

Focus Review Article

A Concise Review on Synthesis of Sulfoxides and Sulfones with Special Reference to Oxidation of Sulfides

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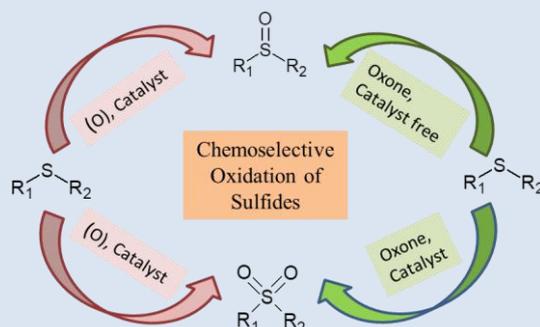
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Abstract:

A large variety of organosulfur compounds have been shown to having diverse biological effects such as anti-oxidant effects, anti-inflammatory properties, inhibition of platelet aggregation, reduction of systolic blood pressure, and reduction of cholesterol. Among these, sulfoxides and sulfones show wide and significant applications as commodity chemical in various fields of chemistry. Therefore, synthesis of sulfoxides as well as sulfones has remained a point of attraction for synthetic organic chemists. Among array of methods used to synthesize the sulfoxides or sulfones, oxidation of sulfide is the most convenient way. This review precises chemoselective methods for the synthesis of the sulfoxides as well as sulfones focusing on oxidative protocols. This review will aid researchers to explore and utilise the mentioned protocols for different organic transformations.

Key words: Sulfide, Oxidation, Sulfoxide, Sulfone, Oxone

Graphical Abstract:



Biography:



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1. Introduction

Sulfur has been known for centuries and it is widely distributed in nature. Owing to the presence of sulfur in all living organisms as well as vegetables in the form of organic or inorganic compounds, sulfur is regarded as an important biogenic element. Many organosulfur compounds are present in a variety of food stuffs including, garlic, onion, chive, cabbage,

broccoli, leek, radish, asparagus, mushroom, coffee, mustard, truffle, and pineapple [1].

At present, sulfur is an integral component of the world economy due to its use in the manufacture of numerous products ranging from fertilizers [2], agrochemicals [3], food stuffs [4] polymers as well as pharmaceuticals. Organosulfur compounds are used as inhibitors of polymerization and as stabilizers of polymer materials (e.g. mercaptobenzimidazole).

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Even vulcanization of rubber by sulfur (and sulfur derivatives) is based on the formation of organosulfur compounds [5,6]. On the other hand, tetramethylene sulfone as well as dimethyl sulfoxide are the well-known and highly useful solvents in organic synthesis. It is worthy to note that in most of the commercially available organosulfur compounds, sulfur is present in two different forms viz. thiol or thioether. Among these, thioether function is more attractive because this group can easily be converted to corresponding sulfoxide or sulfone at any stage of the synthesis. Resultant sulfoxides as well as sulfones serve as pivotal intermediates in synthetic organic chemistry. Among these, sulfoxides serve as valuable synthons in C-C bond forming reactions [7-10], Diels-Alder reactions [11,12], as chiral auxiliaries [13] and in medicinal chemistry as antiulcer, antihypertensive, cardiostimulant agents, CNS stimulants as well as

vasodilators [14]. They are also known to play an important role in enzyme activation [15] while a few sulfoxides find application in the separation of radioactive and less common metals [16].

Sulfoxides are either colorless liquids or solids with low melting points. For instance, dimethyl sulfoxide is one of the common amphiphatic solvent of low toxicity. It is used as a solvent in a wide variety of industrial processes, such as manufacture of polyacrylonitrile fibers, pesticides, in the extraction of aromatic hydrocarbons from refinery streams and for industrial cleaning. It is also used as a solvent for in vivo administration of water insoluble drugs and antioxidants. The significance of sulfoxides as commodity chemicals, their efficacy as versatile building blocks for the assembly of chemically and biologically useful molecules, including therapeutic agents is increasing [17,18].

