

An efficient and direct route to the synthesis of diaryl sulfoxides catalyzed by heteropoly acid

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Abstract

Heteropoly acid tungstophosphoric acid ($H_3PW_{12}O_{40}$) was found to be an excellent catalyst for the synthesis of symmetrical diaryl sulfoxides. The reaction was carried out in various organic solvents or ionic liquids and under solventfree condition. The reaction exhibited better results in terms of the yield and rate under solventfree condition. The catalyst was efficiently recovered from the reaction mixture and reused. The highlighting features of the present protocol are short reaction times, high yields of the products, ambient conditions, and simple workup.

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1. Introduction

Sulfoxides are fascinating organic molecules. Because of the multifarious conversions of sulfoxides into a myriad of organosulfur compounds, they are extremely important to organic chemists. This class of compounds finds immense use in the field of drugs, sulfur-substituted natural products and pharmaceuticals [1,2]. Much exploration has been carried out to understand its importance as chiral auxiliary in asymmetric synthesis [3–5] and particularly in carbon–carbon bond forming reactions [6,7]. In addition, the synthesis of diaryl sulfoxides leads to triarylsulfonium salts which are used extensively as photoactive cationic initiators [8] and for the photogeneration of protonic acid in the lithographic resist field [9].

The methodology for the direct synthesis of sulfoxides is, however, not explored to a great extent. Some indirect methods for synthesizing sulfoxides comprise of the reduction of sulfones, the oxidation of sulfides, and the reaction of organometallic reagents with sulfinic acid esters, mixed anhydrides or sulfines [10]. Friedel–Crafts sulfonylation of arenes using Brønsted acids [11,12] as well as Lewis acids [13–15], the addition of aryl Grignard reagents to thionyl chloride [10] and

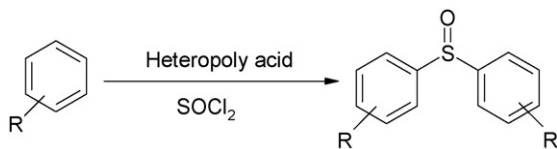
the reaction of SO_2 with arenes in the presence of magic acid [16] are some of the direct methods of preparation of sulfoxides. Quite recently, trifluoromethanesulfonic acid and scandium triflate have also been employed as catalysts in the reaction of arenes with thionyl chloride to obtain sulfoxides.

It is important to bring to light the fact that many of the methods suffer from certain drawbacks such as the use of corrosive, hazardous, oxidizing and difficult to handle reagents, lack of selectivity, longer reaction times, high temperature and the formation of a mixture of products containing sulfonium salts and chlorinated byproducts along with desired sulfoxides.

In recent years, the use of solid acids as heterogeneous catalysts has received considerable attention in different areas of organic synthesis [17]. Amongst the various heterogeneous catalysts, heteropoly acids (HPAs) are the most attractive, because of their flexibility in modifying the acid strength, environmental compatibility, nontoxicity and experimental simplicity [18–20]. The use of HPA as a catalyst makes the process convenient and environmentally benign. HPAs due to their unique physicochemical properties are widely used as homogeneous and heterogeneous acid and oxidation catalysts.

Earlier in our laboratory, we have successfully synthesized diaryl sulfoxides by an efficient direct route employing chloroaluminate ionic liquid [21]. With growing interest in similar study and in view of the emerging importance of the use of heteropoly acids as catalyst in organic synthesis, we herein wish

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Scheme 1. Heteropoly acid catalyzed synthesis of symmetrical diaryl sulfoxides.

to report the synthesis of symmetrical diaryl sulfoxides from arenes and thionyl chloride using catalytic amount of heteropoly acid (Scheme 1).

2. Experimental

2.1. Material

All chemicals and reagents were of analytical grade and used as received.

