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Symmetric Diarylsulfoxides as Asymmetric Sulfinylating Reagents for Dialkylmagnesium Compounds

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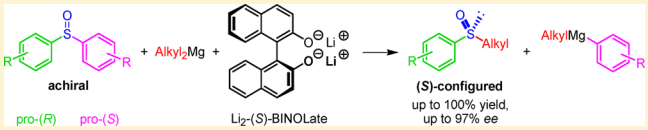
Supporting Information

ABSTRACT: At −78 °C, primary dialkylmagnesium compounds reacted with diarylsulfoxides when 1.5 equiv of the dilithium salt of (*S*)-BINOL was added as a promotor. Alkyl aryl sulfoxides resulted in up to quantitative yield and with up to 97% *ee*. This demonstrates the feasibility of asymmetric sulfinylations by achiral sulfinylating agents (from the perspective of $Alkyl_2Mg$) as well as the feasibility of asymmetric sulfoxide−magnesium exchanges (from the perspective of Ar_2SO).



INTRODUCTION

Nonracemic, i.e., enantioenriched or enantiomerically pure, sulfoxides[1] occur widely in asymmetric synthesis[2]—either stoichiometrically as carriers of chiral information[3] or catalytically as ligands for transition metals[4]—and natural product synthesis.[5] Nonracemic sulfoxides[6] are prepared, inter alia, by the asymmetric oxidation of sulfides[7] (the enantioselective oxidation leading to esomperazole—one of the top-selling drugs for gastric diseases—is a prominent example[8]), by the functionalization of organometallics with enantiomerically pure sulfinylating agents (e.g., refs 9, 11−21), and by the asymmetric alkylation (or arylation) of sulfenate anions by alkyl (or aryl) halides.[10] Grignard reagents have provided nonracemic sulfoxides upon functionalization by enantiomerically pure sulfinic acid derivatives−e.g., by menthyl (*S*)-*para*-toluenesulfinate,[11] (4*S*)-4-benzyl-*N*-[(*S*)-*para*-toluenesulfinyl]oxazolidinone,[12] and *tert*-butyl [(*R*)-*tert*-butylsulfinyl] sulfide[13]—or by enantiomerically pure sulfoxides (**1**,[14] **2**,[15] **3**,[16] **7**,[17] **8**,[18] (*S*)-**9**,[18] **12**,[19,20] **13**,[20] **14**,[21] or **15**,[21] Figure 1; ref 22). When one of the mentioned sulfinic acid derivatives sulfinylates a Grignard reagent, the leaving group is a magnesium alkoxide, a magnesium carbamate, or a magnesium sulfide. When such sulfinylations are carried out with one of the sulfoxides **1**−**3**, **7**−(*S*)-**9**, or **12**−**15**, the leaving group is a(nother) Grignard reagent. That feature makes the latter processes sulfoxide-magnesium exchange reactions.[23]

In 2012, we reported that *nonracemic* isopropyl aryl sulfoxides are accessible by sulfinylating *i*-Pr_2Mg[24] by *symmetric* (achiral!) diarylsulfoxides.[25] The best-working sulfinylating agent of the latter kind was the diarylsulfoxide **18** (Scheme 1). One of its enantiotopic 2,4-dimethylphenyl groups was replaced by the isopropyl group with a 95.5:4.5 preference over the other, i.e., with 91% *ee*. The underlying enantiocontrol was exerted by 3.0 equiv of the dilithium salt "Li_2-(*S*)-BINOLate" (**20**) of (*S*)-BINOL. **20** forms a 1:1 complex with Et_2Mg in the solid state.[26] An analogous interaction between **20** and *i*-Pr_2Mg was expected to arise upon mixing "THF"[27] solutions of the two components at −78 °C.

RESULTS AND DISCUSSION

The present study demonstrates that symmetric diarylsulfoxides sulfinylate *primary* dialkylmagnesium compounds in good yields,[28] too, and even with up to 97% *ee* (Schemes 2−6). This required fulfilling three prerequisites: (1) In the preparatory phase of the reaction, the dialkylmagnesium reagent had to be separated from the Schlenk equilibrium of the initially prepared Grignard reagent by precipitating the accompanying $MgBr_2$ with diglyme (0.39 equiv) and 1,4-dioxane (0.60 equiv). (2) The resulting dialkylmagnesium reagent (1.2 equiv) had to be complexed by "Li_2-(*S*)-BINOLate" (**20**; 1.5 equiv) prior to adding the sulfoxide. (3) The duration of the sulfinylation had to be monitored carefully. At −78 °C,[29] the optima ranged from 10 s to 26 h. Even moderately longer reaction times could decrease the yield and/or the enantioselectivity when we used Et_2Mg or Bu_2Mg. As previously,[25] the inducing ligand was recoverable as (*S*)-BINOL in almost quantitative yield by flash chromatography on silica gel;[30] it elutes prior to no matter which sulfoxide.

Scheme 2 shows Li_2-(*S*)-BINOLate (**20**)-induced sulfinylations of Me_2Mg, Bn_2Mg,[31] five other examples of $(R_{prim})_2Mg$, and $(c\text{-}C_6H_{11})_2Mg$ with the symmetric diarylsulfoxide **18**. They proceeded with 15%, 2%,[31] 85−97%, and 92% *ee*, respectively. In most cases, the yield surpassed 90%. The preferentially formed sulfoxide enantiomer was levorotatory without an exception;[32] the products, whose absolute configurations we clarified [(−)-**21**, (−)-**22**], were (*S*)-configured.[32] According to the survey of Scheme 2, Et_2Mg, Bu_2Mg, and *i*-Bu_2Mg were sulfinylated by a mixture of sulfoxide **18** and Li_2-(*S*)-BINOLate (**20**) with the highest enantiomeric excesses, namely, with 96%, 96%, and 97%, respectively. This led us to explore how the same organometallics are sulfinylated by mixtures of Li_2-(*S*)-BINOLate (**20**; 1.25 equiv) and symmetric diarylsulfoxides (0.83 equiv) other than **18** (Schemes 3−6).

The Li_2-(*S*)-BINOLate (**20**)-induced asymmetric sulfinylations of Et_2Mg (Scheme 3) reached completion at −78 °C

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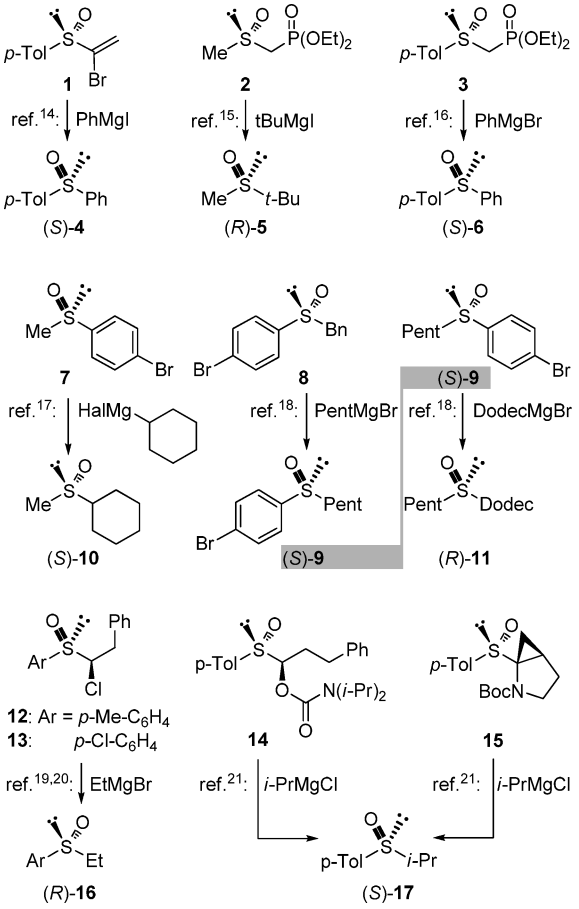
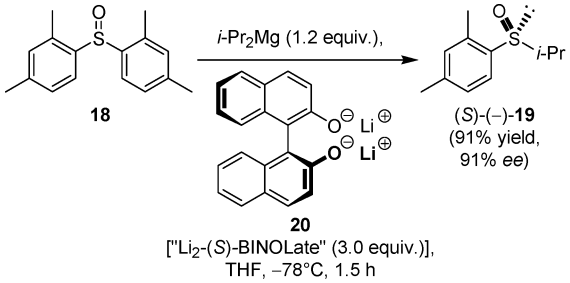


Figure 1. Enantiomerically pure sulfinylating agents, which convert Grignard reagents into nonracemic sulfoxides while expelling another Grignard compound as a leaving group.

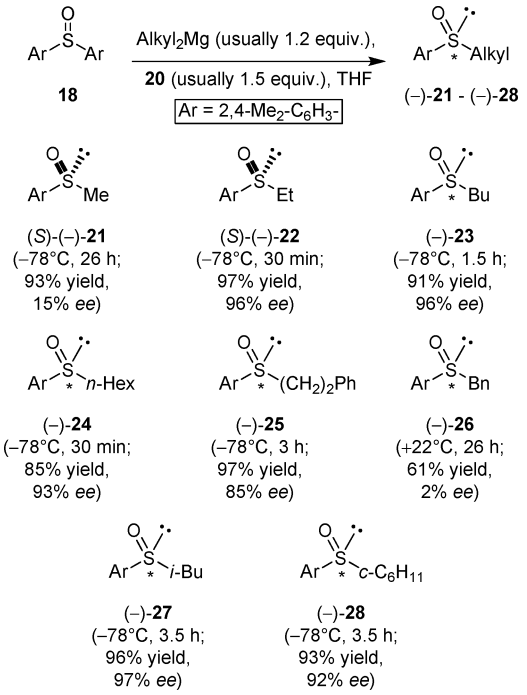
Scheme 1. Asymmetric Sulfinylation of a Secondary Dialkylmagnesium Compound by the Symmetric Diarylsulfoxide 18 in the Presence of an Excess of the Dilithium Salt "Li_2-(*S*)-BINOLate" (20) of (*S*)-BINOL (ref 25)



between as little as 10 s [→ (*S*)-(−)-**32**] and 1 h at maximum [→ (*S*)-(−)-**31**].[33] The ethyl aryl sulfoxides **22** and **29**−**35** resulted in an average yield of 70%. They were uniformly levorotatory and (*S*)-configured.[32] The highest enantiocontrol resulted from (2,4-dimethylphenyl)sulfinyl transfer [→ 97% (*S*)-(−)-**22**, 96% *ee*]. The runners-up were *para*-tolylsulfinyl transfer (94% *ee*) and α-naphthylsulfinyl transfer (93% *ee*).

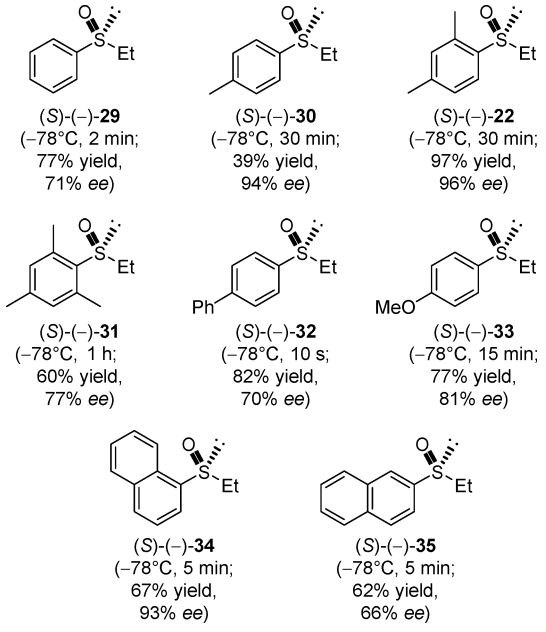
The Li_2-(*S*)-BINOLate (**20**)-induced asymmetric sulfinylations of Bu_2Mg (Scheme 4) were even faster than the analogous sulfinylations of Et_2Mg (cf. above). This rendered the nonracemic sulfoxides **23**, **36**−**37**, and **39**−**42** in 62−91% yield.

Scheme 2. Li_2-(*S*)-BINOLate (20)-Promoted Asymmetric Sulfinylations of Primary Dialkylmagnesium Compounds and of Dicyclohexylmagnesium by the Symmetric Diarylsulfoxide 18 (Configurational Assignments: ref 32)[a]



[a]The sulfoxides **21** and **28** were obtained from differently composed reactant mixtures than the other sulfoxides, using the sulfoxide **18** and more of the exchange-inducing reagents Me_2Mg (2.4 equiv), Bn_2Mg (2.4 equiv), and **20** (3.0 equiv). Under the "usual" conditions, lower yields were obtained.

Scheme 3. Nonracemic Sulfoxides [(*S*)-Configurations: ref 32] from Li_2-(*S*)-BINOLate (20)-Promoted Asymmetric Sulfinylations of Et_2Mg by Symmetric Diarylsulfoxides[a33]



[a]The aryl ethyl sulfoxides depicted here were prepared from a symmetric diarylsulfoxide and the exchange-inducing reagents Et_2Mg (1.2 equiv) and **20** (1.5 equiv), i.e., under the "usual" conditions of Scheme 2.

