Mild and Facile Preparation of Sulfoxides from Sulfides using Titanium(III) Chloride/Hydrogen Peroxide

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Because of the synthetic versatility of sulfoxides, the selective oxidation of sulfides to corresponding sulfoxides without generation of sulfones has been explored rather extensively and several procedures have been reported in recent years[1-8]. However, the selective oxidation of sulfides bearing bulky groups or highly electron-withdrawing substituents still remains a difficult problem.

In this paper we report a mild and facile preparation of sulfoxides using the titanium(III) trichloride/hydrogen peroxide reagent (Scheme **A**). This procedure was found to satisfy the following requirements: (a) the oxidation is highly selective and mild, yielding only sulfoxides but no sulfones even in the oxida-

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Table. Oxidation of Sulfides **1** using Titanium(III) Chloride/Hydrogen Peroxide

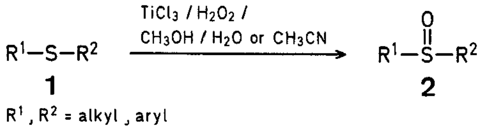
Sulfide 1 No.	R^1	R^2	Reaction time	Molar ratio 1/H_2O_2/$TiCl_3$	Yield[a] [%]	m.p. [°C] or b.p. [°C]/torr	
						found	reported
1a	—$(CH_2)_4$—		5 min	1/7/2	98	45°/3	—[b]
1b	t-C_4H_9	t-C_4H_9	5 min	1/10.5/2	95	104–105°/3	105°/3[12]
1c	CH_3	C_6H_5	5 min	1/7/2	100	104°/3	83–85°/0.1[6]
1d	C_6H_5	$C_6H_5CH_2$	5 min	1/7/2	98	122–123°	122–123°[13]
1e	CH_3	4-O_2N—C_6H_4	10 min	1/7/2	100	157–159°	157–160°[14]
1f	$C_6H_5CH_2$	$C_6H_5CH_2$	15 min	1/7/2	98	132–134°	132–135°[6]
1g	C_6H_5	C_6H_5	5 min	1/5.6/2	100	69–72°	69–71°[6]
1h	dibenzothiophene		20 min	1/7/2	99	181–183°	185–187°[8]
1i	C_6H_5	CH_2CN	15 min[c]	1/7/2	95	64–65°	63.5°[15]
1j	2-pyridyl	CH_3	5 min[c]	1/7/2	93	117°/6	117°/6[9]

[a] Yield of isolated, crude product of 95% purity as determined by G.L.C. analysis (conditions: 20% OV-1,1 m glass column).

[b] Compared with a commercial sample of 96% purity as supplied by Alderich Chemical Co.

[c] Reaction at 0 °C.

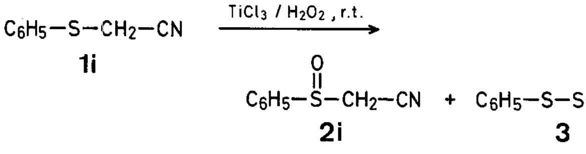
tion of diphenyl sulfide; (b) the oxidation is complete within a few minutes; (c) the procedure is very simple and the isolation of sulfoxides can be carried out readily.



$$R^1-S-R^2 \xrightarrow[CH_3OH\,/\,H_2O\text{ or }CH_3CN]{TiCl_3\,/\,H_2O_2\,/} R^1-\overset{O}{\overset{\|}{S}}-R^2$$

Scheme A

The oxidation of a small amount, e.g. 1.3 g, of diphenyl sulfide (**1g**) with the reagent was found to be complete within 5 min at room temperature without any formation of the corresponding sulfone. After extracting the reaction mixture with chloroform, only the sulfoxide **2g** was obtained quantitatively. The results of oxidations of a few representative sulfides are listed in the Table. In the oxidation of di-t-butyl sulfide (**1b**), a relatively large amount of hydrogen peroxide was necessary because of the low reactivity due to the bulkiness. When a phenyl sulfide having an α-active methylene group (e.g. **1i**) was oxidized with the reagent at room temperature, both diphenyl disulfide (**3**; as the S-dealkylated product) and the sulfoxide **2i** were formed. However, this undesirable side reaction can be avoided by performing the reaction at 0 °C (Scheme **B**).

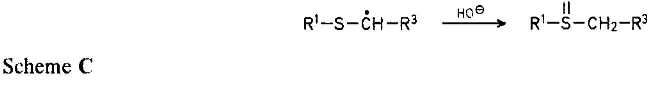


$$C_6H_5-S-CH_2-CN \xrightarrow{TiCl_3\,/\,H_2O_2,\text{ r.t.}} C_6H_5-\overset{O}{\overset{\|}{S}}-CH_2-CN + C_6H_5-S-S-C_6H_5$$

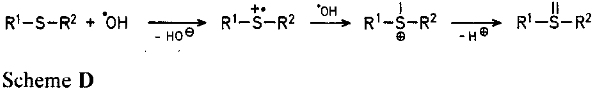
Scheme B

Recently, much attention has been focussed on pyridyl methyl sulfoxide (**2j**) because of its metal chelating ability[9]. The oxidation of the sulfide **1j** to the sulfoxide **2j** with m-chloroperbenzoic acid or hydrogen peroxide requires long reaction times, however, the sulfide **1j** was oxidized smoothly by the present reagent to the corresponding sulfoxide **2j** in a quantitative yield at 0 °C. In the case of **1e**, the mixed solvent system acetonitrile/methanol was used instead of methanol/water, since p-nitrophenyl methyl sulfide was not soluble in aqueous media.

It has been suggested[10,11,12] that in reactions between sulfides and hydroxyl radicals, the α-sulfenyl radical is formed after the initial formation of the sulfenium cation radical as the key intermediate (Scheme **C**). However, the facile formation of di-t-butyl or diphenyl sulfoxide in this reaction may be interpreted in terms of a direct coupling of the hydroxyl radical with the cation radical formed at the sulfur atom of di-t-butyl or diphenyl sulfide (Scheme **D**)[11].



Scheme C



Scheme D

Oxidation of Sulfides 1 to Sulfoxides 2 using the Titanium(III) Chloride/Hydrogen Peroxide Reagent; Typical Procedure:

To a solution of diphenyl sulfide (**1g**; 1.3 g, 7 mmol) and titanium(III) chloride (16% aqueous solution, 10 ml; from Wako Chemicals) in methanol + water (100 ml + 20 ml), hydrogen peroxide (30% aqueous solution, 3.2 ml) in methanol (15 ml) is added dropwise at room temperature with stirring and monitoring the consumption of the sulfide by T.L.C. (alumina plates, Merck GF$_{254}$, type 60/E, eluent: 1:1 chloroform/ethyl acetate). When the starting sulfide has completely disappeared (within $\sim$5 min), the reaction is stopped at once by adding water (50 ml). The reaction mixture is extracted with chloroform (4 × 100 ml). The extract is dried with anhydrous magnesium sulfate. Upon removing chloroform in vacuo, the corresponding sulfoxide **2g** is obtained as the only product; yield: 1.4 g (100%).

In the oxidation of p-nitrophenyl sulfide, a mixture of acetonitrile/methanol (5:2) is used as solvent. In all cases, only the sulfoxides were formed as oxidation products, as shown by T.L.C. and G.L.C. analyses (Table).

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