Chemoselectivity and Enantioselectivity in Copper-Catalysed Oxidation of Aryl Benzyl Sulfides

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Abstract: Enantioselective copper-catalysed oxidation of aryl benzyl sulfides yields enantioenriched sulfoxides (up to 81% ee) in modest yield. This is the highest enantioselectivity reported using a copper catalyst in enantioselective sulfide oxidation. The enhancement of the enantioselectivity of this method through the use of additives is discussed.

Key words: asymmetric catalysis, oxidation, copper, sulfoxides, Schiff bases

Enantiopure sulfoxides are widely used in asymmetric synthesis both as building blocks and pharmaceutical agents.[1] Accordingly, the preparation of enantiopure sulfoxides has been the focus of considerable research. The principal routes to prepare enantiopure sulfoxides are i) the substitution of a chiral precursor and ii) the asymmetric oxidation of a prochiral sulfide.

The preparation of enantiopure sulfoxides through the substitution of chiral precursors was first reported by Andersen in the 1960's.[2] Despite the high yields of enantiopure sulfoxides obtained using this methodology, the scope of the methodology is curtailed by the difficult preparation and limited availability of suitable chiral precursors. The development of chiral precursors that possess two leaving groups has extended the scope of this methodology.[3]

Asymmetric sulfide oxidation has attracted considerable interest as a route to enantiopure sulfoxides. Very efficient biological sulfide oxidations have been reported using both whole cell systems and isolated enzymes.[4] Metal-free asymmetric sulfide oxidation has been reported using oxaziridines[5] and hydroperoxides.[6] Metal-catalysed asymmetric sulfide oxidation is the most popular route to enantiopure sulfoxides. Kagan[7] and Modena[8] independently reported a very efficient titanium-mediated sulfide oxidation based on the Sharpless asymmetric epoxidation procedure. Further investigations improved the scope and utility of this titanium-mediated oxidation.[9] Following a report of vanadium-catalysed asymmetric sulfide oxidation under very mild conditions[10] considerable investigations have taken place into vanadium Schiff base catalysed sulfide oxidations.[11] Manganese,[12a] iron,[12b–12d] niobium,[12e] zirconium,[12f] tungsten,[12g] molybdenum[12h] and osmium[12i] have also been successfully used to catalyse asymmetric sulfide oxidation.

Copper has received relatively little attention in metal-catalysed asymmetric sulfide oxidation. A copper–salen complex was used by Cross to oxidise thioanisole but enantioselectivity was limited (14% ee).[13a] Iglesias, using a different ligand to form the copper-catalyst complex, reported better enantioselectivity for the oxidation of thioanisole (<30% ee).[13b] Kraemer et al. also investigated copper-catalysed asymmetric sulfide oxidation using chiral copper–salen complexes but reported the catalyst complex used was inactive.[13c] In comparison to other metal catalysts used for asymmetric sulfide oxidation, the reactivity and enantioselectivity of copper catalysts are only modest; Iglesias speculated that this may be due to the fact the formation of the copper-oxo oxidising species is kinetically unfavourable.[13b]

Recently we have reported that vanadyl Schiff base complexes can be successfully used for both asymmetric sulfide oxidation and the kinetic resolution of sulfoxides, particularly for aryl benzyl sulfides and sulfoxides.[14] Extension of this methodology using copper instead of vanadium to form the Schiff base complex was explored.

Initial experiments were based on our recent report of vanadium-catalysed asymmetric sulfide oxidation[14] employing copper(II) acetylacetonate and a Schiff base ligand **1** developed by Anson[15] and indicated that modest asymmetric induction was occurring (Table 1, entries 1–4) in agreement with previous reports. Optimisation of the reaction established that the best catalyst loading was 4 mol% ligand and 2 mol% copper acetylacetonate relative to the sulfide, while the optimum amount of oxidant was 1.1 equivalents. No increase in either selectivity or yield was observed using more than 1.1 equivalents of H_2O_2. The optimum temperature was found to be room temperature and optimum reaction time was found to be 16 hours. A significant improvement in enantioselectivity was observed using carbon tetrachloride as the solvent instead of dichloromethane (Table 1, entry 7). A number of ligands were screened to see if they would give better results than **1**. Ligand **2**[16] was found to be the best ligand for this oxidation (Table 1, entries 8 and 9). Ligands **3**–**5** were also investigated but resulted in lower enantioselectivity than that observed for **2**. Utilising the optimised conditions for the preparation of a range of sulfoxides yielded the following results (Table 1, entries 10–20).

