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Preparation of optically active *ortho*-chloro- and *ortho*-bromophenyl sulfoxides

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Abstract

The preparation of the diastereomerically pure menthyl (*S*)-2-chloro- and (*S*)-2-bromophenyl sulfinates by esterification of the corresponding sulfinic acids with (1*R*,2*S*,5*R*)-(−)-menthol and recrystallization/epimerization is reported. The two sulfinates have been converted into enantiomerically pure aryl, vinyl and alkyl sulfoxides by reaction with organomagnesium reagents. These sulfoxides are useful chiral auxiliaries to control the stereochemical outcome of radical reactions.

1. Introduction

The use of sulfoxides as chiral templates has been intensively investigated in carbanion alkylations, Michael additions and cycloadditions.[1] They have been found to have wide applications in the synthesis of biologically active compounds.[2] In our recent work, we found that good stereochemical control could be achieved in radical alkylation and cyclization of simple sulfinylated alkyl radicals by using either *ortho*-chloro- or *ortho*-bromophenyl sulfoxides.[3] Moreover, we have very recently used *ortho*-bromophenyl sulfoxides to run efficient hydrogen abstraction–fragmentation cascades leading to enantiomerically enriched alkenes.[4] In this article, we report an efficient method for the preparation of enantiomerically pure *ortho*-chloro- and *ortho*-bromophenyl sulfoxides.

2. Results and discussion

Different attempts to prepare optically active *ortho*-chloro- and *ortho*-bromophenyl methyl sulfoxides by enantioselective oxidation of the corresponding methyl sulfides (‘sulfoxidation’) have been reported. However, only low to moderate enantioselectivities have been achieved.[5,6]

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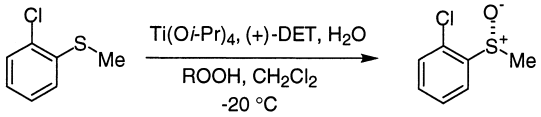
2.1. Enantioselective sulfoxidation approach

Our first attempt to prepare the *ortho*-chlorophenyl methyl sulfoxides **2** was based on the Kagan procedure using Ti(O*i*-Pr)$_4$/(*R*,*R*)-(+)-diethyl tartrate/H_2O.[7] Oxidation of the methyl sulfide **1** gave the desired methyl sulfoxides **2** with low to moderate enantioselectivities depending on the oxidant (cumene hydroperoxide: 27% ee, 91% yield; *tert*-butyl hydroperoxide: 88% ee, 91% yield) (Eq. 1). With this last oxidant, the best enantioselectivity (88% ee) was not reproducible and enantioselectivities as low as 40% ee were obtained in some runs. Moreover, sulfoxide **2** was not crystalline and it was therefore impossible to use recrystallization to enhance its enantiomeric excess. As a consequence, this approach was abandoned for a more convenient preparation procedure.



1

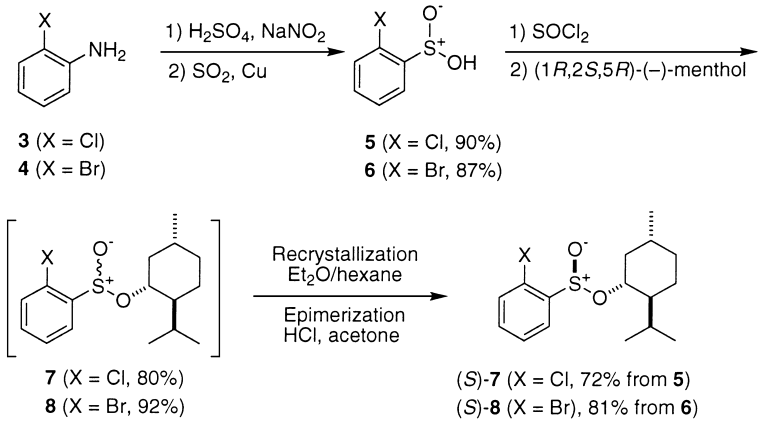
2 (R = cumyl: 27% ee, 91% yield)
(R = *tert*-butyl: 88% ee, 91% yield)

(1)

