

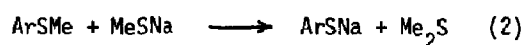
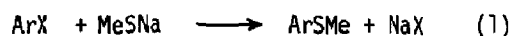
## A CONVENIENT SYNTHESIS OF AROMATIC THIOLS FROM UNACTIVATED ARYL HALIDES

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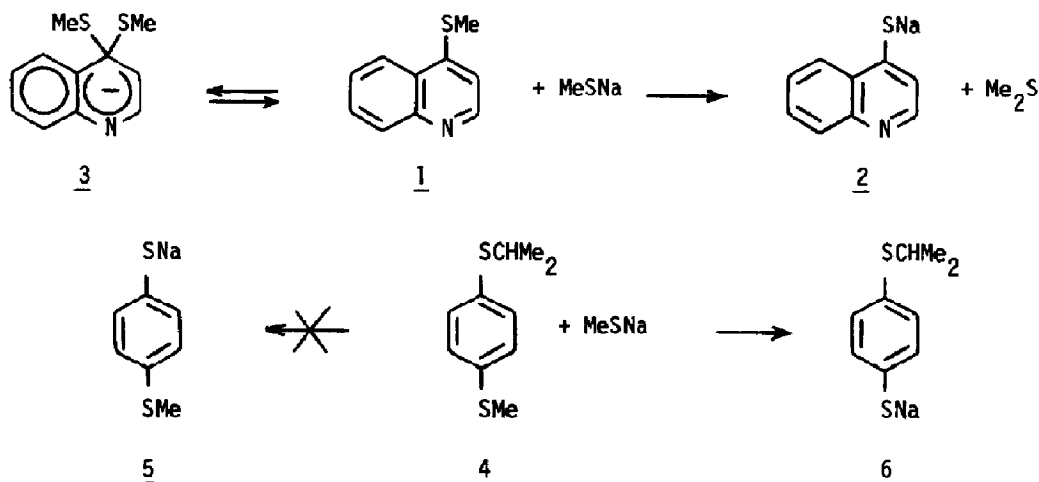
**Summary:** Aromatic thiols are obtained in good yields from unactivated aryl halides and excess MeSNa in HMPA.

In connection with other work<sup>1,2</sup> on the reactivity of halogeno benzenes with sodium alkane-thiolates in HMPA, we report in this communication some preliminary results concerning a simple, high yield synthesis of aromatic thiols which can be effected in a one-pot treatment of unactivated aryl halides with MeSNa in HMPA. This synthesis is based on two remarkable consecutive reactions: a nucleophilic aromatic substitution on unactivated aryl halides<sup>3</sup> which affords aryl methyl sulfides (1) followed by a nucleophilic aliphatic substitution which effects the cleavage of these sulfides to afford the aromatic thiols (2). The ease with which these reactions



occur is probably due to the enhanced reactivity of the nucleophile in the reaction medium employed.<sup>1</sup> The reactions are carried out by heating at 100°C the solution of the aromatic halide (1 mol) and MeSNa (3 mol) in HMPA. After acidification and extraction with ether, the following thiols were obtained (X in ArX, reaction times and % yields are given in the order): thiophenol (Cl, 5h, 90),  $\alpha$ -mercaptanaphthalene (Br, 3.5h, 90),  $\beta$ -mercaptanaphthalene (Br, 5h, 97), 4-mercaptobiphenyl (Br, 2h, 96), 2-mercaptothiophene<sup>4</sup> (Br, 2h, 88), 4-mercaptoquinoline<sup>4</sup> (Cl, 25h, 80), and 4-isopropylthio-thiophenol<sup>4</sup> (Cl, 2h, 90).<sup>5</sup> Otherwise, the final solution of the ArSNa in HMPA can be directly used for other reactions; thus, for instance, addition of ethyl iodide gave the corresponding aryl ethyl sulfides. In most cases reaction (1) is much faster than reaction (2) and thus the process can be stopped to obtain the aryl methyl sulfides in high yields; in the case of chlorobenzene reactions (1) and (2) have comparable rates and the thiophenolate is therefore present in the reaction mixture even at low conversions. In the case of the 4-chloroquinoline the first step is obviously very fast; 4-methylthioquinoline, 1, is formed quantitatively, at room temperature, a few minutes after the addition of MeSNa. The dealkylation reaction to give 2, on the contrary, required longer reaction times; very likely the preferred process in this case is the attack at the 4-position to give the intermediate 3 which then reverts to 1. Reaction of 4-chloro-

phenyl isopropyl sulfide with MeSNa affords the bis-sulfide 4, which selectively gives the



thiophenol 6 with no traces of 5. This result is in agreement with the previously observed difficulty of effecting the carbon-sulfur cleavage in the aryl isopropyl sulfides<sup>1,2</sup> and supports the hypothesis that reaction (2) is proceeding via an S<sub>N</sub>2 mechanism.

The results now described also indicate that methyl can be used as a protective group of the thiol function which can then be regenerated by treatment with MeSNa in HMPA; this procedure seems to present several advantages in respect to other methods described in the literature.<sup>6</sup> Further work is in progress to investigate this aspect as well as to test the general application of the procedure described above for the synthesis of substituted aromatic thiols. Preliminary results indicate that reactions (1) and (2) can be also applied to vinyl halides.

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#### REFERENCES and NOTES

- 1) P.Cogolli, F.Maiolo, L.Testaferri, M.Tingoli, and M.Tiecco, *J.Org.Chem.*, **44**, 2642 (1979); P.Cogolli, L.Testaferri, M.Tingoli, and M.Tiecco, *J.Org.Chem.*, **44**, 2636 (1979).
- 2) L.Testaferri, M.Tingoli, and M.Tiecco, *J.Org.Chem.*, submitted for publication.
- 3) Reactions (1) are believed to occur through the S<sub>N</sub>Ar mechanism.<sup>1</sup>
- 4) Isolated as the ethyl sulfide obtained by adding EtI to the cooled reaction mixture.
- 5) The obtained thiols and sulfides have physical properties identical to those described in the literature; the structures were easily confirmed by nmr and ir spectra.
- 6) Y.Wolman, "The Chemistry of the Thiol Group", S.Patai Ed., Vol.2, Wiley, London, 1974, p.669; N.Kornblum and A.Scott, *J.Amer.Chem.Soc.*, **96**, 590 (1974).

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