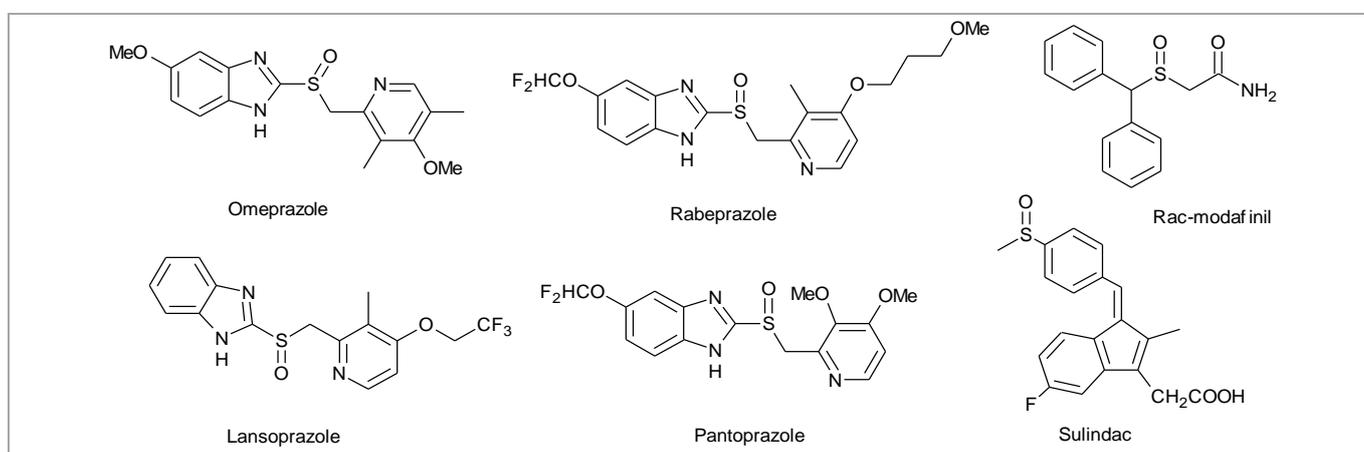


Figure 1. Structures of few medicinally privileged sulfoxides

Enantiopure sulfoxides, owing to their important biological activities are highly useful in the pharmaceutical industry. Omeprazole is a proton pump inhibitor used to treat acid-induced inflammation and ulcers of stomach and duodenum [19, 20]. A number of other acid secretion inhibitors such as Rabeprazole, Lansoprazole, Pantoprazole, have also been developed (Figure 1). Other biologically active compounds containing sulfonyl moiety include Modafinil and Sulindac which have been used in the treatment of narcolepsy and inflammation respectively [21, 22]. A few compounds containing sulfoxide as the structural motif serve as important intermediates in the manufacture of certain veterinary drugs and a few others are engaged in lubricants industry [23]. They are also engaged in the large scale separation of radioactive and less-common metals [24, 25].

Alike sulfoxides, sulfones also play very prominent role in the field of organic synthesis [26,27], pharmaceuticals [28, 29], agrochemicals [30, 31] as well as polymers [32]. They constitute key skeletal

framework of many natural products as well as pharmaceuticals and have attracted considerable attention because of their important biological properties [33]. Particularly, aryl sulfones show various pharmacological properties such as anti-tumor, anti-inflammatory, and anti-fungal activities, including inhibition of HIV-1 reverse transcriptase [34]. Many compounds containing sulfonyl group are known to exhibit antileprotic, antitumor, antiproliferative, antiresorptive and anticancer properties [35-42]. A few medicinally privileged compounds containing “sulfone” as the structural motif are shown in Figure 2.

Synthesis of sulfoxides or sulfone has attracted a great deal of attention from the researchers. Numerous protocols have been reported describing variety of methodologies used to synthesize the sulfoxides and sulfones. This review accounts the concise report of various protocols regarding synthesis of sulfoxides and sulfones. It also focuses on oxidative transformation of sulfides to corresponding sulfoxides and sulfones.