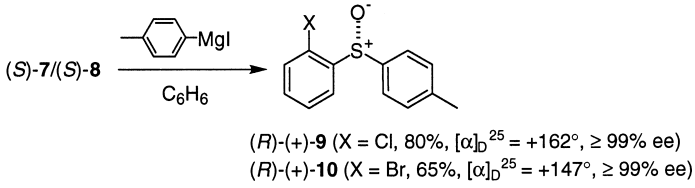
2.2. The Andersen approach

The preparation of enantiomerically pure sulfoxides by nucleophilic substitution at the sulfur center is very well documented since the pioneering work of Andersen with menthyl sulfinate.[8] Many different types of sulfinic acid derivatives have been developed[9] but the original Andersen procedure using menthyl sulfinates is still highly attractive for the preparation of aryl sulfoxides because of its efficiency and low cost. The crucial step of this approach is the preparation of diastereomerically pure sulfinates followed by nucleophilic displacement of the alkoxy moiety with organomagnesium compounds. We decided to investigate the preparation of the menthyl sulfinates **7** and **8** and to study the separation of the diastereomers. Starting from the commercially available *ortho*-chloro- and *ortho*-bromoanilines **3** and **4**, we prepared the sulfinic acids **5** and **6** according to a literature procedure by diazonation and reaction with SO_2 (Scheme 1).[10] The crude sulfinic acids were directly esterified by treatment with oxalyl chloride followed by reaction with (1*R*,2*S*,5*R*)-(−)-menthol. Menthyl sulfinates **7** and **8** were isolated as white solids (1:1 mixture of diastereomers) in 80 and 92% yield from the corresponding aniline, respectively. Several cycles of crystallization (Et_2O/hexane)–epimerization of the mother liquor (conc. HCl, acetone[11,12]) afforded the diastereomerically pure sulfinates (*S*)-**7** and (*S*)-**8** in 72% and 81% yield from the sulfinic acids **5** and **6**, respectively.

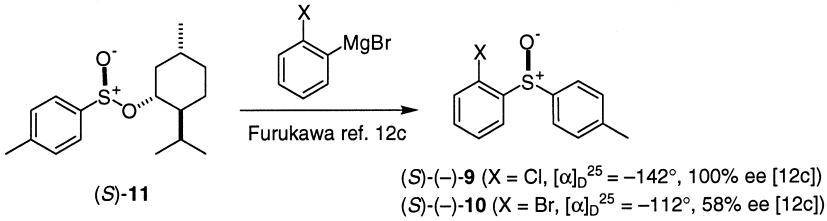
The absolute (*S*) configurations at sulfur of the sulfinate esters **7** and **8** were determined by chemical correlation according to Eqs. 2 and 3. The *para*-tolyl sulfoxides (*R*)-(+)-**9** and (*R*)-(+)-**10**[13] were synthesized from diastereomerically pure **7** and **8** by reaction with *para*-tolylmagnesium iodide in 80% and 65% yield, respectively (Eq. 2). The enantiomeric excess of these two sulfoxides was found to be over 99% by HPLC analysis with a chiral column (Daicel Chiralcel OB-H). The (*S*)-(−)-enantiomers of **9** and **10** have been prepared by Furukawa from the menthyl sulfinate (*S*)-**11** by reaction with *ortho*-chloro- and *ortho*-bromophenylmagnesium bromide (Eq. 3).[13c] Since the nucleophilic substitution at the sulfur atom of the sulfinate is known to occur with inversion of configuration,[14] it was possible to assign the (*S*) configuration for the sulfinates **7** and **8**.



Scheme 1.

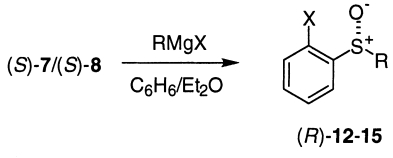


(2)



(3)

Methyl ((*R*)-**12**, (*R*)-**13**) and vinyl ((*R*)-**14**, (*R*)-**15**) sulfoxides were synthesized from the diastereomerically pure sulfinate (*S*)-**7** and (*S*)-**8** in good yields and excellent enantiomeric excess (Eq. 4, Table 1). For analytical reasons, the racemic sulfoxides were synthesized by oxidation of the corresponding sulfide with *m*-CPBA.



(4)

3. Conclusion

We have shown that the Andersen method is efficient for the preparation of enantiomerically pure *ortho*-chloro- and *ortho*-bromophenyl sulfoxides. The key menthyl sulfinates (*S*)-**7** and (*S*)-**8** were synthesized in good yields from the corresponding *ortho*-chloro- and *ortho*-bromoaniline. The absolute configuration of the sulfinates has been proved by chemical correlation via preparation of the known *ortho*-chloro- and *ortho*-bromophenyl *para*-tolyl sulfoxides. These sulfoxides are actually being applied

Table 1
Preparation of methyl and vinyl sulfoxides (*R*)-**12**–**15** from (*S*)-**7** and (*S*)-**8** according to Eq. 4

Entry	X	RMgX	Product	yield	ee[a]
1	Cl	CH_3MgI	**12**	75%	98%
2	Br	CH_3MgI	**13**	80%	99%
3	Cl	CH_2=CHMgBr	**14**	80%	99%
4	Br	CH_2=CHMgBr	**15**	75%	99%

[a]Measured by HPLC (*Daicel Chiralcel OB-H*, 0.42 cm × 25 cm).

for the control of the relative and absolute stereochemistry of radical cyclization and fragmentation reactions.