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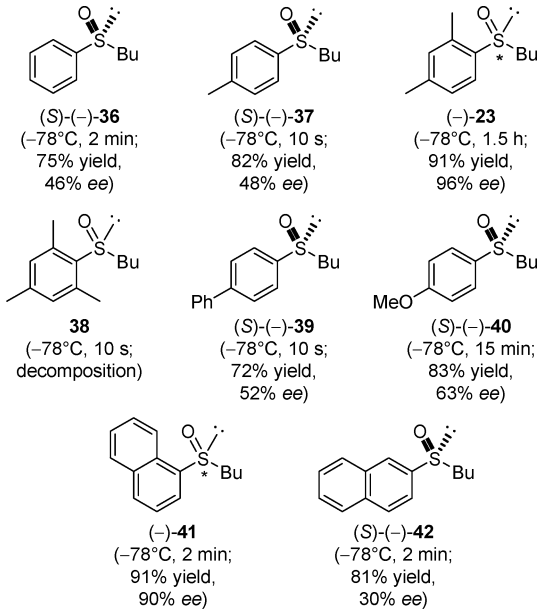
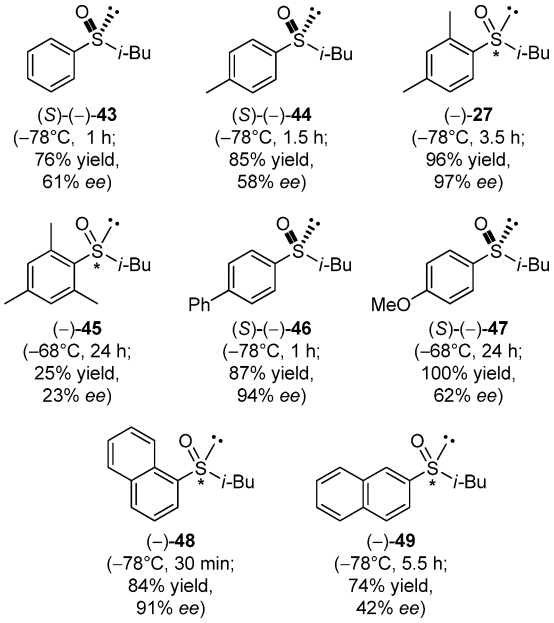
Scheme 4. Nonracemic Sulfoxides (Configurational Assignments: ref 32) from Li_2-(*S*)-BINOLate (20**)-Promoted Asymmetric Sulfinylations of Bu_2Mg by Achiral Diarylsulfoxides**[a]



[a]The aryl butyl sulfoxides depicted here were prepared from a symmetric diarylsulfoxide and the exchange-inducing reagents Bu_2Mg (1.2 equiv) and **20** (1.5 equiv), i.e., under the "usual" conditions of Scheme 2.

Scheme 5. Nonracemic Sulfoxides (Configurational Assignments: ref 32) from Li_2-(*S*)-BINOLate (20**)-Promoted Asymmetric Sulfinylations of *i*-Bu_2Mg by Achiral Diarylsulfoxides**[a]



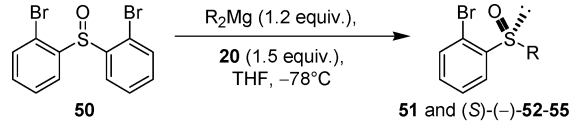
[a]The aryl isobutyl sulfoxides depicted here were prepared from a symmetric diarylsulfoxide and the exchange-inducing reagents *i*-Bu_2Mg (1.2 equiv) and **20** (1.5 equiv), i.e., under the "usual" conditions of Scheme 2.

In contrast, butyl 2,4,6-trimethylphenyl sulfoxide (**38**) did not form because of an almost instantaneous decomposition of a mixture of its precursors. The other sulfoxides of Scheme 4 were consistently levorotatory, and the five sulfoxides, whose 3D structure we clarified, were (*S*)-configured.[32] The highest *ee* value in this series (96%) was observed for the (2,4-dimethylphenyl)-sulfinylation [→ 91% (−)-**23**].

The third dialkyl magnesium reagent, which was sulfinylated asymmetrically in the presence of Li_2-(*S*)-BINOLate (**20**) by a variety of symmetric diarylsulfoxides, was *i*-Bu_2Mg (Scheme 5). It was less reactive than Et_2Mg and Bu_2Mg so that full conversions required 0.5−24 h and possibly a slightly elevated temperature (−68 °C instead of −78 °C). The newly formed sulfoxides were levorotatory, and those, whose absolute configurations we clarified (**43**, **44**, **46**, and **47**), were (*S*)-configured.[32] Enantiocontrol was best when the (2,4-dimethylphenyl)sulfinyl group was transferred [→ 96% (*S*)-(−)-**27**, 97% *ee*] or the (4-phenylphenyl)sulfinyl group [→ 87% (*S*)-(−)-**46**, 94% *ee*].

In the presence of Li_2-(*S*)-BINOLate (**20**), bis(2-bromophenyl) sulfoxide (**50**) had been a capricious sulfinylating agent for *i*-Pr_2Mg:[25] 3.9 equiv of this additive was required for accelerating the sulfinylation [→ 70% (*S*)-**55**] at the expense of an ensuing Br → Mg exchange; the latter interfered unavoidably under standard conditions.[25] No Br → Mg exchanges occurred when mixtures of bis(2-bromophenyl) sulfoxide (**50**) and Li_2-(*S*)-BINOLate (**20**) sulfinylated Et_2Mg, Bu_2Mg, and *i*-Bu_2Mg—yet not Me_2Mg—asymmetrically (Scheme 6). The corresponding brominated sulfoxides (*S*)-**52**−(*S*)-**54**[32] resulted in 69−83% yield and with 53−89% *ee*.

Scheme 6. Nonracemic (2-Bromophenyl) Sulfoxides [(*S*)-Configurations: ref 32] from Li_2-(*S*)-BINOLate (20**)-Promoted Asymmetric Sulfinylations by the Symmetric Bis(2-bromophenyl) Sulfoxide 50**



R = Me: **51**	R = Et: (*S*)-(−)-**52**	R = Bu: (*S*)-(−)-**53**	R = *i*-Bu: (*S*)-(−)-**54**	R = *i*-Pr:[23] (*S*)-(−)-**55**
(decomp.)	(−78°C, 10 s; 69% yield, 89% *ee*)	(−78°C, 10 s; 79% yield, 86% *ee*)	(−78°C, 1.5 h; 83% yield, 53% *ee*)	(−78°C, 1.5 h; 70% yield, 36% *ee*)

CONCLUSION

In summary, we have shown that symmetric diarylsulfoxides transfer arylsulfinyl groups on di(*prim*-alkyl) magnesium compounds *asymmetrically* when 1.5 equiv of Li_2-(*S*)-BINOLate (**20**) is present. This transformation is a novel entry into the synthesis of nonracemic alkyl aryl sulfoxides.

Ethyl, butyl, and isobutyl aryl sulfoxides arose with up to 97% *ee*. Hexyl and phenylethyl 2,4-dimethylphenyl sulfoxide resulted with 93% and 87% *ee*, respectively. In stark contrast, methyl 2,4-dimethylphenyl sulfoxide resulted with little enantiocontrol (15% *ee*) and benzyl 2,4-dimethylphenyl sulfoxide virtually without (2% *ee*). We are at a loss interpreting these substituent dependencies. Hence, it remains unclear to which extent—and in the affirmative case, where—steric effects and/or electronic effects and/or other effects are operative in the *ee*-determining or the yield-determining step. This is not least because the

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sulfoxide/magnesium exchange—let alone our asymmetric variant thereof—is only poorly understood mechanistically.[26]

The strategy, which underlies our present synthesis of alkyl aryl sulfoxides, would become more generally useful if enantiomerically pure additives like Li_2-(*S*)-BINOLate (**20**) allowed one to sulfinylate organometallics asymmetrically also by other symmetric sulfoxides than diarylsulfoxides. At least there are many kinds of (admittedly, unsymmetric) sulfoxides, which sulfinylate Grignard reagents while expelling a magnesium-containing leaving group (examples: Figure 1). The latter may be stable,[34] β-eliminate,[35] α-eliminate/rearrange,[36] or undergo a semipinacol rearrangement.[37] If a *pair* of progenitors of any such leaving group binds to a −S(=O)− linchpin, a symmetric sulfoxide candidate for effecting another asymmetric sulfinylation like contemplated above would be defined. Such a sulfoxide might act not just on R_2Mg but also on RMgHal, RMgOC(=O)R′, RMgOS(=O)$_2$R′, R_3MgLi, or other organometallics.[38,39]

EXPERIMENTAL SECTION

General. Working Technique: All reactions were carried out under an atmosphere of N_2. Prior to use, reaction flasks were dried in vacuo with a heat gun. Liquids were added with a syringe through a septum. Prior to use, THF, Et_2O, and diglyme were distilled over sodium or potassium under an atmosphere of N_2. *i*-Pr_2NH was distilled over CaH_2 similarly. Other solvents and reagents were employed as obtained commercially, i.e., without further purification. **Flash chromatography on silica gel**: Purification by flash chromatography was conducted on silica gel 60 (230−400 mesh). All eluents were distilled prior to use. Chromatography conditions are documented in a shorthand form like, e.g., "(*c*-C_6H_{12}:EtOAc a:b, F. 10−20)", which means we eluted with an a:b mixture (v:v) of *c*-C_6H_{12} and EtOAc and that the product was isolated from fractions 10−20. Fraction and column size were chosen in accordance to the parameters described by Still et al.[40] **Nuclear magnetic resonance spectra**: NMR spectra were registered with 300 and 400 MHz spectrometers (^{1}H NMR) and with a 100 MHz spectrometer (^{13}C NMR), referenced internally to the ^{1}H and ^{13}C NMR signals of the solvent [$CDCl_3$: 7.26 ppm (^{1}H) and 77.10 ppm (^{13}C)]. ^{1}H NMR data are reported as follows: chemical shift (δ in ppm), multiplicity (s for singlet; d for doublet; t for triplet; q for quartet; m for multiplet; m_c for symmetric multiplet; br for broad signal), coupling constant(s) (Hz), integral, assignment. ^{13}C NMR data are reported in terms of chemical shift and assignment. Assignments of ^{1}H NMR and ^{13}C NMR resonances refer to the IUPAC nomenclature except within substituents (where primed numbers are used) or where explicitly indicated otherwise. NMR assignments were supported by a combination of 1D and 2D techniques (DQF-COSY and ed-HSQC). **High-resolution mass spectra** were obtained employing a CI/NH_3 (110 eV) mode and using an orbitrap analyzer. **Elemental analyses** were obtained with a CHNS analyzer. **Melting points** are uncorrected and were determined using open glass capillaries. **IR spectra** were measured with an FT-IR spectrometer irradiating sample films spread on a NaCl plate. The *ee* values were determined by **chiral HPLC**. **Optical rotations** were measured at 365, 436, 546, 578, and 589 nm at 20 °C and were calculated by the Drude equation {$[\alpha] = (\alpha_{exp} \times 100)/(c \times d)$}; rotational values are the average of five measurements of α_{exp} in a given solution of the respective sample.

Preparation of Reactants. *Preparation of Alkyl$_2$Mg Solutions in Et$_2$O (Alkyl = Et, Bu, n-Hex, (CH$_2$)$_2$Ph, Bn, i-Bu and c-C$_6$H$_{11}$).*[41] At room temperature, the appropriate alkyl bromide (128 mmol) was added dropwise to a suspension of Mg turnings (3.14 g, 129 mmol, 1.0 equiv) in Et_2O (60 mL) within 1.5 h. The dark gray suspension was heated under reflux for 4 h. After cooling to 0 °C, diglyme (7.20 mL, 6.75 g, 50.3 mmol, 0.39 equiv) in Et_2O (9 mL) and thereafter dioxane (6.60 mL, 6.80 g, 77.2 mmol, 0.60 equiv) in Et_2O (6 mL) were added dropwise with a syringe pump within 75 and 50 min, respectively. The white suspension was stirred at −10 °C for 16 h and then filtered with suction in an atmosphere of nitrogen. The clear and colorless filtrate was concentrated to about half its volume by a stream of nitrogen. Usually a small amount of a white precipitate formed concomitantly; it remained in the solution without decreasing its activity. The resulting solution of Alkyl$_2$Mg could be stored at 4 °C for several weeks. Its concentration was determined by titration with salicylic aldehyde phenylhydrazone.[42]

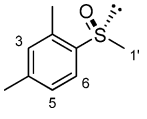
Preparation of Me$_2$Mg and Hex$_2$Mg Solutions in Et$_2$O.[43] At room temperature, MeLi or HexLi (solutions in THF, 12.0 mmol, 1.0 equiv) was added dropwise to a solution of the corresponding AlkylMgCl (solution in THF, 12.0 mmol, 1.0 equiv). After 5 min, the solvent was removed by applying high vacuo (~0.4 mbar). The residue was extracted with Et_2O (3 × 10 mL) from precipitated LiCl. The concentration of the resulting clear and colorless solution was determined by titration with salicylic aldehyde phenylhydrazone.[42] At 4 °C, such solutions could be stored for several weeks.