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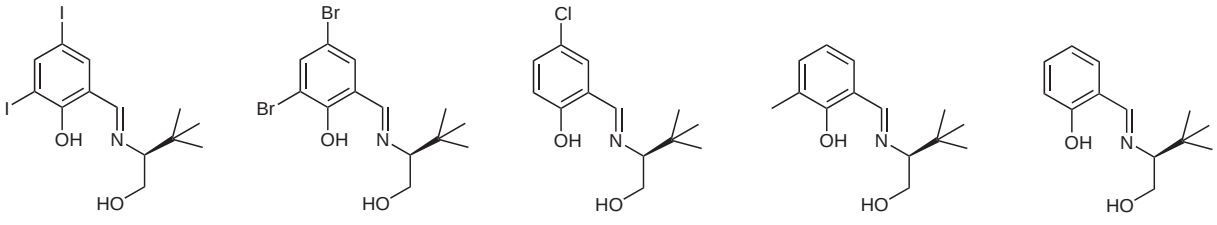
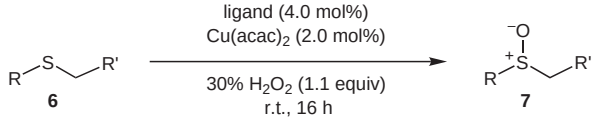
Table 1 Copper-Catalysed Asymmetric Sulfide Oxidation





Entry	6	R	R′	7	Solvent	Ligand	6:7[a]	Yield (%)[b]	ee (%, *R*)[c]
1	**6a**	4-FC_6H_4	Ph	**7a**	CH_2Cl_2	**1**	67:33	31	14
2	**6b**	4-BrC_6H_4	Ph	**7b**	CH_2Cl_2	**1**	68:32	29	13
3	**6c**	4-FC_6H_4	4-FC_6H_4	**7c**	CH_2Cl_2	**1**	–[d]	19	17
4	**6d**	Ph	Ph	**7d**	CH_2Cl_2	**1**	72:28	22	22
5	**6d**	Ph	Ph	**7d**	MeCN	**1**	74:26	34	12
6	**6d**	Ph	Ph	**7d**	$CHCl_3$	**1**	70:30	27	29
7	**6d**	Ph	Ph	**7d**	CCl_4	**1**	75:25	22	43
8	**6d**	Ph	Ph	**7d**	CH_2Cl_2	**2**	53:47	34	33
9	**6d**	Ph	Ph	**7d**	CCl_4	**2**	26:74	27	61
10	**6a**	4-FC_6H_4	Ph	**7a**	CCl_4	**2**	71:29	13	39
11	**6b**	4-BrC_6H_4	Ph	**7b**	CCl_4	**2**	80:20	23	30
12	**6c**	4-FC_6H_4	4-FC_6H_4	**7c**	CCl_4	**2**	–[d]	18	47
13	**6d**	Ph	Ph	**7d**	CCl_4	**2**	26:74	27	61
14	**6e**	4-$MeOC_6H_4$	Ph	**7e**	CCl_4	**2**	63:37	17	39
15	**6f**	2-$MeOC_6H_4$	Ph	**7f**	CCl_4	**2**	57:43	29	79
16	**6g**	4-MeC_6H_4	4-$MeOC_6H_4$	**7g**	CCl_4	**2**	47:53	42	27
17	**6h**	4-MeC_6H_4	3-$MeOC_6H_4$	**7h**	CCl_4	**2**	67:33	22	41
18	**6i**	4-MeC_6H_4	4-FC_6H_4	**7i**	CCl_4	**2**	63:37	32	48
19	**6j**	4-MeC_6H_4	4-ClC_6H_4	**7j**	CCl_4	**2**	56:44	37	51
20	**6k**	4-MeC_6H_4	Ph	**7k**	CCl_4	**2**	46:54	38	55

[a] Ratio of **6**:**7** determined by ^{1}H NMR analysis of the crude product.
[b] Yield of **7** after purification.
[c] Determined by HPLC analysis on chiral column (Daicel Chiracel OD-H); absolute configuration determined by comparing HPLC retention times to those of enantiopure sulfoxides prepared using Andersen Method for **7h**–**j**; absolute configuration determined by comparison of specific rotation values for **7b**,**d**,**k** to known literature values (see experimental section); for **7a**,**c**,**e**–**g** proposed configuration based on HPLC elution order and the direction of the specific rotations.
[d] Not determined by ^{1}H NMR due to signal overlap.