4. Experimental

4.1. General

THF was freshly distilled from potassium under N_2, CH_2Cl_2, pyridine and benzene from CaH_2, Et_2O from sodium/benzophenone. Flash column chromatography (FC) and filtration: silica gel Merck or Baker (60 870–230 mesh); elution with EtOAc and hexane or petroleum ether (p.e.); m.p.: not corrected; Büchi–Tottoli apparatus and Reichert Thermovar Kofler hot stage. FT-IR: Mattson–Unicam 5020. NMR: Varian Gemini 200 (^{1}H=200 MHz, ^{13}C=50.3 MHz); Bruker AM-360 (^{1}H=360.13 MHz); Bruker Avance DRX-500 (^{1}H=500 MHz, ^{13}C=125.77 MHz); unless otherwise indicated, spectra were recorded in $CDCl_3$ solns; for ^{1}H chemical shifts δ in ppm relative to $CHCl_3$ (=7.27 ppm); for ^{13}C chemical shifts δ in ppm relative to $CHCl_3$ (=77.0 ppm); MS: Finnigan 1020; Nermag R10-10C; vacuum generators micromass E70/70 and Hewlett–Packard 5988A; CI, chemical ionization with NH_3 or CH_4; EI, electron ionization at 70 eV; FAB, fast atom bombardment, matrix 3-nitrobenzyl alcohol (NBA), Xe-bombardment (8 kV, 1 mA); microanalyses: Ciba, Mikrolabor, CH-1700 Fribourg–Marly, Switzerland. HPLC: Daicel Chiralcel OB-H (0.46 cm diameter, 25 cm length), flow rate 0.5 ml/min.

4.2. General procedure 1. Preparation of sulfinic acids[10]

4.2.1. Preparation of copper catalyst[15]

A cold saturated soln of $CuSO_4$ (500 g, 3.13 mol) in H_2O (1.4 l) was placed in a beaker and stirred as Zn dust (200 g, 3.06 mol) was added very slowly. Too rapid addition makes the copper go lumpy. The addition was discontinued before complete decoloration of the $CuSO_4$ soln took place. The temperature reached 80°C at the end of the addition. The aqueous layer was removed and the copper stayed at the bottom of the beaker as a heavy dark red layer that was washed twice with cold H_2O. Traces of Zn were removed by covering the copper with twice its volume of H_2O and addition of 1 N HCl until hydrogen formation stopped. The copper took an intensive red color and was washed with H_2O until the H_2O stayed neutral. The catalyst was highly air sensitive and was stored as a wet paste.

4.2.2. Preparation of the sulfinic acids

2-Haloaniline (0.24 mol) was dissolved in H_2O (640 ml) and conc. H_2SO_4 (97%, 176 ml) was added. On cooling to 0°C, the 2-haloaniline sulfate crystallized as a white solid. At 0°C, a soln of $NaNO_2$ (0.28 mol) in H_2O (110 ml) was added dropwise to the white suspension. The solid disappeared and a cooled soln (0°C) of conc. H_2SO_4 (95–97%, 88 ml) in H_2O (60 ml) was added. The flask and its contents were weighed and SO_2 was passed through the soln at −25°C until the weight ceased to increase (200 g). It is important to keep the soln at −25°C in order to increase the absorption of SO_2 and the yield, since both the diazo compound and the sulfinic acid are unstable. The SO_2 absorption was finished within 1 h. The mixture was transferred to an ice cooled 3 l beaker and a catalytic amount of copper was added in portions with constant stirring until the violent gas evolution was finished. During the addition of copper, a slow stream of SO_2 was passed through the soln. The sulfinic acid precipitated and was isolated by filtration and washed with H_2O. The solid was treated with 10% Na_2CO_3 (1000 ml). The copper stayed in the filter and the clear aq. soln was acidified with cold 50% H_2SO_4. The white precipitate was extracted with Et_2O (2000 ml). Drying (Na_2SO_4) and evaporation gave the sulfinic acid as a white solid, which was used without further purification for the next step. The sulfinic acids can be stored at −25°C for several days.

4.3. General procedure 2. Preparation of sulfinate esters[12]

Freshly prepared sulfinic acid (0.144 mol) was added at rt in small portions to a soln of $SOCl_2$ (0.722 mol, 85.9 g, 52.5 ml) in benzene (250 ml). The mixture was stirred until all the solid was dissolved and no more gas evolution was observed. The excess of $SOCl_2$ was removed by azeotropic distillation with benzene (3×200 ml). The mixture was concentrated to 50 ml and the residue was diluted with anhydrous Et_2O (250 ml). A soln of (1*R*,2*S*,5*R*)-(−)-menthol (0.155 mol, 24.2 g) in anhydrous pyridine (25 ml) was added dropwise at 0°C. The mixture was stirred for 1 h at rt and then hydrolyzed with H_2O (100 ml). The organic layer was washed with 10% HCl (100 ml) and brine (50 ml). The organic layer was dried (Na_2SO_4), filtered and evaporated to give the sulfinate ester as a white solid (1:1 mixture of two diastereoisomers).

