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An efficient solvent free catalytic oxidation of sulfides to sulfoxides with hydrogen peroxide catalyzed by a binaphthyl-bridged Schiff base titanium complex

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Abstract—A titanium binaphthyl-bridged Schiff base complex proved to be an efficient catalyst for the hydrogen peroxide oxidation of aromatic and aliphatic sulfides to the corresponding sulfoxides in satisfactory yields under solvent-free conditions.

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1. Introduction

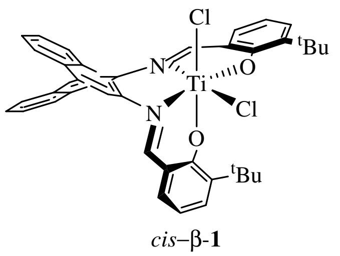
The oxidation of sulfides is the major method for the synthesis of sulfoxides which are versatile intermediates in organic synthesis (usable for C–C bond formation[1] and functional group transformations[2]) and are useful for the preparation of biologically and medically important compounds.[3]

Although many reagents are available for the oxidation of sulfides to sulfoxides,[4] the catalytic processes with environmentally benign oxidants have become increasingly important.

Apart from molecular oxygen, recently, hydrogen peroxide has been a very attractive 'green oxidant' offering the advantages that it is cheap, environmentally benign, readily available and produces only water as a by-product.[5] Nevertheless, hydrogen peroxide alone has to be used carefully due to the possibility of an over-oxidation reaction.[6]

Many catalysts have been specifically developed for hydrogen peroxide: tungsten catalyst systems,[7] a dinuclear iron complex,[8] a tungsten catalyst coupled with an acidic phase-transfer catalyst under organic solvent and halogen-free conditions,[9] an iron tetrakis-(pentafluorophenyl)-porphyrin complex,[10] HPA having Keggin structure,[11] a silica-based tungstate interphase catalyst.[12] A variety of Mt-(salen) complexes[13–15] are able to catalyze the asymmetric oxidation of sulfides to sufoxides with hydrogen peroxide, as the terminal oxidant, but a drawback of these convenient methods is often the use of chlorohydrocarbon solvents or anhydrous H_2O_2 in ethanol[6] and the over-oxidation to sulfones as side products.

Recently, we became interested in the use of titanium (salen)-catalysts in oxidation reactions and we reported the preparation and the characterization of a new octahedral titanium complex bearing a bulky binaphthyl-bridged Schiff base ligand (*rac*-**1**, Fig. 1) and we showed that the C_1-symmetric *cis*-β isomer is preferentially formed.[16]



cis–β-**1**

Figure 1. The titanium binaphthyl-bridged Schiff base complex **1**.

Keywords: Salen ligands; Ti(IV) complexes; Sulfoxidation; Hydrogen peroxide; Sulfoxide; Oxidation.

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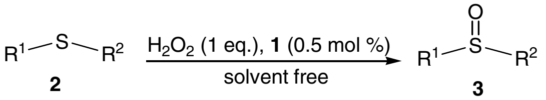
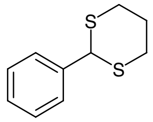
Table 1. Oxidation of methyl *p*-tolyl sulfide using 30% aqueous H_2O_2 catalyzed by **1**

Entry	Catalyst (mol %)	Reaction time (min)/*T* (°C)	Yield of Sulfoxide (%)	Yield of Sulfone (%)
1[a]	1	1200/rt	60	10
2	1	15/rt	80	12
3	—	180/rt	39	—
4	0.5	15/rt	82	12
5	0.5	120/4	72	4
6	0.5	360/4	92	8

[a] CH_2Cl_2 was used as the solvent in the reaction.