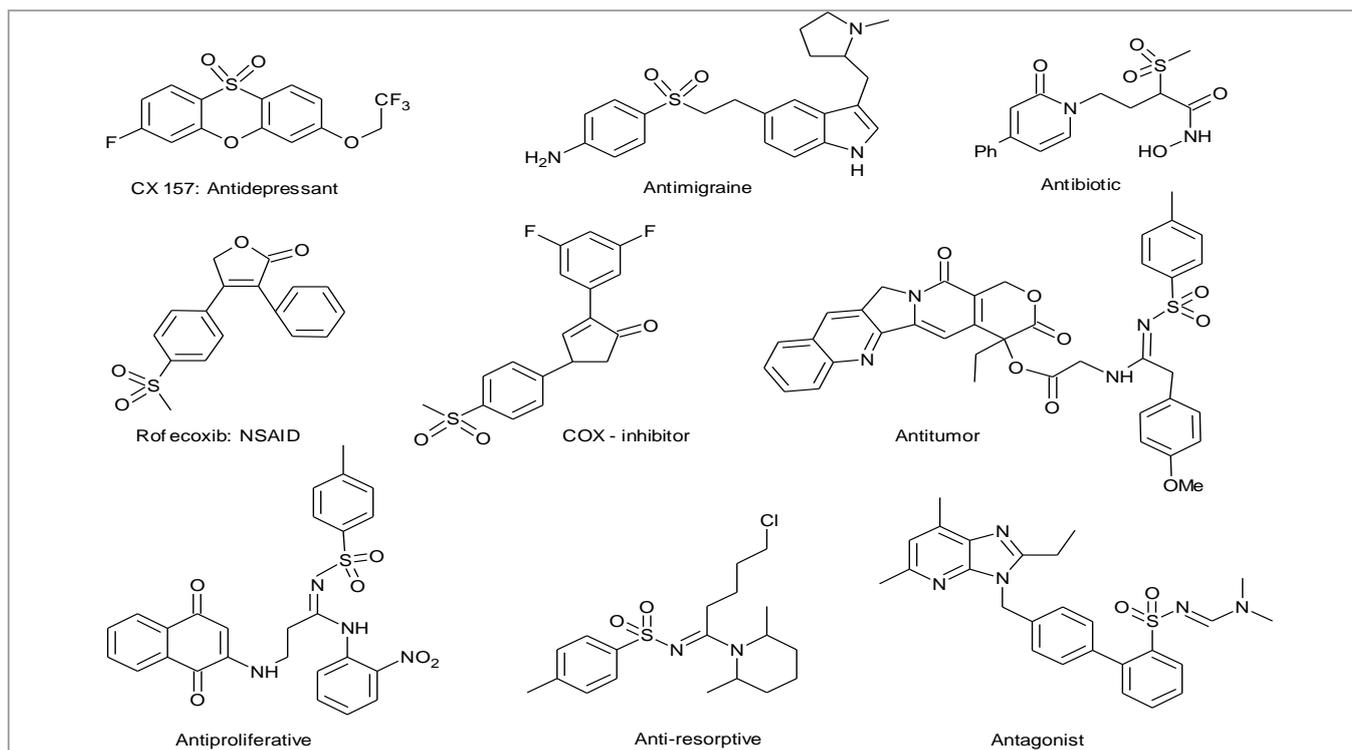


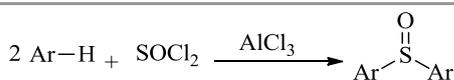
Figure 2. Structures of few medicinally privileged sulfones

2. Synthesis of sulfoxides

Synthesis of sulfoxides can be achieved employing two different routes. (A) Non-oxidative routes (B) Oxidative routes

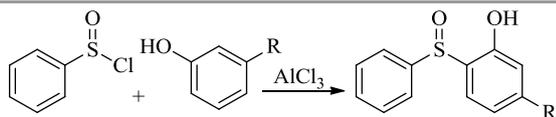
2.1. Non-oxidative routes

The most attractive pathway for the synthesis of aryl ketones involves Lewis acid catalysed acylation of arenes with acid chloride. Similarly, Lewis acid catalyzed sulfonylation of arenes with thionyl chloride is a well-known path for the synthesis of diaryl sulfoxides (Scheme 1) [43].



Scheme 1. AlCl_3 catalyzed sulfonylation of arenes using thionyl chloride

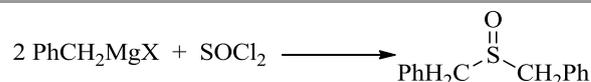
Chasar and Pratt extended this protocol for the synthesis of ortho substituted diaryl sulfoxides by the reaction of aryl sulfinyl chloride with substituted phenols (Scheme 2) [44].



Scheme 2. AlCl_3 catalyzed sulfonylation of arenes using aryl sulfinyl chloride

Both the aforementioned Lewis acid catalysed protocols suffer from the drawbacks as regards the use of environmentally non-benign anhydrous aluminium chloride as the catalyst [45]. In circumventing this problem a Lewis acid-free protocol was proposed by

Strecker. In which, the synthesis of dibenzyl sulfoxides was achieved by using methyl magnesium halide and thionyl chloride (Scheme 3) [46].



Scheme 3. Nucleophilic substitution of Grignard's reagent on thionyl chloride

The most popular non-oxidative approach for synthesis of the sulfoxides involve sulfinate methodology, wherein sulfoxides can be obtained by nucleophilic displacement on sulfinyl derivatives like sulphites, sulfinamides, sulfinyl chloride or sulfinic esters with organometallic reagents. Strecker reported for the first time that, the reaction of diethyl sulphite with two equivalents of Grignard's reagent in ether medium is a useful route for the synthesis of symmetrical sulfoxides (Scheme 4) [46].



Scheme 4. Substitution of Grignard's reagent on diethyl sulfite

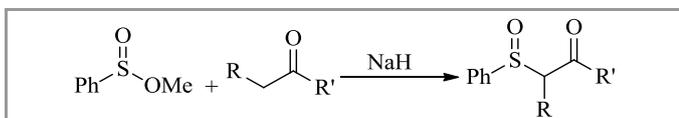
On the other hand, Montanari [47], Mislow [48] and Wudl [49] independently reported the synthesis of optically active sulfoxides using sulfinamides as precursors (Scheme 5).



Scheme 5. Substitution of methyl lithium on sulfinamide

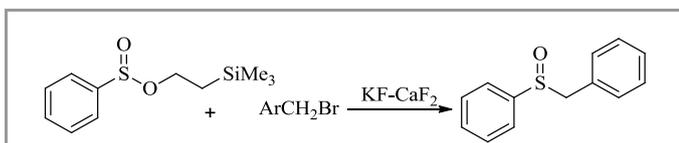


Monteiro *et al.* synthesized a series of racemic β -keto sulfoxides by the reaction of arenesulfonate esters (methyl benzenesulfonate) with α -methylene carbonyl compounds in presence of sodium hydride (Scheme 6) [50].



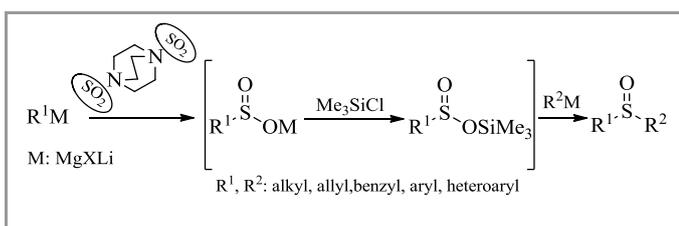
Scheme 6. Synthesis of sulfoxide using α -methylene carbonyl compound

In an approach towards the synthesis of unsymmetrical sulfoxides, 2-trimethylsilylethyl benzene sulfinate was used as a precursor. It was prepared by the reaction between sodium benzene sulfinate and 2-trimethylsilylethyl chloride and it was then allowed to react with alkyl or aryl halide in the presence of potassium fluoride–calcium fluoride mixture as the catalyst. In this process, alkylation at sulfur with concomitant loss of trimethylsilyl fluoride as well as ethene furnishes the desired unsymmetrical sulfoxide (Scheme 7) [51].



