been confirmed by comparison with an authentic sample[3] obtained by the action of nitrous acid on 2-hydrazino pyridine.

The generality of this new reaction has been shown by the formation of tetrazolo[1,5-a]quinoline (9-B) and tetrazolo[5,1-a]isoquinoline[4] in good yields (70-75%), by reaction of 3 with 6 and isoquinoline N-oxide, respectively.

Mechanistically formation of tetrazoloazines from N-oxide may proceed through a direct nucleophilic displacement of the azide group by the N-oxide oxygen with concomitant attack of the displaced azide on the α-position of the heterocycle giving rise to a Reissert-type of intermediate (8). A facile loss of arylsulfonic acid from 8 can be visualised resulting in the α-azido compound (9-A) which can isomerise[5] readily to the tetrazole form (9-B). In the above mechanism the assumption made about the intermediacy of 8 is ratified by reacting the quinolinium salt 7 prepared from 6 and benzenesulfonyl chloride with aqueous sodium azide solution which afforded the tetrazoloquinoline 9 in moderate yields (45%). Formation of 9 directly under the reaction conditions[6] suggests the lability of the intermediate 8 which spontaneously loses benzene sulfonic acid. Attempted reaction of the pyridinium salt obtained from 2 with benzenesulfonyl chloride resulted in a very low yield of 5. The lower yield of 5 (5% vs. 45% of 9) may be attributed to the considerable loss of resonance energy caused by the formation of dihydro intermediates in monocyclic compounds.[7]

In light of the mechanism it is reasonable to assume the formation of tetrazoloazines by the reaction of hydrazoic acid with pyridine N-oxide and its benzoanalogues. However, the reaction of 2 with hydrazoic acid in chloroform did not give any tetrazolopyridine, but resulted in the recovery of starting material.



A noteworthy feature of this reaction is that the heterocyclic N-oxides suppress the normal decomposition pattern in arenesulfonyl azides and effect a novel azido-transfer. This result is interestingly different from the earlier literature reports where a diazo-transfer or arenesulfonyl nitrene derived products have been observed during the decomposition of arenesulfonyl azides in the presence of heterocyclic substances.[1,8)]

The reaction of heterocyclic N-oxides with arenesulfonyl azides appears to be more promising route for the synthesis of tetrazoloazines than the nitrosation[3] of difficultly accessable α-hydrazinoheterocycles or the reaction of α-chloroheterocycles with azide ions,[9] where the yields are less than 50%. The nitrosation method though comparable in yields with the present one suffers from disadvantage of increased synthetic step involved in the preparation of hydrazino compounds.[10]

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References

1) R. A. Abramovitch and T. Takaya, J. Org. Chem., 37, 2023 (1972).
2) The reaction is carried out by gradually heating the reactants to the dissociation temperature of the azides and maintaining the mixture at that temperature for 1 h. The product is isolated by column chromatography over silica gel eluting with pet. ether/$CHCl_3$ (1:1).
3) R. G. Fargher and R. Furness, J. Chem. Soc., 107, 688 (1915).
4) Authenticated by comparing with the samples prepared by the reaction of sodium azide in DMSO with 2-chloroquinoline and 1-chloroisoquinoline respectively.
5) 2-Azidopyridine and its benzoanalogues have been reported to exist predominantly in the tetrazole form. Some aspects of the azidoazomethine-tetrazolo isomerism have been reviewed by M. Tisler, Synthesis, 1973, 123.
6) The reaction between the N-sulfonyloxyquinolinium chloride suspended in chloroform and an aqueous solution of sodium azide proceeded smoothly by stirring the reaction mixture for 2 h at room temperature.
7) A. R. Katritzky and E. Lunt, Tetrahedron, 22, 4291 (1969).
8) A. S. Bailey and J. J. Merrer, J. Chem. Soc., C, 1966, 1345.
9) M. D. Nair and S. R. Mehta, Indian J. Chem., 5, 403 (1967).
10) W. H. Perkin and R. Robinson, J. Chem. Soc., 103, 1978 (1913).

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