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Stereoisomeric 2-butylphenylsulfoxides and their binding modes in the adduct formation with an enantiopure dirhodium tetracarboxylate complex

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This paper is dedicated to Prof. Dr. Heinz Oberhammer, Eberhard Karls Universität Tübingen, Tübingen, Germany, on the occasion of his 70th birthday.

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ABSTRACT

All stereoisomers of the 2-butylphenylsulfoxides **1a** and **2a** and their *p*-substituted derivatives **1b**–**1e** and **2a**–**2e** (X = F, Br, NO_2, and OCH_3) were synthesized. Absolute configurations were derived from commercial enantiopure 2-butanols used as starting materials, by X-ray diffraction and by polarimetry. Preferred conformations were determined by density functional and second-order Møller–Plesset calculations. Oxygen atoms dominate in the adduct formation equilibria of 2-butylsubstituted sulfoxides and the chiral dirhodium complex **Rh*** although the sulfur atom is, in principle, the stronger donor. This is due to steric shielding of the sulfur atom produced by the aromatic ring and the secondary 2-butyl substituent. Enantiodifferentiation of sulfoxides is easily accomplished by the dirhodium experiment, i.e. recording NMR spectra in the presence of an equimolar amount of **Rh***. Complex formation shifts ($\Delta\delta$) and diastereomeric dispersion effects ($\Delta\nu$) differ in the dirhodium experiment for nonracemic mixtures of sulfoxides as compared to pure enantiomers. This, however, does not affect the efficiency of the dirhodium experiment at all.

1. Introduction

Dirhodium complexes and their adducts have been the focus of interest for many years [1]. They were introduced as homogeneous catalysts in various reactions [2] and found even medicinal application [3]. During the last decade, we have shown that the enantiomers of many chiral ligands, particularly those of soft Lewis bases, can be differentiated easily by adding an equimolar amount of the dirhodium complex $Rh_2^{(II)}$ [(*R*)-(+)-MTPA]$_4$ (**Rh***, MTPA-H = methoxytrifluoromethylphenylacetic acid ≡ Mosher's acid; see Scheme 1) [4] to their $CDCl_3$ solution and monitoring the diastereomeric dispersion $\Delta\nu$ of their ^{1}H or ^{13}C NMR signals at room-temperature (dirhodium method) [5–7].

The complexation site of ligand molecules **L** in dirhodium complex adducts (**Rh*** ← **L**) can be identified by moderate deshieldings of nearby ^{1}H and – particularly – ^{13}C nuclei (complexation shifts $\Delta\delta$). In a qualitative interpretation of positive $\Delta\delta$ values, one can assume that an adduct formation induces an increase of the electron-acceptor properties of the binding atom [5]. Recently, we investigated some ethers **3** (Scheme 2) with oxygen binding sites attached to aromatic and aliphatic ring systems [8]. In ethers, the binding energy is based primarily on electrostatic interaction [9]. As expected, we found that the inductive effect of the oxygen on the aliphatic α-carbons is enhanced when it is complexed to the rho atom ($\Delta\delta > 0$). However, deshielding complexation shifts $\Delta\delta$ at the aromatic *ipso*-carbons (also α-positioned) turned out to be minute whereas *ortho*- and *para*-carbon signals are influenced significantly by the resonance effect of oxygen and its interaction with substituents in *para*-position [8].

In order to gain further insight into the complexation mechanisms of chalcogen ligands, we extended this study to structurally analogous thioethers **4** (Scheme 2) [10]. Whereas ethers are hard ligands, thioethers are soft [11] and represent a different ligand category in the dirhodium experiment as compared to ethers [5]; i.e., thioethers can make use of an additional orbital interaction (HOMO–LUMO) for complexation. Indeed, this can be monitored by inspecting the dependence of complexation shifts at the aliphatic α carbon (C-2) and the *ortho*-carbon (C-2′) on Hammetťs inductive and resonance parameters, respectively [10]. For each carbon site and each parameter the correlations are opposite as compared to those of ethers, and this can be rationalized semi-quantitatively by effects of HOMO–LUMO energy changes on ^{13}C chemical shifts [10].

Then, we extended these studies to sulfoxides offering both types of donors simultaneously, soft sulfur and hard oxygen atoms; the results are presented here.

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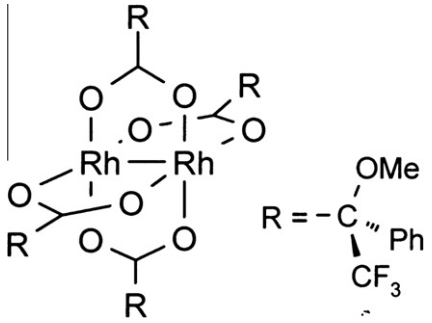


Scheme 1. Structure of the dirhodium complex **Rh***.

