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A NOVEL METHOD FOR HETEROAROMATIC N-IMINES

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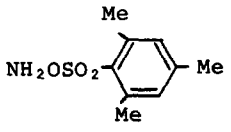
Recently heteroaromatic N-imines which are isoelectronic with N-oxides, have acquired considerable importance as intermediates in organic syntheses.[1] However, we[2] and others[3-5] found the scope of the known methods of preparation to be severely limited. In this communication a new and general method for heteroaromatic N-imines using O-mesitylenesulfonylhydroxylamine (MSH) (I) as an aminating agent is described.

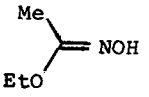
MSH, first reported by Carpino,[6] was prepared by the following improved method; mesitylenesulfonyl chloride was added with stirring to a solution of ethyl acetohydroxamate (II)[7] and triethylamine in dimethylformamide at room temperature. After one hour, the reaction mixture was poured into ice-water to give 86 per cent yield of ethyl O-mesitylenesulfonylacetohydroxamate (III), mp. 57-58°. Treatment of III with 70 per cent perchloric acid and then water gave white crystals of MSH in 79 per cent yield.

In a typical procedure for the N-amination, equimolar admixture of pyridine and MSH in methylene chloride was allowed to stand at room temperature for a few minutes. After addition of ether, the precipitated crystals of N-aminopyridinium mesitylenesulfonate were recrystallized from a mixture of methanol and ethyl acetate.

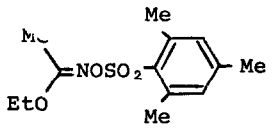
The results obtained for some representative heteroaromatics, were summarized in Table. The structures of the products (IV) were proved by elemental analysis,



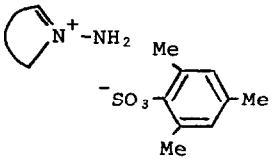
I



II



III



IV

infrared and ultraviolet spectra[3a,1a]; in addition, the N-amino derivatives from pyridine, 2,6-lutidine, quinoline, isoquinoline, quinaldine, 1-methylisoquinoline, and α- and β-naphthyridines were converted to the corresponding N-benzoylimino derivatives, which were easily characterized either by direct comparison with authentic specimens or by infrared[2,1a] and mass spectrometry.[8]

The advantage of this method becomes clear by comparison of the results noted in Table with those by other reactions recorded in the literature. For

Parent Heterocycles	M.p.	Yield(%)	Parent Heterocycles	M.p.	Yield(%)
pyridine	125-126°	80	2-benzoylpyridine	178-179°	78
2-picoline	120-121°	94	4-benzoylpyridine	178-179°	93
2,6-lutidine	180-181°	89	2-chloropyridine	116-117°	61
2-cyanopyridine	236-237°	57	3-nitropyridine	169-170°	68
3-cyanopyridine	181-182°	72	pyridazine	154-155°	68[a)]
4-cyanopyridine	196-197°	90	quinoline	132-133°	67
2-carbomethoxypyridine	136-137°	84	quinaldine	201-202°	83
3-carbethoxypyridine	132-133°	86	isoquinoline	134-135°	70
4-carbethoxypyridine	57-58°	87	1-methylisoquinoline	175-176°	61
3-carboxypyridine	183-184°	74	α-naphthyridine	254-255°	93
3-acetylpyridine	152-153°	98	β-naphthyridine	195-196°	99

a) mono-N-amine salt.

example, Gösl's procedure[9] using hydroxylamine O-sulfonic acid which appears to be most widely utilized at present, fails to give the N-amino derivatives of cyano-, nitro-, carboxy-, and ethoxycarbonylpyridine,[3] and gives lower yields of N-amino derivatives of pyridine (63-72%), 2-picoline (57%), 2,6-lutidine (34%) and quinoline (32%).

The mesitylenesulfonates (IV) thus obtained are soluble in water and readily generate the corresponding unisolable N-imines[10] by treatment with base.

Footnotes and References

1. For example, see a) T. Okamoto and M. Hirobe, J. Syn. Org. Chem. (Japan), 26, 746 (1968); b) V. Boekelheide and N.A. Fedoruk, J. Org. Chem., 33, 2062 (1968); c) Y. Tamura, N. Tsujimoto, Y. Sumida, and M. Ikeda, Tetrahedron, 28, 21 (1972); d) Y. Tamura, H. Ishibashi, N. Tsujimoto, and M. Ikeda, Chem. Pharm. Bull. (Japan), 19, 1285 (1971), and references cited therein; e) T. Sasaki, K. Kanematsu, and A. Kakehi, Tetrahedron, 28, 1469 (1972).
2. Y. Tamura, Y. Miki, T. Honda, and M. Ikeda, J. Heterocyclic Chem., in press.
3. a) J. Epsztajn, E. Lunt, and A.R. Katritzky, Tetrahedron, 26, 1665 (1970); b) unpublished data in our laboratory.
4. A. Ohsawa, M. Hirobe, and T. Okamoto, Yakugaku Zasshi, 92, 73 (1972).
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6. L.A. Carpino, J. Am. Chem. Soc., 82, 3133 (1960).
7. J. Houben and E. Schmidt, Ber., 46, 3616 (1913).
8. M. Ikeda, N. Tsujimoto, and Y. Tamura, Org. Mass Spectrom., 5, 61 (1971).
9. R. Gösl and A. Meuwsen, Org. Synth., 43, 1 (1963).
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11. R. Huisgen, R. Grashey and R. Krischke, Tetrahedron Letters, 1962, 387.