One-pot synthesis of aryl sulfoxides and sulfonium salts from sulfinic acid as a novel sulfurizing agent

Kimihisa Yamamoto, Kenji Miyatake, Yukio Nishimura and Eishun Tsuchida*†

Department of Polymer Chemistry, Advanced Research Institute for Science and Engineering, Waseda University, Tokyo 169, Japan

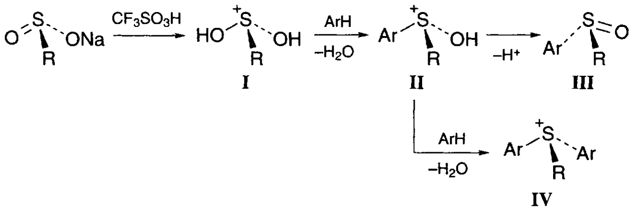
Sodium sulfinate reacts electrophilically with aromatics in trifluoromethanesulfonic acid to give the corresponding aryl sulfoxides and sulfonium salts.

Sulfoxide and sulfonium groups are interesting functional moieties possessing manifold reactivity for transformation into a variety of organic sulfur compounds. These transformations are useful for the synthesis of drugs and sulfur-substituted natural compounds.[1,2] In addition, aryl sulfonium salts have also been used extensively as photoactive cationic initiators[3,4] and for the photogeneration of protonic acid in the lithographic resist field.[5,6]

Sulfoxides are usually prepared by oxidation of the corresponding sulfides through a one-electron transfer mechanism. Aryl sulfoxides are also prepared directly by electrophilic substitution using aryl sulfinyl chlorides[7] or $SOCl_2$, but this process suffers not only from low conversions due to the lower reactivity of the reagents but also from low selectivity due to their thermal and chemical instability. Most sulfonium compounds have been synthesized *via* sulfides or sulfoxide compounds, *e.g.* the reaction of aryl Grignard reagents with diphenyl sulfoxide,[8] condensation of benzene with S_2Cl_2 in the presence of Cl_2 and $AlCl_3$,[9] copper-catalysed arylation of aryl sulfides with a diaryl iodonium hexafluorophosphate,[10] reaction of aryl sulfides with methyl trifluoromethanesulfonate[11] or oxidative coupling of aryl alkyl sulfides.[12]

Sulfinic acids, as a result of their high reactivity and the ambident character of the sulfinate anion, are convenient starting materials for the synthesis of sulfones, sulfinic esters, sulfinamides and so on. However, electrophilic reaction of sulfinic acids through protonation of the sulfinyl group has not been reported. Here we report a novel one-pot synthesis of aryl sulfoxides and aryl sulfonium salts from the electrophilic reaction of sodium methane- or benzene-sulfinate and aromatics (Scheme 1).

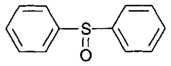
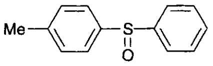
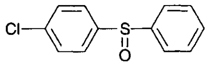
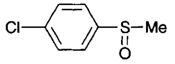
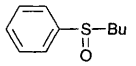
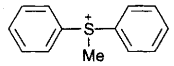
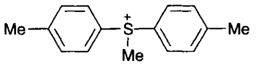
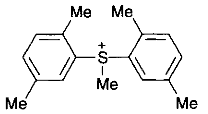
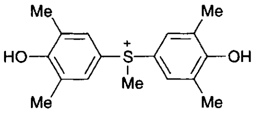
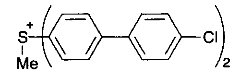
The reaction of sodium sulfinates with aromatics was performed in trifluoromethanesulfonic acid.‡ The sulfinates, barely soluble in the solvent, are gradually dissolved as the reaction progresses. After the reaction, the usual work-up gave the corresponding aryl sulfoxides and sulfonium salts (Table 1). In the case of the reaction of sodium benzenesulfinate with benzene, toluene or 4-chlorobenzene, the corresponding aryl sulfoxides were preferentially formed. This reaction is also applicable to aliphatic sulfinic acids, *e.g.* the reaction of sodium methanesulfinate§ and chlorobenzene resulted in the formation of 4-chlorophenyl methyl sulfoxide in 73% yield. Butyl phenyl sulfoxide was also obtained in 36% yield from sodium butanesulfinate and benzene. In the case of the reaction of toluene with sodium methanesulfinate, methylbis(4-tolyl)sulfonium trifluoromethanesulfonate was isolated in 86% yield; no other products were detected except for a 13% yield of the *ortho*-isomer, methyl(2-tolyl)(4-tolyl)sulfonium trifluoromethanesulfonate. Methanesulfinic acid reacts with *p*-xylene and 2,6-dimethylphenol to yield the corresponding sulfonium salts almost quantitatively.



