RSC Advances

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

Journal Name RSCPublishing

COMMUNICATION

The First Zinc-Catalyzed Oxidation of Sulfides to Sulfones Using H_2O_2 as Green Oxidant

Cite this: DOI: 10.1039/x0xx00000x

Jian-Bo Feng,[a] Jin-Long Gong,[a] and Xiao-Feng Wu[a,b]*

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

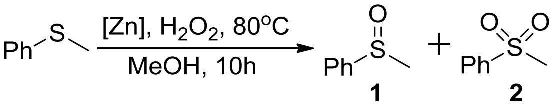
An interesting procedure for the oxidation of sulfides to sulfones has been developed. By using catalytic amount of zinc salt as the catalyst, DBU as the ligand, various sulfones were produced in good yields with hydrogen peroxide as the terminal green oxidant. Notably, this is the first example on zinc-catalyzed oxidation of sulfides to sulfones.

Under the requests of green chemistry, the developments of efficient and selective methodologies are under current interests.[1] In more detail, methodologies without the need of expensive or hazard reagents and with high reaction selectivity are more desired. From this respect, procedures with zinc as the catalyst and hydrogen peroxide as the reagent are highly matched with these standards.[2] Among all the transition metal catalysts, zinc salts are abundant, inexpensive, environmental benign, non-toxic, etc. With those non-fully listed advantages of zinc catalysts in mind, exploring the potentials of zinc catalysts in organic synthesis is absolutely interesting and necessary.[3] Additionally, hydrogen peroxide is considered as green oxidant with water as the only theoretical by-product.[4]

In organic synthesis, zinc is more known as zinc reagent for Negishi coupling and dialkylzinc as alkyl reagents or radical initiator. Zinc salts have been applied as catalysts in reduction reactions, addition reactions (Henry-, Michael-, Mannich-reaction, and so on), etc. as well. Because of the special electronic properties of zinc, zinc catalysts are rarely explored in oxidation reactions.[2b] Under this state, we have been working on the exploration of the potential of zinc catalysts in oxidation reactions during the last three years.[5] Various benzylic substrates were transformed into the corresponding products in a selective manner. Among them, a general zinc-catalyzed oxidation of sulfides to sulfoxides at room temperature using hydrogen peroxide as a green oxidant was developed in 2012.[6] Twenty-one examples of sulfoxides were prepared in moderate to excellent yields. During the optimization process of that study, sulfone was detected as an over oxidized product in most of the cases. Because of the absence of report on zinc-catalyzed oxidation of sulfides to sulfones, we started our further study on this topic and focus on sulfones formation.

Based on our former studied, we decide to choose thioanisole as the model substrate for further optimization. The first experiment was carried out with $ZnBr_2$ (10 mol%) as the catalyst, bipyridine (25 mol%) as the ligand, in methanol at 80 ^{o}C, using 8 equivalents of H_2O_2 as the oxidant. Total conversion of starting material was achieved; the ratiol of sulfoxide and sulfone was 25:75 (Table 1, entry 1). As the known strong influence of ligand on zinc-catalyzed oxidation of sulfides,[6] the testing of others typical nitrogen ligands were performed subsequently (Table 1, entries 2-9). Full conversion can be achieved in all the cases, but 7-30% of sulfoxide was detected as well. To our delight, the situation changed when DBU was applied as the ligand (Table 1, entry 10). Full conversion and full selectivity was achieved in this case. Then we use DBU as the ligand to test the effect of zinc salts (Table 1, entries 11-15). Except the case of ZnI_2, full conversion and selectivity were resulted in all the cases. Considering the price differences of zinc salts, we decide to choose $ZnCl_2$ as the catalyst for further studies on oxidative synthesis of sulfones.[7] Full conversion and selectivity can be achieved with 4 equivalents of H_2O_2 as well, and gave sulfone in 91% isolated yield (Table 1, entry 16). In the case of further decreasing the loading of H_2O_2 or $ZnCl_2$, the conversion and selectivity of thioanisole decreased (Table 1, entries 17 and 18). Low conversion was observed in the absence of $ZnCl_2$ (Table 1, entry 19). With the best combination system, the conversion and selectivity decreased as well under lower temperature.

