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Selective oxidation of sulfides to sulfoxides catalyzed by ruthenium (III) *meso*-tetraphenylporphyrin chloride in the presence of molecular oxygen

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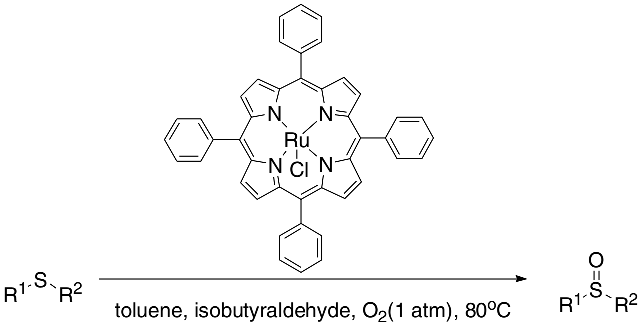
Abstract—Highly efficient selective oxidation of sulfides to sulfoxides by molecular oxygen catalyzed by ruthenium (III) *meso*-tetraphenylporphyrin chloride (Ru(TPP)Cl) with isobutyraldehyde as oxygen acceptor has been reported. In large-scale experiment of thioanisole oxidation, the isolated yield of sulfoxide of 92% was obtained and the turnover number reached up to 92,000.

Selective oxidation of sulfides to the corresponding sulfoxides remains a challenge and is interesting because of the importance of sulfoxides as synthetic intermediates in organic synthesis.[1] Metalloporphyrins, as model catalysts of cytochrome P-450, have been used to mimic various oxidation reactions, for example, hydroxylation of hydrocarbon, epoxidation of olefins and oxidation of sulfide.[2] The sulfoxidation of sulfides catalyzed by cytochrome P-450 and peroxidases is a subject of current interest since the pioneering work of Oae and co-workers,[3] in which various oxidants, for example, PhIO,[4] NaOCl,[5] and Oxone,[6] were used. Hydrogen peroxide is usually applied in metalloporphyrin catalytic sulfoxidation system since it is an environmentally benign oxidant.[7] However, although selective oxidation by molecular oxygen is more attractive because of its cost-effectiveness and environmentally friendly nature of the oxidant,[8] few reports were found for such oxidation of sulfides catalyzed by metallporphyrins. Mansuy[9] ever reported selective aerobic oxidation of di-*n*-butylsulfide to the corresponding sulfoxide in 68% yield in the presence of Mn(TPP)Cl catalysts and 1-methylimidazole as co-catalyst.

In our earlier studies[10] on cyclohexane and nitrotoluene oxidation with dioxygen, high production yields and TONs have been observed for the catalysts metalloporphyrins and metallophthalocyanines applied. Recently,[11] we developed a controllable procedure for the oxidation of sulfides to the corresponding sulfoxides and sulfones by hydrogen peroxide in the presence of β-cyclodextrin as catalyst. As a part of our ongoing interest in metalloporphyrin-catalyzed oxidations with green oxidants, the aerobic oxidation of sulfide to sulfoxide catalyzed by Ru(TPP)Cl in the presence of isobutyraldehyde has been developed (Scheme 1). It should be mentioned for the procedure that the selectivity from sulfides to sulfoxides could be perfectly controlled by choosing suitable metalloporphyrin. In the present paper, a highly efficient selective oxidation system for sulfides to sulfoxides by molecular oxygen catalyzed by ruthenium (III) *meso*-tetraphenylporphyrin chloride



Scheme 1. Ruthenium *meso*-tetraphenylporphyrin chloride catalyzed sulfoxidation.

Keywords: Ruthenium porphyrin; Sulfide; Sulfoxide; Dioxygen.

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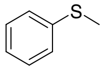
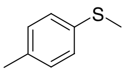
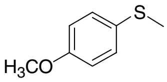
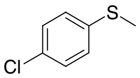
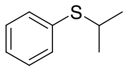
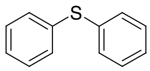
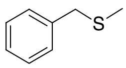
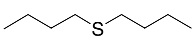
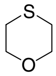
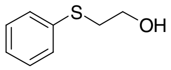
(Ru(TPP)Cl)[12] with isobutyraldehyde as oxygen acceptor has been developed.

With thioanisole as model compound, the effects of reaction conditions on the sulfoxidation with molecular oxygen as oxidant and catalyzed by Ru(TPP)Cl have been investigated.[13] Toluene was chosen as solvent for the reaction, and the results were listed in Table 1.