Preparation of the Symmetric Diarylsulfoxides. The symmetric diarylsulfoxides used in this work were materials from our previous study.[25]

Preparation of Alkyl Aryl Sulfoxides. *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides.*[44] Alkyl$_2$Mg (0.38−0.80 M solutions in Et_2O, 0.55−1.2 equiv) was added to a solution of the appropriate diarylsulfoxide (0.148−0.494 mmol, 1.0 equiv) in THF (1 mL) at room temperature (for further details and deviations from this procedure: cf. individual descriptions). After complete conversion, the reaction was quenched by the addition of MeOH (1 mL) and a saturated aqueous solution of NH_4Cl (1 mL). The layers were separated. The aqueous layer was extracted with *t*-BuOMe (3 × 2 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel[40] (further details: cf. individual descriptions).

Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides. At 0 °C, *n*-BuLi [2.05−2.27 M solution in hexane, 3.0 equiv.] was added to a precooled solution of (*S*)-BINOL (1.5 equiv) in THF (2 mL). After 10 min, stirring was continued at room temperature for another 10 min. Subsequently, a solution of Alkyl$_2$Mg (0.38−0.80 M in Et_2O, 1.2 equiv) was added dropwise. After 10 min, the reaction mixture was cooled to −78 °C and a solution of the appropriate diarylsulfoxide (0.174−0.786 mmol, 1.0 equiv) in THF (1.5 mL) was added during 10 min. If Alkyl$_2$Mg was Et_2Mg or Bu_2Mg, the solution of the appropriate diarylsulfoxide had to be (1) precooled to −78 °C and (2) added to the Li_2-(*S*)-BINOLate/Alkyl$_2$Mg mixture very fast. After full conversion was achieved (10 s to 24 h), the reaction was quenched by the addition of MeOH (2 mL). The resulting mixture was warmed to room temperature and diluted with *t*-BuOMe (5 mL). A saturated, aqueous solution of NH_4Cl (3 mL) was added. The layers were separated. The aqueous layer was extracted with *t*-BuOMe (3 × 2 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel[40] (details: cf. individual descriptions) to yield the title compound.

*(2,4-Dimethylphenyl) Methyl Sulfoxide (**21**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] did not follow the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides*: At 0 °C, *n*-BuLi (2.1 M in hexane, 0.56 mL, 1.2 mmol, 6.1 equiv) was added to a solution of *rac*-BINOL (169 mg, 0.591 mmol, 3.0 equiv) in THF (1 mL). After 10 min, Me_2Mg (0.40 M in Et_2O, 1.18 mL, 0.472 mmol, 2.4 equiv) was added. After another 10 min, a solution of bis(2,4-dimethylphenyl) sulfoxide (50.9 mg, 0.197 mmol) in THF (0.75 mL) was added. After stirring at room temperature for 9 h, the reaction was quenched and the resulting mixture was worked up. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 55:45, F. 30−42) delivered *rac*-**21** (26.2 mg, 79%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (101 mg, 0.391 mmol), (*S*)-BINOL (3.0 equiv), and Me_2Mg (2.4 equiv). After 72 h, this delivered (*S*)-(−)-**21** (61.4 mg, 93%; 15% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 2.34 (s, 3 H, Ar-CH_3), 2.37 (s, 3 H, Ar-CH_3),

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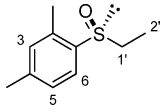
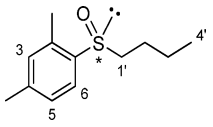
2.66 (s, 3 H, 1′-H_3), 7.01 (br. s, 1 H, 3-H), 7.25 (d, low-field branch superimposed by the singlet of $CHCl_3$, $J_{5,6}$ = 7.9 Hz, 1 H, 5-H), 7.83 ppm (d, $J_{6,5}$ = 8.1, 1 H, 6-H). The preceding data are consistent with those reported in the literature.[46] The *ee* was determined by chiral HPLC (Chiralcel OD-H, *n*-heptane/*i*-PrOH 90:10, 1 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(R)$ = 16.83 min, $t_r(S)$ = 22.21 min. $[\alpha]^{20}_{365} = -163.1$, $[\alpha]^{20}_{436} = -81.2$, $[\alpha]^{20}_{546} = -40.2$, $[\alpha]^{20}_{578} = -34.6$, $[\alpha]^{20}_{589} = -32.1$ (c = 2.00 in EtOH; the respective sample had 15% *ee*); Lit.:[47] $[\alpha]^{20}_{589} = -87.8$ [c = 1.3 in acetone, a sample of the (*S*)-enantiomer with 73% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[47]

*(2,4-Dimethylphenyl) Ethyl Sulfoxide (**22**): (S)-(−)-Enantiomer and Racemic.*[45]



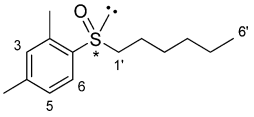
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (100 mg, 0.387 mmol) with Et_2Mg (0.52 M in Et_2O, 0.91 mL, 0.47 mmol, 1.2 equiv) within 30 min. Flash chromatography on silica gel[40] (c-C_6H_{12}:EtOAc 60:40, F. 24−38) delivered *rac*-**22** (34.3 mg, 49%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (200 mg, 0.774 mmol). After 30 min, this delivered (*S*)-(−)-**22** (137 mg, 97%; 96% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.23 (dd, $J_{2',1'\text{-A}} = J_{2',1'\text{-B}}$ = 7.3 Hz, 3 H, 2′-H_3), 2.34 (s, 3 H, Ar-CH_3), 2.36 (s, 3 H, Ar-CH_3), AB signal (δ_A = 2.71, δ_B = 2.86, $J_{A,B}$ = 13.6 Hz, A part additionally split by q, $J_{1'\text{-A},2'}$ = 8.0 Hz, 1′-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 6.9 Hz, 1′-H_B), 7.01 (m_c, 1 H, 3-H), 7.22 (m_c,[49] $J_{5,6}$ = 7.9 Hz, 1 H, 5-H), 7.75 ppm (d, $J_{6',5'}$ = 8.1 Hz, 1 H, 6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 6.4 (C-2′), 18.3 (Ar-CH_3), 21.3 (Ar-CH_3), 48.5 (C-1′), 124.4 (C-6), 127.9 (C-5), 131.5 (C-3), 134.5, 138.6, 141.2 ppm (C-1, C-2, and C-4). The preceding data are consistent with those reported in the literature.[46] The *ee* was determined by chiral HPLC (Chiralcel OD-3, *n*-heptane/*i*-PrOH 96:4, 22 °C, 1 mL/min, $\lambda_{detector}$ = 204 nm): $t_r(R)$ = 9.06 min, $t_r(S)$ = 13.49 min. $[\alpha]^{20}_{365} = -1247.6$, $[\alpha]^{20}_{436} = -614.3$, $[\alpha]^{20}_{546} = -305.5$, $[\alpha]^{20}_{578} = -261.8$, $[\alpha]^{20}_{589} = -248.7$ (c = 1.64 in EtOH; the respective sample had 96% *ee*). The absolute configuration was assigned by chemical correlation (cf. Supporting Information).

*Butyl (2,4-Dimethylphenyl) Sulfoxide (**23**): (−)-Enantiomer and Racemic.*[45]



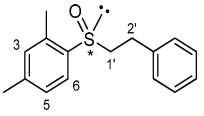
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (95.7 mg, 0.370 mmol) with Bu_2Mg (0.69 M in Et_2O, 0.65 mL, 0.45 mmol, 1.2 equiv) within 1.5 h at 0 °C. Flash chromatography on silica gel[40] (c-C_6H_{12}:EtOAc 80:20, F. 24−40) delivered *rac*-**23** (60.0 mg, 77%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (102 mg, 0.393 mmol). After 1.5 h, this delivered (−)-**23** (75.3 mg, 91%; 96% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.93 (t, $J_{4',3'}$ = 7.6 Hz, 3 H, 4′-H_3), 1.35−1.56 (m, 2 H, 3′-H_2), 1.59−1.83 (m, 2 H, 2′-H_2), 2.33 (s, 3 H, Ar-CH_3), 2.36 (s, 3 H, Ar-CH_3), AB signal (δ_A = 2.70, δ_B = 2.75, $J_{A,B}$ = 13.3 Hz, A part additionally split by dd, $J_{1'\text{-A},2'\text{-A}}$ = 9.4, $J_{1'\text{-A},2'\text{-B}}$ = 5.2 Hz, 1-H_A; B part additionally split by dd, $J_{1'\text{-B},2'\text{-B}}$ = 9.4 Hz, $J_{1'\text{-B},2'\text{-A}}$ = 5.7 Hz, 1-H_B), 7.01 (d, $J_{3,5}$ = 0.7 Hz, 1 H, 3-H), 7.22 (dd, $J_{5,6}$ = 8.1 Hz, $J_{5,3}$ = 0.8 Hz, 1 H, 5-H), 7.77 ppm (d, $J_{6,5}$ = 8.4 Hz, 1 H, 6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.9 (C-4′), 18.3 (Ar-CH_3), 21.3 (Ar-CH_3), 22.0 (C-3′), 24.5 (C-2′), 55.5 (C-1′), 124.2 and 128.2 (C-5, and C-6′), 131.7 (C-3), 134.3, 139.4, and 141.3 ppm (C-1, C-2, and C-4). IR ($CDCl_3$): $\tilde{\nu}$ = 3900, 3450, 3530, 3225, 3030, 2960, 2930, 2870, 2735, 2615, 2295, 2280, 2260, 2055, 1920, 1635, 1605, 1575, 1455, 1400, 1380, 1345, 1280, 1230, 1185, 1155, 1070, 1035, 970, 915, 880, 820, 730 cm^{-1}. HRMS (CI, NH_4Cl): $C_{12}H_{19}SO$ (M + H^+), calculated: 211.11566, found: 211.11560 (Δ = −0.3 ppm). Elemental analysis: calculated (%) for $C_{12}H_{18}SO$ (210.3 g/mol): C 68.52, H 8.63, S 15.24; found: C 68.53, H 8.74, S 15.26. The *ee* was determined by chiral HPLC (Chiralpak AD-H, *n*-heptane/*i*-PrOH 90:10, 1 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(1)$ = 8.02 min, $t_r(2)$ = 9.05 min. $[\alpha]^{20}_{365} = -1273.5$, $[\alpha]^{20}_{436} = -634.2$, $[\alpha]^{20}_{546} = -391.3$, $[\alpha]^{20}_{578} = -273.6$, $[\alpha]^{20}_{589} = -253.9$ (c = 1.74 in EtOH; the respective sample had 96% *ee*).

*Hexyl (2,4-Dimethylphenyl) Sulfoxide (**24**): (−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (38.0 mg, 0.147 mmol) with $Hexyl_2Mg$ (1.4 M in Et_2O, 0.13 mL, 0.18 mmol, 1.2 equiv) within 15 min. Flash chromatography on silica gel[40] (c-C_6H_{12}:EtOAc 85:15, F. 27−36) delivered *rac*-**24** (17.0 mg, 48%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (50.0 mg, 0.193 mmol). After 30 min, this delivered (−)-**24** (39.1 mg, 85%; 93% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$, sample contained 10% of the starting material): δ = 0.86−0.89 (m, 3 H, 6′-H_3), 1.26−1.51 (m, 6 H, 3′-, 4′-, and 5′-H_2), 1.61−1.84 (m, 2 H, 2′-H_2), 2.34 (s, Ar-CH_3), 2.36 (s, Ar-CH_3), AB signal (δ_A =2.70, δ_B = 2.75, $J_{A,B}$ = 13.1 Hz, A part additionally split by dd, $J_{1'\text{-A},2'\text{-A}}$ = 7.2 Hz, $J_{1'\text{-A},2'\text{-B}}$ = 5.5 Hz, 1′-H_A; B part additionally split by dd, $J_{1'\text{-B},2\text{-A}}$ = 9.3 Hz, $J_{1'\text{-B},2'\text{-B}}$ = 6.7 Hz, 1′-H_B), 7.01 (m_c, 1 H, 3-H), 7.22 (m_c, 1 H, 5-H), 7.77 ppm (d, $J_{6,5}$ = 7.9 Hz, 1 H, 6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.0 (C-1′), 18.2 (Ar-CH_3), 21.3 (Ar-CH_3), 22.49, 22.55, 28.5, 31.5, 55.9 (C-1′), 124.1 (C-6), 128.0 (C-5), 131.5 (C-3), 134.4, 139.5, 140.7 ppm (C-1, C-2, and C-4). IR ($CDCl_3$): $\tilde{\nu}$ = 3470, 2955, 2930, 2860, 1605, 1570, 1480, 1465, 1455, 1400, 1380, 1275, 1230, 1160, 1060, 1035, 920, 820, 725 cm^{-1}. HRMS (CI, NH_4Cl): $C_{14}H_{23}SO$ (M + H^+), calculated: 239.14696, found: 239.14660 (Δ = −1.5 ppm). The *ee* was determined by chiral HPLC (Chiralcel OD-H, *n*-heptane/*i*-PrOH 90:10, 1 mL/min, $\lambda_{detector}$ = 209 nm): $t_r(1)$ = 7.35 min, $t_r(2)$ = 9.76 min. $[\alpha]^{20}_{365} = -1098.5$, $[\alpha]^{20}_{436} = -550.5$, $[\alpha]^{20}_{546} = -282.0$, $[\alpha]^{20}_{578} = -224.0$, $[\alpha]^{20}_{589} = -225.5$ (c = 0.20 in EtOH; the respective sample had 93% *ee*).

