Tetrahedron Letters 55 (2014) 1818–1821

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

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

Bing Yu, Chun-Xiang Guo, Chun-Lai Zhong, Zhen-Feng Diao, Liang-Nian He *

State Key Laboratory and Institute of Elemento-Organic Chemistry, Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), Nankai University, Tianjin 300071, People's Republic of China

ARTICLE INFO

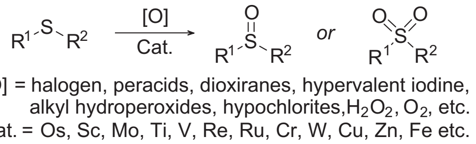
Article history:
Received 12 December 2013
Revised 17 January 2014
Accepted 27 January 2014
Available online 31 January 2014

Keywords:
Phenyliodine diacetate
Sulfide
Oxidation
Aqueous reaction

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 $PhI(OAc)_2$ at room temperature; whereas sulfones were obtained in the presence of 2.1 equiv of $PhI(OAc)_2$ 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.

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.[1–3] In particular, sulfoxides have also emerged as oxotransfer reagents[4] and as ligands.[5] On the other hand, the strong inductive ability of the sulfone group makes it attractive in the field of asymmetric organocatalysis.[6] 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,[7] hydrogen peroxide,[8,9] organic hydroperoxide,[10] hypervalent iodine,[11] and other halogen derivatives.[12] However, it is worth mentioning that a transition metal catalyst is often required to perform the reaction smoothly,[13,14] 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.



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

As powerful electrophiles[15] and highly selective oxidants,[16] hypervalent iodine reagents have found broad application in organic chemistry due to their low toxicity, mild reactivity, ready availability, high stability, and easy handling.[17] In particular, hypervalent iodine compounds have also been employed in the oxidation of sulfides. Togo and co-workers have prepared (diacetoxyiodo)arenes containing heteroaromatics as novel oxidant to oxidize diaryl sulfides to corresponding sulfoxides.[18] Kobayashi group[19] 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,[20] 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.[21] Moreover, Yusubov and Wirth disclosed the reaction between PIDA and *p*-toluenesulfonic acid (TsOH), which gave Koser's reagent with reasonable yields.[22] 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, $NaHSO_4$). Therefore, we assumed that if the Koser's reagent

---

* Corresponding author. Tel./fax: +86 22 23503878.
E-mail address: heln@nankai.edu.cn (L.-N. He).

http://dx.doi.org/10.1016/j.tetlet.2014.01.116

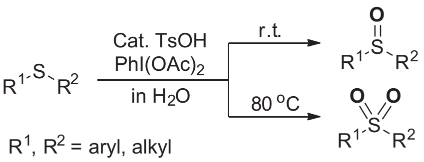
could be generated from PIDA and TsOH, then the possibility of employing TsOH as a catalyst should be considered for the reaction using PIDA as oxidant in the oxidation of sulfides.

As a part of our continuous interest on selective oxidation reactions,[23,24] 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_3CN 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 yield of phenyl methyl sulfone **3a** to 7% (entry 2). Interestingly, the reaction in water gave 44% yield of **2a** and 55% yield of **3a** (entry 3). The addition of a catalytic amount of Ag_2CO_3, $CuBr_2$, and $FeBr_2$ 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, 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).

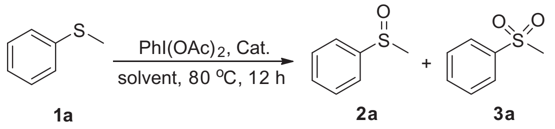
With the optimized conditions in hand, the utility and generality of this transition-metal-free process for the selective oxidation of sulfides were further examined. As shown in Table 2, a series of aromatic sulfides can be transformed into the corresponding sulfoxide. Various substituents including $-CH_3$, $-OCH_3$, –Cl, and –CN could 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**



Scheme 2. Chemoselective oxidation of sulfides.

Table 1
Optimization of the reaction conditions[a]



Entry	Solvent	PIDA (equiv)	Cat.	Conv.[b] (%)	Yield[b] (%)	
					2a	3a
1	CH_3CN	1.1	–	99	98	<1
2	CH_3CN	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	$CuBr_2$	>99	50	49
6	H_2O	2.1	$FeBr_2$	>99	43	56
7	H_2O	2.1	SDS	>99	33	66
8[c]	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[d]	H_2O	1.1	TsOH	>99	89	10

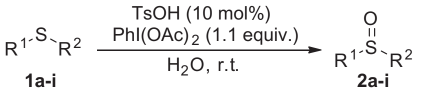
[a] Reaction conditions: To a glass tube equipped with a magnetic stir bar, thioanisole (24.8 mg, 0.2 mml), indicated amount of PIDA, catalyst (10 mol %), solvent (1.5 mL) as solvent were added, and the mixture was stirred for 12 h at 80 °C. SDS = sodium dodecyl sulfate.

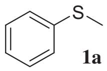
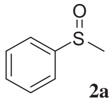
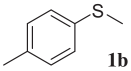
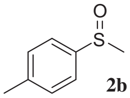
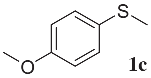
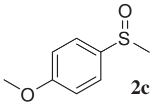
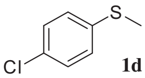
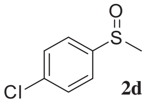
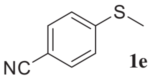
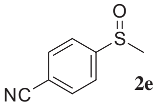
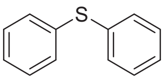
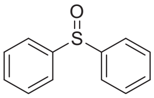
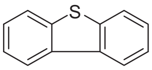
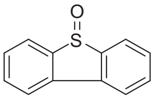
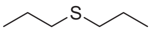
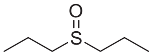
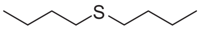
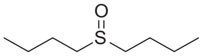
[b] Determined by GC with area normalization.

[c] 40 mol % of AcOH was added.

[d] Reaction at rt for 5 h.

Table 2
Oxidation of sulfides to sulfoxides[a]



Entry	Substrate	Sulfoxide	time (h)	Yield[b] (%)
1	 **1a**	 **2a**	4	88
2	 **1b**	 **2b**	5	85
3	 **1c**	 **2c**	5	84
4	 **1d**	 **2d**	5	85
5	 **1e**	 **2e**	12	87
6	 **1f**	 **2f**	5	78
7	 **1g**	 **2g**	24	0
8	 **1h**	 **2h**	12	81
9	 **1i**	 **2i**	12	90

[a] 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.

[b] Isolated yield.