As shown in Table 1, it can be known that the catalytic activity of metalloporphyrins is related with the nature of central ions in the thioanisole sulfoxidation (entries 1–4). Compared with manganese, iron, and cobalt porphyrin catalysts, Ru(TPP)Cl was the most effective catalyst in the sulfoxidation system since thioanisole could be completely converted to sulfoxide within 30 min. Various amounts of Ru(TPP)Cl catalyst were examined in the oxidation of thioanisole with molecular oxygen as an oxidant. Poorer selectivity of sulfoxide and poorer activity of sulfide were obtained in thioanisole oxidation when the molar ratios of catalyst to thioanisole were 1×10^{-3} and 1×10^{-5}, respectively (entries 5 and 6), and the optimal molar ratio of catalyst to substrate was 1×10^{-4}. When the substrate/isobutyraldehyde molar ratio was 1/4, 79% thioanisole could be converted (entry 8), and higher molar ratio of substrate to isobutyraldehyde gave higher conversion of thioanisole (entries 1 and 9). However, no significant difference was observed when the substrate/isobutyraldehyde molar ratio reached 1/5 for the present system.

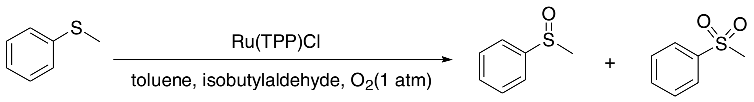
Both the Ru(TPP)Cl catalyst and the additive isobutyraldehyde were necessary for the smooth conversion. In the absence of the catalyst, only 18% thioanisole could be converted, indicating that the Ru(TPP)Cl catalyst is crucial for the sulfoxidation (entry 7). Without the addition of isobutyraldehyde, only 12% sulfoxide could be obtained even by conducting the reaction for 90 min (entry 10). According to the previous works,[14] the aerobic oxidation catalyzed by metal complexes plus isobutyraldehyde should proceed via a radical mechanism. In the process, the metal complexes reacts with aldehyde to generate acylperoxy radicals, which acts as initiation in the chain mechanism.

Table 2. Oxidation of various sulfides by molecular oxygen catalyzed by Ru(TPP)Cl[a]

Entry	Substrate	Time (min)	Conv. (%)	Selectivity (%)	
				Sulfoxide	Sulfone
1		30	99	>99	<1
2		30	97	96	4
3		30	98	95	5
4		45	96	95	5
5		45	93	96	4
6		60	98	92	8
7		30	>99	>99	<1
8		20	>99	>99	<1
9		60	94	97	3
10		45	>99	90	<1

[a] Reaction conditions: substrate (2 mmol), molar ratio of substrate/isobutylaldehyde (1/5), molar ratio of catalyst/substrate (1/10,000), toluene (5 mL), O_2 (bubbling), 80 °C.

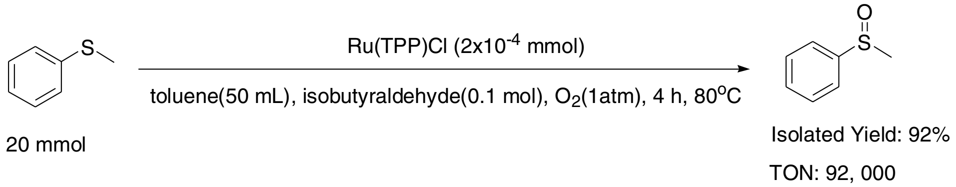
Table 1. Oxidation of thioanisole catalyzed by Ru(TPP)Cl in the presence of molecular oxygen[a]



Entry	Catalyst	Time (min)	Isobutylaldehyde/substrate (molar ratio)	T (°C)	Conv. (%)	Selectivity (%)	
						Sulfoxide	Sulfone
1	Ru(TPP)Cl	30	5/1	80	>99	>99	<1
2	Mn(TPP)Cl	60	5/1	80	79	>99	<1
3	Fe(TPP)Cl	90	5/1	80	63	94	6
4	Co(TPP)Cl	90	5/1	80	56	95	5
5[b]	Ru(TPP)Cl	30	5/1	80	>99	40	60
6[b]	Ru(TPP)Cl	30	5/1	80	52	>99	<1
7	—	90	5/1	80	18	89	11
8	Ru(TPP)Cl	30	4/1	80	79	>99	<1
9	Ru(TPP)Cl	30	6/1	80	>99	>99	<1
10	Ru(TPP)Cl	90	0	80	12	>99	<1
11	Ru(TPP)Cl	90	5/1	70	75	98	2
12	Ru(TPP)Cl	30	5/1	90	>99	45	55

[a] Substrate (2 mmol), molar ratio of catalyst/substrate (1/10,000), toluene (5 mL), O_2 bubbling (1 atm).

[b] Catalyst/substrate (molar ratio) = 1/1000, 1/100,000, respectively.