*(2,4-Dimethylphenyl) (2-Phenylethyl) Sulfoxide (**25**): (−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (91.8 mg, 0.355 mmol) with 2-$Phenylethyl_2Mg$ (0.98 M in Et_2O, 0.40 mL, 0.39 mmol, 1.1 equiv) within 30 min. Flash chromatography on silica gel[40] (c-C_6H_{12}:EtOAc 80:20, F. 21−36) delivered *rac*-**25** (31.6 mg, 34%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (600 mg, 2.32 mmol).[48] After 3 h, this delivered (−)-**25** (581 mg, 97%; 85% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, Ar-CH_3), 2.36 (s, 3 H, Ar-CH_3), 2.90−3.15 (m, 4 H, 1′- and 2′-H_2), 7.01 (m_c, 1 H, 1 × Ar-H), 7.17−7.25 (m, 4 H, 4 × Ar-H), 7.26−7.30 (m, 2 H, 2 × Ar-H), 7.80 ppm (d, $^3J_{6,5}$ = 8.0 Hz, 1 H, 6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.1 (Ar-CH_3), 21.3 (Ar-CH_3), 28.6 (C-2′), 56.6 (C-1′), 124.2 (C-6), 126.7, 128.0, 128.6, 128.8, 131.6, 134.3, 138.9, 139.1, 141.2 ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3455, 3060, 3030, 2965, 2920, 2865, 2095, 1640, 1605, 1495, 1480, 1455, 1400, 1380, 1325, 1275, 1232, 1155, 1060, 1030, 965, 920, 875, 820, 750, 700 cm^{-1}. HRMS (CI, NH_4Cl): $C_{16}H_{19}SO$ (M + H^+),

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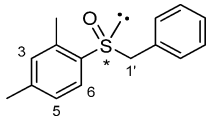
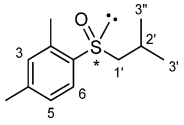
calculated: 259.11566, found: 259.11580 (Δ = +0.5 ppm). Elemental analysis: calculated (%) for $C_{16}H_{18}SO$ (258.4 g/mol): C 74.38, H 7.02, S 12.41; found: C 74.05, H 6.94, S 12.02. The *ee* was determined by chiral HPLC (Chiralpak AD-3, *n*-heptane/*i*-PrOH 95:5, 1 mL/min, $\lambda_{detector}$ = 206 nm): $t_r(1)$ = 8.17 min, $t_r(2)$ = 15.73 min. $[\alpha]^{20}_{365} = -885.7$, $[\alpha]^{20}_{436} = -432.8$, $[\alpha]^{20}_{546} = -216.2$, $[\alpha]^{20}_{578} = -185.6$, $[\alpha]^{20}_{589} = -175.0$ (c = 0.90 in EtOH; the respective sample had 85% *ee*).

*Benzyl (2,4-Dimethylphenyl) Sulfoxide (**26**): (−)-Enantiomer and Racemic.*[45]



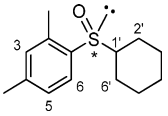
The **racemic synthesis**[44] did not follow the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides*: At 0 °C, *n*-BuLi (2.1 M in hexane, 0.56 mL, 1.2 mmol, 6.1 equiv) was added to a solution of *rac*-BINOL (167 mg, 0.583 mmol, 3.0 equiv) in THF (1 mL). After 10 min, Bn_2Mg (0.40 M in Et_2O, 1.18 mL, 0.473 mmol, 2.4 equiv) was added. After another 10 min, a solution of bis(2,4-dimethylphenyl) sulfoxide (50.9 mg, 0.197 mmol) in THF (0.75 mL) was added. After stirring for 9 h at room temperature, the reaction was quenched and the resulting mixture was worked up. Flash chromatography on silica gel[40] (c-C_6H_{12}:EtOAc 80:20, F. 30−42) delivered *rac*-**26** (38.0 mg, 79%) as a colorless solid (mp. = 65−66 °C). The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis (2,4-dimethylphenyl) sulfoxide (101 mg, 0.391 mmol), (S)-BINOL (3.0 equiv), and Bn_2Mg (2.4 equiv). After 72 h, this delivered (−)-**26** (58.3 mg, 61%; 2% *ee*) as a colorless solid (mp. = 65−66 °C). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 2.01 (s, 3 H, Ar-CH_3), 2.35 (s, 3 H, Ar-CH_3), AB signal (δ_A = 3.98, δ_B = 4.09, $J_{A,B}$ = 12.4 Hz, 2 H, 1′-H), 6.91 (d, $J_{3,5}$ = 0.6 Hz, 1 H, 3-H), 6.98−7.01 (m, 2 H, 2 × Ar-H), 7.15 (dd, $J_{5,6}$ = 6.3 Hz, $J_{5,3}$ = 0.6 Hz, 1 H, 5-H), 7.21−7.30 (m, 3 H, 3 × Ar-H superimposed by the singlet of $CHCl_3$), 7.61 ppm (d, $J_{6,5}$ = 7.0 Hz, 1 H, 6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.0 (Ar-CH_3), 21.4 (Ar-CH_3), 62.7 (C-1′), 124.4 (C-6), 128.0 (C-5), 128.3, 128.5, 129.6, 130.5, 131.0 (C-3), 135.6, 138.4, 141.3 ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3895, 3545, 3255, 3030,2920, 2860, 2610, 2260, 1650, 1795, 1775, 1675, 1625, 1600, 1600, 1565, 1550, 1515, 1490, 1450, 1400, 1380, 1340, 1235, 1155, 1060, 1035, 925, 820, 765, 700 cm^{-1}. HRMS (CI, NH_4Cl): $C_{15}H_{17}SO$ ($M + H^+$), calculated: 245.10000, found: 245.10001 (Δ = ± 0.0 ppm). Elemental analysis: calculated (%) for $C_{15}H_{16}SO$ (244.4 g/mol): C 73.73, H 6.60, S 13.12; found: C 73.52, H 6.64, S 12.82. The *ee* was determined by chiral HPLC (Chiralcel OD-H, *n*-heptane/*i*-PrOH 90:10, 1 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(1)$ = 14.85 min, $t_r(2)$ = 20.81 min. $[\alpha]^{20}_{365} = -18.8$, $[\alpha]^{20}_{436} = -9.0$, $[\alpha]^{20}_{546} = -5.6$, $[\alpha]^{20}_{578} = -6.5$, $[\alpha]^{20}_{589} = -6.3$ (c = 0.53 in EtOH; the respective sample had 2% *ee*).

*(2,4-Dimethylphenyl) Isobutyl Sulfoxide (**27**): (−)-Enantiomer and Racemic.*[45]



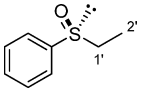
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (100 mg, 0.387 mmol) with *i*-Bu_2Mg (0.80 M in Et_2O, 0.59 mL, 0.47 mmol, 1.2 equiv) within 5 h at 0 °C. Flash chromatography on silica gel[40] (c-C_6H_{12}:EtOAc 75:25, F. 12−20) delivered *rac*-**27** (54.2 mg, 67%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (601 mg, 2.33 mmol) and delivered after 3.5 h (−)-**27** (470 mg, 96%; 97% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.05 (d, $J_{3',2'}$ = 6.8 Hz, 3 H, 3′-H_3), 1.17 (d, $J_{3'',2'}$ = 6.5 Hz, 3 H, 3″-H_3), 2.25−2.35 (m, 1 H, 2′-H superimposed by the singlet of Ar-CH_3 at 2.33 ppm), 2.33 (s, 3 H, Ar-CH_3), 2.36 (s, 3 H, Ar-CH_3), AB signal (δ_A = 2.67, δ_B = 2.46, $J_{A,B}$ = 13.1 Hz, A part additionally split by d, $J_{1'-A,2'}$ = 9.7 Hz, 1′-H_A; B part additionally split by dd, $J_{1'-B,2'-A}$ = 4.3 Hz, $J_{1'-B,2'-B}$ = 0.4 Hz, 1′-H_B), 7.01 (m_c, 1 H, 3-H), 7.23 (m_c,[49] $J_{5,6}$ = 7.9 Hz, 1 H, 5-H), 7.79 ppm (d, $J_{6',5'}$ = 8.0 Hz, 1 H, 6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.1 (Ar-CH_3), 21.3 (Ar-CH_3) 23.0 (C-3′), 24.4 (C-3″), 66.3(C-1′), 123.8 (C-6), 128.2 (C-5), 131.5 (C-3), 134.1, 140.0, 140.9 ppm (C-1, C-2, and C-4). IR ($CDCl_3$): $\tilde{\nu}$ = 2910, 2510, 2960, 2925, 2870, 2735, 2195, 1775, 1605, 1460, 1380, 1330, 1230, 1170, 1075, 1030, 820, 695 cm^{-1}. HRMS (CI, NH_4Cl): $C_{12}H_{19}SO$ ($M + H^+$), calculated: 211.11566, found: 211.11570 (Δ = +0.2 ppm). The *ee* was determined by chiral HPLC (Chiralpak AD-H, *n*-heptane/*i*-PrOH 90:10, 1 mL/min, $\lambda_{detector}$ = 209 nm): $t_r(1)$ = 6.95 min, $t_r(2)$ = 8.96 min. $[\alpha]^{20}_{365} = -1425.9$, $[\alpha]^{20}_{436} = -720.6$, $[\alpha]^{20}_{546} = -366.2$, $[\alpha]^{20}_{578} = -314.5$, $[\alpha]^{20}_{589} = -299.1$ (c = 1.90 in EtOH; the respective sample had 97% *ee*).

*Cyclohexyl (2,4-Dimethylphenyl) Sulfoxide (**28**): (−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (100 mg, 0.387 mmol) with (c-C_6H_{11})$_2$Mg (0.38 M in Et_2O, 1.24 mL, 0.472 mmol, 1.2 equiv) within 6 h at 0 °C. Flash chromatography on silica gel[40] (c-C_6H_{12}:EtOAc 70:30, F. 12−21) delivered *rac*-**28** (86.3 mg, 94%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2,4-dimethylphenyl) sulfoxide (100 mg, 0.387 mmol). After 3.5 h, this delivered (−)-**28** (84.9 mg, 93%; 92% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.16−1.31 (m, 3 H), 1.43−1.57 (m, 2 H), 1.61−1.67 (m, 1 H), 1.76−1.88 (m, 4 H), 2.35 (s, 3 H, Ar-CH_3), 2.36 (s, 3 H, Ar-CH_3), 2.57 (dddd, $J_{1',2'-ax} = J_{1',6'-ax}$ = 11.7 Hz, $J_{1',2'-eq} = J_{1',6'-eq}$ = 3.4 Hz, 1 H, 1′-H), 7.01 (m_c, 1 H, 3-H), 7.20 (m_c,[49] $J_{5,6}$ = 8.1 Hz, 1 H, 5-H), 7.70 ppm (d, $J_{6,5}$ = 8.1 Hz, 1 H, 6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.7 (Ar-CH_3), 21.4 (Ar-CH_3), 24.0, 25.47, 25.57, 25.9, 26.8, 62.1 (C-1), 125.3 (C-6), 127.8 (C-5), 131.4 (C-3), 135.7, 137.7, 141.0 ppm (C-1, C-2, and C-4). IR ($CDCl_3$): $\tilde{\nu}$ = 3935, 3760, 3525, 3280, 3030, 3005, 2930, 2855, 2735, 2655, 2615, 2360, 2295, 2240, 2055, 1920, 1720, 1635, 1605, 1475, 1450, 1380, 1340, 1270, 1230, 1180, 1155, 1120, 1060, 1035, 920, 890, 820, 745, 710 cm^{-1}. HRMS (CI, NH_4Cl): $C_{14}H_{21}SO$ ($M + H^+$), calculated: 237.13131, found: 237.13150 (Δ = +0.8 ppm). The *ee* was determined by chiral HPLC (Chiralcel OD-H, *n*-heptane/*i*-PrOH 96:4, 1 mL/min, $\lambda_{detector}$ = 254 nm): $t_r(1)$ = 6.84 min, $t_r(2)$ = 9.98 min. $[\alpha]^{20}_{365} = -1168.7$, $[\alpha]^{20}_{436} = -564.0$, $[\alpha]^{20}_{546} = -275.7$, $[\alpha]^{20}_{578} = -237.9$, $[\alpha]^{20}_{589} = -226.2$ (c = 1.10 in EtOH; the respective sample had 92% *ee*).