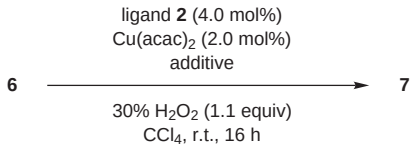
While moderate enantioselectivity was observed, the limited amount of sulfoxide formed was disappointing. These results are in agreement with previous results reported using copper in asymmetric sulfide oxidation, which indicated the reactivity of copper was poor.[13b] Evidence for product inhibition of the oxidation was seen, presumably through complexation of the sulfoxide to the copper catalyst. Significantly, the substitution patterns on the aryl

benzyl sulfoxides are seen to have an influence on the enantioselectivity of the oxidation. For example an interesting trend is observed for the oxidation of **6e** and **6f** (Table 1, entries 14 and 15). It would seem that the more sterically demanding *ortho*-methoxy-substituted sulfide **6f** is oxidised with greater enantioselectivity than the corresponding *para*-substituted sulfide **6e**. Similarly the *meta*-methoxy-substituted **6h** is oxidised with greater enantioselectivity than **6g** (Table 1, entries 16 and 17), though the effect of substitution on the benzyl substituent is not as significant as that observed when the substituent is on the aryl ring adjacent to the sulfur as for **6e** and **6f**. These results indicate steric hindrance may play a crucial role in this oxidation, suggesting that using sterically hindered Schiff base ligands such as those used by Berkessel,[17a] Katsuki[17b] and more recently by Jeong et al.[17c] may give superior results to those obtained using ligand **2**.

The use of additives has resulted in the enhancement of some asymmetric sulfide oxidations.[12c,17b,18] Bolm reported a significant enhancement in the efficiency of iron Schiff base catalysed sulfide oxidation in the presence of 4-methoxybenzoic acid or its lithium salt.[12c]

No such improvement was observed carrying out this oxidation in the presence of 4-methoxybenzoic acid and it would seem that this additive may only be beneficial when using an iron-based catalyst as it has also been reported ineffective in vanadium Schiff base catalysed asymmetric sulfide oxidations.[19] Iglesias carried out his copper-catalysed asymmetric sulfide oxidations in the presence of 4-methylmorpholine-*N*-oxide (NMO).[13b] NMO was used as an additive in a manganese-catalysed sulfide oxidation as it was believed to stabilise the Mn(V)=O complex.[20] Carrying out the above oxidation in the presence of NMO resulted in an improvement in the yield of sulfoxide and in nearly all cases, an improvement in enantioselectivity also (Table 2, entries 1 and 4–14).

Table 2 Copper-Catalysed Asymmetric Sulfide Oxidation in the Presence of Additives



Entry	6	R	R′	7	Additive[a]	6:7[b]	Yield (%)[c]	ee (%, *R*)[d]
1	**6d**	Ph	Ph	**7d**	NMO	43:57	44	60
2	**6d**	Ph	Ph	**7d**	DMSO[e]	54:46	25	62
3	**6d**	Ph	Ph	**7d**	Ionic liquid[f]	43:57	21	71
4	**6a**	4-FC_6H_4	Ph	**7a**	NMO	71:29	21	40
5	**6b**	4-BrC_6H_4	Ph	**7b**	NMO	72:28	20	37
6	**6c**	4-FC_6H_4	4-FC_6H_4	**7c**	NMO	–[g]	26	52
7	**6e**	4-$MeOC_6H_4$	Ph	**7e**	NMO	35:65	45	44
8	**6l**	3-$MeOC_6H_4$	Ph	**7l**	NMO	44:56	42	69
9	**6f**	2-$MeOC_6H_4$	Ph	**7f**	NMO	43:57	49	81
10	**6g**	4-MeC_6H_4	4-$MeOC_6H_4$	**7g**	NMO	45:55	27	38
11	**6h**	4-MeC_6H_4	3-$MeOC_6H_4$	**7h**	NMO	68:32	14	47
12	**6i**	4-MeC_6H_4	4-FC_6H_4	**7i**	NMO	48:52	29	65
13	**6j**	4-MeC_6H_4	4-ClC_6H_4	**7j**	NMO	57:43	26	50
14	**6k**	4-MeC_6H_4	Ph	**7k**	NMO	45:55	33	57