Scheme 7. 2-trimethylsilylethyl benzene sulfinate and aryl halide

In an interesting approach, unsymmetrical sulfoxides have been prepared by the reaction of organo lithium or organo magnesium compounds with DABSO {1,4-Diazabicyclo[2.2.2]octane bis(sulfur dioxide)}. The necessary DABSO was prepared by the reaction of DABCO with sulfur dioxide. In this protocol the formation of sulfoxide was proposed to proceed through the generation of trimethylsilyl sulfinate intermediate (Scheme 8) [52].



Scheme 8. Synthesis of sulfoxide using organometallic compound and DABSO

Apart from the aforementioned protocols, a few more non-oxidative protocols are also available for synthesis of sulfoxides [53–61]. However, most of them are associated with some limitations such as handling of lachrymatory reagents, expensive starting materials, and drastic reaction conditions. Hence, these methods are not preferred for the synthesis of the sulfoxides. On the other hand, chemoselective oxidation of sulfides to sulfoxides is the most preferred pathway in the synthesis of sulfoxides. In this chapter we have also relied on this approach. Thus, it would be quite relevant to take a brief account

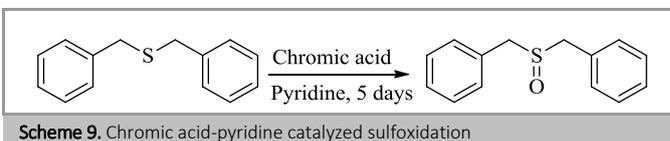
of the protocols reported earlier for chemoselective oxidation of sulfides to sulfoxides.

2.2. Oxidative routes

Chemoselective and controlled oxidation of sulfur from organosulfur compounds to sulfoxides is a challenging research topic in the synthetic organic chemistry. A useful number of methods are available for the oxidation of sulfides to sulfoxides. Traditionally, although strong oxidants, like nitric acid or KMnO_4 can be used for sulfoxidation, in tune with current demands of green chemistry, an array of reagents and reagent-catalyst combinations have been introduced for this oxidative transformation. The methods or the reagents available for the oxidation of sulfides to sulfoxides can be broadly classified into following categories.

2.2.1. Chromic acid

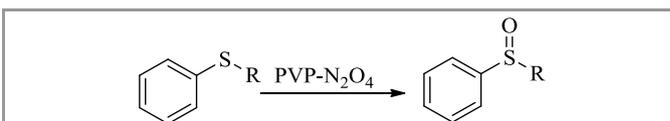
Chromic acid in glacial acetic acid is a promising reagent-reaction medium consisting of many oxidation reactions. However, due to the high tendency of sulfides to undergo over oxidation to sulfones, it is not conventionally used for the oxidation of sulfides. Chromic acid-pyridine combination has been demonstrated to be highly effective in chemoselective and controlled oxidation of sulfide to sulfoxides (Scheme 9) [62].



Scheme 9. Chromic acid-pyridine catalyzed sulfoxidation

2.2.2. Nitric acid and oxides of nitrogen

Nitric acid had been the reagent of choice in oxidation of sulfides to sulfoxides. However, the main drawback associated with the use of nitric acid is the possibility of concomitant nitration of the substrate or other side reactions. Few other oxides of nitrogen employed for the oxidation of sulfides are: acyl nitrates [63], nitroniumhexafluorophosphate [64], thallium nitrate [65], ceric ammonium nitrate [66], nitrogen tetroxide [67], polyvinylpyrrolidone supported dinitrogen tetroxide (PVP- N_2O_4) (Scheme 10) [68] etc.



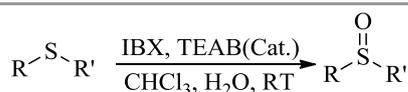
Scheme 10. PVP supported dinitrogen tetroxide catalyzed sulfoxidation

2.2.3. Halogen, Hypohalites

Organic sulfides on reaction with molecular halogen are known to form halosulfonium salts, which can undergo hydrolysis at the presence of water to yield sulfoxides. Based upon this concept, halogens,

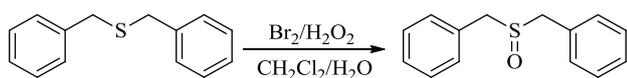


especially bromine or *in situ* generated bromine has been employed in oxidation of sulfides. The process suffers from the drawbacks as regards formation of sulfonic acid and sulfinic acid as the by-products and the possibility of halogenation of the aromatic ring. By using hypochlorites as oxidant, lower dialkyl sulfides are reported to undergo oxidation directly to sulfones while higher sulfides get converted to sulfoxides [69]. Sodium meta-periodate (NaOI₄) in excess amount has also been reported for selective sulfoxidation [70]. Using NaOCl as an oxidant, TEMPO-linked metalloporphyrins have been shown to be efficient catalysts in selective oxidation of sulfides to sulfoxides [71]. Iodosobenzene has emerged as an efficient oxidizing agent for the oxidation of unsaturated or otherwise sensitive sulfides to corresponding sulfoxides [72, 73]. Iodoxybenzoic acid (IBX)-tetraethyl ammonium bromide has also been shown to be efficient oxidant-catalyst combination in chemoselective oxidation of numerous sulfides. The method offers the advantages of short reaction times, functional group compatibility and non-formation of over oxidation products (Scheme 11) [74].



