Enantioselective chromatographic resolution and one-pot synthesis of enantiomerically pure sulfoxides over a homochiral Zn-organic framework t

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Supporting Information

Materials and NMR spectrocsopy

CH_2Cl_2 for chromatographic separation and CCl_4 for NMR spectroscopy were analytical grade Fluka reagents. All other solvents were reagent grade and used without further purification. $[Zn_2(bdc)(L\text{-lac})(dmf)]\cdot(DMF)_m$ ($\mathbf{1}\cdot DMF_m$, $m= 0.4$ or 1) was prepared as described.[4] In the communication text and below, $\mathbf{1}$ stands for $\mathbf{1}\cdot DMF_1$. In cases we need to specify the number of DMF guest molecules, the $\mathbf{1}\cdot DMF_m$ notation is used.

^{1}H NMR spectra were measured on a Bruker DPX-250 spectrometer at 250.13 MHz in 5 mm glass tubes. Measurement parameters: spectral width 5 kHz, acquisition frequency 0.2 Hz, 45° pulse at 4.1 μs.

Preparation of the column for chiral liquid chromatography

Solid crystals of the homochiral porous polymer $\mathbf{1}$ was powdered in a mortar and sifted, collecting the fraction with particle size ≤0.09 mm. The latter was suspended in 10% DMF solution in CH_2Cl_2. This suspension containing 14 g of the grinded $\mathbf{1}$ was transferred in a glass tube (8 mm inner diameter) to obtain a 330 mm long column.

Enantioselective chromatographic separation procedure

Prior to use, the column was washed with 8 cm^3 of 0.01 M solution of DMF in CH_2Cl_2. Solutions of racemic mixtures of the sulfoxides (0.1-0.2 mmol) were placed on the top of the column and then elution was started with 0.01 M solution of DMF in CH_2Cl_2. The elution rate was maintained constant (2 cm^3 h^{-1}) using an appropriate narrow steel nozzle, 1 cm^3 fractions were collected. In some experiments the polarity of the eluent was increased (1% DMF in CH_2Cl_2 was used) after elution of the first 10-15 cm^3. After the separation, the column was regenerated: 10 ml of 10% DMF solution in CH_2Cl_2 was eluted through the column, the latter was capped and stored at room temperature.

Each fraction was dried in a flow of air, dissolved in 0.6 cm^3 of CCl_4 or $CDCl_3$ for p-$NO_2PhSOMe$) and placed in an NMR tube. Using ^{1}H NMR, the net concentration of the sulfoxide (for $CDCl_3$ solutions, the spectra were referenced to the residual $CHCl_3$ (δ 7.27); for CCl_4 solutions, an admixture of trichloroethylene in CCl_4 was used as an internal reference (δ 6.46)) and the enantiomeric excess (by addition of $Eu(hfc)_3$) were measured as described in the Experimental details of Ref. 1. Based on these data, curves of the concentrations of each enantiomer vs. eluted volume were plotted.

Measurement of sorption constants

Sorption experiments were conducted as described.[4]. The uncertainty of the constants measurements were ca. 30%.

Method A. (Based on Lengmuir adsorption model)

Known quantity of a pure enantiomer was placed in a small flask with a magnetic stirbar containing CH_2Cl_2 (0.5-1 cm^3), and weighed quantity of $\mathbf{1}\cdot(DMF)_x$ ($x= 0.4$ or 1) was added. After stirring for 2.5 h at room temperature, the polymer was filtered off and washed with hexane (1 cm^3). Then CH_2Cl_2 and hexane fractions were combined and volatiles were removed in a flow of air, and the amount of the remaining sulfoxide was measured by ^{1}H NMR. Thus, provided that the remaining concentration of the sulfoxide and the amount sorbed in the pores of $\mathbf{1}$ are known, the sorption constant was estimated from linear dependence of sorption vs. concentration (in 3 separate experiments with 3 differing concentrations of the sulfoxide).