[a] 2.5 mol% of the additive used, added before the addition of the oxidant.
[b] Ratio of **6**: **7** determined by ^{1}H NMR analysis of the crude product.
[c] Yield of **7** after purification.
[d] Determined by HPLC analysis on chiral column (Daicel Chiracel OD-H); absolute configuration determined by comparing HPLC retention times to those of enantiopure sulfoxides prepared using Andersen Method for **7h**–**k**; absolute configuration determined by comparison of specific rotation values for **7b** and **7d**, to known literature values (see experimental section); for **7a**,**c**,**e**–**g**,**l** proposed configuration based on HPLC elution order and the direction of the specific rotations.
[e] 10.0 mol% of the DMSO used, added before the addition of the oxidant.
[f] 10.0 mol% of the ionic liquid (1-butyl-3-methylimidazolium hexafluorophosphate) used, added before the addition of the oxidant.
[g] Not determined by ^{1}H NMR due to signal overlap.

The use of dimethyl sulfoxide (DMSO) as an additive resulted in a slight improvement in enantioselectivity (Table 2, entry 2) while using the ionic liquid, 1-butyl-3-methylimidazolium hexafluorophosphate, as an additive resulted in a further improvement in the enantioselectivity of the oxidation (Table 2, entry 3).

Again, introducing a methoxy substituent into the aryl ring showed interesting trends with the enantioselectivity increasing as the methoxy group moves from the *para* to *meta* to *ortho* positions (Table 2, entries 7–9). Enantiopurities of up to 81% ee can be achieved albeit in modest yield (Table 2, entry 9). Presumably, a copper–Schiff base–oxo complex mediates this oxidation, however, no investigation was undertaken to establish the nature and structure of this complex.

The results reported above reflect the highest enantioselectivities to date in copper-catalysed asymmetric sulfide oxidation. While the results obtained using this method are modest in comparison to other established asymmetric sulfide oxidation methods, critically no sulfone formation occurs under these conditions. Over-oxidation leading to sulfone formation often accompanies asymmetric sulfide oxidation. In some cases the formation of the sulfone may be the result of kinetic resolution which can enhance the overall enantioselectivity of the oxidation.[14,21] However, the presence of sulfone in the crude product can make isolation of the pure sulfoxide tedious. Sulfone formation also impacts deleteriously on the overall yield of the oxidation. Using an achiral ligand it is possible to use this methodology for the chemoselective preparation of racemic sulfoxides. Furthermore, the sensitivity of the asymmetric sulfide oxidation to the precise structure of the aryl benzyl sulfide is indicative of significant ligand–substrate interactions in the transition state for the oxidation. Therefore, improvement of this method either through ligand modification or the screening of further additives could lead to enhanced enantioselection coupled with high chemoselectivity for sulfoxide formation.

Chemicals and solvents were purchased from commercial suppliers. Sulfides **6a**–**c** and **6e**–**l** were prepared by treatment of an excess of thiolate anion with the appropriate benzyl halide. Sulfide **6d** was purchased from Aldrich. For thin-layer chromatography (TLC), Merck 60 F254 silica gel plates were used and compounds were visualised by UV. Solvents were distilled before use. ^{1}H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were recorded on a Bruker AVANCE300 at 20 °C using $CDCl_3$ as solvent. Chemical shifts are given in ppm relative to TMS as the internal standard. Coupling constants (*J*) are reported in Hz. Mass spectra were recorded on a Waters/Micromass LCT Premier Time of Flight spectrometer (ESI) and a Waters/Micromass Quattron Micro triple quadrupole spectrometer (ESI). Chiral HPLC was performed with a Waters 600E System Controller and a Waters 996 Photodiode Array Detector operating a Chiralpak OD-H column from Daicel Chemical Industries Ltd., eluting with *n*-hexane and 2-PrOH. Specific rotations were recorded on a Perkin Elmer 341 polarimeter, at 20 °C in the solvents indicated. The sodium D-line (589 nm) was used unless otherwise indicated. Samples were analysed in a 1 mL dual-walled, thermostatted glass cell (PE part number: 631136) of path length 10 cm. Sample temperature control was maintained using a Julabo F25-MV immersion circulator. Results were processed on a Dell Optiplex GX260 PC using Bio Light Pol Winlab software (version number 1.00.01). The units of α are 10^{-1} deg cm^{2}g^{-1}. Absolute configurations were assigned by the comparison of the specific rotations with the literature data (**7b**,**d**,**g**,**i**–**k**) or comparison of HPLC retention times with enantiopure samples of known configuration (**7l**). Notably, the direction of the specific rotations were in complete agreement with literature values, however, the magnitudes varied somewhat.

