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An Efficient Method for the Oxidation of Sulfides to Sulfones

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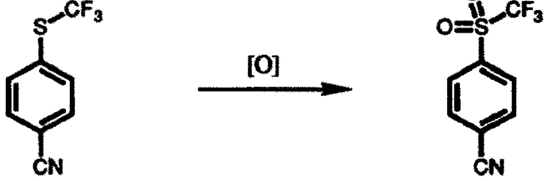
Abstract: Ruthenium trichloride - sodium periodate is a highly efficient and powerful system for the oxidation of unreactive sulfides to sulfones.

Sulfones are useful intermediates in organic synthesis.[1] One general method for the preparation of sulfones is the oxidation of sulfides.[2] Numerous reagents can effect this transformation, as evidenced by recent reports from Kaldor (OsO_4-NMO)[3] and Kende (n-Pr_4NRuO_4-NMO)[4]. However, oxidation of highly electron-deficient sulfides can often be problematic. During our research we required a powerful reagent to oxidize the highly unreactive sulfide **1** to sulfone **2**, since mild conditions (e.g.: OsO_4-NMO, MCPBA, and Jones' reagent) failed to effect this reaction. Chromium trioxide in refluxing acetic acid[5] was effective but yields were relatively low.

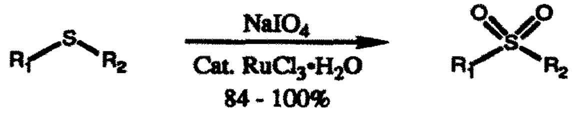
Scheme 1



1 **2**

Djerassi and co-workers reported in 1953 that diphenyl sulfide could be oxidized to the corresponding sulfone in good yield with an equimolar amount of ruthenium tetroxide.[6] More recently, Sharpless has shown that in the presence of a catalytic amount of ruthenium trichloride, sodium periodate can be employed to effect various oxidations,[7] including oxidation of sulfites to sulfates.[8] We report here that the ruthenium trichloride-sodium periodate system oxidizes sulfides to sulfones in excellent yield. Results are summarized in Table 1.[9]

Table 1 **Oxidation of Sulfides to Sulfones**

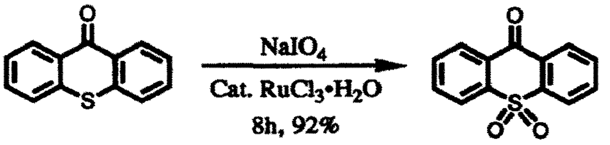


Entry[a]	R_1	R_2	Time (h)[b]	Yield (%)[c]	mp (°C)[d]
A	CF_3	Ph	1.0	91	oil
B	CF_3	*p*-C_6H_4CN	12	98	97-98
C	Ph	Ph	1.0	100	127-128 (lit. 123)[12a]
D	*p*-$C_6H_4NO_2$	*p*-$C_6H_4NO_2$	3.0	85[e]	280-281
E	*t*-Bu	*t*-Bu	1.0	84	128-128.5
F	*i*-Pr	*i*-Pr	1.0	90	oil (lit. 36)[12b]
G	Et	$PhCH_2$	1.0	90	88-88.5 (lit. 84)[12c]
H	Thioxanthen-9-one		8.0	92	218-219
I	allyl	Ph	1.0	multiple products	

a. All reactions were carried out on 1 mmole scale. b. All reactions other than Entries B, D and H were complete by TLC within 20 minutes, though they were allowed to stir for 1 hr. c. All yields are isolated yields. Products were characterized by proton-NMR and mass spectroscopy. d. Melting points were measured on an Electrothermal melting point apparatus and were uncorrected. e. Extracted with THF-EtOAc-CH_2Cl_2 (3:3:1).

This new ruthenium trichloride-based method is a relatively powerful system for oxidation of sulfides to sulfones. The reactions were usually complete in 20 minutes, although they were allowed to proceed for 1 hour. Trifluoromethyl *p*-cyanophenyl sulfide was converted to the sulfone in quantitative yield at room temperature in 12 hours (Entry B). Oxidation of diphenyl sulfide to diphenyl sulfone, which required 24 hours by Kaldor's or Kende's catalytic methods,[3,4] was complete in 20 minutes with sodium periodate in the presence of a catalytic amount of ruthenium trichloride, providing the sulfone in 100% yield (Entry C). Electron-withdrawing groups slow down the reaction, as in, for example, the oxidation of thioxanthen-9-one which required 8 hours at room temperature (*Scheme 2* and Entry H). Steric hinderance, however, did not seem to affect the rate of oxidation, as di-*t*-butyl sulfide was oxidized to di-*t*-butyl sulfone in excellent yield within 20 minutes (Entry E). Although it has been shown that sodium periodate oxidizes sulfides to sulfoxides,[10] it failed to oxidize phenyl trifluoromethyl sulfide in a control experiment. The intermediate sulfoxide was not detected for any of the reactions listed in *Table 1*. The amount of ruthenium trichloride required for the oxidation is as little as 0.05 mole percent. The reaction is exothermic, so cooling with an ice bath is recommended, particularly for large scale reactions.

Scheme 2



Acetate and epoxide functional groups should be tolerated by these conditions, as shown by Sharpless and co-workers.[7] However, carbon-carbon double bonds will be cleaved: the oxidation of allyl phenyl sulfide under these conditions gave multiple products including the starting allyl phenyl sulfide, the product sulfone and the aldehyde and carboxylic acid (Entry I). While Sharpless has shown that benzyl methyl ether can be oxidized to methyl benzoate under these conditions,[7] benzyl ethyl sulfide was converted to the corresponding sulfone in 90% yield, indicating that sulfide oxidation is much faster than benzylic oxidation.

A representative experiment is as follows. To a round-bottomed flask with a magnetic stirrer were sequentially added *p*-cyanophenyl trifluoromethyl sulfide (204 mg, 1 mmol, Fairfield supply), carbon tetrachloride (2 ml), acetonitrile (2 ml), water (4 ml)[11] and sodium periodate (642 mg, 3 mmol). To this suspension was added ruthenium trichloride hydrate (*ca* 0.1 mg, 0.05 mol%). The resulting mixture was stirred at room temperature. A white precipitate was formed during the reaction. After 12 hours, the reaction was complete by TLC analysis. Water (30 ml) and ether (30 ml) were introduced. After separation, the ether layer was washed successively with saturated sodium bicarbonate and sodium chloride solutions. Drying over magnesium sulfate, filtration through a pad of silica gel and concentration provided pure *p*-cyanophenyl trifluoromethyl sulfone (230 mg, 98%) as a white solid (m.p. 97-98 °C).

In conclusion, we have demonstrated that sodium periodate-ruthenium trichloride is a powerful, yet chemoselective, reagent for the oxidation of sulfides to sulfones. The catalytic turnover is very efficient and only about 0.05 mol% of ruthenium catalyst is required. This method is particularly useful for the oxidation of electron-deficient sulfides.

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9. Satisfactory spectral data were obtained for all products.

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11. In contrast to Sharpless' observation,[7] the ratio of the solvents did not seem to affect the rate of the oxidation of sulfides to sulfones, although use of acetonitrile as co-solvent is important for a rapid reaction rate. In a control experiment in the absence of acetonitrile, the oxidation of diphenyl sulfide was extremely slow.

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