Scheme 2. Large-scale oxidation of thioanisole catalyzed by Ru(TPP)Cl.

Temperature is another important factor to influence the selectivity of thioanisole oxidation to sulfoxide catalyzed by Ru(TPP)Cl in presence of molecular oxygen. Only 75% thioanisole could be oxidized by conducting the reaction under 70 °C for 90 min (entry 11), and when the temperature rose to 90 °C, the poorer selectivity of sulfoxide could be obtained accordingly (entry 12).

Encouraged by the excellent catalytic performance for the thioanisole oxidation to sulfoxide, different sulfides were subjected to the reaction system in the presence of molecular oxygen, and the results are listed in Table 2.

As in Table 2, all substrates could be smoothly converted to sulfoxides with high conversion rates, and excellent selectivities were obtained by Ru(TPP)Cl catalyst and molecular oxygen as the sole oxidant. Moreover, it can be observed that the electronic property of substrate affects the reaction rate (entries 1–4). It required a slightly longer reaction time for substrate with electron-withdrawing groups (entry 4). The influence of steric effects could further be found from the oxidation of diphenyl sulfide and isopropyl phenyl sulfide. The conversion rates of diphenyl sulfide and isopropyl phenyl sulfide were 98%, 93% after much longer reactions time (entries 5 and 6). Comparing with thianisole, methyl benzyl sulfide presents the similar reaction behavior, and it could be stoichiometrically converted under the same conditions (entry 7). Sulfoxidation of the linear chain di-*n*-butyl sulfide smoothly proceeded in less reaction time with high conversion and yields (entry 8). Cyclic sulfide, that is, 1,4-thioxane, could also be efficiently sulfoxidated to the corresponding sulfoxide with 94% conversion and 97% selectivity (entry 9).

Despite high efficiency, another salient feature of the present sulfoxidation system is its high chemo-selectivity. For oxidation of hydroxyl group-containing sulfide, for example, 2-(phenylthio) ethanol (entry 10), sulfide can be entirely converted and the yields of sulfoxide could reach 90%, and 10% yield of the corresponding aldehyde was found in products. It demonstrates that the sulfide functional group is highly reactive, but hydroxyl group could hardly be activated under such reaction conditions.

It should be mentioned that the present reaction system was highly selective. Sulfoxides could be nearly stoichiometrically produced, and the generation of the corresponding sulfones was well controlled, which makes this process a good alternative for sulfoxide production.

Large-scale thioanisole oxidation experiment was carried out as shown in Scheme 2.[15] When the amount of Ru(TPP)Cl catalyst was 2×10^{-4} mmol, sulfoxide could be obtained with the isolated yield of 92% by conducting the reaction for 4 h. It should be mentioned that the turnover number of the present catalyst could exceed 90 thousands. To our best knowledge, the oxidation reaction system for sulfide to sulfoxide catalyzed by metalloporphyrins in the presence of molecular oxygen has never been reported before with such high TON value.

Conclusions. Sulfoxidation of sulfides by molecular oxygen was efficiently enhanced by using Ru(TPP)Cl as catalyst and isobutyraldehyde as oxygen acceptor. Under 80 °C and atmospheric pressure, the catalytic system presented high activity and selectivity for the oxidation of sulfides to sulfoxides. In a large-scale experiment of thioanisole oxidation, the isolated yield of sulfoxide was 92%. The turnover number of the present catalyst could exceed 90 thousands.

Acknowledgments

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11. Ji, H. B.; Hu, X. F.; Shi, D. P.; Li, Z. *Russ. J. Org. Chem.* **2006**, *42*, 959.
12. *meso*-Tetraphenylporphyrin (TPP) was prepared according to the known procedure, see Alder, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476, Metalloporphyrins were prepared according to our previously works, see: Ref. 10.
13. General oxidation procedure for oxidation of sulfide. Ru(TPP)Cl (2×10^{-4} mmol) was added to a stirring mixture solution of toluene (5 mL), sulfide (2 mmol), and isobutylaldehyde (0.01 mol). Dioxygen was bubbled through the solution. The consumption of sulfides and formation of products were monitored by GC (Shimadzu GC14C) and GC–MS (Shimadzu GCMS-QP5050A).
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15. General procedure for thioanisole oxidation in large scale. To a stirring solution of toluene (50 mL), thioanisole (20 mmol), isobutylaldehyde (0.1 mol), and Ru(TPP)Cl (2×10^{-4} mmol) were added in the presence of molecular oxygen. After reaction, the crude products were purified via column chromatography (silica gel, eluting agent: $V_{\text{acetic ester}}/V_{\text{petroleum ether}} = 1/3$) to obtain 2.58 g pure sulfoxide (92%).