2.2. Procedure for sulfonylation of anisole in organic solvent or ionic liquid

To a suspension of anisole (10 mmol), organic solvent or ionic liquid (1 ml) and $\text{H}_3\text{PW}_{12}\text{O}_{40}$ (5 mol%), thionyl chloride (6 mmol) was added dropwise and the reaction mixture was stirred at ambient temperature under N_2 atmosphere for specified period of time (Table 3). After completion of the reaction, as indicated by TLC, the reaction mixture was extracted with diethyl ether (3 ml \times 15 ml), the combined extract was then treated with saturated sodium bicarbonate and dried over anhydrous Na_2SO_4 , concentrated in vacuo and the resulting product was purified by silica gel column chromatography to afford pure dianisyl sulfoxide.

2.3. General procedure for sulfonylation under solventfree condition

To a suspension of arene (10 mmol), and the tungstophosphoric acid ($\text{H}_3\text{PW}_{12}\text{O}_{40}$) (2 mol%), thionyl chloride (6 mmol) was added dropwise and the reaction mixture was stirred at ambient temperature under N_2 atmosphere for an appropriate time (Table 4). After completion of the reaction, as indicated by TLC, the reaction mixture was extracted with diethyl ether (3 ml \times 15 ml) and the catalyst was filtered off. The combined ether extract was treated with saturated sodium bicarbonate and dried over anhydrous Na_2SO_4 , concentrated in vacuo and the resulting product was purified by silica gel column chromatography to afford pure diaryl sulfoxide. The products were characterized by IR, ^1H NMR and GC–MS spectroscopy. The filtered catalyst was repeatedly washed with diethyl ether and reused.

2.4. General procedure for recycling of system of ionic liquid and catalyst

After the crude product was extracted from the reaction mixture with diethyl ether, the system of ionic liquid and

Table 1

Screening of different heteropoly acids for the synthesis of dianisyl sulfoxide from anisole in dichloromethane at room temperature

Entry	Catalyst ^a	Time (h)	Yield (%)
1	$\text{H}_3\text{PW}_{12}\text{O}_{40}$	3.0	94
2	$\text{H}_3\text{SiW}_{12}\text{O}_{40}$	6.5	86
3	$\text{H}_3\text{PMo}_{12}\text{O}_{40}$	10	83

^a A 5 mol% of the catalyst was used.

tungstophosphoric acid was reused for subsequent runs and the above mentioned procedure mentioned in Section 2.2 was followed.

3. Results and discussion

Preliminary investigations involved screening of three different heteropoly acids, namely tungstophosphoric acid ($\text{H}_3\text{PW}_{12}\text{O}_{40}$), silicotungstic acid ($\text{H}_3\text{SiW}_{12}\text{O}_{40}$) and molybdophosphoric acid ($\text{H}_3\text{PMo}_{12}\text{O}_{40}$) for the conversion of anisole into dianisyl sulfoxide in dichloromethane (DCM), which was chosen as the prototype. The experiments were carried out at room temperature. Analysis of the reaction mixture on TLC showed complete conversion of the starting material. Anisole reacted smoothly with SOCl_2 to afford the dianisyl sulfoxide in good yield. The protocol exhibited excellent regioselectivity as the para product was formed exclusively. However, it was noticed that tungstophosphoric acid with an optimum quantity of 5 mol% exhibited a high reaction rate in comparison with other two heteropoly acids chosen for the study (Table 1). One interesting observation that needs to be mentioned is that though heteropoly acid did not dissolve in DCM, the reaction performed well under heterogeneous conditions.

Further, we contemplated to illustrate a comparison between tungstophosphoric acid and other conventional acid catalysts, which have not been employed for the synthesis of diaryl sulfoxide, in terms of the yield and rate of the reaction. We chose various acid catalysts such as montmorillonite K10, InBr_3 , etc., to carry out the study. It was evidently observed (Table 2) that the yield and rate of the reaction were significantly low in all the cases except tungstophosphoric acid. Even on prolonging the reactions, the yields did not increase in the case of other acid catalysts.

