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# Metal-free chemoselective oxidation of sulfides by in situ generated Koser's reagent in aqueous media



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Sulfoxides and sulfones are important compounds due to their properties and reactivity. They have been widely used in the preparation of biologically and pharmaceutically significant compounds.<sup>1-3</sup> In particular, sulfoxides have also emerged as oxotransfer reagents<sup>4</sup> and as ligands.<sup>5</sup> On the other hand, the strong inductive ability of the sulfone group makes it attractive in the field of asymmetric organocatalysis.<sup>6</sup> In this context, a considerable effort has been devoted toward the preparation of sulfoxides and sulfones. One of the most favored and straightforward synthetic methods could be selective oxidation of sulfides to sulfoxides or sulfones (Scheme 1), which has been extensively studied by using different oxidants such as molecular oxygen,<sup>7</sup> hydrogen peroxide,<sup>8,9</sup> organic hydroperoxide,<sup>10</sup> hypervalent iodine,<sup>11</sup> and other halogen derivatives.<sup>12</sup> However, it is worth mentioning that a transition metal catalyst is often required to perform the reaction smoothly,<sup>13,14</sup> which may limit the application in terms of safety, toxicity, and abolishment of heavy metals. In addition, metal-free catalyzed processes are interesting alternatives to classical organic transformations since they are often more economical and environmentally friendly.

hypervalent iodine reagents have found broad application in organic chemistry due to their low toxicity, mild reactivity, ready availability, high stability, and easy handling.<sup>17</sup> In particular, hyperva nploved in the

# ABSTRACT

Selective oxidation of sulfides was successfully performed by employing phenyliodine diacetate as an oxidant with the catalysis of TsOH in aqueous solution under mild conditions. Sulfoxides were formed with 1.1 equiv of PhI(OAc)<sub>2</sub> at room temperature; whereas sulfones were obtained in the presence of 2.1 equiv of PhI(OAc)<sub>2</sub> at 80 °C under otherwise identical conditions. Notably, various sulfides were converted to corresponding sulfoxides or sulfones in good to high yields by this metal-free protocol. © 2014 Elsevier Ltd. All rights reserved.

As powerful electrophiles<sup>15</sup> and highly selective oxidants,<sup>16</sup>

lent	iodine	compounds	have	also	been	en





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[O] Cat. [O] = halogen, peracids, dioxiranes, hypervalent iodine, alkyl hydroperoxides, hypochlorites, H<sub>2</sub>O<sub>2</sub>, O<sub>2</sub>, etc. Cat. = Os, Sc, Mo, Ti, V, Re, Ru, Cr, W, Cu, Zn, Fe etc.

Scheme 1. Catalytic oxidation of sulfides to afford sulfoxides or sulfones.

oxidation of sulfides. Togo and co-workers have prepared (diacetoxyiodo)arenes containing heteroaromatics as novel oxidant to oxidize diaryl sulfides to corresponding sulfoxides.<sup>18</sup> Kobayashi group<sup>19</sup> developed immobilized ruthenium catalysts for the oxidation of sulfides to corresponding sulfones by using phenyliodine diacetate (PIDA) as oxidant. In addition, Zhdankin and co-workers,<sup>20</sup> reported a sulfoxidation protocol by using oligomeric iodosylbenzene sulfate, which was in situ generated from PIDA and a stoichiometric amount of sodium bisulfate, as oxidant in aqueous solution. On the other hand, Koser's reagent, hydroxy(tosyloxy)iodobenzene, was found to be efficient in a variety of transformations such as oxytosylation, dioxytosylation, phenyliodination, and oxidation.<sup>21</sup> Moreover, Yusubov and Wirth disclosed the reaction between PIDA and *p*-toluenesulfonic acid (TsOH), which gave Koser's reagent with reasonable yields.<sup>22</sup> In view of these precedents, sulfide oxidation involving hypervalent iodine reagents required prior preparation of catalyst or synthesis of Koser's reagent as oxidant with a stoichiometric amount of additives (e.g. TsOH, NaHSO<sub>4</sub>). Therefore, we assumed that if the Koser's reagent

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could be generated from PIDA and TsOH, then the possibility of employing TsOH as a catalyst should be considered for the reaction using PIDA as oxidant in the oxidation of sulfides.

