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An Efficient Oxidation of Sulfides to Sulfones Using 2-Methylpropanal and Dioxygen

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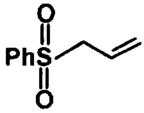
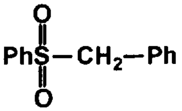
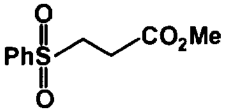
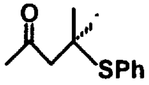
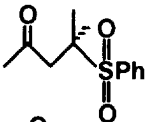
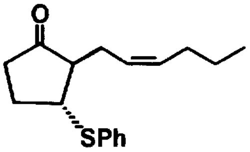
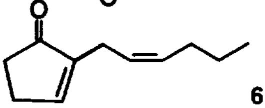
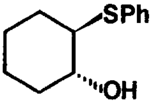
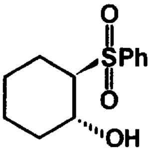
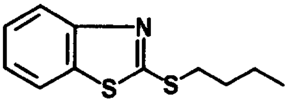
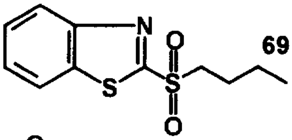
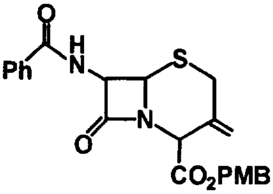
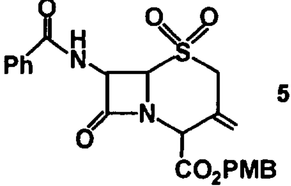
Abstract: *A wide range of sulfides can be oxidized to the corresponding sulfones in high yields in the presence of molecular oxygen and five equivalent of 2-methylpropanal at 70°C.*

Sulfoxides and sulfones play an important role as they can stabilize an anion and thereby promote formation of a new bond on the carbon atom alpha to it[1]. Optically pure sulfoxides have also proven to be versatile chiral auxiliaries during asymmetric carbon-carbon bond formation[2,3]. Sulfoxides and sulfones can be obtained from the corresponding sulfides on treatment with peracids[4], periodates or hydrogen peroxide. Peracid mediated sulfoxidation is normally carried out under low temperature, and it usually suffers from over oxidation of sulfoxide to sulfone whereas periodate and hydrogen peroxide mediated oxidation of sulfide have the disadvantage that aqueous conditions are required for these transformations. Our interest in cobalt catalyzed oxidation of organic substrates with molecular oxygen led to the discovery of oxidation of sulfides to sulfones under the aegis of cobalt salophen[5,6]. Thus various sulfides were oxidized to the corresponding sulfones by using a combination of molecular oxygen, 2-methylpropanal and a catalytic amount of cobalt salophen (Table 1, entries 1, 2, 7 & 8). While exploring these reactions we were pleasantly surprised to discover that in the absence of cobalt salophen a five fold excess of 2-methylpropanal and molecular oxygen converts sulfides to the corresponding sulfones in high yields. Accordingly, a wide range of sulfides can be oxidized to the corresponding sulfones under these conditions and as indicated, allylsulphide and benzyl sulfide underwent smooth transformation to the corresponding sulfones in good yields (Table 2, entries 1 & 2). Functionalized sulfides with an ester or ketone group can also be oxidized to sulfones in reasonably good yields (Table 1, entries 3 & 4). A cyclic β-phenylthioketone underwent elimination to give an enone which is arising due to the thermal syn elimination of the *in situ* generated sulphoxide (Table 1, entry 5). Any attempt to overoxidize this ketone to the corresponding sulfone met with no success. A hydroxysulphide could also be oxidized in a similar manner to afford the corresponding sulfone in good yields (Table 1, entry 6).

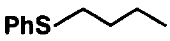
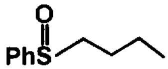
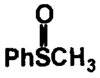
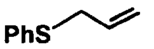
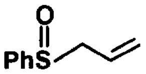
Table 1: Oxidation of Sulfides to Sulfones in the Presence of Dioxygen and 2-Methylpropanal

Entry	Sulfide	Sulfone	(Yield%)[a,b]
1.			72, (73)[c]
2.	$PhS-CH_2-Ph$	 $PhS(=O)_2-CH_2-Ph$	70, (81)[c]
3.			68
4.			69
5.			62
6.			78
7.			69, (60)[c]
8.			51, (31)[c]

a) Isolated yield b) Reaction conditions: A mixture of sulfide (5mmol) and 2-methyl propanal (25 mmol) were heated in dry acetonitrile (15ml) for 3-6h under dioxygen at 70°C. c) Yield of sulfone obtained by cobalt(II) salophen catalyzed reaction using two equivalents of 2-methylpropanal under dioxygen at 70° C.