Table 1. Zinc-catalyzed sulfone synthesis: Optimization.[a]

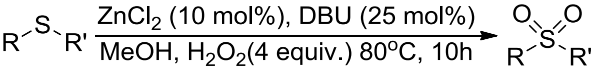


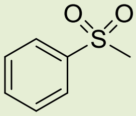
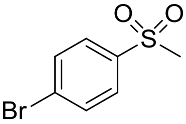
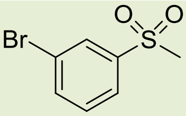
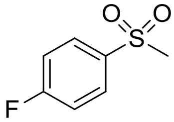
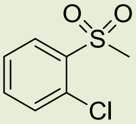
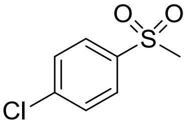
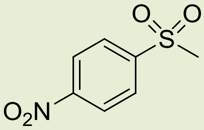
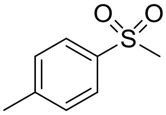
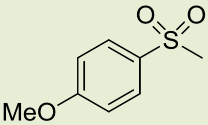
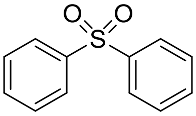
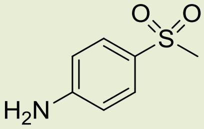
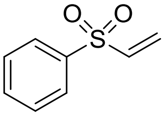
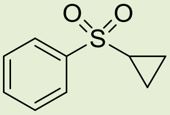
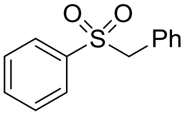
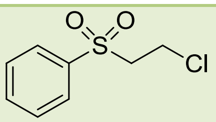
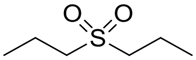
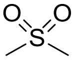
Entry	[Zn]	Ligand	Conv. [%][b]	Ratiol 1:2[b]
1	$ZnBr_2$	Bipyridine	100	25:75
2	$ZnBr_2$	DABACO	100	30:70
3	$ZnBr_2$	DMEDA	100	26:74
4	$ZnBr_2$	TMEDA	100	25:75
5	$ZnBr_2$	1,10-Phen	100	17:83
6	$ZnBr_2$	2-Aminopyridine	100	12:88
7	$ZnBr_2$	Pyridine	100	7:93
8	$ZnBr_2$	Tryptophan	100	11:89
9	$ZnBr_2$	Tyrosine	100	9:91
10	$ZnBr_2$	DBU	100	0:100
11	$ZnCl_2$	DBU	100	0:100
12	ZnI_2	DBU	70	80:20
13	$Zn(OTf)_2$	DBU	100	0:100
14	$Zn(OAc)_2$	DBU	100	0:100
15	$Zn(AcAc)_2$	DBU	100	0:100
16	$ZnCl_2$	DBU	100	0:100[c] 91%[f]
17	$ZnCl_2$	DBU	79	30:70[d]
18	$ZnCl_2$	DBU	100	89:11[e]
19	/	DBU	33	80:20

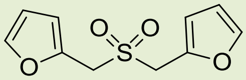
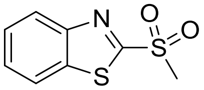
[a] Substrate (1 mmol), zinc catalyst (10 mol%), ligand (25 mol%), H_2O_2 (8 equiv.; 30 mol% in water), MeOH (2 mL), 80 °C, 10 h. [b] Conversion and ratiol were detected by GC using dodecane as internal standard. [c] H_2O_2 (4 equiv.). [d] H_2O_2 (2 equiv.). [e] H_2O_2 (4 equiv.), $ZnCl_2$ (5 mol%), DBU (5 mol%). [f] Isolated yield. DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene.

With the best reaction conditions in our hand, we started the substrates testing.[8] As shown in Table 2, 19 substrates were tested and succeeded. Halogen-substituted sulfones were isolated in good to excellent yields (70-94%; Table 2, entries 2-6). Nitro-substituted sulfone was formed in 70% yield from the corresponding sulfide (Table 2, entry 7). 98% of 1-methyl-4-(methylsulfonyl)benzene was isolated under our conditions (Table 2, entry 8). Methoxy- functional group can be tolerated as well (Table 2, entry 9).