Table 2

Comparison between tungstophosphoric acid and other conventional acid catalysts for synthesis of dianisyl sulfoxide in dichloromethane at room temperature

Entry	Catalyst ^a	Time (h)	Yield (%)
1	$\text{H}_3\text{PW}_{12}\text{O}_{40}$	3.0	94
2	Montmorillonite-K10	20	40
3	Amberlyst-15H	20	25
4	BiCl_3	20	50
5	InBr_3	24	20
6	Molten $(\text{Bu})_4\text{NBr}$	24	No reaction
7	$[\text{Hmim}]\text{Tfa}^b$	24	No reaction

^a A 5 mol% of the catalyst was used.

^b Methylimidazolium trifluoroacetate ionic liquid.

Next, we considered it worthwhile to study the effect of various organic solvents on the yield and rate of the reaction. Our interest in the field of ionic liquids for organic transformations of high synthetic value [22–24] encouraged us to employ ionic liquids for the reaction. Ionic liquids have proven their utility as recyclable reaction media for a wide variety of organic transformations. This aspect made us consider that ionic liquid would serve as a reservoir for the catalyst and that hence the catalyst along with the ionic liquid could be recycled.

Various organic solvents such as dichloroethane, chloroform, THF and acetonitrile, and ionic liquids such as 1-butyl-3-methylimidazolium hexafluorophosphate, [bmim]PF₆ and 1-butyl-3-methylimidazolium tetrafluoroborate, [bmim]BF₄ were selected for the study. Heteropoly acid does not dissolve in halogenated organic solvents like dichloroethane and chloroform but is soluble in acetonitrile, THF. However, this difference did not have profound effect on the outcome of the reaction as all the solvents gave the desired product in excellent yields with 5 mol% of the catalyst. In the case of ionic liquids, the catalyst dissolved in hydrophilic ionic liquids such as [bmim]BF₄ but did not dissolve in hydrophobic ionic liquids such as [bmim]PF₆. This behavior of the catalyst in ionic liquids did not affect the yield or rate of the reaction either as can be inferred from Table 3.


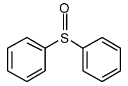

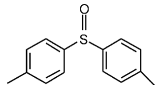
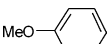
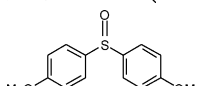
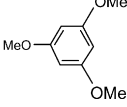
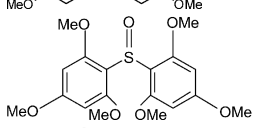

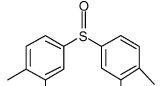

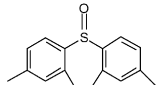

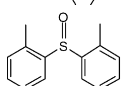

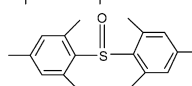

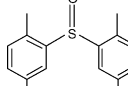

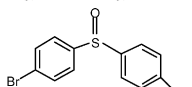

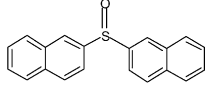

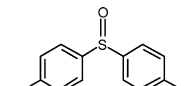

Keeping all these results in view, we were then prompted to study the reaction under solventfree conditions. Quite interestingly, we observed that with 5 mol% of the catalyst, there was appreciable increment in the rate of the reaction (Table 3). However, on reducing the amount of the catalyst from 5 to 2 mol%, we obtained results similar to those obtained with organic solvents and ionic liquids using 5 mol% of the catalyst in terms of both the yield and rate of the reaction.

Considering low loading of the catalyst as beneficial, we decided to generalize the protocol by treating different arenes with thionyl chloride and 2 mol% of the catalyst under solvent-free conditions. All the selected arenes afforded corresponding sulfoxides in high to excellent yields. Tungstophosphoric acid was found to be an efficient catalyst for the synthesis of aryl sulfoxides from activated arenes, and interestingly, the catalyst was also effective for the sulfonylation of unactivated arenes such as chlorobenzene and bromobenzene albeit requiring longer reaction time (Table 4). In the case of solid arenes such as naphthalene (entry 11) and biphenyl (entry 12), we employed the

Table 3
Comparative study between organic solvent, ionic liquids and solventfree condition for the sulphonylation of anisole at room temperature

