A Mild and Highly Efficient Oxidation of Sulfides to Sulfoxides with Periodic Acid Catalyzed by $FeCl_3$

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In memory of Professor Sang Chul Shim who passed away on 11 April, 2002. Professor Shim has provided significant contribution to Organic Photochemistry and made tremendous efforts for the betterment of The Korean Chemical Society.

Abstract: An excellent method for the selective oxidation of sulfides to sulfoxides with periodic acid (H_5IO_6) catalyzed by $FeCl_3$ in MeCN has been devised. The reported procedure is fast, simple and the yields are excellent (>98%) in most cases with reaction time of less than 2 minutes.

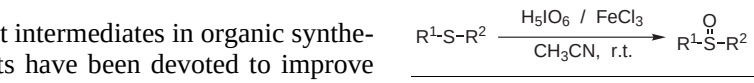
Key words: sulfides, sulfoxides, periodic acid, iron chloride, hypervalent

Sulfoxides are important intermediates in organic synthesis and numerous efforts have been devoted to improve their method of preparation.[2] The use of H_2O_2 as a terminal oxidant utilizes hexafluoropropan-2-ol[3] as the *catalytic* solvent for efficient sulfoxidations. Tetrabromoaurate(III)[4] is a catalyst for the oxidation of sulfides by nitric acid in a biphasic system. Iodosylbenzene[5] in the presence of benzeneseleninic acid oxidizes sulfides to sulfoxides. The combination of mercury(II) oxide/iodine[6] serves as a good oxidizing agent of sulfides. Rhenium(V) oxo complex plus diphenyl sulfoxide[7] is a mild oxidant for sulfoxidation. Sulfides[8] are transformed into sulfoxides through the catalytic action of camphorsulfonic acid on *tert*-butyl hydroperoxide. Oxo(salen) chromium(V) complexes[9] transfer oxygen to sulfides for the sulfoxidation. Silica gel has been found to mediate the oxidation of sulfides with the help of *meso*-tetraphenylporphyrineiron chloride/iodosylbenzene,[10] magnesium monoperoxyphthalate,[11] molecular bromine,[12] and *tert*-butyl hydroperoxide.[13] Similar reaction[14] can occur on the surface of moist alumina with calcium hypochlorite.

In recent years, hypervalent iodine atoms[15–19] are employed to oxidize various organic substrates with or without catalyst. Very recently, oxidation of alcohols with H_5IO_6/2,2,6,6-tetramethylpiperidinyl-1-oxyl[20] has been found to yield the corresponding carbonyl compounds. We would like to report here an effective method of oxidation of sulfides to sulfoxides utilizing $H_5IO_6/FeCl_3$.

H_5IO_6[18] alone exhibits substantial oxidative ability to oxidize sulfides to sulfoxides in pyridine for longer reaction time (3.5 h). *p*-Bromothioanisole is used as a model compound for sulfoxidation by H_5IO_6 with or without catalyst in MeCN in control experiments. The oxidation without $FeCl_3$ takes longer period (17 min) than the reaction with the catalyst (1.5 min) indicating the catalytic effect (Table 1, entry 3). The optimum quantity of $FeCl_3$ turns out to be 3 mol% that produces 96% yield of diphenyl sulfoxide in 10 min (Table 1, entry 11).

Table 1 Transformation of Sulfides into Sulfoxides[a]



Entry	Sulfide		Time (min)	Yield of Sulfoxide (%)[b]
	R^1	R^2		
1	Ph	Me	2	99
2	*p*-MeC_6H_4	Me	1.5	99
3	*p*-BrC_6H_4	Me	1.5 (17)[c]	99 (99)[c]
4	*m*-ClC_6H_4	Me	2	98
5	*p*-ClC_6H_4	Me	1	98
6	*p*-CNC_6H_4	Me	5	97
7	*p*-$NO_2C_6H_4$	Me	15	96
8	Ph	Et	1.5	99
9	$PhCH_2$	Me	1.5	99
10	$PhCH_2$	Et	1	97
11	Ph	Ph	10	96
12	$PhCH_2$	Ph	2	99
13	$PhCH_2$	$PhCH_2$	2	99
14	$Me(CH_2)_2$	$Me(CH_2)_2$	1	99
15	$Me(CH_2)_3$	$Me(CH_2)_3$	1	99
16	Ph	CH_2Cl	5	80
17		-	60	64

[a] Reagents and conditions: $FeCl_3$: 0.03 mmol, H_5IO_6: 1.1 mmol, sulfide: 1 mmol, MeCN: 1 mL.
[b] Yields of isolated products.
[c] Reaction time and yield without $FeCl_3$.