Table 2. Zinc-catalyzed sulfones synthesis.[a]



Entry	Product	Yield[%][b]
1		91
2		92
3		94
4		83
5		70
6		88
7		70
8		98
9		97
10		96
11		97
12		46
13		98
14		85
15		50
16		98
17		85

18		62
19		22

[a] Substrate (1 mmol), ZnCl$_2$ (10 mol%), DBU (25 mol%), H$_2$O$_2$ (4 equiv.; 30 mol% in water), MeOH (2 mL), 80 ^{o}C, 10 h. [b] Isolated yield.

Amino as a potentially oxidizable group can be tolerable under our conditions as well, the corresponding 4-(methylsulfonyl)aniline was isolated in 97% yield (Table 2, entry 11). Additionally, vinyl-, cyclopropyl-, benzyl-, and 2-chloroethyl- substituted sulfides were tested as substrates as well, and succeeded to give the desired sulfones in 48-98% yields (Table 2, entries 12-15). Furthermore, aliphatic sulfides were oxidized and gave the corresponding sulfones in 62-98% yields (Table 2, entries 16-18). 2-(Methylthio)benzo[*d*]thiazole as an examples of heterocyclic substituted sulfides was tested under our standard conditions, 22% of the desired sulfone was isolated. The decomposition of benzo[*d*]thiazole under oxidative conditions is responsible for the low yield.

Conclusions

In conclusion, an efficient methodology on oxidation of sulfides to the corresponding sulfones has been developed. In the presence of catalytic amount of ZnCl$_2$, using DBU as unusual ligand and H$_2$O$_2$ as green oxidant, 19 examples of sulfones were isolated in moderate to excellent yields. Notably, this is the first example of zinc-catalyzed oxidation of sulfides to sulfones.

Notes and references

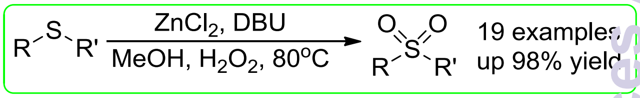
[a] Department of Chemistry, Zhejiang Sci-Tech University, Xiasha Campus, Hangzhou, Zhejiang Province, 310018, People's Republic of China
E-mail: xiao-feng.wu@catalysis.de

[b] Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Strasse 29a, 18059 Rostock (Germany)

Electronic Supplementary Information (ESI) available: [NMR data and spectrum]. See DOI: 10.1039/c000000x/

Acknowledgments: The authors thank the financial support from Zhejiang Sci-Tech University (1206838-Y). X. -F Wu appreciates the general support from Matthias Beller in LIKAT.