As a part of our continuous interest on selective oxidation reactions,<sup>23,24</sup> we herein would like to report selective oxidation of sulfides in aqueous solution with the in situ formed Koser's reagent, from PIDA and a catalytic amount of TsOH, as reactive oxidant to afford the corresponding sulfoxides or sulfones under mild conditions (Scheme 2).

The exploratory experiments started using thioanisole **1a** as the model substrate. As shown in Table 1, the oxidation of 1a using PIDA (1.1 equiv) as oxidant in CH<sub>3</sub>CN under 80 °C for 12 h, provided phenyl methyl sulfoxide 2a in almost quantitative yield (Table 1, entry 1). An increase in the PIDA amount to 2.1 equiv caused a slight increase in the vield of phenyl methyl sulfone **3a** to 7% (entry 2). Interestingly, the reaction in water gave 44% yield of **2a** and 55% vield of **3a** (entry 3). The addition of a catalytic amount of Ag<sub>2</sub>CO<sub>3</sub>, CuBr<sub>2</sub>, and FeBr<sub>2</sub> did not lead to a significant improvement in sulfone yield (entries 4-6). When sodium dodecyl sulfate (SDS) was employed as phase-transfer catalyst, the yield of 3a was increased to 66% (entry 7). Moreover, 40 mol % of AcOH was also demonstrated to be inefficient (entry 8). Surprisingly, excellent conversion and selectivity were achieved in the presence of TsOH (10 mol %) with water as a solvent (entry 9). Nevertheless, only 12% yield of 3a was obtained in ethanol (entry 10). Compared with other solvent, water was demonstrated to be essential for the TsOH-catalyzed oxidation process. On the other hand, the aqueous reaction gave 2a with 89% yield using PIDA (1.1 equiv) as oxidant under room temperature for 5 h (entry 11). As a consequence,



Scheme 2. Chemoselective oxidation of sulfides.

### Table 1

Optimization of the reaction conditions<sup>a</sup>



Entry	Solvent	PIDA (equiv)	Cat.	Conv. <sup>b</sup> (%)	Yield <sup>b</sup> (%)	
					2a	3a
1	CH₃CN	1.1	_	99	98	<1
2	CH <sub>3</sub> CN	2.1	_	>99	92	7
3	$H_2O$	2.1	_	>99	44	55
4	$H_2O$	2.1	$Ag_2CO_3$	>99	47	52
5	$H_2O$	2.1	CuBr <sub>2</sub>	>99	50	49
6	$H_2O$	2.1	FeBr <sub>2</sub>	>99	43	56
7	$H_2O$	2.1	SDS	>99	33	66
8 <sup>c</sup>	$H_2O$	2.1	AcOH	96	35	60
9	$H_2O$	2.1	TsOH	>99	8	91
10	EtOH	2.1	TsOH	86	73	12
11 <sup>d</sup>	$H_2O$	1.1	TsOH	>99	89	10

<sup>a</sup> Reaction conditions: To a glass tube equipped with a magnetic stir bar, thioanisole (24.8 mg, 0.2 mml), indicated amount of PIDA, catalyst (10 mol %), solvent (1.5 mL) as solvent were added, and the mixture was stirred for 12 h at 80 °C. SDS = sodium dodecyl sulfate.

<sup>b</sup> Determined by GC with area normalization.

<sup>c</sup> 40 mol % of AcOH was added.

<sup>d</sup> Reaction at rt for 5 h.

the synthesis of sulfoxide **2a** and sulfone **3a** from sulfide **1a** could be accessed efficiently by using PIDA as oxidant, *p*-toluenesulfonic acid as catalyst in water (entries 9 and 11).

With the optimized conditions in hand, the utility and generality of this transition-metal-free process for the selective oxidation of sulfides were further examined. As shown in Table 2, a series of aromatic sulfides can be transformed into the corresponding sulfoxide. Various substituents including  $-CH_3$ ,  $-OCH_3$ , -Cl, and -CNcould be tolerated and the sulfoxides were obtained in almost excellent yields (Table 2 entries 1–5). With sulfide **1e**, the yield was improved to 87% after increasing the reaction time to 12 h (entry 5). In the case of diphenyl sulfide **1f**, the isolated yield of sulfoxide **2f** was 78% (entry 6). However, the sulfoxidation of dibenzothiophene sulfoxide **1g** was failed, probably due to its poor solubility in water (entry 7). Dialkyl sulfides (**2h** and **2i**) could convert to the corresponding sulfoxide in good to excellent yield under the reaction condition for 12 h (entries 8 and 9).