Method B. (Via sorption of racemic mixtures)

It is assumed that sorption equilibrium is established within the experiment time and only one type of sorption centers is present in the homochiral polymer. The amount of the polymer (and the number of structural units $[Zn_2(bdc)(L\text{-lac})(dmf)]$), the amount of racemic sulfoxide and solution volume are known. Then, the amount of the remaining sulfoxide was measured as in *Method A*, and the

ee of the sulfoxide in solution was measured by ^{1}H NMR with Eu(hfc)$_3$. Further, the *ee* of the sorbed sulfoxide was measured as described in Ref. 1. These data were used to calculate the ratio of the sorption constants. Then, using Lengmuir isotherm for simultaneous sorption of both enantiomers and the balance equilibrium, one could obtain a linear dependence of the sorption vs. concentration. The constant for one of the enantiomers could be estimated in 3 experiments with differing concentrations. The other constant was calculated using the experimentally determined constant ratio (see above).

Effect of particle size and elution rate on the enantioseparation effectiveness

Particle size ≤0.160 mm;
Elution rate: 12 cm^3 h^{-1}

Particle size ≤0.160 mm;
Elution rate: 4 cm^3 h^{-1}

Particle size ≤0.090 mm;
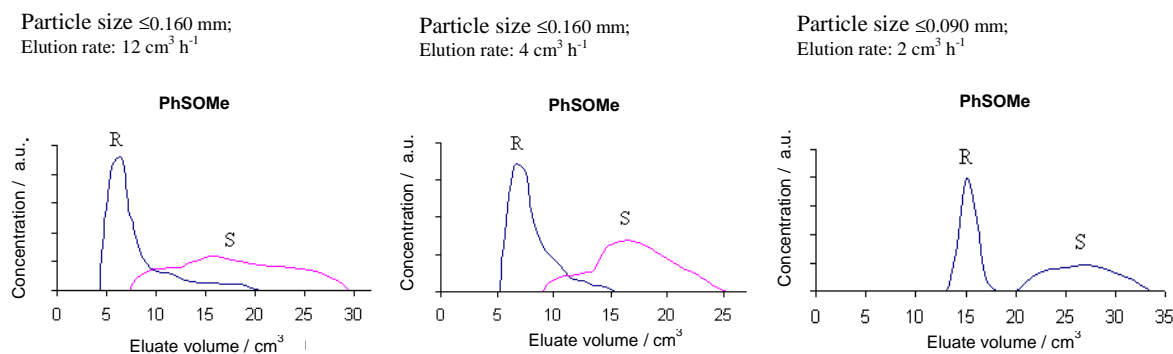Elution rate: 2 cm^3 h^{-1}

Figure S1. Enantiomeric separation of PhSOMe using **1** as the chiral stationary phase, with differing particle size and elution rates. Eluent: (a) 11 cm^3 of 0.01 M DMF solution in CH$_2$Cl$_2$, then 1% DMF in CH$_2$Cl$_2$; (b) 8 cm^3 of 0.01 M DMF solution in CH$_2$Cl$_2$, then 1% DMF in CH$_2$Cl$_2$; (c) 12 cm^3 of 0.01 M DMF solution in CH$_2$Cl$_2$, then 1% DMF in CH$_2$Cl$_2$.

It is seen that decreasing the elution rate (at constant particle size of less than 0.160 mm) leads to a better resolution of enantiomers (Figure S1). The use of **1** with smaller particles (less than 0.090) and further decrease of elution rate allows the complete resolution. Apparently, it is due to relatively low rate of diffusion inside the granules of **1** that the local sorption eluilibria are not established at high elution rates, leading to wide chromatographic peaks with long tails. We foresee that elaboration of a procedure to prepare uniform particles of **1** with the size typically used in liquid chromatography (i.e. 0.005 or 0.010 mm) would allow achieving complete enantioseparation at much higher elution rates.