1. a) *Metal-Catalyzed reactions in water*, Eds: P. H. Dixneuf, V. Cadierno, Wiley-VCH, 2013; b) R. Noyori, *Chem. Commun.* 2005, 1807-1811; c) M. -O. Simon, C. -J. Li, *Chem. Soc. Rev.* 2012, **41**, 1415-1427; d) X. Han, M. Poliakoff, *Chem. Soc. Rev.* 2012, **41**, 1428-1436; e) R. B. N. Baig, R. S. Varma, *Chem. Soc. Rev.* 2012, **41**, 1559-1584.
2. a) X. -F. Wu, H. Neumann, *Adv. Synth. Catal.* **2012**, *354*, 3141-3160; b) X. -F. Wu, *Chem. Asian J.* **2012**, *7*, 2502-2509; c) S. Enthaler, *ACS Catal.* **2013**, *3*, 150-158.
3. For selected examples on zinc catalysts, see: a) D. E. Frantz, R. Fassler, E. M. Carreira, *J. Am. Chem. Soc.* **1999**, *121*, 11245–11246; b) D. E. Frantz, R. Fassler, E. M. Carreira, *J. Am. Chem. Soc*. **2000**, *122*, 1806–1807; c) D. Boyall, F. Lopez, H. Sasaki, D. Frantz, E. M. Carreira, *Org. Lett.* **2000**, *2*, 4233–4236; d) N. K. Anand, E. M. Carreira, *J. Am. Chem. Soc.* **2001**, *123*, 9687–9688; e) R. Fassler, D. E. Frantz, J. Oetiker, E. M. Carreira, *Angew. Chem., Int. Ed.* **2002**, *41*, 3054–3056; f) C. Fischer, E. M. Carreira, *Org. Lett.* **2004**, *6*, 1497–1499; g) D. Topic, P. Aschwanden, R. Fassler, E. M. Carreira, *Org. Lett.* **2005**, *7*, 5329–5330; h) N. A. Marinos, S. Enthaler, M. Driess, *ChemCatChem* **2010**, *2*, 846–853; i) S. Enthaler, B. Eckhardt, S. Inoue, E. Irran, M. Driess, *Chem. Asian J.* **2010**, *5*, 2027–2035; j) S. Enthaler, K. Schröder, S. Inoue, B. Eckhardt, K. Junge, M. Beller, M. Driess, *Eur. J. Org. Chem.* **2010**, 4893–4901; k) S. Enthaler, Catal. Lett. 2011, 141, 55–61; l) S. Enthaler, *Catal. Sci. Technol.* **2011**, *1*, 104–110; m) S. Enthaler, S. Inoue, *Chem. Asian J.* **2012**, *7*, 169–175; n) S. Enthaler, M. Weidauer, *Chem. Eur. J.* **2012**, *18*, 1910–1913; o) S. Enthaler, *Angew. Chem. Int. Ed.* **2014**, *53*, 2716-2721; p) S. Enthaler, M. Weidauer, *ChemSusChem* **2012**, *5*, 1195–1198*;* q) S. Enthaler, *Eur. J. Lipid Sci. Technol.* **2013**, *115*, 239–245; r) S. Enthaler, A. Trautner, *ChemSusChem* **2013**, *6*, 1334–1336.
4. C. W. Jones, J. H. Clark. *Applications of Hydrogen Peroxide and Derivatives*. Royal Society of Chemistry, **1999**.
5. a) X. -F. Wu, *Chem. Eur. J.* **2012**, *18*, 8912-8915; b) X. -F. Wu, *Tetrahedron Lett.* **2012**, *53*, 3397-3399; c) X. -F. Wu, *Tetrahedron Lett*. **2012**, *53*, 4328-4331; d) Z. -Z. Song, J. -L. Gong, M. Zhang, X. -F. Wu, *Asian. J. Org. Chem.* **2012**, *1*, 214-217; e) X. -F. Wu, *Tetrahedron Lett.* **2012**, *53*, 6123-6126; f) X. -F. Wu, C. B. Bheeter, H. Neumann, P. H. Dixneuf, M. Beller, *Chem. Commun.* **2012**, *48*, 12237-12239; g) M. Zhang, X. -F. Wu, *Tetrahedron Lett.* **2013**, *54*, 1059-1062; h) X. -F Wu, M. Sharif, A. Pews-Davtyan, P. Langer, K. Ayub, M. Beller, *Eur. J. Org. Chem.* **2013**, 2783-2787; i) M. Sharif, J. Opalach, P. Langer, M. Beller, X. -F Wu, *RSC Adv.* **2014**, *4*, 8-17.
6. X. -F. Wu, *Tetrahedron Lett.* **2012**, *53*, 4328-4331.
7. Sigma-Aldrich Product Catalogue.
8. Under air, in a 50 mL tube, ZnCl$_2$ (10 mol %), DBU (25 mol%), and a stirring bar was added. Then H$_2$O$_2$ [4 mmol; 30 % aq] was added slowly to the tube after the addition of substrate (1 mmol) and MeOH (2 mL) by syringe. Then close the tube and keep the final solution at 80 ^{o}C for 10 h. When the reaction was finished, the solvent was removed in vacuo, and the residue was purified by flash column (petroleum ether/ethyl acetate). All the products are commercially available.



The first example on zinc-catalyzed oxidation of sulfides to sulfones has been developed. By using catalytic amount of zinc salt as the catalyst, DBU as the ligand, various sulfones were produced in good yields with hydrogen peroxide as the terminal green oxidant.