*Ethyl Phenyl Sulfoxide (**29**): (S)-(−)-Enantiomer*[33] *and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using diphenyl sulfoxide (39.8 mg, 0.197 mmol) with Et_2Mg (0.33 M in Et_2O, 0.33 mL, 0.11 mmol, 0.55 equiv) within 30 min. Flash chromatography on silica gel[40] (c-C_6H_{12}:EtOAc 55:45, F. 32−46) delivered *rac*-**29** (25.1 mg, 83%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using diphenyl sulfoxide (39.8 mg, 0.197 mmol). After 2 min, this delivered (*S*)-(−)-**29** (23.3 mg, 77%; 71% *ee*) as a colorless oil. After 30 min, (*S*)-(−)-**29** was obtained in a lower yield with a lower *ee* (34%; 31% *ee*). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 1.20 (dd, $J_{2',1'-A} = J_{2',1'-B}$ = 7.5 Hz, 3 H, 2′-H_3), AB signal (δ_A = 2.76, δ_B = 2.90, $J_{A,B}$ = 13.4 Hz, A part additionally split by q, $J_{1'-A,2'}$ = 7.5 Hz, 1′-H_A; B part additionally split by q, $J_{1'-B,2'}$ = 7.4 Hz, 1′-H_B), 7.46−7.55 (m, 3 H, 3 × Ar-H), 7.59−7.64 ppm (m, 2 H, 2 × Ar-H). The preceding data are consistent with those reported in the literature.[50] The *ee* was determined by chiral HPLC (Chiralcel OJ-H, *n*-heptane/EtOH 95:5, 1 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(R)$ = 11.86 min,

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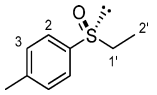
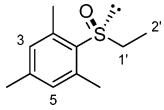
$t_r(S)$ = 12.76 min. $[\alpha]^{20}_{365}$ = −354.0, $[\alpha]^{20}_{436}$ = −179.5, $[\alpha]^{20}_{546}$ = −92.5, $[\alpha]^{20}_{578}$ = −78.0, $[\alpha]^{20}_{589}$ = −73.5 (*c* = 0.20 in EtOH; the respective sample had 31% *ee*); Lit.:[51] $[\alpha]^{20}_{589}$ = −219.6 [*c* = 1.4 in EtOH, a sample of the (*S*)-enantiomer with 99% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[51]

*Ethyl (p-Tolyl) Sulfoxide (**30**): (S)-(−)-Enantiomer[33] and Racemic.[45]*



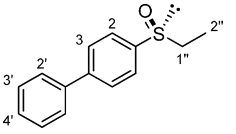
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(*p*-tolyl) sulfoxide (45.4 mg, 0.197 mmol) with Et_2Mg (0.16 M in Et_2O, 1.35 mL, 0.216 mmol, 1.1 equiv) within 1.25 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 50:50, F. 27−40) delivered *rac*-**30** (7.0 mg, 21%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(*p*-tolyl) sulfoxide (45.3 mg, 0.197 mmol). After 10 s, this delivered (*S*)-(−)-**30** (29.8 mg, 90%; 69% *ee*) as a colorless oil. After 30 min, (*S*)-(−)-**30** was obtained in a lower yield with a higher *ee* (39%; 94% *ee*). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 1.19 (dd, $J_{2',1'\text{-A}} = J_{2',1'\text{-B}}$ = 7.4 Hz, 3 H, 2′-H_3), AB signal (δ_A = 2.75, δ_B = 2.87, $J_{A,B}$ = 14.8 Hz, A part additionally split by q, $J_{1'\text{-A},2'}$ = 7.3 Hz, 1′-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 7.4 Hz, 1′-H_B), AA′BB′ signal with signal centers at δ_A = 7.32 and δ_B = 7.50 ppm (4 H, 2 × 2-H and 2 × 3-H). The preceding data are consistent with those reported in the literature.[50] The *ee* was determined by chiral HPLC (Chiralcel OJ-H, *n*-heptane/EtOH 98:2, 1 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(R)$ = 17.63 min, $t_r(S)$ = 20.92 min. $[\alpha]^{20}_{365}$ = −723.5, $[\alpha]^{20}_{436}$ = −361.6, $[\alpha]^{20}_{546}$ = −183.6, $[\alpha]^{20}_{578}$ = −157.3, $[\alpha]^{20}_{589}$ = −148.5 (*c* = 0.55 in EtOH; the respective sample had 69% *ee* was used); Lit.:[50] $[\alpha]^{20}_{589}$ = −247 [*c* = 2.60 in $CHCl_3$; the respective sample had 94% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[50]

*Ethyl (2,4,5-Trimethylphenyl) Sulfoxide (**31**): (S)-(−)-Enantiomer and Racemic.[45]*



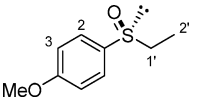
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2,4,6-trimethylphenyl) sulfoxide (56.5 mg, 0.197 mmol) with Et_2Mg (0.42 M in Et_2O, 0.52 mL, 0.22 mmol, 1.1 equiv) within 2 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 60:40, F. 24−30) delivered *rac*-**31** (16.2 mg, 42%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2,4,6-trimethylphenyl) sulfoxide (56.4 mg, 0.197 mmol). After 1 h, this delivered (*S*)-(−)-**31** (23.2 mg, 60%; 77% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$, the sample contained a small amount of inseparable impurity with signals at 1.23, 2.26, 2.68−2.75, 2.80−2.87, 6.97, and 7.60 ppm): δ = 1.28 (dd, $J_{2',1'\text{-A}} = J_{2',1\text{-B}}$ = 7.5 Hz, 3 H, 2′-H_3), 2.28 (s, 3 H, Ar-CH_3), 2.54 (s, 6 H, 2 × Ar-CH_3), AB signal (δ_A = 2.95, δ_B = 3.21, $J_{A,B}$ = 12.9 Hz, A part additionally split by q, $J_{1'\text{-A},2'}$ = 7.6 Hz, 1′-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 7.5 Hz, 1′-H_B), 6.86 ppm (s, 2 H, 2 × Ar-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 8.6 (C-1′), 19.5 (2 × Ar-CH_3), 21.2 (Ar-CH_3), 46.2 (C-2′), 131.0 (C-3 and C-5), 134.5, 138.6, 141.1 ppm (C-1, C-2, C-4, and C-6). IR ($CDCl_3$): $\tilde{\nu}$ = 3290, 2970, 2925, 2855, 2450, 2045, 1600, 1570, 1455, 1380, 1295, 1250, 1070, 1045, 1015, 965, 850, 775, 715, 665 cm^{-1}. HRMS (CI, NH_4Cl): $C_{11}H_{17}SO$ ($M + H^+$), calculated: 197.10001, found: 197.10020 (Δ = +1.0 ppm). The *ee* was determined by chiral HPLC (Chiralcel OD-3, *n*-heptane/*i*-PrOH 98:2, 1.0 mL/min, $\lambda_{detector}$ = 205 nm): $t_r(R)$ = 11.91 min, $t_r(S)$ = 20.69 min. $[\alpha]^{20}_{365}$ = −1256.8, $[\alpha]^{20}_{436}$ = −552.7, $[\alpha]^{20}_{546}$ = −255.5, $[\alpha]^{20}_{578}$ = −219.5, $[\alpha]^{20}_{589}$ = −210.0 (*c* = 0.22 in EtOH; the respective sample had 77% *ee*). The absolute configuration was assigned by chemical correlation (cf. Supporting Information).

*Ethyl (4-Phenylphenyl) Sulfoxide (**32**): (S)-(−)-Enantiomer[33] and Racemic.[45]*



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(4-phenylphenyl) sulfoxide (74.1 mg, 0.209 mmol) with Et_2Mg (0.33 M in Et_2O, 0.35 mL, 0.116 mmol, 0.55 equiv) within 30 min. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 52:48, F. 26−42) delivered *rac*-**32** (37.3 mg, 77%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(4-phenylphenyl) sulfoxide (69.8 mg, 0.197 mmol). After 10 s, this delivered (*S*)-(−)-**32** (37.4 mg, 82%; 70% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.24 (dd, $J_{2'',1''\text{-A}} = J_{2'',1''\text{-B}}$ = 7.5 Hz, 3 H, 2″-H_3), AB signal (δ_A = 2.82, δ_B = 2.94, $J_{A,B}$ = 13.3 Hz, A part additionally split by q, $J_{1''\text{-A},2''}$ = 7.3 Hz, 1″-H_A; B part additionally split by q, $J_{1''\text{-B},2''}$ = 7.5 Hz, 1″-H_B), 7.37−7.42 (m, 1 H, 4′-H), 7.45−7.49 (m, 2 H, 2 × 2′-H*), 7.59−7.62 (m, 2 H, 2 × 3′-H*), AA′BB′ signal with signal centers at δ_A = 7.67 and δ_B = 7.74 ppm (4 H, 2 × 2-H and 2 × 3-H); *assignments interchangeable. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 6.2 (C-2″), 50.5 (C-1″), 124.8 (C-2), 127.3 (C-2′*), 127.9 (C-3), 128.2 (C-4′), 129.1 (C-3′*), 139.9, 142.2, 144.1 ppm (C-1, C-4, and C-1′); *assignments interchangeable. IR ($CDCl_3$): $\tilde{\nu}$ = 3520, 3055, 3030, 3000, 2920, 2850, 2455, 2065, 1660, 1595, 1560, 1480, 1390, 1265, 1110, 1090, 1045, 1025, 965, 915, 935, 835, 760, 720, 695, 655 cm^{-1}. HRMS (CI, NH_4Cl): $C_{14}H_{15}SO$ ($M + H^+$), calculated: 231.08436, found: 231.08460 (Δ = +1.0 ppm). Elemental analysis: calculated (%) for $C_{14}H_{14}SO$ (230.3 g/mol): C 73.01, H 6.13, S 13.92; found: C 72.74, H 6.08, S 13.73. The *ee* was determined by chiral HPLC (Chiralcel OJ-H, *n*-heptane/EtOH 95:5, 1.0 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(R)$ = 27.54 min, $t_r(S)$ = 29.81 min. $[\alpha]^{20}_{365}$ = −834.0, $[\alpha]^{20}_{436}$ = −374.6, $[\alpha]^{20}_{546}$ = −178.7, $[\alpha]^{20}_{578}$ = −153.0, $[\alpha]^{20}_{589}$ = −145.4 (*c* = 1.4 in EtOH; the respective sample had 70% *ee*). The absolute configuration was assigned by chemical correlation (cf. Supporting Information).

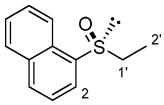
*Ethyl (4-Methoxyphenyl) Sulfoxide (**33**): (S)-(−)-Enantiomer and Racemic.[45]*



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(4-methoxyphenyl) sulfoxide (51.8 mg, 0.197 mmol) with Et_2Mg (0.16 M in Et_2O, 1.35 mL, 0.216 mmol, 1.1 equiv) within 1.25 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 40:60, F. 21−36) delivered *rac*-**33** (11.5 mg, 32%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(4-methoxyphenyl) sulfoxide (51.7 mg, 0.196 mmol). After 15 min, this delivered (*S*)-(−)-**33** (28.0 mg, 77%; 81% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 1.18 (dd, $J_{2',1'\text{-A}} = J_{2',1'\text{-B}}$ = 7.5 Hz, 3 H, 2′-H_3), AB signal (δ_A = 2.84, δ_B = 2.77, $J_{A,B}$ = 13.1 Hz, A part additionally split q, $J_{1'\text{-A},2'}$ = 7.4 Hz, 1′-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 7.5 Hz, 1′-H_B), 3.86 (s, 3 H, O-CH_3), AA′BB′ signal with signal centers at δ_A = 7.03 and δ_B = 7.55 ppm (4 H, 2 × 2-H and 2 × 3-H). The preceding data are consistent with those reported in the literature.[52] The *ee* was determined by chiral HPLC (Chiralcel OD-3, *n*-heptane/*i*-PrOH 98:2, 1.0 mL/min, $\lambda_{detector}$ = 230 nm): $t_r(R)$ = 20.03 min, $t_r(S)$ = 22.32 min. $[\alpha]^{20}_{365}$ = −819.1, $[\alpha]^{20}_{436}$ = −396.6, $[\alpha]^{20}_{546}$ = −196.0, $[\alpha]^{20}_{578}$ = −167.6, $[\alpha]^{20}_{589}$ = −161.8 (*c* = 0.82 in EtOH; the respective sample had 81% *ee*); Lit.:[52] $[\alpha]^{20}_{589}$ = +130.0 [*c* = 1.4 in MeOH for a sample of the (*R*)-enantiomer. The *ee* of this sample is not stated in ref 52]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[52]