Catalytic oxidation of alkyl aryl sulfides
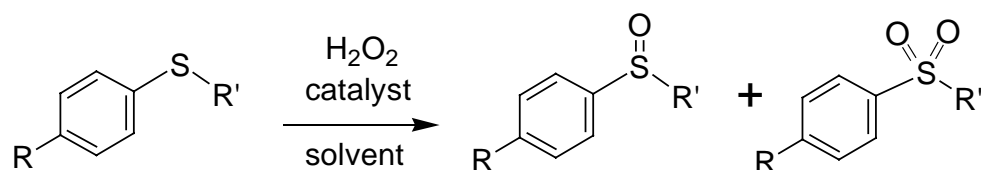
Scheme S1 Catalytic oxidation of alkyl aryl sulfides.

General procedure for the oxidation of sulfides catalyzed by Zn(NO$_3$)$_2$·6H$_2$O.
Sulfide (0.15 mmol) was dissolved in an appropriate solvent (CH$_3$CN, MeOH or H$_2$O, 1.5 mL), followed by the addition of the catalyst (10-20 mol.-%) and H$_2$O$_2$ (0.3 mmol). The mixture was stirred for 3-24 h at room temperature, followed by the solvent removal *in vacuo*. The reaction products were separated by column chromatography (SiO$_2$, hexane/ethyl acetate) and analyzed by ^{1}H NMR in CCl$_4$ or CDCl$_3$.
General procedure for the oxidation of sulfides catalyzed by 1·(DMF)$_m$:

Sulfide (0.1 mmol), **1** and H_2O_2 (as 90% or 30% aqueous solution) were mixed in CH_3CN or CH_3CN/CH_2Cl_2 mixture (2 mL). The mixture was stirred for 16 h at room temperature. Solids were filtered off and the adsorbed sulfoxide was extracted with methanol (3×3 mL). Extracts and filtrate were combined and solvent was removed *in vacuo*. Products concentrations were analyzed by ^{1}H NMR in CCl_4 or $CDCl_3$.

Selected ^{1}H NMR data for the compounds involved (δ, ppm, 20 °C): in $CDCl_3$, PhSCH_3 2.34, PhSOCH_3 2.61, PhSO$_2$CH_3 2.92; *p*-NO$_2$PhSCH_3 2.55, *p*-NO$_2$PhSOCH_3 2.77, *p*-NO$_2$PhSO$_2$CH_3 3.08. In CCl_4, *p*-BrPhSCH_3 2.44, *p*-BrPhSOCH_3 2.62, *p*-BrPhSO$_2$CH_3 2.94. In CCl_4, PhSCH_2Ph 4.16, PhSOCH_2Ph 3.90(m), PhSO$_2$CH2Ph 4.05.

The *ee*s were measured by ^{1}H NMR with Eu(hfc)$_3$ chiral shift reagent in CCl_4. The absolute configuration was determined by comparing Eu(hfc)$_3$-shifted NMR patterns of sulfoxides with those of the sulfoxides with known absolute configuration (for details see Supporting Information for

Table S1 Oxidation of alkyl aryl sulfides to sulfoxides with H_2O_2 catalyzed by Zn-containing compounds.

№	Sulphide	Catalyst	S:Zn.	Time. h	Solvent	Conversion. % [b]	Selectivity. % [c]
1	PhSMe [a]	Zn(NO$_3$)$_2$·6H$_2$O	10	16	CH$_3$CN	100	95
2	PhSMe [a]	Zn(NO$_3$)$_2$·6H$_2$O	10	16	H$_2$O	100	97
3	p-MePhSMe [a]	Zn(NO$_3$)$_2$·6H$_2$O	10	16	CH$_3$CN	77	100
4	PhSCH$_2$Ph [a]	Zn(NO$_3$)$_2$·6H$_2$O	10	16	CH$_3$CN	80	100
5	p-BrPhSMe [a]	Zn(NO$_3$)$_2$·6H$_2$O	10	24	CH$_3$CN	100	100
6	PhSiPr [a]	Zn(NO$_3$)$_2$·6H$_2$O	5	3	MeOH	100	100
7	2-naphthylSMe [a]	Zn(NO$_3$)$_2$·6H$_2$O	5	3	CH$_3$CN	100	100
8	PhSMe [d]	**1**·(DMF)$_{0.4}$	1.5	16 [e]	CH$_3$CN	92	100
9	p-BrPhSMe [d]	**1**·(DMF)$_{0.4}$	1.5	16 [e]	CH$_3$CN	8	100
10	PhSMe [d]	**1**·(DMF)$_{0.4}$	1.5	16 [f]	CH$_3$CN/CH$_2$Cl$_2$ (1:10)	100	87
11	p-BrPhSMe [d]	**1**·(DMF)$_{0.4}$	25	16 [f]	CH$_3$CN/CH$_2$Cl$_2$ (1:10)	58	100
12	p-BrPhSMe [d]	**1**	1.5	16 [f]	CH$_3$CN/CH$_2$Cl$_2$ (1:10)	59	99