Scheme 11. TEAB catalyzed oxidation of sulfides using IBX

Bravo and co-workers demonstrated the use of molecular bromine and H₂O₂ combination for sulfoxidation. The reaction is known to follow free-radical pathway to furnish the desired product (Scheme 12) [75].



Scheme 12. Br-H₂O₂ combination for oxidation of sulfides

Cetyltrimethylammonium tribromide (CTMATB) prepared by the reaction between molecular bromine and cetyltrimethylammonium bromide has been demonstrated as an efficient reagent in controlled and chemoselective oxidation of sulfides to sulfoxides. In fact, CTMATB serves as a slow release source of bromine. The reagent mainly offers the advantages of easy handling of the oxidant and controlled oxidation (Scheme 13) [76].



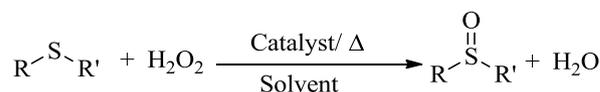
Scheme 13. Sulfoxidation using Cetyltrimethylammonium tribromide

2.2.4. Peroxides, peracids and ozone

Peroxy compounds such as hydrogen peroxide, organic hydroperoxides, peracids and ozone are well known sources of active oxygen and have been used for the oxidation of sulfides to sulfoxides. Among organic hydroperoxides, urea-hydrogen peroxide (UHP) [77], *tert*-butyl hydroperoxide (TBHP) [78], 2-hydroperoxyhexafluoro-2-propanol [79], flavin hydroperoxide [80] and α -azohydroperoxide [81] are well documented as oxidants for sulfoxidation.

In 1928 Lewin reported the use of perbenzoic acid for sulfoxidation of sulfides at room temperature [82] while Sakuraba *et al.* reported the use of peracetic acid for the same oxidation [83]. On the other hand, *meta*-chloroperbenzoic acid, although shock sensitive and potentially explosive in nature, is the most preferred oxidant in the oxidation of sulfides to sulfoxides [84].

Amongst several peroxy compounds, hydrogen peroxide is an economical and commercially available oxidizing agent. Water being the only by-product in hydrogen peroxide mediated oxidation, it has dragged more attention (Scheme 14). It is worthy to note that, hydrogen peroxide is although a good oxidant from environmental point of view, its activity is low and the same can be increased by using appropriate reaction medium, catalyst or temperature. The efficacy of H₂O₂ in combination with number of catalysts or using different solvents has been reviewed [85].



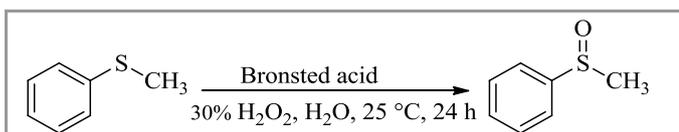
Scheme 14. Oxidation of sulfides using H₂O₂ as an oxidant

Several catalysts and reaction conditions have been reported to accelerate the sulfoxidation using H₂O₂ and to take an account of all of them is a herculean task. Thus, only a few representative methods have been discussed here. For instance Molybdenum salt [86], immobilized vanadyl, cobalt or nickel alkyl phosphonates [87], zinc bromide [88], Ga(OTf) [89], glacial acetic acid [90], poly(N-vinylpyrrolidone) (PVP) and poly(4-vinylpyridine) [91], vanadium complex [VO₂F(dmpz)₂] (dmpz = 3, 5-dimethyl pyrazole) [92] have been reported for the oxidation of sulfides. Recently Kulkarni *et al.* [93] reported the use of magnetically separable nickel ferrite-H₂O₂ as an efficient catalyst-oxidant combination in chemoselective oxidation sulfides. Besides this array of acid catalysts supported on MPNs for oxidation of sulfides to sulfoxides have been reported by many researchers [94]. On the other hand, Atul Kumar and Akanksha have reported the use of human haemoglobin-H₂O₂ as a highly efficient biocatalyst-



oxidant combination for this oxidation [95]. This combination necessitates the use of phosphate buffer as the reaction medium. Very recently Ghorbani-Choghamarani *et al.* have demonstrated immobilized cobalt complex on the surface of SBA-15 as an efficient and green catalyst for sulfoxidation [96].

Rostami *et al.* [97] and Zolfigol *et al.* [98] described the use of boric acid and silica vanadic acid as highly efficient Bronsted acid catalysts in chemoselective oxidation of sulfides using hydrogen peroxide as oxidant under solvent-free conditions. Recently, Shen *et al.* reported on the influence of pH in Bronsted acid catalyzed sulfoxidation of sulfides using H_2O_2 as an oxidant. He has concluded that, the performance of the catalyst in this oxidation does not depend upon the amount of the catalyst but it depends upon the pH of the reaction medium. With the choice of any Bronsted acid as catalyst at pH 1.30, more than 98 % conversion with high selectivity and excellent substrate tolerance has been reported (Scheme 15) [99].



