

CHEMOSELECTIVE OXIDATION OF SULFIDES TO SULFONES

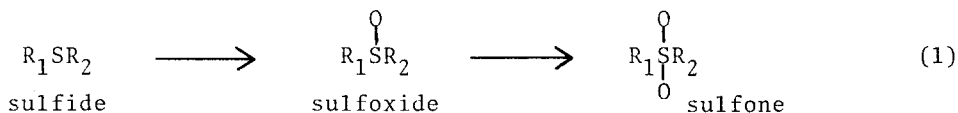
WITH POTASSIUM HYDROGEN PERSULFATE

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ABSTRACT:

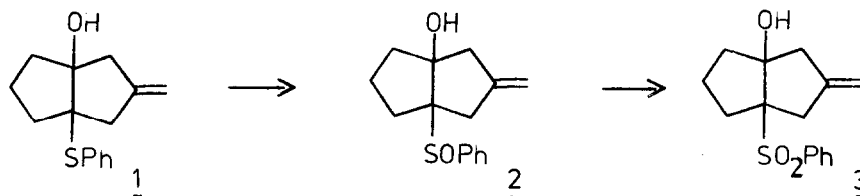
Potassium hydrogen persulfate in aqueous methanol was found to be a convenient, inexpensive, and chemoselective reagent for the oxidation of sulfides to sulfones and sulfoxides in the presence of other common functional groups.

As the use of organosulfur compounds in organic synthesis has continually expanded², so has the need for chemoselective interconversion of the various oxidation states of sulfur (sulfide → sulfoxide → sulfone, see equation 1). We now wish to report that the little used, but convenient and inexpensive oxidizing agent, potassium hydrogen persulfate (KHSO₅)^{3,4,5} commercially sold as oxone, is an excellent reagent for the oxidation of sulfides to sulfones with potential usefulness in the oxidation of sulfides to sulfoxides.



Most commonly, organic peracids (perbenzoic acid, mCPBA) have been used for the oxidation of sulfides to sulfones. Although these peracids rapidly oxidize sulfides to sulfoxides at low temperatures (~-78°), the higher temperatures often required for the sulfoxide to sulfone interconversion (0° to room temperature) can cause oxidation of other functional groups. Specifically, isolated olefins are often epoxidized under these conditions. For example, oxidation of sulfide 1 with 2.0 equivalents mCPBA (4h, -78°; 5h, -20°; 16h, 25°; CH₂Cl₂) produced a 45% isolated yield of the sulfone 3 with epoxide containing compounds accounting for the bulk of the remaining products.

We have found that KHSO₅ in aqueous methanol is a highly chemoselective oxidizing agent for the conversion of sulfides to sulfones. In a typical experimental procedure, thioanisole (10 mmol) was dissolved in methanol (40 ml) and cooled

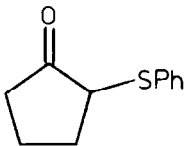
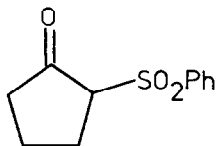
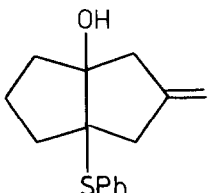
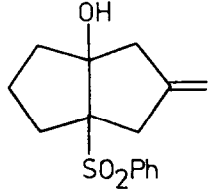
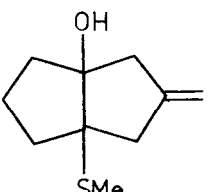
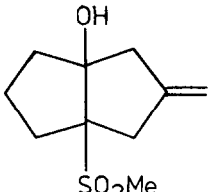
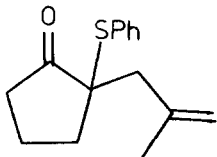
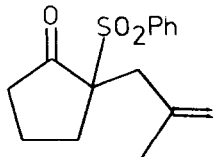
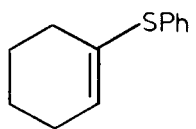
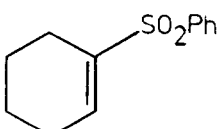


to 0°. To this was added a solution of 49.5% KHSO_5^3 (30 mmoles) in water (40 ml). The resulting cloudy slurry was stirred for 4h at room temperature, diluted with water, and extracted with chloroform (3X). The combined organic layers were washed with water and brine, dried over Na_2SO_4 , and concentrated under reduced pressure to give a quantitative recovery of methyl phenyl sulfone as a white solid. Solid sulfones were purified by simple recrystallization.

Several comments about the reaction are in order. (1) The reaction medium is acidic, pH 2-3. A buffer can be added to bring the pH to ~ 5 , at which time gas evolution is observed. (2) An excess of KHSO_5 is required for rapid completion of the reaction. Generally, 3 mmoles of KHSO_5 per 1 mmole sulfide (50% excess) was the ratio used. (3) The initial reaction is exothermic and controlled addition of the aqueous phase may be advisable for larger scales. Concentration of the methanol prior to workup is also recommended for larger reactions. (4) The reaction is readily followed by analytical TLC. Upon addition of the aqueous KHSO_5 , complete disappearance of the starting sulfide was noted along with the presence of the polar sulfoxide. Over the period of 20 min to 4h at room temperature, the sulfoxide was completely converted to the sulfone, which generally showed an intermediate polarity.

Table I lists the oxidations performed. Generally, the crude product was isolated in high yield and was pure by analytical TLC and ^1H nmr. These examples illustrate the chemoselectivity of KHSO_5 . Entry 2 illustrates that ketones are unaffected by these oxidation conditions. Entries 3 and 4 show that isolated olefins are unaffected by KHSO_5 in aqueous methanol. No evidence for epoxidation was observed. This is in direct contrast to the results obtained with mCPBA (vide supra) in which epoxidation was a significant problem. Entry 5 shows the selectivity in a poly-functional molecule. Although epoxidation might have been expected⁵, again, none was observed. Entry 6 shows the useful transformation of a vinyl

TABLE I

<u>Entry</u>	<u>Starting Sulfide</u>	<u>Sulfone Product</u>	<u>Yield^{a,b}</u>	<u>MP</u>
1	PhSCH ₃	PhSO ₂ CH ₃	100 (95)	85-88.5
2			98 (83)	114-114.5
3			94	115-116
4			98	c
5			92 (77)	129.5-130.5
6			98 (85)	43-44

^aYields are of crude product which was pure by nmr and homogeneous by TLC. Values in parentheses refer to recrystallized yields.

^bSatisfactory elemental analysis and/or high resolution mass spectra were obtained for all new compounds.

^cOil.

sulfide to an α,β -unsaturated sulfone.

In one experiment, the potential usefulness of KHSO_5 for the oxidation of sulfides to sulfoxides was investigated. Treatment of sulfide 1 with 1.3 equivalents of KHSO_5 at 0° in aqueous methanol (2 min) followed by reductive workup (sodium bisulfite) produced sulfoxide 2 in 84% isolated yield along with a small amount of sulfone 3. Thus, by controlling the reaction time and temperature, it is possible to isolate good yields of sulfoxides.

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References

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3. Potassium hydrogen persulfate, available under the trade name oxone, is a safe, air stable, free flowing mixture containing 2 moles KHSO_5 , 1 mole K_2SO_4 , 1 mole KHSO_4 . Oxone is sold by the Alfa Division of Ventron Corp.
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