Interestingly, a selective oxidation of 2-benzothiazolebutylsulfide was achieved where oxidation of the side chain sulfide was the predominant pathway (Table 1, entry 7). Similarly, cephalosporin also underwent oxidation to give the corresponding sulfone in moderate yields. Apart from this sulfone some minor amount of the corresponding sulfoxide was also obtained (Table 1, entry 8). It is note-worthy though not particularly surprising that the oxidation of these products can be controlled at the sulfoxide level by discontinuing the reaction after 1h and in the case of thioanisole, butyl and allylsulfide the corresponding sulfoxides were isolated in high yields (Table 2). However, prolonging the reaction to 3-4 h results in complete formation of sulfones in quantitative yields. On a comparison of the uncatalyzed reaction with cobalt salophen catalyzed reactions, it became clear that in the latter case the sulfoxides could not be isolated and the reaction mixture consisted of the corresponding sulfones. Also, cobalt salophen catalyzed reactions do not offer any great advantage over the uncatalyzed one except for that in the latter case five equivalents of the aldehyde are required as compared to the former where two equivalents are sufficient to convert sulfide to the corresponding sulfone .

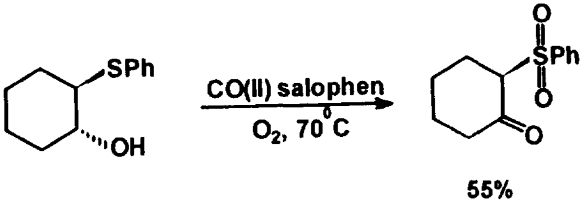
Table 2: Oxidation of Sulfides to Sulfoxides in the Presence of Dioxygen and 2-Methylpropanal

Entry	Sulfide	Sulfone	(Yield%)^{a,b}
1.			82
2.	$PhSCH_3$	 $PhS(=O)CH_3$	78
3.			84

a) Isolated yield b) Reaction conditions: A mixture of sulfide (5mmol) and 2-methylpropanal (25 mmol) were heated in dry acetonitrile (15ml) for 1h under dioxygen at 70°C.

The mechanism of the catalyzed and the uncatalyzed reactions may be different as in the latter case the reactive species is likely to be a peracid, whereas in the former case it may be a metal stabilized oxo-species which is responsible for these oxidations. The difference in the nature of the species formed under these conditions is clearly evident during oxidation of the hydroxysulfide which is oxidized to the corresponding hydroxysulfone in the uncatalyzed reactions (Table 1, entry 6) whereas the corresponding β -ketosulfone is formed under cobalt salophen catalyzed conditions (eq. 1).

Irrespective of the mechanism, the combined use of molecular oxygen and 2-methylpropanal constitutes a extremely useful method for the oxidation of sulfides to sulfones in a preperatively useful manner.



(eq. 1)

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References and Notes

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2. a) For a review on the synthetic uses of β-ketosulfoxides, sulfones and sulfides, see Trost, B. M. *Chem. Rev.*, **1978**, 78, 363. b) For a review on asymmetric synthesis with chiral sulfoxides, see Solladie, G. *Synthesis* **1981**, 185. c) Solladie, G. *Chimia* **1984**, 38, 233.

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5. Cobalt salophen is a complex of cobalt(II) derived from the Schiff's base of salicylaldehyde and o-phenylenediamine and cobalt(II) chloride.

6. For related metal catalysed oxidations see : a) Mastorolli, P. and Nobile C. F. ; *Tetrahedron Lett.*, **1994**, 35, 4193. b) Vincent, S. ; Lion, C. ; Heyatullah, M. ; Challier, A. ; Delmas, G. ; Magnud- G. *Phosphorous, Sulfur, Silicon and Related Elements* , **1994**, 92, 1-4, 189. c) Imigawa, K. ; Nagata, T.; Yamada, T. and Mukaiyama, T. *Chem. Lett.*, **1995,** 335.

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