A mild, efficient and selective oxidation of sulfides to sulfoxides

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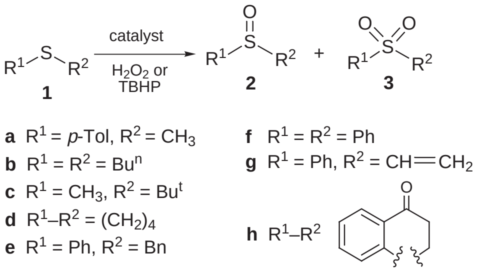
Several titanium derivatives supported on silica have been investigated as catalysts in the sulfide→sulfoxide oxidation; the supported titanium/tartaric acid catalyst is highly suited to reactions carried out with H_2O_2, leading to high yields and high sulfoxide/sulfone selectivities, while small asymmetric inductions (up to 13%) are observed.

The selective oxidation of sulfides to sulfoxides has been a challenge for many years, partly due to the importance of sulfoxides as intermediates in organic synthesis.[1] In recent years selective oxidation of sulfides to sulfoxides has been carried out with a large number of supported reagents.[2] Recently, the use of H_2O_2 has taken on a new importance due to environmental implications, however, a catalyst is necessary to activate this oxidant. TS-1[3,4] and TS-2,[5] promote sulfide oxidation, but the use of bulky sulfides is precluded by their limited access to the Ti active sites. In order to overcome this limitation other molecular sieves have been used.[3–6] Ti-MCM-41 allows the oxidation of bulky sulfides,[6] but with low sulfoxide/sulfone selectivity.

Following a methodology closely related to that used by Shell to prepare $TiCl_4$-modified silica,[7] we have treated silica with $Ti(OPr^i)_4$ and shown[8] that this solid is an efficient catalyst in the epoxidation of alkenes of any size with hydroperoxides. We considered it interesting to test these silica-supported titanium compounds as catalysts in the selective oxidation of sulfides to sulfoxides (Scheme 1).

Firstly we tested the silica treated with $Ti(OPr^i)_4$ (**cat-1**, Ti content: 1.02 mmol g^{-1}) as a catalyst in the oxidation of methyl *p*-tolyl sulfide with TBHP and with H_2O_2 (Table 1, entries 1–4). Although the oxidation is faster with TBHP, a better sulfoxide/sulfone selectivity is obtained with H_2O_2. The recovered catalysts show a similar activity, but the product selectivity increases, mainly in the reaction carried out with H_2O_2, which indicates that the recovered catalyst does not have the same structure. It seems logical that in the presence of a large excess of water (we use 30% H_2O_2), the isopropoxy groups are hydrolysed to hydroxy groups, and that this modification of the Ti environment influences the course of the reaction.

In view of these results we decided to assess the effect of the introduction of polar groups near the titanium and we treated the original catalyst with diethyl (*R*)-tartrate (Scheme 2) to obtain **cat-2** (1.06 mmol Ti g^{-1}). The modification of the catalyst was monitored by IR spectroscopy, which shows the appearance of a broad carbonyl band. The width of this band indicated the presence of several kinds of carbonyl groups, and Scheme 2 shows only one of the possibilities. The catalytic tests (Table 1, entries 4–7) show that the introduction of diethyl tartrate reduces the catalytic activity and increases the sulfoxide/sulfone

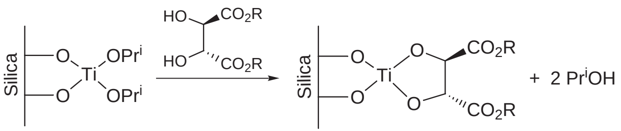


Scheme 1

Table 1 Results obtained in the oxidation of methyl *p*-tolyl sulfide **1a** promoted by different supported titanium catalysts[a]

				Yield (%)				
Entry	Catalyst	Sulfide	Oxidant	*t*/h	Total	sulfoxide **2**	sulfone **3**	**2:3**
1	**cat-1**	**1a**	TBHP	0.5	79	59	20	75:25
2	**cat-1**[b]	**1a**	TBHP	2	85	71	14	83:17
3	**cat-1**	**1a**	H_2O_2	3	87	75	12	86:14
4	**cat-1**[b]	**1a**	H_2O_2	3	88	84	4	95:5
5	**cat-2**	**1a**	TBHP	4	90	83[c]	7	92:8
6	**cat-2**	**1a**	H_2O_2	3	89	77[d]	12	87:13
7	**cat-2**[b]	**1a**	H_2O_2	3.5	85	84	1	99:1
8	**cat-3**	**1a**	TBHP	4	91	82[e]	9	90:10
9	**cat-3**	**1a**	H_2O_2	4	96	95[f]	1	99:1
10	**cat-3**[b]	**1a**	H_2O_2	4.5	96	95	1	99:1
11	—	**1a**	H_2O_2	24	49	47	2	96:4
12	**cat-3**	**1a**	H_2O_2	24	97	94	3	97:3
13	**cat-3**	**1b**	H_2O_2	4	100	100	0	—
14	**cat-3**	**1c**	H_2O_2	24	97	94	3	97:3
15	**cat-3**	**1d**	H_2O_2	4	98	96	2	98:2
16	**cat-3**	**1e**	H_2O_2	24	94	93	1	99:1
17	**cat-3**	**1f**	H_2O_2	24	97	95	2	98:2
18	**cat-3**	**1g**	H_2O_2	24	97	94	3	97:3
19	**cat-3**	**1h**	H_2O_2	24	95	92	3	97:3