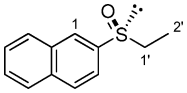
dx.doi.org/10.1021/jo502417j | J. Org. Chem. 2015, 80, 897−910

*Ethyl (1-Naphthyl) Sulfoxide (**34**): (S)-(−)-Enantiomer and Racemic.*[45]



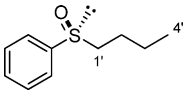
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using di(1-naphthyl) sulfoxide (59.8 mg, 0.198 mmol) with Et_2Mg (0.33 M in Et_2O, 0.33 mL, 0.109 mmol, 0.55 equiv) within 1.5 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 55:45, F. 14−24) delivered *rac*-**34** (17.0 mg, 42%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using di(1-naphthyl) sulfoxide (59.6 mg, 0.197 mmol). After 5 min, this delivered (*S*)-(−)-**34** (27.0 mg, 67%; 93% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.22 (dd, $J_{2',1'\text{-A}} = J_{2',1'\text{-B}}$ = 7.3 Hz, 3 H, 2′-H_3), AB signal (δ_A = 2.85, δ_B = 3.12, $J_{A,B}$ = 13.6 Hz, A part additionally split q, $J_{1'\text{-A},2'}$ = 7.5 Hz, 1′-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 7.6 Hz, 1′-H_B), 7.55−7.61 (m, 2 H, 2 × Ar-H), 7.67 (dd, ^3J = 8.2 Hz, ^3J = 7.0 Hz, 1 H, 1 × Ar-H), 7.93−7.99 (m, 3 H, 3 × Ar-H), 8.11 ppm (dd, ^3J = 7.2 Hz, ^4J = 1.2 Hz, 1 H, 1 × Ar-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 6.2 (C-2′), 48.8 (C-1′), 121.7, 123.6, 125.6, 126.7, 127.3, 129.1, 129.2, 131.2, 133.6, 139.1 ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3470, 3055, 2955, 2925, 2870, 2850, 2425, 2045, 1645, 1590, 1505, 1455, 1405, 1370, 1345, 1260, 1190, 1140, 1065, 1055, 1045, 1020, 965, 920, 865, 805, 775, 740, 665 cm^{-1}. HRMS (CI, NH_4Cl): $C_{12}H_{13}SO$ ($M + H^+$), calculated: 205.06871, found: 205.06860 (Δ = −0.5 ppm). The *ee* was determined by chiral HPLC (Chiralcel OJ-H, *n*-heptane/*i*-PrOH 80:20, 0.8 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(R)$ = 9.17 min, $t_r(S)$ = 10.45 min. $[\alpha]^{20}_{365}$ = −1098.4, $[\alpha]^{20}_{436}$ = −512.3, $[\alpha]^{20}_{546}$ = −277.6, $[\alpha]^{20}_{578}$ = −221.8, $[\alpha]^{20}_{589}$ = −248.7 (*c* = 1.40 in EtOH; the respective sample had 93% *ee*). The absolute configuration was assigned by chemical correlation (cf. Supporting Information).

*Ethyl (2-Naphthyl) Sulfoxide (**35**): (S)-(−)-Enantiomer and Racemic.*[45]



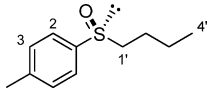
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using di(2-naphthyl) sulfoxide (59.6 mg, 0.197 mmol) with Et_2Mg (0.33 M in Et_2O, 0.33 mL, 0.109 mmol, 0.55 equiv) within 1.5 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 55:45, F. 42−50) delivered *rac*-**35** (30.0 mg, 75%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using di(2-naphthyl) sulfoxide (59.6 mg, 0.197 mmol). After 5 min, this delivered (*S*)-(−)-**35** (25.1 mg, 62%; 66% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 1.22 (dd, $J_{2',1'\text{-A}} = J_{2',1'\text{-B}}$ = 7.4 Hz, 3 H, 2′-H_3), AB signal (δ_A = 2.99, δ_B = 2.84, $J_{A,B}$ = 13.4 Hz, A part additionally split by q, $J_{1'\text{-A},2'}$ = 7.3 Hz, 1′-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 7.4 Hz, 1′-H_B), 7.55−7.62 (m, 3 H, 3 × Ar-H), 7.90−7.99 (m, 3 H, 3 × Ar-H), 8.18x ppm (br. s, 1 H, 1-H). The preceding data are consistent with those reported in the literature.[53] The *ee* was determined by chiral **HPLC** (Chiralcel OJ-H, *n*-heptane/EtOH 95:5, 1 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(R)$ = 17.24 min, $t_r(S)$ = 18.35 min. $[\alpha]^{20}_{365}$ = −501.0, $[\alpha]^{20}_{436}$ = −244.7, $[\alpha]^{20}_{546}$ = −123.9, $[\alpha]^{20}_{578}$ = −106.3, $[\alpha]^{20}_{589}$ = −99.8 (*c* = 0.49 in EtOH; the respective sample had 66% *ee*); Lit.:[51] $[\alpha]^{20}_{589}$ = −180.5 [*c* = 1.3 in acetone; the respective sample of the (*S*)-enantiomer had >99% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[51]

*Butyl Phenyl Sulfoxide (**36**): (S)-(−)-Enantiomer and Racemic.*[45]



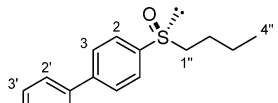
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using diphenyl sulfoxide (39.8 mg, 0.197 mmol) with Bu_2Mg (0.75 M in Et_2O, 0.14 mL, 0.105 mmol, 0.53 equiv) within 30 min. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, 28−40) delivered *rac*-**36** (24.1 mg, 67%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using diphenyl sulfoxide (39.7 mg, 0.196 mmol). After 2 min, this delivered (*S*)-(−)-**36** (27.0 mg, 75%; 46% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 0.92 (t, $J_{4',3'}$ = 7.2 Hz, 3 H, 4′-H_3), 1.35−1.82 (m, 4 H, 2′- and 3′-H_2), AB signal (δ_A = 2.79, δ_B = 2.80, $J_{A,B}$ = 7.1 Hz, 2 H, 1′-H_A and 1′-H_B), 7.48−7.55 (m, 3 H, 3 × Ar-H), 7.60−7.64 ppm (m, 2 H, 2 × Ar-H). The preceding data are consistent with those reported in the literature.[53] The *ee* was determined by chiral HPLC (Chiralcel OJ-H, *n*-heptane/EtOH 98:2, 1 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(R)$ = 11.72 min, $t_r(S)$ = 12.45 min. $[\alpha]^{20}_{365}$ = −498.7, $[\alpha]^{20}_{436}$ = −254.5, $[\alpha]^{20}_{546}$ = −131.6, $[\alpha]^{20}_{578}$ = −113.9, $[\alpha]^{20}_{589}$ = −107.2 (*c* = 0.86 in EtOH; the respective sample had 46% *ee*); Lit.:[53] $[\alpha]^{20}_{589}$ = +150 [*c* = 0.1 in CH_2Cl_2, a sample of the (*R*)-enantiomer with 75% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[53]

*Butyl (p-Tolyl) Sulfoxide (**37**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(*p*-tolyl) sulfoxide (45.6 mg, 0.198 mmol) with Bu_2Mg (0.75 M in Et_2O, 0.14 mL, 0.105 mmol, 0.53 equiv) within 30 min. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 60:40, F. 12−18) delivered *rac*-**37** (23.8 mg, 62%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(*p*-tolyl) sulfoxide (45.5 mg, 0.198 mmol). After 10 s, this delivered (*S*)-(−)-**37** (31.8 mg, 82%; 48% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 0.92 (t, $J_{4',3'}$ = 7.2 Hz, 3 H, 4′-H_3), 1.34−1.51 (m, 2 H, 3′-H_2), 1.52−1.74 (m, 2 H, 2′-H_2), 2.42 (s, 3 H, Ar-CH_3), 2.70−2.86 (m, 2 H, 1′-H_2), AA′BB′ signal with signal centers at δ_A = 7.32 and δ_B = 7.51 ppm (2 × 2-H and 2 × 3-H). The preceding data are consistent with those reported in the literature.[54] The *ee* was determined by chiral HPLC (Chiralcel OD-3, *n*-heptane/*i*-PrOH 98:2, 1 mL/min, $\lambda_{detector}$ = 205 nm): $t_r(R)$ = 12.21 min, $t_r(S)$ = 15.35 min. $[\alpha]^{20}_{365}$ = −507.6, $[\alpha]^{20}_{436}$ = −257.8, $[\alpha]^{20}_{546}$ = −131.6, $[\alpha]^{20}_{578}$ = −113.5, $[\alpha]^{20}_{589}$ = −108.1 (*c* = 0.37 in EtOH; the respective sample had 48% *ee*); Lit.:[55] $[\alpha]^{20}_{589}$ = −162.3 (*c* = 3.2 in acetone, a sample of the (*S*)-enantiomer with 91% *ee*). The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[55]

*Butyl (4-Phenylphenyl) Sulfoxide (**39**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(4-phenylphenyl) sulfoxide (69.9 mg, 0.197 mmol) with Bu_2Mg (0.75 M in Et_2O, 0.14 mL, 0.11 mmol, 0.55 equiv) within 30 min. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 27−44) delivered *rac*-**39** (27.3 mg, 54%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(4-phenylphenyl) sulfoxide (83.1 mg, 0.234 mmol). After 10 s, this delivered (*S*)-(−)-**39** (43.5 mg, 72%; 52% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.94 (t, $J_{4'',3''}$ = 7.3 Hz, 3 H, 4″-H_3), 1.37−1.56 (m, 2 H, 3″-H_2), 1.58−1.72 (m, 1 H, 2″-H_A), 1.73−1.80 (m, 1 H, 2″-H_B), 2.78−2.89 (m, 2 H, 1″-H_2), 7.37−7.42 (m, 1 H, 4′-H), 7.45−7.49 (m, 2 H, 2 × 2′-H*), 7.59−7.62 (m, 2 H, 2 × 3′-H*), AA′BB′ signal with signal centers at δ_A = 7.68 and δ_B = 7.74 ppm (4 H, 2 × 2-H and 2 × 3-H); *assignments interchangeable. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.8 (C-4″), 22.0 (C-3″), 24.3 (C-2″), 57.2 (C-1″), 124.7 (C-2), 127.3 (C-2′*), 128.0 (C-3), 128.2 (C-4′), 129.1 (C-3′*), 139.9, 142.9,

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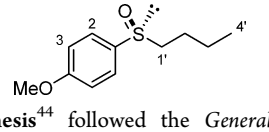
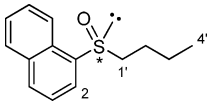
144.1 ppm (C-1, C-4, and C-1′); *assignments interchangeable. IR ($CDCl_3$): $\tilde{\nu}$ = 3650, 3240, 3055, 2955, 2930, 2870, 2395, 1950, 1560, 1480, 1465, 1450, 1395, 1165, 1095, 1075, 1030, 1015, 105, 915, 835, 750, 715, 690, 655 cm^{-1}. HRMS (CI, NH_4Cl): $C_{16}H_{19}SO$ ($M + H^+$), calculated: 259.11566, found: 259.11590 (Δ = +0.9 ppm). Elemental analysis: calculated (%) for $C_{16}H_{18}SO$ (258.4 g/mol): C 73.38, H 7.02, S 12.41; found: C 74.23, H 6.93, S 12.49. The *ee* was determined by chiral HPLC (Chiralcel OD-3, *n*-heptane/*i*-PrOH 96:4, 1.0 mL/min, $\lambda_{detector}$ = 206 nm): $t_r(R)$ = 12.47 min, $t_r(S)$ = 13.65 min. $[\alpha]^{20}_{365} = -561.3$, $[\alpha]^{20}_{436} = -255.5$, $[\alpha]^{20}_{546} = -124.7$, $[\alpha]^{20}_{578} = -106.6$, $[\alpha]^{20}_{589} = -100.9$ (*c* = 0.47 in EtOH; the respective sample had 52% *ee*). The absolute configuration was assigned by chemical correlation (cf. Supporting Information).

