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A Convenient Acid-catalyzed Oxidation of Sulfides to Sulfoxides by *t*-Butyl Hydroperoxide

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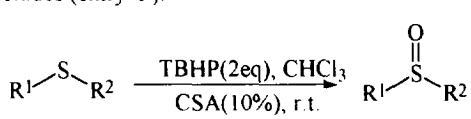
Abstract: a very efficient synthesis of sulfoxides is achieved by oxidation of sulfides with *t*-butyl hydroperoxide catalyzed by camphorsulfonic acid. Copyright © 1996 Published by Elsevier Science Ltd

In connection with our researches on the enantioselective oxidation of sulfoxides to sulfones,[1] we needed considerable amounts of arylalkyl and dialkyl sulfoxides. The typical procedure for the synthesis of compounds of type **2** is represented by the oxidation of sulfides **1**. However, although many methodologies are available,[2] only few have general validity. In fact, undesired side reactions (overoxidation, C-C and C-S bond fission)[3,4] can often be observed with many oxidant, so that satisfactory selectivity requires a careful control of the reaction conditions and/or the use of not readily available reagents.[5,6]

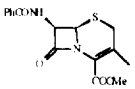
Now, we wish to report a very simple and convenient procedure for the synthesis of sulfoxides through acid-catalyzed oxidation of sulfides by *t*-butyl hydroperoxide (TBHP). In fact, when starting materials **1** are submitted to the action of a twofold excess of TBHP in the presence of catalytic amounts (10 %) of camphorsulfonic acid (CSA) in $CHCl_3$ solution at room temperature, the selective oxidation to sulfoxides **2** takes place with very good yields (table).

It has to be noted that, although overoxidation of diaryl sulfides to sulfones is rather diffucult to prevent, especially in the presence of an excess of oxidant, no evidence of formation of diphenyl sulfone has been detected in entry b. Furthermore, non aqueuos medium and work-up (see experimental) allow the ready isolation of water soluble sulfoxides (entry f).



1 **2**

Table - Oxidation of sulfides by TBHP/CSA

Entry	R^1	R^2	React. time (h)	Yield(%) [a]
a	Ph	Me	3	100
b	Ph	Ph	18	95
c	*p*-ClC_6H_4	Me	4	97
d	*p*-Tolyl	Me	4	97
e	*n*-Bu	n-Bu	1	98
f	*t*-Bu	Me	1	95
g			23	80 [b]

[a] *All the yields refer to isolated chromatographically pure compounds, whose structures have been confirmed by spectroscopic data (IR, ^{1}H-NMR, MS).*
[b] *Obtained as 1/1 α/β sulfoxides mixture, which has been resolved by chromatographic purification on SiO_2 (eluent: ethyl acetate/ether 8/2)*

The oxidation of the cephalosporin derivative (entry g) merits consideration. In the presence of the 7-β-acylamino side chain, the NH assisted approach of the oxidation reagent generally leads to the most sterically hindered (*S*)-sulfoxide.[7] Conversely, under our reaction conditions, an almost equimolar mixture of the two isomeric (*R*)- and (*S*)-sulfoxides is obtained in fairly good overall yield, thus allowing the isolation of the otherwise less accessible (*R*)-isomer.[8] Under a mechanistic point of view, there does not seem to be any major stereochemical influence, neither hydrogen bond controlled nor steric, directing TBHP oxidation, so that no discrimination between the α and β faces occurs.

***Experimental*:** a mixture of **1** (3 mmol), TBHP (3M isooctane solution, 6 mmol), CSA (0.3 mmol) in $CHCl_3$ (15 ml) is stirred at room temperature under the conditions reported in table. The reaction is monitored by TLC. Then, the solution is directly poured onto the top of a silica-gel chromatographic column and elution with *n*-hexane/ethyl acetate mixtures affords pure **2**.

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