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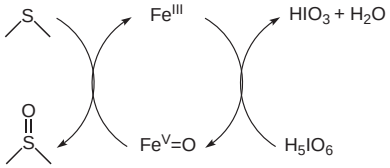
Numerous sulfides were subject to sulfoxidation under the stoichiometric condition given in Table 1. Substituted thioanisoles (entries 2–7) undergo very smooth oxidation but indicate modest rate retardation due to the presence of electron-withdrawing groups (entries 6 and 7). Unsubstituted (entry 1) and some substituted thioanisoles (entries 2–5) react in less than 2 minutes with over 98% yield. The *sluggish* reaction of *p*-$NO_2C_6H_4SMe$ showing 96%/15 minutes (entry 7) can be regarded as very effective and fast when compared with other oxidations of *p*-$NO_2C_6H_4SMe$ employing different methods.[4,5,10,11,12,14] Insertion of methylene on either side of sulfur atom of thioanisole may engender again the similar reactivity in terms of yield and reaction time (entries 8–10). Our yield (%)/time for ethyl phenyl sulfide (entry 8) indicates 99%/1.5 minutes that is even better than the previous oxidation of ethyl phenyl sulfide[4] which is known to be one of the fast reaction. Diphenyl sulfide may exert a little steric hindrance for the oxidation as exhibited by the longer time of 10 minutes with 96% yield (entry 11). Such a rate retardation[4,8,10–12,14,17] has already been clearly observed in the oxidation of diphenyl sulfide with longer reaction time (1–28 h) giving low yield (60–100%). However, the slow process can be nearly overcome when diphenyl sulfide is oxidized with present method. The insertion of methylene into diphenyl sulfide (entries 12 and 13) reduces the reaction time from 10 to 2 minutes indicating the release of steric hindrance. Similarly, linear dialkyl sulfides (entries 14 and 15) also react very quickly with excellent yields. Chloromethyl phenyl sulfide gave the corresponding sulfoxide in 80% yield (entry 16) and 1,4-thioxane (entry 17) gave 64% of product within one hour. The possible pathway for the sulfoxidation may due to the dissociation of H_5IO_6 to iodic acid and nascent oxygen, that reacts with Fe(III) to form Fe(V)=O. This hypervalent Fe(V)=O state transfers oxygen to sulfide for the sulfoxidation (Scheme 1).



Scheme 1

In summary, we have presented a most convenient and effective method of sulfoxidation. The rates of oxidation of substituted thioanisoles are slightly reduced when *p*-CN and *p*-NO_2 occupy the phenyl ring. Steric effect caused by the phenyl ring of diphenyl sulfide slightly delays the formation of diphenyl sulfoxide. This indicates that the rate of sulfoxidation is only modestly influenced by electronic and steric effects. Therefore, our method can be considered as the most outstanding methodology of sulfoxidation.

Sulfoxidation; General Procedure

$FeCl_3$ (5 mg, 0.03 mmol) and sulfide (1 mmol) were dissolved in MeCN (1 mL) and stirred for 5 min. To this solution was added H_5IO_6 (1.1 mmol) at once. The reaction was monitored by TLC at regular intervals. The reaction was quenched by the addition of a sat. aq solution of $Na_2S_2O_3$ and extracted with CH_2Cl_2 (4 × 5 mL). The combined organic layers was dried (Na_2SO_4) and evaporated to dryness. The products were purified by flash column chromatography on silica gel and identified by ^1H, ^{13}C NMR and GC-MS. All sulfoxides thus obtained were identified by comparing NMR data with the values reported in the literature[11,12,17,22] and those of the authentic samples.

Methyl Phenyl Sulfoxide (Entry 1)[11]

^1H NMR ($CDCl_3$, 200 MHz): δ = 2.73 (s, 3 H), 7.51–7.55 (m, 3 H), 7.64–7.69 (m, 2 H).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 43.83, 123.36, 129.24, 130.92, 145.51.

Methyl *p*-Tolyl Sulfoxide (Entry 2)[11]

Mp 40 °C (Lit.[21] mp 41–42 °C).

^1H NMR ($CDCl_3$, 200 MHz): δ = 2.42 (s, 3 H), 2.72 (s, 3 H), 7.34 (d, 2 H, *J* = 8.2 Hz), 7.55 (d, 2 H, *J* = 8.2 Hz).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 21.36, 44.06, 123.50, 130.00, 141.48, 142.53.

4-Bromophenyl Methyl Sulfoxide (Entry 3)[22]

Mp 81 °C (Lit.[21] mp 82–84 °C).

^1H NMR ($CDCl_3$, 200 MHz): δ = 2.72 (s, 3 H), 7.53 (d, 2 H, *J* = 8.8 Hz), 7.68 (d, 2 H, *J* = 8.8 Hz).

^{13}C NMR ($CHCl_3$, 50 MHz): δ = 43.86, 125.03, 125.30, 132.44, 144.81.

3-Chlorophenyl Methyl Sulfoxide (Entry 4)

^1H NMR ($CDCl_3$, 200 MHz): δ = 2.71 (s, 3 H), 7.43–7.50 (m, 3 H) 7.64 (s, 1 H).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 43.99, 121.57, 123.60, 130.56, 131.16, 135.67, 147.77.

MS (EI, 70 eV): *m*/*z* = 176, 174, 159, 131, 111, 99, 75, 63, 50, 39.

4-Chlorophenyl Methyl Sulfoxide (Entry 5)[6]

Mp 45 °C (Lit.[21] mp 47–48 °C).

^1H NMR ($CDCl_3$, 200 MHz): δ = 2.72 (s, 3 H), 7.51 (d, 2 H, *J* = 8.8 Hz), 7.61 (d, 2 H, *J* = 8.8 Hz).