[a] At 25 °C with 187 mg cat per mmol sulfide and 1 equiv. oxidant, in CH_2Cl_2 (with TBHP) or MeOH (with H_2O_2). The reactions were monitored by GC and the final results determined by ^1H NMR spectroscopy after filtering and washing the catalyst. [b] Catalyst recovered from a reaction with the same oxidant. [c] 7% ee. [d] 2% ee. [e] 8% ee. [f] 13% ee.



cat-1

cat-2 R = Et
cat-3 R = H

Scheme 2

selectivity in the reaction carried out with TBHP, while the catalytic performance is almost unchanged when H_2O_2 is used. The recovered catalyst gives an exceptional sulfoxide/sulfone selectivity (entry 7), which points to a new structure of the catalytic sites after recovery, as shown by the modification of the IR carbonyl band, which suggests the hydrolysis of the ester groups.

In view of this we decided to treat the initial catalyst with (*R*)-tartaric acid and to test the catalytic activity of this solid (**cat-3**, 0.82 mmol Ti g^{-1}). The results obtained with TBHP (entry 8) are very similar to those obtained using the catalyst containing diethyl (*R*)-tartrate (**cat-2**). However, the reactions carried out with H_2O_2 (entries 9 and 10) lead to an excellent sulfoxide/sulfone ratio and a very high selectivity (97%) with respect to the H_2O_2.

(*R*)-Tartaric acid is strongly adsorbed onto silica, thus it is important to assess the modification of the titanium centres and the catalytic role of these centres. The modification of the environment of titanium can be estimated from the amount of Pr^{i}OH lost during the preparation of the catalyst. Although it is not possible to obtain quantitative conclusions, given that some Pr^{i}OH may remain adsorbed on the silica surface, GC analysis shows that 65 ± 5% of the Pr^{i}O groups present in the original solid are lost during treatment. This result agrees with the modification of most of the titanium atoms. The catalytic role of the titanium was confirmed by adsorbing onto silica gel the same amount of (*R*)-tartaric acid used to modify the catalyst and carrying out the reaction in the presence of this solid. The results obtained are the same as those reached in the absence of catalyst, showing that the catalytic activity is related to the presence of titanium.

Although it was not the aim of the present work, the introduction of chiral centers may produce an asymmetric reaction, and so this possibility was considered. The ee of the sulfoxides was determined as previously described,[9] and the absolute configuration was determined by polarimetry.[10] The low ee obtained for the (*R*)-sulfoxide provides additional evidence for the modification of the catalytic centers.

Given that the catalyst obtained by treatment with (*R*)-tartaric acid (**cat-3**) leads to the best selectivity, we tested the effect of using a smaller amount of catalyst. Very good results were obtained, with a sulfide/titanium ratio = 140, by simply increasing the reaction time. In order to test the general scope of this method it was applied to several other sulfides (Scheme 1, Table 1, entries 12–19).

This solid promotes the reaction with a very small amount of catalyst and leads to high yields and selectivities. The methodology is applicable to bulky sulfides and is compatible with the presence of other oxidisable functions, as shown in the last two examples where epoxidation of the double bond (**1g**) or Baeyer–Villiger oxidation of the ketone (**1h**) were not observed.

As far as the mechanism is concerned, either the H_2O_2 may be the oxidation agent, *via* a Ti–OOH intermediate, or a supported peracid intermediate may be formed.

We tested the recovery of the catalyst in the oxidation of dibutyl sulfide **1b** (Table 2). A gradual leaching of titanium takes place. However, this leaching is very slow given that after five reactions each mmol of titanium has been treated with about 5000 mmol of water. Furthermore, even the fifth reaction takes place with reasonable yield and selectivity. The existence of leaching suggests that the reaction can take place, at least in part, in the homogeneous phase. In order to clarify this point we treated **cat-3** with H_2O_2 for 4 h. The solid was separated by filtration and the filtrate used in the oxidation of a corresponding amount of sulfide **1a**. The filtrate promotes the reaction with a 83:17 sulfoxide/sulfone ratio. In another experiment we carried out the reaction of **1a** until 85% conversion (15 min), then the catalyst was separated by filtration and both the solid and the filtrate were used in a new reaction. The sulfide was consumed in both reactions at almost the same rate.

Table 2 Recovery of the catalyst in the oxidation of **1b** with H_2O_2 promoted by **cat-3**

Run	*t*/h	Yield (%)			Ti/mmol $g^{-1\,a}$
		Total	Sulfoxide **2b**	Sulfone **3b**	
1	4	100	100	0	0.82
2	5	98	96	2	—
3	8	96	92	4	—
4	8	90	82	8	—
5	9	91	82	9	—
6	—	—	—	—	0.22

[a] Determined by plasma emission spectroscopy.

In our opinion these results indicate the co-existence of the homogeneous and heterogeneous reactions and that a very active homogeneous catalyst is obtained under these conditions. Therefore, it seems that the identification of the homogeneous species and the improvement of the behaviour of the heterogeneous system against leaching are important aims.

These results clearly show that modification of the environment of titanium *via* introduction of organic molecules can modify the performance of the catalysts. This strategy opens the way to the preparation of new families of supported chiral catalysts in which grafting is carried out through the metal instead of through the chiral auxiliary.

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