Entry	Solvent	Amount of catalyst (mol%)	Time (h)	Yield (%)
1	Dichloroethane	5	3.0	94
2	Chloroform	5	3.5	96
3	Acetonitrile	5	4.5	92
4	THF	5	5.0	89
5	[bmim]BF ₄	5	3.0	95
6	[bmim]PF ₆	5	3.5	95
7	[moemim]OMs	5	3.0	92
8	Solventfree	2	3.0	93
9	Solventfree	5	0.5	95

Table 4
Synthesis of diaryl sulfoxides under solventfree conditions catalyzed by 2 mol% of tungstophosphoric acid

Entry	Arene	Product ^a	Time (h)	Yield ^b (%)
1			3.0	87
2			3.0	90 ^c
3			2.5	94
4			2.0	95
5			3.0	92
6			3.0	92
7			3.0	88
8			3.0	95
9			4.5	87
10			3.5	81
11			4.5	86 ^d
12			4.5	84 ^d
13		No reaction	24	–

^a The products were characterized by ¹H NMR, IR, GC–MS and by comparison with authentic samples [25].

^b Isolated yields.

^c An ortho to para ratio of 10:90 was obtained, which was confirmed by ¹H NMR and GC–MS spectroscopy.

^d The ionic liquid 1-butyl 3-methylimidazolium tetrafluoroborate, [bmim]BF₄ (1 ml) was used as solvent.

ionic liquid [bmim]BF₄. However, deactivated arenes such as nitrobenzene remained unchanged under similar reaction conditions even after 24 h.

The reaction exhibited high selectivity as no sulfonium salts, sulfides and sulfones were obtained. The methodology showed

Table 5
Recyclability of system of ionic liquid and tungstophosphoric acid for synthesis of dianisyl sulphoxide

Run	Yield (%)
1	94
2	92
3	90
4	90

excellent regioselectivity as the para products were formed exclusively.

Keeping in view the constraints of environmental legislation, the recovery and reusability of heteropoly acid needed some investigation. In this context, as the reaction mixture was heterogeneous under solventfree condition, diethyl ether was added to the reaction mixture and heteropoly acid was filtered out. When ionic liquid was used as the reaction mixture, the product was removed by diethyl ether extraction and the entire system of ionic liquid and heteropoly acid could be reused for three consecutive runs. This recovered heteropoly acid showed a decline in its catalytic activity as the product was obtained in lower yield; however, the regioselectivity remained exclusive (Table 5).

4. Conclusion

In summary, a highly effective and environment friendly synthesis of diaryl sulfoxides from arenes and thionyl chloride in presence of tungstophosphoric acid ($H_3PW_{12}O_{40}$) is reported. The ionic liquid serves as a good reservoir for the catalyst. Even under solventfree condition, the catalyst could be easily recovered and reused. Excellent regioselectivity, high yields and ambient conditions are the striking features of the present protocol.

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- [25] Representative spectral data for products: di-(4-methoxyphenyl) sulfoxide: 1H NMR (300 MHz, $CDCl_3$): (δ = 3.74 (s, 6H), 7.05 (dd, 8H). EIMS: m/z : 262, 232, 202, 126, 78, 57. IR (KBr): 2930, 2859, 1584, 1475, 1357, 1256, 1208, 1035, 850, 790 cm^{-1} . Di-(2,4-dimethylphenyl) sulfoxide: 1H NMR (300 MHz, $CDCl_3$): (δ = 2.29 (s, 12H), 6.90 (d, 2H), 6.96 (d, 2H), 7.20 (d, 2H). EIMS: m/z : 258, 240, 226, 169, 141, 105, 77, 43. IR (KBr): 2925, 2845, 1580, 1450, 1330, 1215, 1035, 765, 610 cm^{-1} . Di-(2,4,6-trimethylphenyl) sulfoxide: 1H NMR (300 MHz, $CDCl_3$): (δ = 2.37 (s, 18H), 6.96 (s, 4H). EIMS: m/z : 286, 228, 208, 196, 105, 91, 77, 57. IR (KBr): 2934, 2848, 1589, 1462, 1321, 1024, 780, 601 cm^{-1} .