4.4. General procedure 3. Preparation of the sulfoxides[12]

A 1 M soln of the Grignard reagent was prepared from Mg (0.121 g, 5 mmol) and halide (5.5 mmol) in Et_2O (5 ml). Part of this soln (1.5 ml, 1.5 mmol) was added dropwise at 0–10°C to a soln of sulfinate ester (1 mmol) in benzene (2 ml). The soln was stirred at rt for 2–3 h and the reaction mixture was hydrolyzed with sat. NH_4Cl (2 ml) and extracted with Et_2O (5 ml). The collected organic layers were washed with brine (5 ml), dried (Na_2SO_4), filtered and evaporated to give the crude sulfoxide.

*4.5. 2-Chloro-1-benzenesulfinic acid **5***

From compound **3** (30 g, 0.235 mol) and $NaNO_2$ (19.47 g, 0.282 mol) according to general procedure 1, crude **5** (36.5 g, 90%) was obtained and used without further purification for the next step. White solid, m.p.: 120°C. ^{1}H NMR (200 MHz, DMSO): 7.90–7.80 (*m*, 1 arom. H); 7.70–7.41 (*m*, 3 arom. H). ^{13}C NMR (50.3 MHz, DMSO): 145.53 (*s*), 132.92 (*d*), 130.87 (*s*), 129.88 (*d*), 127.65 (*d*), 124.77 (*d*). IR (KBr): 3081, 1572, 1283, 1244. MS (FAB): 221 (78), $[M+Na]^+$, 187 (50), 175 (10), 159 (15), 153 (33), 137 (100), 127 (15), 115 (55), 110 (33).

4.6. 2-Bromo-1-benzenesulfinic acid **6**

From compound **4** (40 g, 0.233 mol) and $NaNO_2$ (19.47 g, 0.282 mol) according to general procedure 1, crude **6** (44.8 g, 87%) was obtained and used without further purification for the next step. White solid, m.p.: 130°C. ^{1}H NMR (200 MHz, DMSO): 7.90–7.35 (*m*, 4 arom. H). ^{13}C NMR (50.3 MHz, DMSO): 147.19 (*s*), 133.08 (*d*), 132.97 (*d*), 128.13 (*d*), 125.03 (*d*), 119.72 (*s*). IR (KBr): 2879, 2461, 2112, 1830, 1633, 1444, 1332, 1282. MS (FAB): 267 (40, $[M+Na]^+$), 187 (15), 175 (45), 153 (80), 137 (100), 125 (25), 115 (25), 79 (35), 63 (85).

4.7. (*S*S,*1*R,*2*S,*5*R)-(−)-1-(2-Chlorophenylsulfinyloxy)-2-isopropyl-5-methylcyclohexane (S)-**7**

From compound **5** (25 g, 0.142 mol) and (1*R*,2*S*,5*R*)-(−)-menthol (23.9 g, 0.153 mol) according to general procedure 2, crude **7** (35.8 g, 80%) was obtained as a 1:1 mixture of diastereomers. Recrystallization procedure for compound **7** (10 g, 1:1 mixture of diastereomers): the white solid was dissolved in acetone and conc. HCl (3 drops) was added. The colorless soln was stirred for 10 min at rt After evaporation, the resulting crystals were dissolved in Et_2O (21.5 ml). The slightly yellowish soln was diluted with hexane (215 ml) and the colorless soln was allowed to crystallize at −24°C for 16 h. The resulting white solid (6.4 g of a 1:12 mixture of diastereoisomers) was removed by filtration. The filtrate was concentrated and the remaining solid (3.6 g, 1:1 mixture of diastereomers) was dissolved in Et_2O (7.8 ml) and hexane (78 ml). One drop of conc. HCl was added and the clear soln was allowed to crystallize at −24°C for 16 h. This procedure was repeated 7 times. The collected solid was recrystallized in Et_2O:hexane (1:10) at −24°C to give diastereomerically pure (*S*)-**7** (32.2 g, 72%) as white crystals, m.p.: 99–100°C. $[\alpha]_D^{25}$=−277 (c=1, acetone). ^{1}H NMR (500 MHz): 8.05–7.97 (*m*, 1 arom. H); 7.50–7.42 (*m*, 2 arom. H); 7.42–7.36 (*m*, 1 arom. H); 4.12 (*dt*, J=4.5, 10.7, CHOSO); 2.40–2.33 (*m*, C*H*HCHOSO); 2.18–2.07 (*m*, C*H*$(CH_3)_2$); 1.72–1.62 (*m*, C*H*HCHCH$_3$); C*H*HCHCH$(CH_3)_2$); 1.53–1.40 (*m*, C*H*CH$_3$); 1.38–1.30 (*m*, C*H*CHOSO); 1.27–1.17 (*m*, CH*H*CHOSO); 1.09–0.98 (*m*, CH*H*CHCH$(CH_3)_2$); 0.95 (*d*, J=6.5, CH$_3$); 0.91–0.80 (*dm*, 4H, J=7.07, CH*H*CHCH$_3$, isopropyl CH$_3$); 0.67 (*d*, J=6.9, isopropyl CH$_3$). ^{13}C NMR (125 MHz): 143.44 (*s*), 133.01 (*d*), 132.03 (*s*), 130.04 (*d*), 127.38 (*d*), 125.70 (*d*), 80.44 (*d*), 47.83 (*d*), 42.51 (*t*), 33.94 (*t*), 31.72 (*d*), 25.11 (*d*), 23.16 (*t*), 22.04 (*q*), 20.81 (*q*), 15.37 (*q*). IR (KBr): 3065, 2930, 2890, 1576, 1451, 1387, 1372, 1245, 1181, 1097. MS (EI): 315 (56, $[M+1]^+$), 205 (10), 177 (100), 139 (31), 97 (3), 83 (22). Anal. calcd for $C_{16}H_{23}ClO_2S$ (314.87): C 61.03, H 7.36; found C 60.93, H 7.38.