^{13}C NMR ($CHCl_3$, 50 MHz): δ = 43.85, 124.86, 129.50, 137.09, 144.16.

4-Cyanophenyl Methyl Sulfoxide (Entry 6)[14]

Mp 85 °C (Lit.[14] mp 86–88 °C).

^1H NMR ($CDCl_3$, 400 MHz): δ = 2.73 (s, 3 H), 7.73 (d, 2 H, *J* = 8.0 Hz), 7.80 (d, 2 H, *J* = 8.0 Hz).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 43.79, 114.68, 117.63, 124.23, 132.92, 151.43.

MS (EI, 70 eV): *m*/*z* = 165, 150, 134, 122, 102, 90, 75, 63, 51, 39.

Methyl 4-Nitrophenyl Sulfoxide (Entry 7)[14]

Mp 146 °C (Lit.[14] mp 147–148 °C).

^1H NMR ($CDCl_3$, 400 MHz): δ = 2.81 (s, 3 H), 7.86 (d, 2 H, *J* = 8.4 Hz), 8.41 (d, 2 H, *J* = 8.4 Hz).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 44.81, 124.43, 124.61, 149.41, 153.16.

Ethyl Phenyl Sulfoxide (Entry 8)[14]
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.20 (t, 3 H, *J* = 7.6 Hz), 2.82 (dq, 2 H, *J* = 12.8 Hz), 7.46–7.65 (m, 5 H).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 5.80, 50.10, 123.99, 128.98, 130.77, 143.07.

MS (EI, 70 eV): *m*/*z* = 126, 110, 97, 78, 65, 51, 39.

Benzyl Methyl Sulfoxide (Entry 9)[22]
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.46 (t, 3 H), 3.87 (d, 1 H, *J* = 12.8 Hz), 4.06 (d, 1 H, *J* = 12.8 Hz), 7.27–7.40 (m, 5 H).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 37.25, 60.26, 128.43, 128.97, 129.59, 129.99.

Benzyl Ethyl Sulfoxide (Entry 10)
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.34 (t, 3 H, *J* = 7.4 Hz), 2.61 (dq, 2 H, *J* = 8 Hz), 3.99 (q, 2 H, *J* = 12.8 Hz), 7.28–7.45 (m, 5 H).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 6.53, 43.96, 57.48, 128.25, 128.90, 129.83, 129.88.

MS (EI, 70 eV): *m*/*z* = 168, 91, 77, 65, 51, 39.

Diphenyl Sulfoxide (Entry 11)[14]
Mp 68 °C (Lit.[23] mp 69–71 °C).

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.43–7.68 (m).

^{13}C NMR ($CHCl_3$, 50 MHz): δ = 124.89, 129.38, 131.10, 145.83.

Benzyl Phenyl Sulfoxide (Entry 12)[14]
Mp 121 °C (Lit.[23] mp 122–123 °C).

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.98 (d, 1 H, *J* = 12.8 Hz), 4.09 (d, 1 H, *J* = 12.8 Hz), 6.95–7.00 (m, 2 H), 7.22–7.28 (m, 3 H), 7.35–7.45 (m, 5 H).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 63.07, 123.95, 127.78, 127.98, 128.39, 128.65, 129.90, 130.71, 142.25.

Dibenzyl Sulfoxide (Entry 13)[14]
Mp 133 °C (Lit.[14] mp 133–135 °C).

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.85 (d, 2 H, *J* = 12.8 Hz), 3.92 (d, 2 H, *J* = 12.8 Hz), 7.25–7.38 (m, 10 H).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 57.12, 128.25, 128.84, 130.06, 130.03.

Dipropyl Sulfoxide (Entry 14)[14]
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.08 (t, 6 H, *J* = 7.2 Hz), 1.85 (sext, 4 H, *J* = 7.6 Hz), 2.50–2.74 (m, 4 H).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 13.41, 16.26, 54.36.

Dibutyl Sulfoxide (Entry 15)[11]
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.92 (t, 6 H, *J* = 7.2 Hz), 1.37–1.50 (m, 4 H), 1.70 (quin, 4 H, *J* = 7.4 Hz), 2.57–2.66 (m, 4 H).

^{13}C NMR ($CHCl_3$, 100 MHz): δ = 13.27, 21.66, 24.22, 51.76.

Chloromethyl Phenyl Sulfoxide (Entry 16)[24]
^{1}H NMR ($CDCl_3$, 200 MHz): δ = 4.41 (s, 2 H), 7.56–7.60 (m, 3 H), 7.69–7.74 (m, 2 H).

^{13}C NMR ($CHCl_3$, 50 MHz): δ = 61.43, 124.91, 129.45, 132.27.

1,4-Thioxane-4-oxide (Entry 17)[11]
Mp 42 °C (Lit.[25] mp 41–43 °C).

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.73 (m, 2 H), 2.99 (m, 2 H), 3.83 (m, 2 H), 4.54 (m, 2 H).

^{13}C NMR ($CHCl_3$, 50 MHz): δ = 46.54, 59.29.

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