Scheme 1

It is supposed that the reaction of sulfinic acid with aromatics proceeds through the electrophilic substitution reaction of dihydroxy(phenyl)- or (alkyl)-sulfonium **I** as an active species, formed by protonation of the oxygen atom (O=S<) of sulfinic acid in trifluoromethanesulfonic acid (Scheme 1) because the acidity of trifluoromethanesulfonic acid (H_o = −14.1) is greater than the pK_b (−2.3) of the sulfoxide group.[13] Besides, **I**

Table 1 Synthesis of aryl sulfoxides and sulfonium salts from sodium sulfinate and aromatics

Entry	R	ArH	σ_p^+	III or IV[a]	Yield[b] (%)
1	Ph	Benzene	0		98
2	Ph	Toluene	−0.31		98
3	Ph	Chlorobenzene	0.11		97
4	Me	Chlorobenzene	0.11		73
5	Bu	Benzene	0		36
6	Me	Benzene	0		92
7	Me	Toluene	−0.31		99[c]
8	Me	*p*-Xylene	−0.24		93
9	Me	2,6-Dimethyl-phenol	−1.06		99
10	Me	4-Chlorobi-phenyl	—		68[d]

[a] As trifluoromethanesulfonate. [b] The yield of the product was determined by gas chromatography. Sulfonium compounds were analysed as the corresponding sulfides, after demethylation. [c] Methylbis(4-tolyl)sulfonium salt = 86%, methyl(4-tolyl)(2-tolyl)sulfonium salt = 13%. [d] Isolated yield, as boiling temperature of the sulfide compound was too high to analyse the yield by GC.

possesses a lower LUMO level (−6.56 eV) in comparison with those of SCl_2 (−2.60 eV), S_2Cl_2 (−3.24 eV), MeSCl (−1.32 eV) and PhSCl (−1.55 eV) which are well-known to be conventional sulfurizing agents.¶ This means that **I** can act as a strong electrophile and can attack the aromatics to form the hydroxy(aryl)sulfonium trifluoromethanesulfonate **II**. The product selectivity (sulfoxide–sulfonium) depends on the relative reactivity of the aromatic and **II**. Aromatics with electron-withdrawing groups such as chlorobenzene (Brown's substituent constant: $\sigma_p^+ = 0.11$) suppress the electrophilic substitution of **II**, which leads to predominant formation of the corresponding sulfoxide **III**, through deprotonation by adding water after the reaction. The sulfonium salt **IV** formation occurs preferentially in high yield in the case of aromatics with lower σ_p^+.

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Footnotes

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‡ *Typical procedure*. Sodium benzenesulfinate dihydrate (0.80 g, 4 mmol) and toluene (0.74 g, 8 mmol) were stirred in trifluoromethanesulfonic acid (5 ml) at room temperature for 12 h. The colour of the mixture turned from colourless to yellow with time. After the reaction, the mixture was poured into 150 ml of water and the organic compound was recovered by extraction with two 100 ml portions of dichloromethane. Evaporation of the organic layer gave 4-tolyl phenyl sulfoxide in 98% yield, determined by gas chromatography. All products were characterised by IR and NMR spectroscopy.

§ Sodium methanesulfinate and sodium butanesulfinate were prepared according to the previously reported method. See; Y. Ueno, A. Kojima and M. Okawara, *Chem. Lett.*, 1984, 2125.

¶ Reactivity (stability) of the sulfonium cations was evaluated from LUMO (lowest unoccupied molecular orbital) energies calculated by a semi-empirical molecular orbital calculation PM3 (MOPAC ver. 6.00). LUMO energies were calculated using the keyword ENPAR. An optimized structure was obtained using the keyword PULAY. PM3 calculations were performed on a Fujitsu VP2200 supercomputer.

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