2. Experiment

2.1. Materials and synthesis

The syntheses of **Rh*** [4], the ethers **3** [8] and the thioethers **4** [10] have been described by us earlier. The sulfoxides **1a**–**1e** and **2a**–**2e** were prepared by H_2O_2 oxidation of the thioethers **4a**–**4e**, respectively [12]. General procedure: the respective 2-butylphenylthioether (2.2 mmol) was dissolved in 5 ml methanol. A solution of H_2SO_4 (16%) in *tert*-butanol and 35% H_2O_2 (0.18 g, 5.1 mmol) was added dropwise. Then, the mixture was stirred for 24 h at room-temperature. Aqueous NaCl solution (5%) was added and the mixture extracted three times with 5 ml chloroform each. The combined organic phases were dried over $MgSO_4$ and the solvent evaporated *in vacuo*. The residue was purified by column chromatography at normal pressure and temperature using silica gel as stationary and mixtures of petrol ether and ethyl acetate as mobile phase (see Section 2). Yields are given below. Synthetic procedures were not optimized. *p*-Nitrophenyl-methylsulfoxide (**5**) was prepared analogously from the respective commercially available thioether [13].

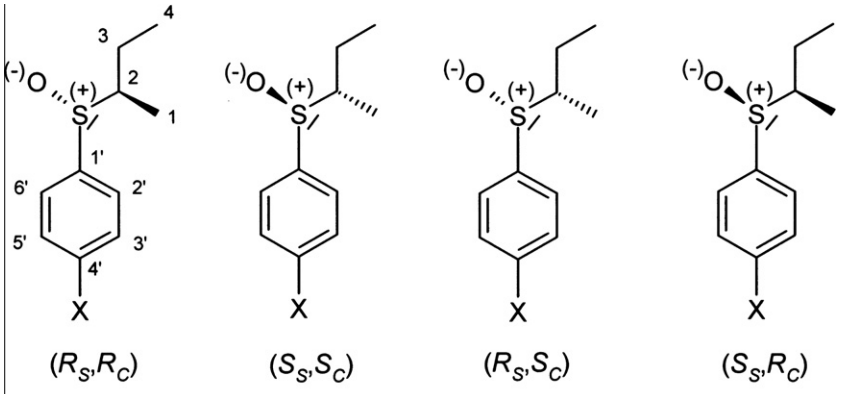
The parent sulfoxides **1a**/**2a** has been described in literature [14]; all others are new. We collected the ^1H and ^{13}C NMR data of all enantiopure 2-butylphenylsulfoxides in Table 2; yields, physical data, infra-red (IR) and mass spectral data (ESI-MS) are listed below. IR spectra were recorded on a Bruker Vector 22 using neat samples and positive ESI-MS spectra on a Micromass LCT.

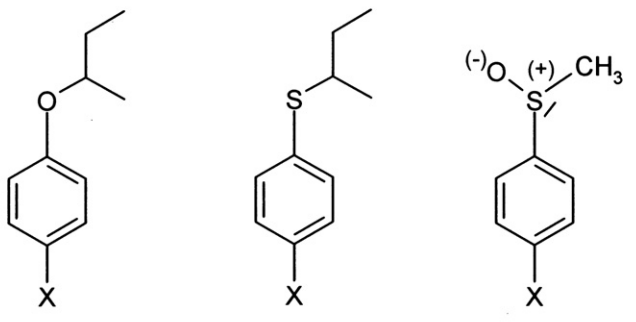
*2.1.1. (R_S,R_C)- or (S_S,S_C)-(1-methylpropylthio)benzene-S-oxide (**1a**)*

Yield: 72%, viscous, slightly yellowish liquid. IR (liquid) $\tilde{\nu}$ (cm^{-1}) 3046, 2966, 2932, 1583, 1443, 1381, 1035, 748, 692. ESI-MS calculated for $C_{10}H_{15}OS$: 183.0844 $[M+H]^+$, found: 183.0840.

*2.1.2. (R_S,S_C)- or (S_S,R_C)-(1-methylpropylthio)benzene-S-oxide (**2a**)*

Yield: 73%, viscous, slightly yellowish liquid. IR (liquid) $\tilde{\nu}$ (cm^{-1}) 3040, 2963, 2932, 1581, 1441, 1384, 1031, 748, 691. ESI-MS calculated for $C_{10}H_{15}OS$: 183.0844 $[M+H]^+$, found: 183.0843.





	a	b	c	d	e
X =	H	F	Br	NO_2	OCH_3

Scheme 2. Structures of stereoisomeric 2-butylphenylsulfoxides **1** (*like*) and **2** (*unlike*); structurally related ethers **3** and thioethers **4** for comparison. Although the atom numbering is not in total agreement with the IUPAC nomenclature, it has been chosen to for a better comparability of NMR data. Correct IUPAC names are given in the Experimental Part.