Sulfoxides **7a**,[22] **7c**[22] and **7e**[23] have been previously reported in racemic form only. Sulfoxides **7b**,**d**,**g**,**i**–**k** have been reported in enantioenriched form.[14b] Sulfoxides **7f**,**h**,**l** have not been previously reported.

Typical Experimental Procedure

Copper(II) acetylacetonate (2.6 mg, 2.0 mol%) was added to a round-bottomed flask containing **2** (15.2 mg, 4.0 mol%) and CCl_4 (1 mL). The resulting solution was stirred at r.t. for 5 min, and then a solution of **6** (1 mmol) in CCl_4 (1 mL) was added. After 5 min stirring at r.t. NMO (3 mg, 2.5 mol%) was added to the reaction mixture and after stirring for a further 5 min at r.t. H_2O_2 (0.11 mL, 30%, 1.1 mmol) was added in one portion, dropwise to the solution. The reaction mixture was then stirred at r.t. for a further 16 h. Then, H_2O (5 mL) was added and the phases separated; the organic layer was washed with H_2O (2 × 5 mL) and brine (5 mL), dried, and concentrated at reduced pressure to give the crude product. The ratio of **6**:**7** in the crude product was determined by ^{1}H NMR. The product was purified by column chromatography on silica gel (6:4, hexane–EtOAc).

(*R*)-(+)-Benzyl-4-fluorophenyl Sulfoxide (7a, Table 2, Entry 4)[22]

Crude product contained a mixture of sulfide and sulfoxide (71:29). Purification by chromatography afforded the product as a white solid (49 mg, 21%, 40% ee).

^{1}H NMR: δ = 3.90–4.02 (1 H, A of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 4.08–4.21 (1 H, B of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 6.92–6.99 (2 H, m, ArH), 7.11 (2 H, t, *J* = 8.5 Hz, ArH), 7.21–7.39 (5 H, m, ArH). HPLC: t_R (*R*) = 34.5 min, t_R (*S*) = 39.9 min [Chiracel OD-H; flow rate 1.0 mL min^{-1}; hexane–2-PrOH (98:2); 20 °C]; $[\alpha]_D^{20}$ +60 (*c* 0.19, acetone).

(*R*)-(+)-Benzyl-4-bromophenyl Sulfoxide (7b, Table 2, Entry 5)[14b]

Crude product contained a mixture of sulfide and sulfoxide (72:28). Purification by chromatography afforded the product as a white solid (59 mg, 20%, 37% ee).

^{1}H NMR: δ = 3.90–4.02 (1 H, A of ABq, *J* = 12.6 Hz, one of $SOCH_2$), 4.05–4.16 (1 H, B of ABq, *J* = 12.6 Hz, one of $SOCH_2$), 6.94–7.01 (2 H, m, ArH), 7.15–7.35 (5 H, m, ArH), 7.51–7.61 (2 H, m, ArH). HPLC: t_R (*R*) = 44.4 min, t_R (*S*) = 50.1 min [Chiracel OD-H; flow rate 0.5 mL min^{-1}; hexane–2-PrOH (94:6); 10 °C]; $[\alpha]_D^{20}$ +39.6 (*c* 0.37, $CHCl_3$); lit. 14b: $[\alpha]_D^{20}$ –65 (*c* 0.2, $CHCl_3$) for *S* >99% ee.