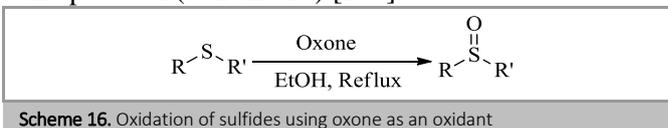
Scheme 15. Bronsted acid catalyzed sulfoxidation using H_2O_2

Attempts have also been made to check the efficacy of hydrogen peroxide in the oxidation of sulfides in various reaction media. In early studies acetone and acetic acid were the preferred solvents for the oxidation of sulfides using H_2O_2 as an oxidant [100-103]. In an interesting study, Drabowicz *et al.* reported that the rate of sulfoxidation can be increased substantially by changing the reaction medium from acetone to methanol [104] while Zu and co-workers have reported the use of phenol as a solvent in expeditious sulfoxidation of sulfides using 30 % H_2O_2 as an oxidant [105].

Oxone is another commercially available oxidant that has attracted considerable attention these days. Chemically it is a 2:1:1 ternary composite of $KHSO_5$, K_2SO_4 and $KHSO_4$. The only drawback with the use of Oxone is its solubility in water. This poses problems in using the same in oxidative transformations carried out in organic solvents. Despite this limitation, the use of Oxone in various organic transformations is well documented [106]. At the same time it is worthy to note that, reports on its use in the oxidation of sulfides are scanty [107-109].

Greenhalgh was the first to report the use of Oxone-wet alumina combination to bring out oxidation of sulfides to sulfoxides in CH_2Cl_2 medium under reflux condition [107]. Kroop *et al.* have reported the use of silica gel-Oxone combination to effect sulfoxidation

[108]. In a recent communication, Yu and his colleagues demonstrated that, selective oxidation of sulfides to sulfoxides can be carried out by using Oxone alone as an oxidant in ethanol medium. However, very long reaction times (12 h) and reflux condition are the two main draw backs associated with this protocol (Scheme 16) [109].



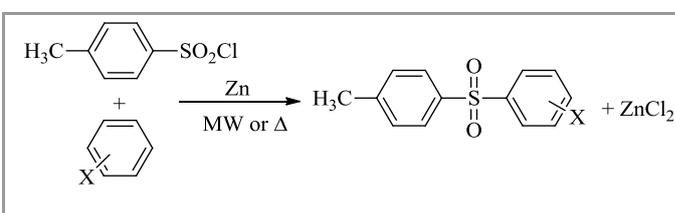
Scheme 16. Oxidation of sulfides using oxone as an oxidant

3. Synthesis of sulfones

Alike sulfoxides, synthesis of sulfones can be achieved following non-oxidative as well as oxidative routes.

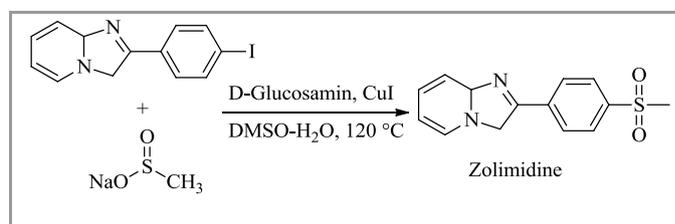
3.1. Non-oxidative routes

Sulfonylation of aromatic compounds with arenesulfonyl halides or arenesulfonic acids has been the most preferred non-oxidative approach for the synthesis of sulfones [110-112]. For instance, Bandgar and co-workers have reported the synthesis of sulfones by zinc catalyzed sulfonylation of arenes using *p*-toluene sulfonyl chloride as the sulfonylating agent. The reaction conditions involve thermal as well as microwave activation (Scheme 17) [113].



Scheme 17. Zn catalyzed sulfonylation of arenes using TsCl

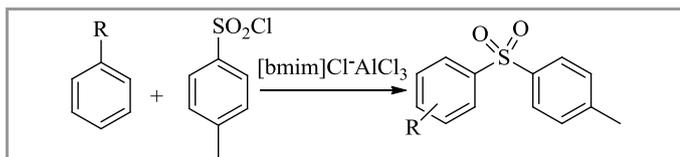
Recently, the marketed antiulcer drug Zolimidine and other aryl sulfones have been synthesized by CuI assisted coupling of sulfinate and aryl halide at the presence of D-glucosamine as a green ligand (Scheme 18) [114].



Scheme 18. CuI assisted coupling of sulfinate and aryl halide

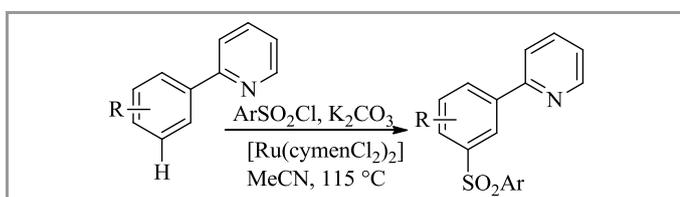
Friedel-Craft's sulfonylation method for the synthesis of diaryl sulfones using ionic liquid was introduced by Salunkhe. In this protocol, the ionic liquid used viz. [bmim]Cl-AlCl₃, has been reported to serve as the reaction medium as well as catalyst (Scheme 19) [115].