4.8. (*S*S,*1*R,*2*S,*5*R)-(−)-1-(2-Bromophenylsulfinyloxy)-2-isopropyl-5-methylcyclohexane (S)-**8**

From compound **6** (40 g, 0.181 mol) and (1*R*,2*S*,5*R*)-(−)-menthol (30.4 g, 0.195 mol) according to general procedure 2, crude **8** (59.8 g, 92%) was obtained as a 1:1 mixture of diastereomers. Recrystallization procedure for compound **8** (10 g, 1:1 mixture of diastereomers): the white solid was dissolved in acetone (56 ml) and conc. HCl (3 drops) was added. The colorless soln was stirred for 10 min at rt. After evaporation, the resulting crystals were dissolved in Et_2O (26 ml). The slightly yellowish soln was diluted with hexane (260 ml) and the resulting colorless soln was allowed to crystallize at −24°C for 16 h. The resulting white solid (6.5 g of a 1:10 mixture of diastereoisomers) was removed by filtration. The filtrate was concentrated and the resulting oily solid (3.5 g, 1:1 mixture of diastereomers) was dissolved in Et_2O (11 ml) and hexane (110 ml). One drop of conc. HCl was added and the clear soln was allowed to crystallize at −24°C for 16 h. This procedure was repeated 6 times. The collected crystals were then recrystallized in Et_2O:hexane (1:10) at −24°C to give diastereomerically pure (*S*)-**8** (52.7 g, 81%) as white crystals, m.p.: 108.7–109.2°C. $[\alpha]_D^{25}$=−221 (c=1, acetone). ^{1}H NMR (500

MHz): 8.01–7.99 (*m*, 1 arom. H); 7.60–7.51 (*m*, 2 arom. H); 7.42–7.39 (*m*, 1 arom. H); 4.12 (*td*, J=10.7, 4.5, CHOSO); 2.46–2.35 (*m*, C*H*HCHOSO); 2.19–2.06 (*m*, C*H*$(CH_3)_2$); 1.72–1.63 (*m*, C*H*HCHCH_3, C*H*HCHCH$(CH_3)_2$); 1.54–1.43 (*m*, C*H*CH_3); 1.40–1.31 (*m*, C*H*CHOSO); 1.29–1.19 (*tm*, J=12.22, CH*H*CHOSO); 1.08–0.98 (*m*, CH*H*CHCH$(CH_3)_2$); 0.96 (*d*, J=6.5, CH_3); 0.92–0.80 (*dm*, 4H, J=7.07, CH*H*CHCH_3, isopropyl CH_3); 0.67 (*d*, J=6.9, isopropyl CH_3). ^{13}C NMR (125 MHz): 145.23 (*s*), 133.27 (*d*), 133.21 (*d*), 128.03 (*d*), 126.12 (*d*), 120.49 (*s*), 80.18 (*d*), 47.86 (*d*), 42.58 (*t*), 33.98 (*t*), 31.76 (*d*), 25.19 (*d*), 23.22 (*t*), 22.06 (*q*), 20.82 (*q*), 15.40 (*q*). IR (KBr): 3443, 2950, 2912, 2890, 1571, 1447, 1386, 1372, 1243, 1131. MS (EI): 360 (30, $[M+1]^+$), 223 (100), 204 (15), 139 (66), 97 (14), 83 (83), 69 (30), 57 (31), 55 (47). Anal. calcd for $C_{16}H_{23}BrO_2S$ (359.32): C 53.48, H 6.45; found C 53.41, H 6.54.