(*R*)-(+)-4-Fluorobenzyl-4′-fluorophenyl Sulfoxide (7c, Table 2, Entry 6)[22]

Crude product contained a mixture of sulfide and sulfoxide. Purification by chromatography afforded the product as a white solid (65 mg, 26%, 52% ee).

^{1}H NMR: δ = 4.00 (2 H, s, $SOCH_2$), 6.89–6.97 (4 H, m, ArH), 7.12–7.21 (2 H, m, ArH), 7.30–7.39 (2 H, m, ArH). HPLC: t_R (*R*) = 34.5 min, t_R (*S*) = 39.9 min [Chiracel OD-H; flow rate 1.0 mL min^{-1}; hexane–2-PrOH (98:2); 20 °C]; $[\alpha]_D^{20}$ +46.7 (*c* 0.38, acetone).

(*R*)-(+)-Benzyl-phenyl Sulfoxide (7d, Table 2, Entry 1)[14b]
Crude product contained a mixture of sulfide and sulfoxide (43:57). Purification by chromatography afforded the product as a white solid (95 mg, 44%, 60% ee).

^{1}H NMR: δ = 3.95–4.05 (1 H, A of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 4.05–4.15 (1 H, B of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 6.96–7.01 (2 H, m, ArH), 7.22–7.29 (3 H, m, ArH), 7.36–7.48 (5 H, m, ArH). HPLC: t_R (*R*) = 28.0 min, t_R (*S*) = 34.6 min [Chiracel OD-H; flow rate 1.0 mL min^{-1}; hexane–2-PrOH (98:2); 20 °C]; $[\alpha]_D^{20}$ +98.8 (*c* 0.25, acetone); lit. 14b: $[\alpha]_D^{20}$ –135.9 (*c* 0.49, acetone) for *S* = 91% ee.

(*R*)-(+)-Benzyl-4-methoxyphenyl Sulfoxide (7e, Table 2, Entry 7)[23]
Crude product contained a mixture of sulfide and sulfoxide (35:65). Purification by chromatography afforded the product as a white solid (111 mg, 45%, 44% ee).

^{1}H NMR: δ = 3.85 (3 H, s, OCH_3), 3.92–3.99 (1 H, A of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 4.09–4.15 (1 H, B of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 6.89–7.02 (4 H, m, ArH), 7.21–7.33 (4 H, m, ArH). HPLC: t_R (*R*) = 54.9 min, t_R (*S*) = 64.2 min [Chiracel OD-H; flow rate 1.0 mL min^{-1}; hexane–2-PrOH (98:2); 20 °C]; $[\alpha]_D^{20}$ +31.9 (*c* 0.28, acetone).

(*R*)-(+)-Benzyl-3-methoxyphenyl Sulfoxide (7l, Table 2, Entry 8)
Crude product contained a mixture of sulfide and sulfoxide (44:56). Purification by chromatography afforded the product as a white solid (103 mg, 42%, 69% ee).

Anal. Calcd (%) for $C_{14}H_{14}O_2S$: C, 68.28; H, 5.73; S, 13.02. Found: C, 68.09; H, 5.87; S, 12.93. ^{1}H NMR: δ = 3.70 (3 H, s, OCH_3), 3.96–4.03 (1 H, A of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 4.04–4.12 (1 H, B of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 6.87–7.02 (5 H, m, ArH), 7.21–7.33 (4 H, m, ArH). ^{13}C NMR: δ = 55.5 (OCH_3), 63.5 ($SOCH_2$), 108.4 (CH_{Ar}), 116.5 (CH_{Ar}), 118.1 (CH_{Ar}), 128.2 (CH_{Ar}), 128.5 (CH_{Ar}), 129.1 ($C_{Ar(q)}$), 129.7 (CH_{Ar}), 130.4 (CH_{Ar}), 144.1 ($C_{Ar(q)}$), 160.1 ($C_{Ar(q)}$), one $C_{(q)}$ not seen. ESI-MS: *m/z* = 247 [M + H]$^+$. ESI-HRMS: *m/z* calcd for $C_{14}H_{14}SO_2$ [M + H]$^+$: 247.0790; found 247.0784. HPLC: t_R (*S*) = 41.6 min, t_R (*R*) = 47.3 min [Chiracel OD-H; flow rate 1.0 mL min^{-1}; hexane–2-PrOH (98:2); 20 °C]; $[\alpha]_D^{20}$ +73.5 (*c* 0.17, acetone).