We next turned our attention to the scope of sulfones' preparation. The results have been listed in Table 3. The sulfides **1a-1d** 

# Table 2

Oxidation of sulfides to sulfoxides<sup>a</sup>



<sup>a</sup> Reaction conditions: To a glass tube equipped with a magnetic stir bar, sulfide (0.2 mmol), PIDA (71 mg, 0.22 mmol), *p*-toluenesulfonic acid (3.4 mg, 0.02 mmol),  $H_2O$  (1.5 mL) as solvent were added, and the mixture was stirred at rt for desired time.

<sup>b</sup> Isolated yield.

#### Table 3

Oxidation of sulfides to sulfones<sup>a</sup>

_1.S、_2	TsOH (10 mol%) PhI(OAc) <sub>2</sub> (2.1 equiv.)	0,0
1a-i	H <sub>2</sub> O, 80 °C	R <sup>1</sup> ~ R <sup>2</sup> 3a-i

Entry	Substrate	Sulfone	Time (h)	Yield <sup>b</sup> (%)
1	S la	S=0 3a	12	86
2	S 1b	O S 3b	20	78
3	S lc	o S 3c	20	80
4	CI Id		20	81
5	NC 1e	NC S 3e	36	40
6	If Street	S S S S S S S S S S S S S S S S S S S	20	42
7	lg state	°, ° S → 3g	24	0
8	S 1h	0,0 ,5 ,5 ,3h	24	89
9	S 1i	0,0 ,5 ,5 ,3i	24	86

<sup>a</sup> Reaction conditions: To a glass tube equipped with a magnetic stir bar, sulfide (0.2 mmol), PIDA (135 mg, 0.42 mmol), *p*-toluenesulfonic acid (3.4 mg, 0.02 mmol), H<sub>2</sub>O (1.5 mL) as solvent were added, and the mixture was stirred for desired time at 80 °C.

<sup>b</sup> Isolated yield.

were oxidized to afford the corresponding sulfones in 78–86% yield under the conditions for 12–20 h, which revealed that the reaction tolerated functional groups such as 4-methyl, 4-methoxyl, and 4halogen (entries 1–4). For 4-cyanophenylmethyl sulfide **1e** and diphenyl sulfide **1f**, low yields were obtained even with prolonged time (entries 5 and 6). Similarly, dibenzothiophene sulfoxide **1g** was inefficient presumably owing to poor solubility in water (entry 7). Gratifyingly, aliphatic substrates (**1h** and **1i**) displayed good reactivity to afford the corresponding sulfones.

To further gain insight into the reaction mechanism, <sup>1</sup>H NMR investigations were performed to get information about the reaction intermediate (Fig. 1). In <sup>1</sup>H NMR spectrum (A), the chemical shift of  $CH_{3-}$  in methyl phenyl sulfide (*a*, 2.25 ppm) and  $CH_{3-}$  in methyl phenyl sulfoxide (*b*, 2.74 ppm) could indicate that the sulfide is converted to sulfoxide efficiently without the formation of the sulfone after stirring for 10 min at room temperature.

After reaction at 80 °C for 2 h, the signal of  $CH_3$ – in methyl phenyl sulfone (c, 3.10 ppm) is observed as shown in Figure 1B. Moreover, the intensity of sulfoxide signal b is declined; whereas the sulfone signal c is augmented as the reaction going (Fig. 1B vs 1C). Consequently, the sulfone is found to be the only product with a trace of sulfide after 24 h (Fig. 1D). As a result, the sulfone is regarded to be formed via further oxidation of the sulfoxide. In particular, the sulfoxide is rapidly formed under the reaction conditions. On the other hand, the oxidation of the sulfoxide **2a** to generate the sulfone **3a** is much slower (see Supporting information).

As outlined in Scheme 3, a possible mechanism is proposed on the basis of the results described above. The presumed intermediate hydroxy(tosyloxy)iodobenzene is generated from phenyliodine diacetate and *p*-toluenesulfonic acid in aqueous solution.<sup>16,18</sup> The in situ formed hypervalent iodine reagent, Koser's reagent, could facilitate the oxygen transfer during the oxidation of the sulfide to the sulfoxide and further to the sulfone, which is converted to PhI and regenerates the catalyst TsOH.