[a] Reaction conditions: sulfhide (0.15 mmol), catalyst and 30% aqueous H_2O_2 (0.3 mmol) in 1.5 ml of the appropriate solvent, 200 rpm stirring at room temperature. [b] Conversion = ([RSOR′] + [RSO$_2$R′]) / ([RSOR′] + [RSO$_2$R′] + [RSR′]). [c] Selectivity = [RSOR′] / ([RSOR′] + [RSO$_2$R′]). [d] Reaction conditions: sulfide (0.1 mmol), catalyst oxidant H_2O_2 (3 equiv.) in 2 ml of the appropriate solvent, 200 rpm stirring at room temperature. [e] 30% aqueous H_2O_2 (3 equiv.) was used as the oxidant [f] 90% aqueous H_2O_2 (3 equiv.) was used as the oxidant.

(Bryliakov, K. P., Talsi, E. P. *Angew. Chem. Int. Ed.* **2004**, *43*, 5228-5230)).

Selected oxidation results are presented in Table S1. *p*-NO$_2$PhSMe and PhSCH$_2$Ph demonstrated very low oxidation conversion of 7% and 3%, respectively, when oxidized over **1**·DMF.[4]

General procedures for the combined oxidation/separation experiments.

Method A. *5-fold excess of H_2O_2.* Prior to the oxidation, 7 mL of 0.01 M DMF solution in CH_2Cl_2 was passed through the column. Then, 2 mL of 0.01 M DMF solution in CH_2Cl_2(85%)/CH_3CN(15%) mixture containing 0.34 mmol of H_2O_2 was eluted. Then PhSMe (0.17 mmol) in 0.2 mL of 0.01 M DMF solution in CH_2Cl_2 was on the top of the column followed by 3 mL of 0.01 M DMF solution in CH_2Cl_2(85%)/CH_3CN(15%) containing 0.51 mmol of H_2O_2. Sulfoxide was eluted with 0.01 M DMF solution in CH_2Cl_2(85%)/CH_3CN(15%), 1 mL fractions being collected at elution rate 2 mL/h. After collecting first 12 mL of the eluate, 1 vol.-% solution of DMF in CH_2Cl_2(85%)/CH_3CN(15%) was used as eluent. Solvent was removed in vacuo from the collected fractions, and the reaction products were analyzed by ^{1}H NMR. The enantiomeric purity was analyzed by ^{1}H NMR with Eu(hfc)$_3$.

Method B. *1.5-fold excess of H_2O_2.* Prior to oxidation, 7 mL of 0.01 M DMF solution in CH_2Cl_2 was eluted through the column, followed by 0.75 mL of 0.01 M DMF solution in CH_2Cl_2(85%)/CH_3CN(15%) mixture containing 0.0975 mmol of H_2O_2. Then PhSMe (0.13mmol) in 0.2 mL of 0.01 M DMF solution in CH_2Cl_2 was loaded on the top of the column followed by 0.75 mL of 0.01 M DMF solution in CH_2Cl_2(85%)/CH_3CN(15%) containing 0.0975 mmol of H_2O_2. Elution and product analysis were performed as in method **A**.