Table 2. Oxidation with 30% aqueous H_2O_2 of sulfides to sulfoxides catalyzed by **1**



Entry	R¹	R²	Time (min)	Yield of sulfoxide (%)	Yield of sulfone (%)
1	*o*-(MeO)C_6H_4	Me	15	95	2
2	*p*-(MeO)C_6H_4	Me	15	86	8
3	*p*-ClC_6H_4	Me	15	77	11
4	*p*-(NO_2)C_6H_4	Me	15	39	3
5	*p*-(NO_2)C_6H_4	Me	120	74	4
6	Me(CH_2)$_7$	Me	15	83	13
7[a]			15	68	—

[a] Diastereoselectivity *trans*/*cis* 98/2 determined by ^{1}H NMR analysis (400 MHz) on the crude reaction mixture.

We also reported some preliminary results concerning its catalytic activity in the epoxidation of allylic alcohols: the epoxyalcohols were obtained in very high regio and chemoselective way by the MW exposure of the mixture in solvent free-conditions.[16]

In the present work we wish to report an efficient, solventless protocol in which H_2O_2 has been used as the oxidizing agent in the presence of the complex **1** for the chemoselective oxidation of sulfides to their sulfoxides in high chemical yield and short reaction times.

Initially, we performed a set of preliminary experiments on methyl *p*-tolyl sulfide as a model substrate using 30% aqueous hydrogen peroxide in the presence of a catalytic amount of **1** at room temperature under solvent free conditions. The results are depicted in Table 1.

The reaction was initially carried out in CH_2Cl_2 (entry 1) using 1% mol of catalyst and produced the sulfoxide in 60% yield while, interestingly, under solvent free conditions (entry 2), methyl *p*-tolyl sulfoxide was obtained in 80% yield and sulfone in 12% yield after only 15 min. A reduction of catalyst loading (entry 4) did not cause a lowering of yield and chemoselectivity. It is noteworthy that in a blank experiment (entry 3), no significant oxidation was observed under similar reaction conditions in the absence of **1**, and only a low conversion was observed in the presence of 2 equiv of H_2O_2 after prolonged reaction times.

In order to improve the chemoselectivity, the reaction was carried out at the lower temperature of 4 °C and under these conditions the sulfoxide was isolated in higher yield simply by prolonging the reaction time (entries 5 and 6) while the occurrence of the process of over-oxidation to sulfone was reduced in a not negligible way.

To study the scope of this procedure, a series of various substituted sulfides including alkyl aryl sulfides and dialkyl sulfides was reacted according to optimized reaction conditions (Table 2).

The results are reported in Table 2: it can be observed that in the series of methyl aryl sulfides (Table 2, entries 1–5) the yields of sulfoxide are high and the electronic nature and the position of the substituents have a minimal effect on the efficiency of the reaction, although the presence of a nitro group on the aromatic ring required longer reaction time to obtain comparable efficiency (cfr. entries 4 and 5). As shown in entry 6, the catalyst **1** under the same reaction conditions is also effective in the oxidation of a dialkyl sulfide affording the corresponding sulfoxide in excellent yield and in a very short time. At last, when the reaction was performed on the cyclic thioacetal (entry 7), an exclusive process of monosulfoxidation was found to take place with high level of *trans*-diastereoselectivity.

In conclusion, the results reported in this letter clearly indicate that using as low as 0.5% mol of catalyst **1** it is possible to obtain a mild and chemoselective synthesis of sulfoxides from both aromatic and aliphatic sulfides. The procedure is solvent-free and requires 1 equiv of benign oxidant H_2O_2. Lastly, very short reaction times are needed to obtain a high yield of sulfoxides.

2. Catalyst preparation

The catalyst **1** was prepared as reported in Ref. 16.

3. General procedure for the oxidation of sulfides to sulfoxides

A 30% hydrogen peroxide solution (1 equiv, 1 mmol) was added to a vial containing the sulfide **2** (1 mmol) and complex **1** (0.5%, 0.005 mmol). After stirring at room temperature for the reported time, 10% solution of Na_2SO_3 (2 ml) was added. The mixture was extracted with AcOEt and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The remaining oil was purified by chromatography on silica gel (Etp/AcOEt 1/1 v/v).

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