(*R*)-(+)-Benzyl-2-methoxyphenyl Sulfoxide (7f, Table 2, Entry 9)
Crude product contained a mixture of sulfide and sulfoxide (43:57). Purification by chromatography afforded the product as a white solid (121 mg, 49%, 81% ee).

Anal. Calcd (%) for $C_{14}H_{14}O_2S$: C, 68.26; H, 5.73; S, 13.02. Found: C, 67.85; H, 5.77; S, 12.63. ^{1}H NMR: δ = 3.88 (3 H, s, OCH_3), 3.92–4.02 (1 H, A of ABq, *J* = 12.8 Hz, one of $SOCH_2$), 4.20–4.30 (1 H, B of ABq, *J* = 12.8 Hz, one of $SOCH_2$), 6.90 (1 H, d, *J* = 7.8, ArH), 7.02–7.08 (3 H, m, ArH), 7.20–7.27 (3 H, m, ArH), 7.38–7.46 (2 H, m, ArH). ^{13}C NMR: δ = 56.2 (OCH_3), 60.0 ($SOCH_2$), 110.7 (CH_{Ar}), 121.8 (CH_{Ar}), 126.2 (CH_{Ar}), 128.3 (CH_{Ar}), 128.6 (CH_{Ar}), 130.5 ($C_{Ar(q)}$), 130.7 (CH_{Ar}), 132.4 (CH_{Ar}), 155.5 ($C_{Ar(q)}$), one $C_{(q)}$ not seen. ESI-MS: *m/z* = 247 [M + H]$^+$. ESI-HRMS: *m/z* calcd for $C_{14}H_{14}SO_2$ [M + H]$^+$: 247.0793; found: 247.0784. HPLC: t_R (*S*) = 34.0 min, t_R (*R*) = 39.0 min [Chiracel OD-H; flow rate 1.0 mL min^{-1}; hexane–2-PrOH (98:2); 20 °C]; $[\alpha]_D^{20}$ +351 (*c* 0.32, $CHCl_3$).

(*R*)-(+)-4-Methoxybenzyl-*p*-tolyl Sulfoxide (7g, Table 2, Entry 10)[14b]
Crude product contained a mixture of sulfide and sulfoxide (45:55). Purification by chromatography afforded the product as a white solid (70 mg, 27%, 38% ee).

^{1}H NMR: δ = 2.40 (3 H, s, $ArCH_3$), 3.79 (3 H, s, OCH_3), 3.97–4.05 (1 H, A of ABq, *J* = 12.7 Hz, one of $SOCH_2$), 4.18–4.24 (1 H, B of ABq, *J* = 12.7 Hz, one of $SOCH_2$), 6.78 (2 H, d, *J* = 8.7 Hz, ArH), 6.91 (2 H, d, *J* = 8.7 Hz, ArH), 7.17–7.32 (4 H, m, ArH). HPLC: t_R (*R*) = 33.4 min, t_R (*S*) = 41.0 min [Chiracel OD-H; flow rate 0.5 mL min^{-1}; hexane–2-PrOH (90:10); 10 °C]; $[\alpha]_D^{20}$ 31.9 (*c* 0.26, $CHCl_3$); lit. 14b: $[\alpha]_D^{20}$ –87 (*c* 0.2, $CHCl_3$) for *S* >99% ee.

(*R*)-(+)-3-Methoxybenzyl-*p*-tolyl Sulfoxide (7h, Table 2, Entry 11)
Crude product contained a mixture of sulfide and sulfoxide (68:32). Purification by chromatography afforded the product as a white solid (36 mg, 14%, 47% ee).