*4.9. (*R*)-(+)-2-Chlorophenyl 4-methylphenyl sulfoxide* **9**

From Mg (122 mg, 5 mmol), 4-iodotoluene (1.2 g, 5.5 mmol) and (*S*)-**7** (314 mg, 1 mmol) according to general procedure 3, the title compound was obtained. The resulting yellow oil was purified by FC (EtOAc:hexane 1:10) to give compound **9** (176 mg, 70%) as a white solid, m.p.: 90–91°C. $[\alpha]_D^{25}$=+162 (c=1, acetone). *R*:*S* >99.5:0.5 (HPLC, *i*-PrOH:hexane 5:95, t_r(*R*)=40 min, t_r(*S*)=44 min). ^{1}H NMR (360 MHz): 8.10–8.04 (*m*, 1 arom. H); 7.65–7.58 (*m*, 2 arom. H); 7.54–7.47 (*m*, 1 arom. H); 7.42–7.30 (*m*, 2 arom. H); 7.27–7.21 (*m*, 2 arom. H); 2.36 (*s*, CH_3). ^{13}C NMR (50 MHz): 143.61 (*s*), 142.02 (*s*), 141.36 (*s*), 131.79 (*d*), 131.10 (*s*), 129.92 (*d*), 127.87 (*d*), 126.07 (*d*), 125.71 (*d*), 21.41 (*q*). IR (KBr): 3443, 3053, 2922, 2361, 1928, 1813, 1593. MS (EI): 250 ($[M]^+$, 57), 233 (27), 202 (30), 184 (31), 167 (12), 139 (21), 111 (33), 91 (92), 77 (100). Anal. calcd for $C_{13}H_{11}ClOS$ (250.74): C 62.27, H 4.42; found C 62.3, H 4.46.

*4.10. (*R*)-(+)-2-Bromophenyl 4-methylphenyl sulfoxide* **10**

From Mg (122 mg, 5 mmol), 4-iodotoluene (1.2 g, 5.5 mmol) and (*S*)-**8** (359 mg, 1 mmol) according to general procedure 3, the title compound was obtained. The resulting yellow oil was purified by FC (EtOAc:hexane 1:10) to give compound **10** (192 mg, 65%) as a white solid, m.p.: 88–89°C. $[\alpha]_D^{25}$=+147 (c=1, THF). *R*:*S* >99.5:0.5 (HPLC, *i*-PrOH:hexane 5:95, t_r(*R*)=48 min, t_r(*S*)=42 min). ^{1}H NMR (360 MHz): 8.11–8.05 (*m*, 1 arom. H); 7.69–7.49 (*m*, 4 arom. H); 7.37–7.30 (*m*, 1 arom. H); 7.29–7.20 (*m*, 2 arom. H); 2.37 (*s*, CH_3). ^{13}C NMR (50.3 MHz): 145.23 (*s*), 142.02 (*s*), 141.43 (*s*), 133.06 (*d*), 132.07 (*d*), 129.90 (*d*), 128.44 (*d*), 126.33 (*d*), 119.96 (*s*), 21.42 (*q*). IR (KBr): 3437, 3050, 2921, 1592, 1492, 1445, 1402, 1310, 1092, 1081. MS (EI): 296 (100, $[M+1]^+$), 279 (61), 247 (15), 215 (60), 199 (22), 184 (14), 139 (42), 123 (31), 107 (91), 91 (43). Anal. calcd for $C_{13}H_{11}BrOS$ (295.20): C 52.9, H 3.76; found C 52.83, H 3.80.

*4.11. (*R*)-(+)-2-Chlorophenyl methyl sulfoxide* **12**

From Mg (122 mg, 5 mmol), iodomethane (5.5 mmol, 781 mg, 0.34 ml) and (*S*)-**7** (314 mg, 1 mmol) in benzene (2 ml) according to general procedure 3, the title compound was obtained. FC (EtOAc:hexane 1:4) gave compound **12** (131 mg, 75%), pale yellow oil. $[\alpha]_D^{25}$=+139 (c=1, THF). *R*:*S* >99:1 (HPLC, *i*-PrOH:hexane 10:90, t_r(*R*)=58 min, t_r(*S*)=28 min). ^{1}H NMR (360 MHz): 7.99–7.91 (*m*, 1 arom. H); 7.58–7.49 (*m*, 1 arom. H); 7.49–7.35 (*m*, 2 arom. H); 2.81 (*s*, CH_3). ^{13}C NMR (50 MHz): 143.72 (*s*), 131.80 (*d*), 129.68 (*s*), 129.63 (*d*), 128.01 (*d*), 125.22 (*d*), 41.63 (*q*). IR (film): 3485, 3059, 2997, 2914, 1566, 1446, 1290, 1093, 1014, 950. MS (EI): 174 (83, $[M]^+$), 159 (100), 131 (66), 111 (25), 99 (9), 75 (35), 63 (9). Anal. calcd for C_7H_7ClOS (174.65): C 48.14, H 4.04; found C 48.15, H 4.11.

