A Simple Preparation of Aromatic or Heteroaromatic Sulphides

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Summary A simple preparation of alkyl- or aryl-thio-aromatic compounds from primary aromatic and hetero-aromatic amines and the appropriate disulphides has been effected using isopentyl nitrite

THE introduction of a sulphur group to the pyridine ring has been accomplished by a variety of methods Nucleophilic substitution of halogens or oxygen has been used to obtain pyridine-2- or -4-thiol[1] and also pyridine-3-thiol,[2] for which the reaction conditions are more severe, particularly in the absence of activating substituents A more satisfactory preparation of the latter involves the reduction of pyridine-3-sulphonyl chloride by tin(IV) chloride[3] The reaction of alkanethiols with pyridinium salts is known to lead to the direct introduction of alkylthio-groups to the pyridine ring, however, the product is a mixture of the regioisomers[4] Although aromatic and heteroaromatic amino-groups have been transformed into sulphides through diazotization,[3,5] the diazotization of some heteroaromatic amines is only moderately successful[6] As the reaction of primary aromatic amines with alkyl nitrites provides a useful method for the generation of aryl radicals,[7] we investigated the synthesis of aromatic and pyridyl sulphides using isopentyl nitrite, which resulted in a simple transformation of amino-groups to the corresponding alkyl- or aryl-thio-groups under neutral conditions

In general, the synthesis involved adding an amine to a solution of isopentyl nitrite and an excess of dimethyl disulphide which was heated to 80—90 °C A gas was evolved immediately and the mixture became deep brown Upon completion of the gas evolution, the resulting methyl aryl sulphide was isolated by distillation, crystallization, or solvent extraction Replacement of dimethyl disulphide by diphenyl disulphide gave the corresponding phenyl derivatives The reaction conditions and yields are summarized in the Table

TABLE One-flask synthesis of sulphides from arylamines[a]

Amine (mol)	Method of addition[b]	Reaction time/h	Product (yield[c]/%)
3-Aminopyridine			3-Methylthiopyridine
(0·05)	A	2[d]	(75)
(0 20)	A	3[d]	(25)
			3-Phenylthiopyridine
(0 025)	A[e]	0 5[d]	(22)
2-Aminopyridine			2-Methylthiopyridine
(0·2)	B	2[f]	(28)
4-Aminopyridine			4-Methylthiopyridine
(0·2)	B	2[f]	(33)
4-Methylaniline			4-Methylthioaniline
(0 05)	A	1[d]	(73)
4-Nitroaniline			4-Methylthioaniline
(0 05)	B	0 3[d]	(84)

[a] All the reactions were carried out in a 3-necked flask immersed in a hot water bath (80—90 °C) under an argon atmosphere The molar ratio of reagents was $ArNH_2$ isopentyl nitrite MeSSMe 1 1 5 11 [b] A Isopentyl nitrite was added to a solution of amine in dimethyl disulphide in one portion at 80—90 °C B Solid amine was added gradually to a solution of isopentyl nitrite and dimethyl disulphide at 80—90 °C. 4-Nitroaniline is so reactive the amine should be added carefully in small portions [c] Isolated yield after distillation or crystallization based on amine used [d] Gas evolution was very fast and ceased within 20 min [e] Diphenyl disulphide (PhSSPh) was used instead of dimethyl disulphide at 120—130 °C The molar ratio of reagents was $ArNH_2$: isopentyl nitrite . PhSSPh 1 : 2 : 2 Gas evolution was very slow, this reaction time reflects the completion of gas evolution

In a large-scale preparation of methyl 3-pyridyl sulphide from 3-aminopyridine, significant amounts of 1,3-bis-(3-pyridyl)triazene were formed. The formation of the triazene was probably due to a reaction of the free amine with the nitrosated amino-compound and so an excess of amino-compound should be avoided for the preparation of sulphides. This procedure can be applied successfully to carbocyclic aromatic amines.

The above procedure offers several advantages over existing synthetic procedures. (i) Unlike the conversion of arenediazonium salts into the thio-products, the above procedure is not affected by electron-donating or withdrawing substituents on the aromatic nucleus; (ii) heteroaromatic amines, *e.g.* aminopyridines, which are generally difficult to diazotize, may be transformed *via* this process; (iii) the starting materials are readily available; and (iv) the disposition of the new substituent on the aromatic ring is determined unequivocally.

We thank the Robert A. Welch Foundation for the support of this research and Dr. Grace Neff for her assistance.

(*Received, 6th May* 1980; *Com.* 473.)

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