In summary, we have developed a metal-free protocol for selective oxidation of sulfides under mild conditions. The reactive oxidant was proposed to be Koser's reagent generated in situ from readily available phenyliodine diacetate and only 10 mol% of TsOH, which avoided the prior synthesis of Koser's reagent with stoichiometric additives. Notably, the transformation was achieved in aqueous medium, resulting in the synthesis of sulfoxides and sulfones by tuning PIDA amount and the reaction temperature. Various sulfides worked well with this metal-free procedure under safe and mild conditions.



Figure 1. <sup>1</sup>H NMR of the oxidative reaction in D<sub>2</sub>O. (A) Reaction at rt after 10 min, (B) the reaction at 80 °C after 2 h, (C) the reaction at 80 °C after 12 h, (D) the reaction at 80 °C after 24 h.



Scheme 3. Proposed mechanism for the oxidation of sulfide by in situ formed Koser's reagent.

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### Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.01. 116.

# **References and notes**

- Carreno, M. C. Chem. Rev. 1995, 95, 1717. 1
- Stingl, K. A.; Tsogoeva, S. B. Tetrahedron: Asymmetry 2010, 21, 1055. 2.
- Wojaczynska, E.; Wojaczynski, J. Chem. Rev. 2010, 110, 4303. 3.
- Khenkin, A. M.; Neumann, R. J. Am. Chem. Soc. 2002, 124, 4198. 4.
- Fernandez, I.; Khiar, N. Chem. Rev. 2003, 103, 3651. 5.
- Nielsen, M.; Jacobsen, C. B.; Holub, N.; Paixao, M. W.; Jorgensen, K. A. Angew. 6. Chem., Int. Ed. 2010, 49, 2668.
- 7. Chinnusamy, T.; Reiser, O. ChemSusChem 2010, 3, 1040.
- Shi, F.; Tse, M. K.; Kaiser, H. M.; Beller, M. Adv. Synth. Catal. 2007, 349, 2425. 8 Ricoux, R.; Allard, M.; Dubuc, R.; Dupont, C.; Marechal, J. D.; Mahy, J. P. Org. 9. Biomol. Chem. 2009, 7, 3208.
- Kumar, S.; Verma, S.; Jain, S. L.; Sain, B. Tetrahedron Lett. 2011, 52, 3393. 10.
- 11. Moorthy, J. N.; Senapati, K.; Parida, K. N.; Jhulki, S.; Sooraj, K.; Nair, N. N. J. Org. Chem. 2011, 76, 9593.
- 12. Kowalski, P.; Mitka, K.; Ossowska, K.; Kolarska, Z. Tetrahedron 2005, 61, 1933.
- 13. Wu, X.-F. Tetrahedron Lett. **2012**, 53, 4328.
- Islam, S. M.; Roy, A. S.; Mondal, P.; Tuhina, K.; Mobarak, M.; Mondal, J. Tetrahedron Lett. **2012**, 53, 127. 14.
- 15. Wirth, T.; Brown, M.; Farid, U. Synlett 2013, 424
- Zhdankin, V. V.; Stang, P. J. Chem. Rev. 2008, 108, 5299. 16
- Wirth, T. Angew. Chem., Int. Ed. 2005, 44, 3656. 17.
- Togo, H.; Nabana, T.; Yamaguchi, K. J. Org. Chem. 2000, 65, 8391. 18.
- Miyamura, H.; Akiyama, R.; Ishida, T.; Matsubara, R.; Takeuchi, M.; Kobayashi, 19. S. Tetrahedron **2005**, 61, 12177.
- 20 Yusubov, M. S.; Yusubova, R. Y.; Funk, T. V.; Chi, K.-W.; Zhdankin, V. V. Synthesis 2009, 2505.
- 21. Koser, G. Aldrichim. Acta 2001, 34, 89.
- 22
- 23.
- Yusubov, M. S.; Wirth, T. Org. Lett. **2005**, 7, 519. Miao, C.-X.; He, L.-N.; Wang, J.-Q.; Wang, J.-L. Adv. Synth. Catal. **2009**, 351, 2209. Yu, B.; Liu, A.-H.; He, L.-N.; Li, B.; Diao, Z.-F.; Li, Y.-N. Green Chem. **2012**, 14, 957. 24