Anal. Calcd (%) for $C_{15}H_{16}O_2S$: C, 69.20; H, 6.19; S, 12.32. Found: C, 68.89; H, 6.33; S, 12.20. ^{1}H NMR: δ = 2.39 (3 H, s, $ArCH_3$), 3.70 (3 H, s, OCH_3), 3.90–3.98 (1 H, A of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 4.05–4.12 (1 H, B of ABq, *J* = 12.5 Hz, one of $SOCH_2$), 6.50 (1 H, br s, ArH), 6.61 (1 H, d, *J* = 7.5, ArH), 6.79–6.86 (1 H, m, ArH), 7.12–7.33 (5 H, m, ArH). ^{13}C NMR: δ = 21.8 ($ArCH_3$), 55.6 (OCH_3), 64.3 ($SOCH_2$), 114.7 (CH_{Ar}), 115.7 (CH_{Ar}), 123.1 (CH_{Ar}), 124.9 (CH_{Ar}), 129.7 (CH_{Ar}), 130.0 (aromatic CH_{Ar}), 131.2 ($C_{Ar(q)}$), 140.1 ($C_{Ar(q)}$), 142.1 ($C_{Ar(q)}$), 159.9 ($C_{Ar(q)}$). ESI-MS: *m/z* = 261 [M + H]$^+$. ESI-HRMS: *m/z* calcd for $C_{15}H_{16}SO_2$ [M + H]$^+$: 261.0949; found: 261.0941. HPLC: t_R (*S*) = 45.3 min, t_R (*R*) = 62.8 min [Chiracel OD-H; flow rate 1.0 mL min^{-1}; hexane–2-PrOH (98:2); 20 °C]; $[\alpha]_D^{20}$ +109 (*c* 0.41, acetone).

(*R*)-(+)-4-Fluorobenzyl-*p*-tolyl Sulfoxide (7i, Table 2, Entry 12)[14b]
Crude product contained a mixture of sulfide and sulfoxide (48:52). Purification by chromatography afforded the product as a white solid (72 mg, 29%, 65% ee).

^{1}H NMR: δ = 2.40 (3 H, s, CH_3), 3.99 (2 H, s, $SOCH_2$), 6.94 (4 H, d, *J* = 7.0 Hz, ArH), 7.23–7.29 (4 H, m, ArH). HPLC: t_R (*R*) = 34.6 min, t_R (*S*) = 40.3 min [Chiracel OD-H; flow rate 0.5 mL min^{-1}; hexane–2-PrOH (93:7); 10 °C]; $[\alpha]_D^{20}$ +71.5 (*c* 0.35, $CHCl_3$); lit. 14b: $[\alpha]_D^{20}$ –109 (*c* 0.4, $CHCl_3$) for *S* = 71% ee.

(*R*)-(+)-4-Chlorobenzyl-*p*-tolyl Sulfoxide (7j, Table 2, Entry 13)[14b]
Crude product contained a mixture of sulfide and sulfoxide (57:43). Purification by chromatography afforded the product as a white solid (69 mg, 26%, 50% ee).

^{1}H NMR: δ = 2.40 (3 H, s, CH_3), 3.98 (2 H, s, $SOCH_2$), 6.90 (2 H, d, *J* 6.5, ArH), 7.18–7.30 (6 H, m, ArH). HPLC: t_R (*R*) = 34.5 min, t_R (*S*) = 40.9 min [Chiracel OD-H; flow rate 0.5 mL min^{-1}; hexane–2-PrOH (93:7); 10 °C]; $[\alpha]_D^{20}$ +89.4 (*c* 0.26, acetone); lit. 14b: $[\alpha]_D^{20}$ –140 (*c* 0.5, $CHCl_3$) for *S* >99% ee.

(*R*)-(+)-Benzyl-*p*-tolyl Sulfoxide (7k, Table 2, Entry 14)[14b]
Crude product contained a mixture of sulfide and sulfoxide (45:55). Purification by chromatography afforded the product as a white solid (76 mg, 33%, 57% ee).

^{1}H NMR: δ = 2.40 (3 H, s, $ArCH_3$), 3.94–4.02 (1 H, A of ABq, *J* = 12.5 Hz, $SOCH_2$), 4.05–4.15 (1 H, B of ABq, *J* = 12.5 Hz, $SOCH_2$), 6.92–7.02 (2 H, m, ArH), 7.15–7.35 (7 H, m, ArH). HPLC: t_R (*R*) = 44.4 min, t_R (*S*) = 51.9 min [Chiracel OD-H; flow rate 1.0 mL min^{-1}; hexane–2-PrOH (98:2); 20 °C]; $[\alpha]_D^{20}$ +69.6 (*c* 0.23, acetone); lit. 14b: $[\alpha]_D^{20}$ –235.2 (*c* 0.7, acetone) for *S* >99% ee.

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