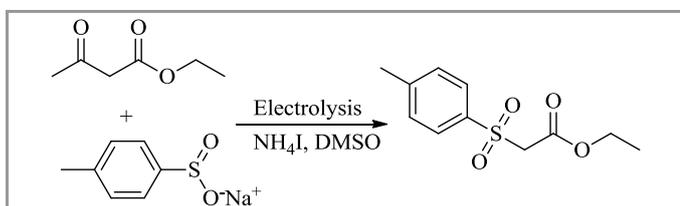
Scheme 19. Ionic liquid mediated oxidation of sulfides to sulfones

For regioselective sulfonylation of heterocycles with aryl sulfonyl chlorides, activation of C–H bond using metal based catalysts has been demonstrated to be essential. Saidi *et al.* have developed a method for activation of *meta* C–H bond in 2-phenylpyridine using Ruthenium complex. Thus, selective sulfonylation of 2-phenylpyridine to afford *meta* phenylsulfonyl -2-phenyl pyridine was achieved (Scheme 20) [116].



Scheme 20. Sulfonylation of heterocycles by C-H bond activation using base

Pan *et al.* recently reported an electrochemical synthesis of β -sulfonylestere using of aryl sulfonates and β -keto ester compounds as substrates and ammonium iodide as an electrolyte (Scheme 21) [117].

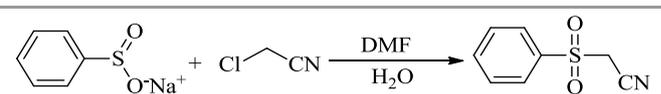
Scheme 21. Electrochemical synthesis of β -sulfonyl esters

Regioselective ring opening of epoxide through addition of salt of sulfonates is another attractive strategy for the synthesis of functionally diverse sulfones. Chumachenko and Sampson have reported the synthesis of aryl sulfones by ring opening of ethylene and propylene oxide with zinc sulfinate in aqueous medium (Scheme 22A) [118]. Murthy *et al.* have recently reported a green and catalyst-free protocol for the synthesis of β -hydroxy arylsulfones by heating together a mixture of sodium salt of aryl sulfonic acid and epoxide in water medium (Scheme

22B) [119]. Resultant of β -hydroxy arylsulfones serve as starting materials in the synthesis of vinyl sulfones as well as β -ketosulfones which serve as important intermediates in organic synthesis.

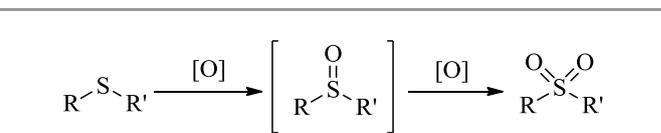
Chawla *et al.* developed a simple protocol for the synthesis of aryl vinyl sulfones by heating together a mixture of sodium benzenesulfinate and terminal epoxide in presence of lithium bromide as the catalyst. The reaction passes through the formation of β -hydroxy arylsulfones as the intermediate but, subsequent elimination of water to furnish corresponding vinyl sulfone is not regioselective. Thus, the resultant vinyl sulfone is a mixture of terminal and internal vinyl sulfone (Scheme 23) [120].

Phenylsulfonyl acetonitrile is an active methylene compound and serves as a valuable synthon in organic synthesis. It could be prepared in excellent yield by heating together a mixture of sodium benzene sulfinate and 2-chloroacetonitrile in aqueous-dimethylformamide (Scheme 24) [121].



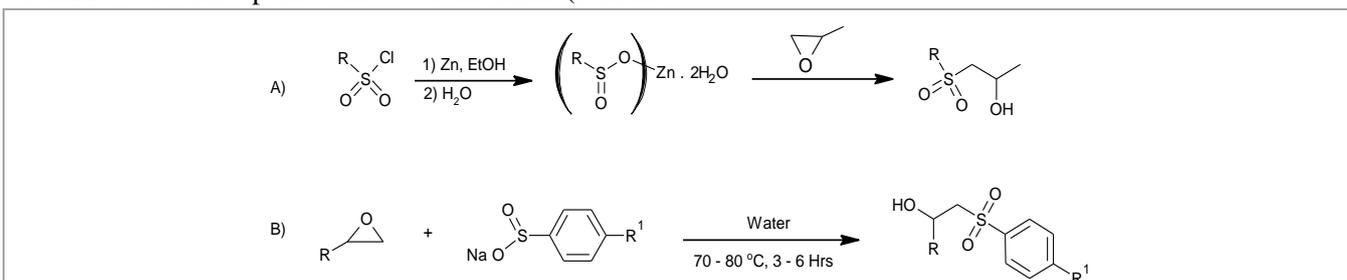
Scheme 24. Synthesis of phenyl sulfonyl acetonitrile using chloroacetonitrile