4.12. (R)-(+)-2-Bromophenyl methyl sulfoxide **13**

From Mg (122 mg, 5 mmol), iodomethane (781 mg, 5.5 mmol, 0.34 ml) and (*S*)-**8** (359 mg, 1 mmol) in benzene (2 ml) according to general procedure 3, the title compound was obtained. FC (EtOAc:hexane 1:4) gave compound **13** (170 mg, 80%) as a pale yellow oil. $[\alpha]_D^{25}$=+251 (c=1, THF). *R*:*S* >99.5:0.5 (HPLC, *i*-PrOH:hexane 5:95, t_r(*R*)=33 min, t_r(*S*)=52 min). ^{1}H NMR (360 MHz): 7.97–7.93 (*m*, 1 arom. H); 7.62–7.54 (*m*, 2 arom. H); 7.42–7.34 (*m*, 1 arom. H); 2.83 (*s*, CH_3). ^{13}C NMR (50 MHz): 145.56 (*s*), 132.85 (*d*), 132.14 (*d*), 128.65 (*d*), 125.66 (*d*), 118.37 (*s*), 41.93 (*q*). IR (film): 3495, 3065, 3001, 2916, 1574, 1450, 1292, 1246, 1060, 1029, 950. MS (EI): 219 (95, $[M]^+$), 204 (100), 177 (38), 155 (16), 139 (57), 124 (11), 108 (29), 96 (93), 75 (62). Anal. calcd for C_7H_7BrSO (219.10): C 38.37, H 3.22; found C 38.36, H 3.46.

4.13. (R)-(+)-2-Chlorophenyl vinyl sulfoxide **14**

From a 1 M soln of vinylmagnesium bromide in THF (13 ml, 13 mmol) and (*S*)-**7** (4.0 g, 12.7 mmol) according to general procedure 3, in THF (50 ml) instead of benzene, the title compound was obtained. FC (EtOAc:hexane 1:4) gave compound **14** (1.4 g, 60%) as a colorless oil. $[\alpha]_D^{25}$=+207 (c=1, THF). *R*:*S* >99.5:0.5 (HPLC, *i*-PrOH:hexane 10:90, t_r(*R*)=21 min, t_r(*S*)=36 min). ^{1}H NMR (360 MHz): 7.81–7.75 (*m*, 1 arom. H); 7.52–7.33 (*m*, 3 arom. H); 6.83 (*dd*, J=16.3, 9.7, CHSO); 6.17 (*d*, J=16.3, C*H*H=C); 5.87 (*d*, J=9.7, CH*H*=C). ^{13}C NMR (50.3 MHz): 141.53 (*s*), 140.30 (*d*), 131.75 (*d*), 130.17 (*s*), 129.63 (*d*), 128.06 (*d*), 125.00 (*d*), 120.73 (*t*). IR (film): 3535, 3061, 3005, 1547, 1450, 1367, 1246. MS (CI): 187 (100, $[M+1]^+$), 170 (6), 159 (2), 138 (13), 135 (2), 75 (2). Anal. calcd for C_8H_7ClOS (186.66): C 51.48, H 3.78; found: C 51.49, H 3.86.

4.14. (R)-(+)-2-Bromophenyl vinyl sulfoxide **15**

From a 1 M soln of vinylmagnesium bromide in THF (10.4 ml, 10.4 mmol) and (*S*)-**8** (2.5 g, 6.9 mmol) according to general procedure 3, in THF (28 ml) instead of benzene, the title compound was obtained. FC (EtOAc:hexane 1:4) gave compound **15** (1.2 g, 75%) as a colorless oil. $[\alpha]_D^{25}$=+305 (c=1, THF). *R*:*S* >99.5:0.5 (HPLC, *i*-PrOH:hexane 10:90, t_r(*R*)=23 min, t_r(*S*)=45 min). ^{1}H NMR (360 MHz): 7.82–7.77 (*m*, 1 arom. H); 7.59–7.50 (*m*, 2 arom. H); 7.39–7.32 (*m*, 1 arom. H); 6.88 (*dd*, J=16.4, 9.4, CHSO); 6.24 (*d*, J=16.4, C*H*H=C); 5.98 (*d*, J=9.4, CH*H*=C). ^{13}C NMR (50 MHz): 143.49 (*s*), 140.59 (*d*), 132.84 (*d*), 132.06 (*d*), 128.69 (*d*), 125.59 (*d*), 120.81 (*t*), 118.90 (*s*). IR (film): 3425, 2955, 1724, 1568, 1446, 1367, 1178, 1068, 1014. MS (EI): 232 (9, $[M+1]^+$), 202 (2), 182 (10), 157 (3), 141 (4), 108 (7), 87 (20), 71 (100). Anal. calcd for C_8H_7BrOS (231.11): C 41.58, H 3.05; found C 41.92, H 3.37.