*Butyl (4-Methoxyphenyl) Sulfoxide (**40**): (S)-(−)-Enantiomer and Racemic.*[45]



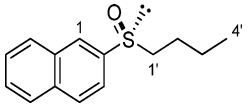
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(4-methoxyphenyl) sulfoxide (51.6 mg, 0.196 mmol) with Bu_2Mg (0.75 M in Et_2O, 0.29 mL, 0.22 mmol, 1.1 equiv) within 1 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 55:45, F. 24−34) delivered *rac*-**40** (15.6 mg, 37%) as a colorless oil. The asymmetric synthesis followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(4-methoxyphenyl) sulfoxide (51.8 mg, 0.197 mmol). After 15 min, this delivered (*S*)-(−)-**40** (34.6 mg, 83%; 63% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 0.92 (t, $J_{4',3'}$ = 7.2 Hz, 3 H, 4′-H_3), 1.34−1.50 (m, 2 H, 3′-H_2), 1.51−1.75 (m, 2 H, 2′-H_2), 2.69−2.86 (m, 1 H, 1′-H_2), 3.86 (s, 3 H, O-CH_3), AA′BB′ signal with signal centers at δ_A = 7.02 and δ_B = 7.56 ppm (4 H, 2 × 2-H and 2 × 3-H). The preceding data are consistent with those reported in the literature.[56] The *ee* was determined by chiral HPLC (Chiralcel OJ-H, *n*-heptane/EtOH 98:2, 1 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(S)$ = 19.94 min, $t_r(R)$ = 21.38 min. $[\alpha]^{20}_{365} = -468.4$, $[\alpha]^{20}_{436} = -238.9$, $[\alpha]^{20}_{546} = -126.6$, $[\alpha]^{20}_{578} = -117.7$, $[\alpha]^{20}_{589} = -114.7$ (*c* = 0.64 in EtOH; the respective sample had 63% *ee*). The absolute configuration was assigned by chemical correlation (cf. Supporting Information).

*Butyl (1-Naphthyl) Sulfoxide (**41**): (−)-Enantiomer and Racemic.*[45]



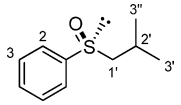
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using di(1-naphthyl) sulfoxide (57.9 mg, 0.192 mmol) with Bu_2Mg (0.75 M in Et_2O, 0.14 mL, 0.11 mmol, 0.57 equiv) within 35 min. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 20−30) delivered *rac*-**41** (25.5 mg, 56%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using di(1-naphthyl) sulfoxide (59.4 mg, 0.197 mmol). After 2 min, this delivered (−)-**41** (41.5 mg, 91%; 90% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.91 (t, $J_{4',3'}$ = 7.3 Hz, 3 H, 4′-H_3), 1.34−1.56 (m, 2 H, 3′-H_2), 1.59−1.69 (m, 1 H, 2′-H_A), 1.81−1.91 (m, 1 H, 2′-H_B), AB signal (δ_A = 2.83, δ_B = 3.03, $J_{A,B}$ = 13.2 Hz, A part additionally split by dd, $J_{1'\text{-}A,2'\text{-}B}$ = 9.5 Hz, $J_{1'\text{-}A,2'\text{-}A}$ = 4.9 Hz, 1′-H_A; B part additionally split by dd, $J_{1'\text{-}B,2'\text{-}B}$ = 10.2 Hz, $J_{1'\text{-}B,2'\text{-}A}$ = 6.8 Hz, 1′-H_B), 7.55−7.61 (m, 2 H, 2 × Ar-H), 7.67 (dd, ^3J = 6.9 Hz, ^3J = 5.9 Hz, 1 H, 1 × Ar-H), 7.94−7.98 (m, 3 H, 3 × Ar-H), 8.13 ppm (dd, ^3J = 7.2 Hz, ^4J = 1.2 Hz, 1 H, 1 × Ar-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.8 (C-4′), 22.0 (C-3′), 24.6 (C-2′), 55.9 (C-1′), 121.6, 123.2, 125.7, 126.7, 127.2, 129.0, 129.2, 131.1, 133.6, 139.9 ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3535, 3055, 2930, 2925, 2870, 2405, 2045, 1645, 1590, 1505, 1465, 1400, 1380, 1345, 1260, 1215, 1190, 1140, 1100, 1070, 1040, 965, 800, 770, 740, 665 cm^{-1}. HRMS (CI, NH_4Cl): $C_{14}H_{17}SO$ ($M + H^+$), calculated: 233.10001, found: 233.10000 (Δ = −0.1 ppm). Elemental analysis: calculated (%) for $C_{14}H_{16}SO$ (232.3 g/mol): C 72.37, H 6.94, S 13.80; found: C 72.00, H 6.90, S 13.83. The *ee* was determined by chiral HPLC (Chiralpak AD-H, *n*-heptane/*i*-PrOH 95:5, 1 mL/min, $\lambda_{detector}$ = 209 nm): $t_r(1)$ = 17.39 min, $t_r(2)$ = 24.68 min. $[\alpha]^{20}_{365} = -2378.2$, $[\alpha]^{20}_{436} = -1147.8$, $[\alpha]^{20}_{546} = -573.0$, $[\alpha]^{20}_{578} = -491.5$, $[\alpha]^{20}_{589} = -466.8$ (*c* = 1.28 in EtOH; the respective sample had 90% *ee*).

*Butyl (2-Naphthyl) Sulfoxide (**42**): (S)-(−)-Enantiomer and Racemic.*[45]



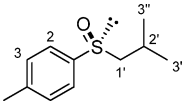
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using di(2-naphthyl) sulfoxide (61.0 mg, 0.202 mmol) with Bu_2Mg (0.75 M in Et_2O, 0.15 mL, 0.11 mmol, 0.55 equiv) within 35 min. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 24−37) delivered *rac*-**42** (20.1 mg, 47%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using di(2-naphthyl) sulfoxide (59.6 mg, 0.197 mmol). After 2 min, this delivered (*S*)-(−)-**42** (37.2 mg, 81%; 30% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 0.92 (t, $J_{4',3'}$ = 7.1 Hz, 3 H, 4′-H_3), 1.36−1.55 (m, 2 H, 3′-H_2), 1.57−1.67 (m, 1 H, 2′-H_A), 1.71−1.86 (m, 1 H, 2′-H_B), 2.85−2.91 (m, 2 H, 1′-H_2), 7.56−7.62 (m, 3 H, 3 × Ar-H), 7.89−7.99 (m, 3 H, 3 × Ar-H), 8.19 ppm (br. s, 1 H, 1-H). The preceding data are consistent with those reported in the literature.[53] The *ee* was determined by chiral HPLC (Chiralcel OD-3, *n*-heptane/*i*-PrOH 98:2, 1 mL/min, $\lambda_{detector}$ = 224 nm): $t_r(R)$ = 13.40 min, $t_r(S)$ = 15.81 min. $[\alpha]^{20}_{365} = -288.0$, $[\alpha]^{20}_{436} = -139.8$, $[\alpha]^{20}_{546} = -71.5$, $[\alpha]^{20}_{578} = -61.3$, $[\alpha]^{20}_{589} = -58.0$ (*c* = 0.61 in EtOH; the respective sample had 30% *ee*); Lit.:[53] $[\alpha]^{20}_{589}$ = +188 [*c* = 0.12 in CH_2Cl_2, a sample of the (*R*)-enantiomer with 67% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[53]

*Isobutyl Phenyl Sulfoxide (**43**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using diphenyl sulfoxide (70.0 mg, 0.346 mmol) with *i*-Bu_2Mg (0.80 M in Et_2O, 0.24 mL, 0.19 mmol, 0.55 equiv) within 1.5 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 27−39) delivered *rac*-**43** (46.6 mg, 74%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using diphenyl sulfoxide (80.5 mg, 0.393 mmol). After 1 h, this delivered (*S*)-(−)-**43** (54.7 mg, 76%; 61% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.06 (d, $J_{3',2'}$ = 6.8 Hz, 3 H, 3′-H_3), 1.16 (d, $J_{3'',2'}$ = 6.5 Hz, 3 H, 3″-CH_3), 2.24 (m_c, 1 H, 2′-H), 2.47 (dd, $J_{1'\text{-}A,1'\text{-}B}$ = 13.0 Hz, $J_{1'\text{-}A,2'}$ = 9.2 Hz, 1 H, 1′-H_A), 2.81 (dd, $J_{1'\text{-}B,1'\text{-}A}$ = 13.0 Hz, $J_{1'\text{-}B,2'}$ = 5.0 Hz, 1 H, 1′-H_B), 7.45−7.54 (m, 3 H, 3 × Ar-H), 7.61−7.65 ppm (m, 2 H, 2 × Ar-H). The preceding data are consistent with those reported in the literature.[57] The *ee* was determined by chiral HPLC (Chiralcel OD-3, *n*-heptane/*i*-PrOH 95:5, 1 mL/min, $\lambda_{detector}$ = 209 nm): $t_r(R)$ = 6.57 min, $t_r(S)$ = 8.23 min. $[\alpha]^{20}_{365} = -721.2$, $[\alpha]^{20}_{436} = -374.3$, $[\alpha]^{20}_{546} = -194.2$, $[\alpha]^{20}_{578} = -167.2$, $[\alpha]^{20}_{589} = -159.8$ (*c* = 1.45 in EtOH; the respective sample had 61% *ee*); Lit.:[57] $[\alpha]^{20}_{589}$ = +129.0 [*c* = 1.0 in $CHCl_3$, a sample of the (*R*)-enantiomer with 48% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[57]

*Isobutyl (p-Tolyl) Sulfoxide (**44**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(*p*-tolyl) sulfoxide (101 mg, 0.439 mmol) with *i*-Bu_2Mg (0.80 M in Et_2O, 0.61 mL, 0.49 mmol, 1.1 equiv) within 1.5 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 37−49) delivered *rac*-**44** (74.3 mg, 86%) as a

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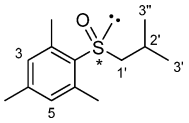
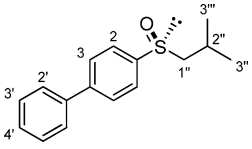
colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(*p*-tolyl) sulfoxide (45.3 mg, 0.197 mmol). After 1 h, this delivered (*S*)-(−)-**44** (32.9 mg, 85%; 58% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 1.05 (d, $J_{3',2'}$ = 5.9 Hz, 3 H, 3′-H_3), 1.14 (d, $J_{3'',2'}$ = 6.3 Hz, 3 H, 3″-H_3), 2.13−2.27 (m, 1 H, 2′-H), 2.41 (s, 3 H, Ar-CH_3 superimposed by AB signal), AB signal (δ_A = 2.44, δ_B = 2.45, $J_{A,B}$ = 8.4 Hz, 2 H, 1′-CH_2), AA′BB′ signal with signal centers at δ_A = 7.31 and δ_B = 7.52 ppm (2 × 2-H and 2 × 3-H). The preceding data are consistent with those reported in the literature.[50] The *ee* was determined by chiral HPLC (Chiralcel OD-3, *n*-heptane/*i*-PrOH 150:1, 1 mL/min, $\lambda_{detector}$ = 249 nm): $t_r(R)$ = 17.66 min, $t_r(S)$ = 20.84 min. $[\alpha]^{20}_{365}$ = −657.2, $[\alpha]^{20}_{436}$ = −334.5, $[\alpha]^{20}_{546}$ = −172.0, $[\alpha]^{20}_{578}$ = −148.3, $[\alpha]^{20}_{589}$ = −139.9 (*c* = 1.27 in EtOH; the respective sample had 58% *ee*); Lit.:[57] $[\alpha]^{20}_{589}$ = −150 [*c* = 0.75 in $CHCl_3$, a sample of the (*S*)-enantiomer with 71% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[50]

*Isobutyl (2,4,6-Trimethylphenyl) Sulfoxide (**45**): (−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] did not follow the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides*: At 0 °C, *n*-BuLi (2.1 M in hexane, 0.56 mL, 1.2 mmol, 3.0 equiv) was added to a solution of *rac*-BINOL (167 mg, 0.584 mmol, 1.5 equiv) in THF (1 mL). After 10 min, *i*-Bu_2Mg (0.80 M in Et_2O, 0.59 mL, 0.47 mmol, 1.2 equiv) was added. After another 10 min, a solution of bis(2,4,6-trimethylphenyl) sulfoxide (113 mg, 0.395 mmol) in THF (1.5 mL) was added. After stirring for 24 h at room temperature, the reaction was quenched and the resulting mixture was worked up. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 18−24) delivered *rac*-**45** (45.9 mg, 52%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2,4,6-trimethylphenyl) sulfoxide (56.4 mg, 0.197 mmol). After 24 h at −68 °C, this delivered (−)-**45** (11.0 mg, 25%; 23% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 1.11 (d, $J_{3',2'}$ = 5.4 Hz, 3 H, 3′-H_3), 1.13 (d, $J_{3'',2'}$ = 5.7 Hz, 3 H, 3″-H_3), 2.17−2.27 (m, 1 H, 2′-H superimposed by singlet of 4-CH_3), 2.27 (s, 3 H, 4-CH_3), 2.50 (dd, $J_{1'-A,1'-B}$ = 13.0 Hz, $J_{1'-A,2'}$ = 8.8 Hz, 1 H, 1′-H_A superimposed by singlet of 2- and 6-CH_3), 2.54 (s, 6 H, 2- and 6-CH_3), 3.27 (dd, $J_{1'-B,1'-A}$ = 13.4 Hz, $J_{1'-B,2'}$ = 5.0 Hz, 1 H, 1′-H_B), 6.85 ppm (s, 2 H, 3- and 5-H). The preceding data are consistent with those reported in the literature.[58] The *ee* was determined by chiral HPLC (Chiralpak AD-H, *n*-heptane/*i*-PrOH 97:3, 1 mL/min, $\lambda_{detector}$ = 265 nm): $t_r(1)$ = 11.33 min, $t_r(2)$ = 12.61 min. $[\alpha]^{20}_{365}$ = −107.3, $[\alpha]^{20}_{436}$ = −73.5, $[\alpha]^{20}_{546}$ = −32.9, $[\alpha]^{20}_{578}$ = −26.7, $[\alpha]^{20}_{589}$ = −22.2 (*c* = 0.80 in EtOH; the respective sample had 23% *ee*).

