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A Convenient Synthesis of Trifluoromethyl Aryl Sulfides

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Abstract : Trifluoromethyl aryl sulfides are obtained in moderate/good yields by heating potassium trifluoroacetate and aryl disulfides in sulfolane Copyright © 1996 Elsevier Science Ltd

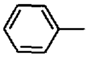
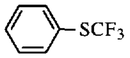
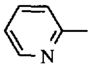
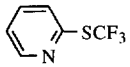
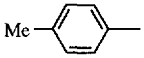
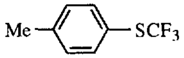
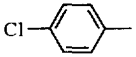
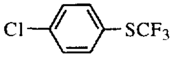
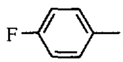
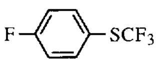
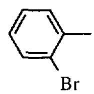
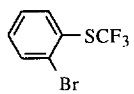
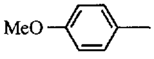
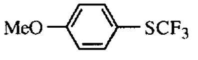
Trifluoromethyl aryl sulfides are important intermediates in the preparation of biologically active compounds,[1] dyes,[2] and useful chemical reagents.[3] So far, compounds of this type have been obtained mainly by multi-step procedures involving chlorination of methyl aryl sulfides followed by chloride/fluoride exchange;[4, 5] however, *o*-substituted derivatives cannot be obtained in this way. More direct methods for the introduction of the trifluoromethylthio group into an aromatic ring include reactions of trifluoromethylsulfenyl halides with aromatic compounds[6] or Grignard reagents,[7] trifluoromethylation of thiols by trifluoromethyl halides,[8] as well as reactions of metallic trifluoromethylthio derivatives with aromatic halides.[9] Most of these methods suffer from harsh reaction conditions, and/or expensive and toxic reagents. Free radical approaches to perfluoroalkylthio derivatives under mild conditions have also been described, and involve the reaction of perfluoroalkyl radicals, generated by decarboxylation[10] or from perfluoroalkyl halides,[11a] with disulfides. Very recently, a similar but ionic reaction of disulfides with trifluoromethyl trimethylsilane has appeared in the literature.[11b]

$$CF_3COOK \quad + \quad Ar-S-S-Ar \quad \xrightarrow[-\,CO_2]{\text{sulfolane} \,/\, \Delta} \quad Ar-SCF_3 \quad + \quad Ar-SK \qquad \text{(eq.1)}$$

We now wish to report a novel and experimentally convenient method for the preparation of various trifluoromethyl aryl sulfides starting from commercially available reagents, based on the thermally induced decarboxylation of potassium trifluoroacetate in the presence of aryl disulfides. It consists in simply heating a mixture of potassium trifluoroacetate and the corresponding disulfide in sulfolane, the product trifluoromethylsulfide being isolated by distillation (eq. 1). A typical experimental procedure is as follows: 4-Fluorophenyl disulfide (3.49 g; 13.72 mM), potassium trifluoroacetate (4.107 g; 27 mM) and sulfolane (3 ml) are added to a flask set for distillation, which is then immersed into a preheated oil bath (180°C). The heterogeneous mixture quickly solubilizes, and is rapidly heated to 230°C with stirring. Soon, trifluoromethyl-4-fluorophenyl sulfide begins to distill, and is collected in the receiving flask. The reaction is complete within 10 min. The crude product contains about 3% by weight of sulfolane. Redistillation affords 2.2 g (82% based on the disulfide used) of analytically pure compound.[12] In this way, various trifluoromethyl aryl sulfides were prepared in moderate/good yields. The results are summarized in Table 1.

The reaction proceeds via the trifluoromethyl carbanionic intermediate, and is mechanistically similar to the previously described malonoester decarboxylation in the presence of diphenyl disulfide.[13] In our case, however, poor yields were obtained when DMSO or HMPA were used as solvents. Heating trifluorocarboxylate salts in the presence of copper salts has been used to introduce a trifluoromethyl group into aromatic compounds.[14]

Tablel. Thermal reaction of potassium trifluoroacetate with aryl disulfides.

Ar in disulfide	product [a]	yield (%)[b]	B. p. / 760 mmHg (b.p. lit.)
		56	75-77°C (77-78°C) [8] (140°C/754 mmHg) [9]
		32	130-132°C (130°C) [9, 10]
 c)		51	163-165°C (166-167°C) [8,9]
 c)		56	162°C (74°C/19 mmHg) [8]
 c)		82	112-115°C
 c)		48	d)
		50	185°C (90°C/19 mmHg) [8]

a) All products are fully characterized by ^{1}H, ^{13}C, IR and MS spectra, which are in agreement with the proposed structures. b) Isolated yields of pure compounds. c) Prepared from the corresponding thiols according to the previously described procedure.[15] d) Purified by column chromatography on SiO_2, eluent: pentane.

In summary, thermal decomposition of potassium trifluoroacetate in presence of aryl disulfides is a novel, short, and experimentally simple route to trifluoromethyl aryl sulfides from commercially available starting materials.

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