4.15. Syntheses of racemic diaryl sulfoxides[16]

4.15.1. (±)-2-Chlorophenyl 4-methylphenyl sulfoxide (±)-**9**

To a soln of 2-chloroaniline (1.3 g, 10 mmol) in H_2O (25 ml) was added at 80°C conc. HCl (5 ml). On cooling to 0°C, the hydrochloride precipitated as a white solid. At 0°C, a soln of $NaNO_2$ (691 mg, 10 mmol) in H_2O (5 ml) was added dropwise to the white suspension. The soln was neutralized with cold sat. NaOAc. The yellow precipitate was filtered and the filtrate was added dropwise at 80°C to a soln of NaOH (480 mg, 12 mmol) and *p*-thiocresol (1.5 g, 12 mmol) in H_2O (10 ml). The reaction mixture was heated at 95°C for 1 h. The mixture was cooled to rt and extracted with Et_2O (100 ml). The organic layer was washed with brine (50 ml), dried (Na_2SO_4), filtered and evaporated to give the crude sulfide. Bulb to

bulb distillation gave pure 2-chlorophenyl 4-methylphenyl sulfide (1.7 g, 74%) as a colorless oil which crystallized to a white solid. B.p.: 160°C/1.3 mbar, m.p: 29°C).

2-Chlorophenyl 4-methylphenyl sulfide (235 mg, 1 mmol) was dissolved in CH_2Cl_2 (20 ml) and treated at −10°C with a dried ($MgSO_4$) soln of *m*-CPBA (172 mg, 1 mmol) in CH_2Cl_2 (10 ml) over a period of 30 min. The soln was stirred for 1 h at −10°C before warming to rt. KF (174 mg, 3 mmol) was added and the resulting suspension was stirred overnight at rt and then filtered through Celite. After removing the solvent, the residue was purified by FC (EtOAc:hexane 1:5) to give (±)-**9** (237 mg, 95%) as a white solid, m.p.: 81.5–82°C. The analytical data was identical to the enantiomerically pure products.

*4.15.2. (±)-2-Bromophenyl 4-methylphenyl sulfoxide (±)-**10***

According to the procedure for the synthesis of (±)-**9** from 2-bromoaniline (1.5 g, 8.7 mmol), $NaNO_2$ (600 mg, 8.7 mmol), *p*-thiocresol (1.3 g, 10.4 mmol) and *m*-CPBA (1.3 g, 8 mmol) the title compound was obtained. FC (EtOAc:hexane 1:5) gave (±)-**10** (2.1 g, 90%) as a white solid, m.p.: 95.5–96°C. The analytical data was identical to the enantiomerically pure products.

*4.15.3. (±)-2-Chlorophenyl methyl sulfoxide (±)-**12***

A soln of CH_3I (1.7 g, 12 mmol) in benzene (10 ml) was added to a soln of 2-chlorothiophenol (1.7 g, 12 mmol), NaOH (680 mg, 17 mmol) and Bu_4NI (111 mg, 0.3 mmol) in H_2O (10 ml). The mixture was vigorously stirred for 24 h at rt. After extraction with Et_2O (3×100 ml), the collected organic layers were washed with brine (3×100 ml), dried (Na_2SO_4), filtered and evaporated to give 2-chlorophenyl methyl sulfide (1.7 g, 89%) as a pale yellow oil which was used without further purification. 2-Chlorophenyl methyl sulfide (159 mg, 1 mmol) was dissolved in CH_2Cl_2 (20 ml) and treated at −10°C with a dried ($MgSO_4$) soln of *m*-CPBA (172 mg, 1 mmol) in CH_2Cl_2 (10 ml) over a period of 30 min. The soln was stirred for 1 h at −10°C before warming to rt. KF (174 mg, 3 mmol) was added and the resulting suspension was stirred overnight and then filtered through Celite. After removing the solvent, the residue was purified by FC (EtOAc:hexane 1:4) to give (±)-**12** (162 mg, 93%) as a pale yellow oil. The analytical data was identical to the enantiomerically pure products.

*4.15.4. (±)-2-Bromophenyl methyl sulfoxide (±)-**13***

According to the procedure for the synthesis of (±)-**12** from CH_3I (1.7 g, 12 mmol), bromothiophenol (2.3 g, 12 mmol) and *m*-CPBA (2.1 g, 12 mmol) the title compound was obtained. FC (EtOAc:hexane 1:4) gave (±)-**13** (2.3 g, 89%) as a pale yellow oil. The analytical data was identical to the enantiomerically pure products.

*4.15.5. (±)-2-Chlorophenyl vinyl sulfoxide (±)-**14***

From a 1 M soln of vinylmagnesium bromide in THF (3 ml, 3 mmol) and compound **7** (850 mg, 2.7 mmol) according to general procedure 3, in THF (15 ml) instead of benzene, the title compound was obtained. FC (EtOAc:hexane 1:4) gave (±)-**14** (327 mg, 65%) as a colorless oil. The analytical data was identical to the enantiomerically pure products.

*4.15.6. (±)-2-Bromophenyl vinyl sulfoxide (±)-**15***

From a 1 M soln of vinylmagnesium bromide in THF (4.2 ml, 4.2 mmol) and compound **8** (1.43 g, 4 mmol) according to general procedure 3, in THF (10 ml) instead of benzene, the title compound was obtained. FC (EtOAc:hexane 1:4) gave (±)-**15** (674 mg, 73%) as a colorless oil. The analytical data was identical to the enantiomerically pure products.

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