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## KINETIC RESOLUTION OF RACEMIC SULFOXIDES BY A MODIFIED SHARPLESS PROCEDURE

Arrigo Scettri<sup>\*a)</sup>, Francesco Bonadies<sup>b)</sup>, Alessandra Lattanzi<sup>b)</sup>, Angela Senatore<sup>a)</sup>,  
 Annunziata Soriente<sup>a)</sup>

<sup>a)</sup>Dipartimento di Chimica, Università di Salerno, 84081 Baronissi (SA) - Italy

<sup>b)</sup>Centro di Studio CNR per la Chimica delle Sostanze Organiche Naturali, Dipartimento di Chimica, Università "La Sapienza", P.le A. Moro 5, 00185 Roma, Italy

**Abstract:** Kinetic resolution of racemic sulfoxides is achieved by enantioselective oxidation to sulfones under Sharpless-type conditions. Copyright © 1996 Elsevier Science Ltd

Chiral sulfoxides are very useful synthons and their preparation can be achieved by many procedures. In particular, the asymmetric oxidation of prochiral sulfides represents one of the typical approaches and the employment of the *t*-butyl hydroperoxide (Ti(O-*i*Pr)<sub>4</sub>)/dialkyl tartrate/H<sub>2</sub>O system has often resulted in a very good degree of enantioselectivity<sup>1</sup>. On the contrary, the possibility of a different approach, based on the kinetic resolution of racemic sulfoxides, has been scarcely explored<sup>2,3</sup>.

We have found that, under the conditions reported by Modena<sup>4</sup>, (Scheme, Table), racemic starting materials **1** undergo an enantioselective oxidation to sulfones **2**, which allows to obtain unreacted enantiomerically enriched sulfoxides **1\***

Scheme

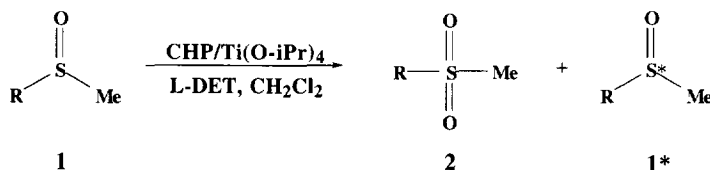


Table - Enantioselective Oxidation of Racemic Sulfoxides **1**<sup>a)</sup>

Entry	R	Reaction Time/h	Temperature	<b>1</b> *(yield) <sup>b)</sup>	e.e. <sup>c)</sup>
<b>a</b>	p-Tol	17	-23°C	75%	13% <sup>d)</sup>
<b>b</b>	p-Tol	91	-23°C	40%	83%
<b>c</b>	Ph	91	-23°C	39%	87%
<b>d</b>	p-ClC <sub>6</sub> H <sub>4</sub>	91	-23°C	31%	94%
<b>e</b>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	91	-23°C	31%	9%
<b>f</b>	p-Tol	16	r.t.	33%	71%
<b>g</b>	Ph	16	r.t.	30%	77%
<b>h</b>	p-ClC <sub>6</sub> H <sub>4</sub>	16	r.t.	31%	64%
<b>i</b>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	16	r.t.	18%	6%
<b>l</b>	p-ClC <sub>6</sub> H <sub>4</sub>	16	r.t.	38%	41% <sup>e)</sup>

<sup>a)</sup>All the reactions have been carried out using Ti(O-iPr)<sub>4</sub>/1/hydroperoxide/L-DET in 1/2/1.3/4 molar ratios.

<sup>b)</sup>All the yields refer to isolated chromatographically pure compounds, obtained as R prevalent enantiomer.

<sup>c)</sup>e.e. have been determined on a representative sample obtained after mixing all the sulfoxide fractions coming from the chromatography<sup>5</sup>, by <sup>1</sup>H-NMR analysis in the presence of R(-)-3,5-dinitro benzoyl- $\alpha$ -methylbenzyl amine as shift reagent.

<sup>d)</sup>t-butyl hydroperoxide has been employed as oxidant.

<sup>e)</sup>In this case Ti(O-iPr)<sub>4</sub> has been used in catalytic amount (20%) with respect to sulfoxide.

In fact, when sulfoxides **1** are submitted to the action of cumyl hydroperoxide (CHP)<sup>6</sup> in the presence of Ti(O-iPr)<sub>4</sub>, as metal catalyst, and L-diethyl tartrate, L-DET, as the chiral auxiliary, in dichloromethane solution at -23°C, the preferential oxidation of the S-enantiomer to sulfone **2** takes place: it has to be noted that, although this procedure has proven to be almost completely unsuccessful in the case of dialkyl sulfoxides (entry **e**) chiral methylaryl sulfoxides **1**\* can be recovered in satisfactory yield and very good enantiomeric excesses (entries **b-d**). Furthermore, although to a lower extent, kinetic resolution has been shown to proceed both at room temperature (entries **f-j**) and under catalytic conditions (entry **e**).

Further investigations, devoted to the improvement of this methodology by other hydroperoxides, are in progress.

**Experimental:** a mixture of **1** (1 mmol), L-DET (2 mmol) and Ti(O-iPr)<sub>4</sub> (0.5 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (10 ml) is stirred for 20 minutes, under the conditions reported in the Table, in atmosphere of argon. Cumyl hydroperoxide (0.65 mmol) is added and the reaction is monitored by TLC. The mixture is poured into the top of a silica gel chromatographic column and the elution with n-hexane/ethyl acetate mixture affords pure chiral sulfoxides **1**\*.

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- Very poor enantiomeric excesses have been observed when t-butyl hydroperoxide was used as oxidant (Table, entry **a**)