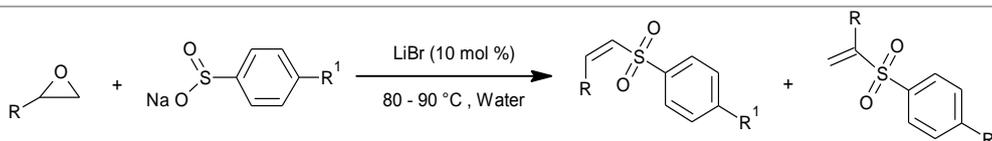
3.2. Oxidative routes



Scheme 25. Complete oxidation of sulfides to sulfones

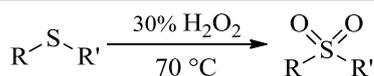
Oxidation of thioethers directly to sulfones is another, simple and most useful route for the synthesis of sulfones (Scheme 25). Literature survey revealed that variety of reagents under the range of experimental conditions has been reported for the direct oxidation of sulfides to sulfones. It is worthy to note that, regardless of medicinal importance of sulfones much attention has earlier been paid towards chemoselective oxidation of sulfides to sulfoxides and the protocols developed for the same have been extended towards the synthesis of sulfones. Nitric acid [122], KMnO_4 [123], bromine [124], NaOCl [125], ozone [126], peracids [127-129], *t*-BuOOH [130] are few of the oxidants used in early days.

Scheme 22. Synthesis of β -hydroxy sulfones through addition of sulfinate salt to epoxide ring



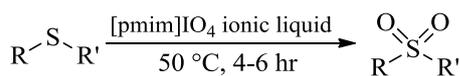
Scheme 23. LiBr catalyzed addition of sodium benzenesulfinate to epoxide

Few reports are also available on the use of magnesium monoperoxyphthalate (MMPP) [131] and polyvalent [132] and hypervalent iodine compounds [133-135]. Besides these, H_2O_2 in combination with variety of catalysts have been most frequently used in the oxidative synthesis of sulfones. For instance, combination of Merrifield resin supported peroxomolybdenum (VI) compounds- H_2O_2 [136], PDDA-SiV₂W₁₀- H_2O_2 [137], polypyridiniumphosphorotungstate- H_2O_2 [138], MnSO_4 - H_2O_2 [139], trifluoroacetophenone- H_2O_2 [140], peroxometalate based polymer immobilised ionic liquid- H_2O_2 [141], polymer-immobilized peroxotungsten compound- H_2O_2 [142], silica bromide- H_2O_2 [143], TaC / NbC- H_2O_2 [144], cyanuric chloride- H_2O_2 [145], borax- H_2O_2 [146], silicasulfuric acid- H_2O_2 [147], TiO_2 - H_2O_2 [148], sulfamic acid- H_2O_2 [149], and H_2O_2 in supercritical carbon dioxide-water [150], are few of the noteworthy and recently reported catalyst – oxidant combinations to effect oxidation of sulfides to sulfones. In addition to these, Jereb *et al.* [151] reported a catalyst-free, solvent-free and functional group compatible protocol for the oxidation of sulfides to sulfones using 30 % H_2O_2 as the oxidant. The main drawback of the developed protocol involves the necessity of elevated temperature (75 °C) and longer time for complete oxidation (Scheme 26).



Scheme 26. Uncatalysed sulfonylation using H_2O_2 at elevated temperature

Recently, task specific bifunctional ionic liquid viz. [pmim]IO₄ has been reported for selective oxidation of sulfides to sulfones. In this reaction, ionic liquid serves as a solvent as well as an oxidant (Scheme 27) [152].

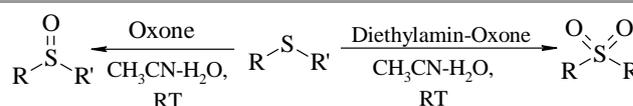


Scheme 27. Sulfonylation using bifunctional ionic liquid

Oxone has also been the choice of a few researchers to bring out oxidation of sulfides to sulfones. However, the developed protocols suffer from the drawbacks like necessity of excess equivalent of Oxone [153], or inorganic supports like montmorillonite [154],

alumina [105] etc. coupled with thermal / MW activation.

The problem of using excess of Oxone was circumvented by Kupwade *et al.* They have reported diethylamine catalysed eco-benign protocol for controlled, selective as well as scalable protocol for oxidation of sulfides to sulfones using Oxone. This report also mentions uncatalysed oxidation of sulfides to sulfoxides (Scheme 28) [156].



Scheme 28. Sulfoxidation and sulfonylation using Oxone as an oxidant

4. Conclusions

Due to the importance of sulfoxides and sulfones in the organic chemistry, biology and polymers development of efficient protocols for the synthesis of sulfoxides and sulfones has been the subject of many research studies. Although the literature is enumerated with several approaches for the synthesis of sulfoxides and sulfones, the most rational and preferred pathway for their synthesis is the oxidation of sulfides. Several protocols have earlier been reported for these oxidative transformations. Among these protocols, oxidation using H_2O_2 are economical and benign. However, the methods developed suffer from the drawbacks as regards necessity of expensive catalyst, long reaction times, high temperatures, generation of unnecessary waste and primly, the unsatisfactory performance in medium to large-scale synthesis. Recently Oxone has emerged as ecobenign alternative for oxidation reaction. It has proven its efficacy for selective and scalable oxidative conversion of sulfides to corresponding sulfoxide or sulfone. Very recently we have mentioned used of Oxone for chemoselective, uncatalysed oxidation sulfides to sulfoxide as well as diethylamine catalysed oxidation of sulfides to sulfone. It is most simple, energy efficient and scalable protocol available for the oxidation of sulfides, complies with several key requirements of green chemistry.

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