*Isobutyl (4-Phenylphenyl) Sulfoxide (**46**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(4-phenylphenyl) sulfoxide (101 mg, 0.286 mmol) with *i*-Bu_2Mg (0.80 M in Et_2O, 0.20 mL, 0.16 mmol, 0.55 equiv) within 1 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 27−48) delivered *rac*-**46** (64.3 mg, 87%) as a colorless solid (mp. = 56−57 °C). The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(4-phenylphenyl) sulfoxide (139.3 mg, 0.393 mmol). After 1 h, this delivered (*S*)-(−)-**46** (87.8 mg, 87%; 94% *ee*) as a colorless solid (mp. = 56−57 °C). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.09 (d, $J_{3'',2''}$ = 6.9, 3 H, 3″-H_3), 1.18 (d, $J_{3''',2''}$ = 6.5 Hz, 3 H, 3‴-H_3), 2.27 (m_c, 1 H, 2″-H), 2.52 (dd, $J_{1''-A,1''-B}$ = 12.9 Hz, $J_{1''-A,2''}$ = 9.2 Hz, 1 H, 1″-H_A), 2.87 (dd, $J_{1''-B,1''-A}$ = 13.0 Hz, $J_{1''-B,2''}$ = 5.0 Hz, 1 H, 1″-H_B), 7.37−7.42 (m, 1 H, 4′-H), 7.44−7.49 (m, 2 H, 2 × 2′-H), 7.59−7.62 (m, 2 H, 2 × 3′-H), AA′BB′ signal with signal centers at δ_A = 7.70 and δ_B = 7.74 ppm (4 H, 2 × 2-H and 2 × 3-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.8 (C-3‴), 22.9 (C-3″), 24.3 (C-2″), 67.7 (C-1″), 124.5 (C-2), 127.3 (C-2′*), 128.1 (C-3), 128.2 (C-4′), 129.1 (C-3′*), 140.0, 143.6, 144.1 ppm (C-1, C-4, and C-1′); *assignments interchangeable. IR ($CDCl_3$): $\tilde{\nu}$ = 3280, 3055, 3030, 2955, 2925, 2855, 2410, 2045, 1665, 1595, 1480, 1465, 1385, 1370, 1240, 1090, 1040, 1005, 840, 810, 760, 720 700, 655 cm^{-1}. HRMS (CI, NH_4Cl): $C_{16}H_{19}SO$ ($M + H^+$), calculated: 259.11566, found: 259.11550 (Δ = −0.6 ppm). Elemental analysis: calculated (%) for $C_{16}H_{18}SO$ (258.4 g/mol): C 74.38, H 7.02, S 12.41; found: C 74.23, H 6.77, S 12.06. The *ee* was determined by chiral HPLC (Chiralpak AD-H, *n*-heptane/*i*-PrOH 90:10, 1 mL/min, 22 °C, $\lambda_{detector}$ = 204 nm): $t_r(S)$ = 12.90 min, $t_r(R)$ = 16.83 min. $[\alpha]^{20}_{365}$ = −1512.3, $[\alpha]^{20}_{436}$ = −819.5, $[\alpha]^{20}_{546}$ = −410.7, $[\alpha]^{20}_{578}$ = −352.5, $[\alpha]^{20}_{589}$ = −334.7 (*c* = 1.16 in EtOH; the respective sample had 94% *ee*). The absolute configuration of the title compound was elucidated by X-ray crystal structure analysis (Figure 2). Detailed information are given in Section 2 of the Supporting Information: Spectra and HPLC Traces. X-ray Details.

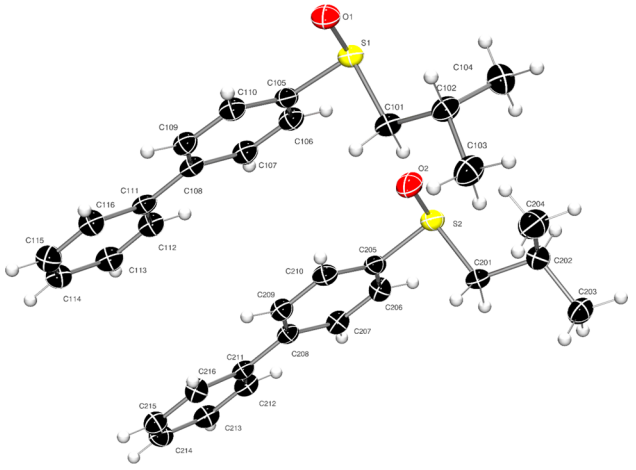
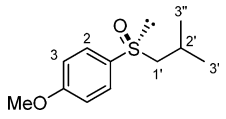


Figure 2. ORTEP plot of the crystal structure of sulfoxide (−)-**46** (at 100 K).[59] The unit cell contains two crystallographically independent molecules.

*Isobutyl (4-Methoxyphenyl) Sulfoxide (**47**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(4-methoxyphenyl) sulfoxide (130 mg, 0.496 mmol) with *i*-Bu_2Mg (0.80 M in Et_2O, 0.68 mL, 0.54 mmol, 1.1 equiv) within 2 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 55:45, F. 17−35) delivered *rac*-**47** (70.8 mg, 67%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(4-methoxyphenyl) sulfoxide (51.7 mg, 0.198 mmol). After 24 h at −68 °C, this delivered (*S*)-(−)-**47** (41.8 mg, 100%; 62% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.06 (d, $J_{3',2'}$ = 6.7 Hz, 3 H, 3′-H_3), 1.13 (d, $J_{3'',2'}$ = 6.5 Hz, 3 H, 3″-H_3), 2.17 (m_c, 1 H, 2′-H), 2.44 (dd, $J_{1'-A,1'-B}$ = 13.3 Hz, $J_{1'-A,2'}$ = 9.0 Hz, 1 H, 1′-H_A), 2.82 (dd, $J_{1'-B,1'-A}$ = 12.8 Hz, $J_{1'-B,2'}$ = 5.5 Hz, 1 H, 1′-H_B), 3.85 (s, 3 H, O-CH_3), AA′BB′ signal with signal centers at δ_A = 7.02 and δ_A = 7.57 ppm (2 × 2-H and 2 × 3-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.9 (C-3″), 22.9 (C-3′), 24.4 (C-2′), 55.8 (O-CH_3), 67.8 (C-1′), 114.9 (C-2), 126.1 (C-3), 135.8,

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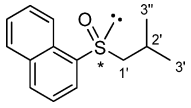
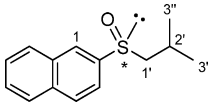
162.1 ppm (C-1 and C-4). IR ($CDCl_3$): $\tilde{\nu}$ = 3460, 3070, 2960, 2870, 2840, 2425, 2045, 1645, 1595, 1580, 1495, 1465, 1445, 1405, 1385, 1370, 1305, 1251, 1170, 1110, 1090, 1070, 1030, 1005, 830, 810, 795 cm^{-1}. HRMS (CI, NH_4Cl): $C_{11}H_{17}SO_2$ ($M + H^+$), calculated: 213.09493, found: 213.09510 (Δ = +0.8 ppm). Elemental analysis: calculated (%) for $C_{11}H_{16}SO_2$ (212.3 g/mol): C 62.23, H 7.60, S 15.10; found: C 62.11, H 7.55, S 14.94. The *ee* was determined by chiral HPLC (Chiralpak AD-H, *n*-heptane/*i*-PrOH 95:5, 1 mL/min, 22 °C, $\lambda_{detector}$ = 204 nm): $t_r(R)$ = 21.00 min, $t_r(S)$ = 24.79 min. $[\alpha]^{20}_{365} = -576.0$, $[\alpha]^{20}_{436} = -284.0$, $[\alpha]^{20}_{546} = -142.5$, $[\alpha]^{20}_{578} = -122.8$, $[\alpha]^{20}_{589} = -117.0$ (c = 1.0 in EtOH; the respective sample had 62% *ee*). The absolute configuration was assigned by chemical correlation (cf. Supporting Information).

*Isobutyl (1-Naphthyl) Sulfoxide (**48**): (−)-Enantiomer and Racemic.*[45]



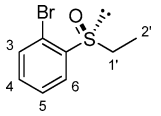
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using di(1-naphthyl) sulfoxide (50.1 mg, 0.166 mmol) with *i*-Bu_2Mg (0.80 M in Et_2O, 0.11 mL, 0.088 mmol, 0.53 equiv) within 2 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 18−25) delivered *rac*-**48** (27.8 mg, 72%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using di(1-naphthyl) sulfoxide (57.5 mg, 0.190 mmol). After 30 min, this delivered (−)-**48** (37.0 mg, 84%; 91% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.06 (d, $J_{3',2'}$ = 6.8 Hz, 3 H, 3′-H_3), 1.27 (d, $J_{3'',2'}$ = 6.6 Hz, 3 H, 3″-H_3), 2.36−2.46 (m, 1 H, 2′-H), 2.72−2.80 (m, 2 H, 1′-H_2), 7.55−7.61 (m, 2 H, 2 × Ar-H), 7.65−7.68 (dd, ^3J = 8.2 Hz, ^3J = 7.3 Hz, 1 H, 1 × Ar-H), 7.91−7.97 (m, 3 H, 3 × Ar-H), 8.15 ppm (dd, ^3J = 7.3 Hz, ^4J = 1.2 Hz, 1 H, 1 × Ar-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.6 (C-3′), 22.9 (C-3″), 24.6 (C-2′), 66.7 (C-1′), 121.5, 122.8, 125.9, 126.7, 127.3, 128.9, 129.2, 131.1, 133.6, 140.8 ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3055, 2960, 2870, 1590, 1505, 1465, 1400, 1380, 1345, 1260, 1170, 1140, 1040, 965, 860, 800, 770, 740, 665, 560 cm^{-1}. HRMS (CI, NH_4Cl): $C_{14}H_{17}SO$ ($M + H^+$), calculated: 233.10001, found: 233.10000 (Δ = −0.1 ppm) and $C_{14}H_{20}SNO$ ($M + NH_4^+$), calculated: 250.12656, found: 250.12660 (Δ = +0.2 ppm). The *ee* was determined by chiral HPLC (Chiralcel OD-H, *n*-heptane/*i*-PrOH 90:10, 1 mL/min, $\lambda_{detector}$ = 209 nm): $t_r(1)$ = 5.29 min, $t_r(2)$ = 24.19 min. $[\alpha]^{20}_{365} = -1512.3$, $[\alpha]^{20}_{436} = -819.5$, $[\alpha]^{20}_{546} = -410.8$, $[\alpha]^{20}_{578} = -352.5$, $[\alpha]^{20}_{589} = -334.7$ (c = 1.10 in EtOH; the respective sample had 91% *ee*).

*Isobutyl (2-Naphthyl) Sulfoxide (**49**): (−)-Enantiomer and Racemic.*[45]



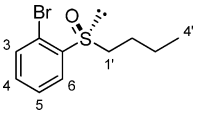
The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using di(2-naphthyl) sulfoxide (101 mg, 0.333 mmol) with *i*-Bu_2Mg (0.8 M in Et_2O, 0.23 mL, 0.18 mmol, 0.55 equiv) within 3 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 21−34) delivered *rac*-**49** (52.1 mg, 67%) as a colorless solid (mp. = 59−60 °C). The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using di(2-naphthyl) sulfoxide (58.1 mg, 0.192 mmol). After 5.5 h, this delivered (−)-**49** (32.8 mg, 74%; 42% *ee*) as a colorless solid (mp. = 59−60 °C). ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.09 (d, $J_{3',2'}$ = 6.9 Hz, 3 H, 3′-H_3), 1.19 (d, $J_{3'',2'}$ = 6.9 Hz, 3 H, 3″-H_3), 2.23−2.33 (m, 1 H, 2′-H), 2.57 (dd, $J_{1'\text{-A},1'\text{-B}}$ = 13.1 Hz, $J_{1'\text{-A},2'}$ = 8.4 Hz, 1 H, 1′-H_A), 2.88 (dd, $J_{1'\text{-B},1'\text{-A}}$ = 13.1 Hz, $J_{1'\text{-B},2'}$ = 4.7 Hz, 1 H, 1′-H_B), 7.58−7.61 (m, 3 H, 3 × Ar-H), 7.89−7.99 (m, 3 H, 3 × Ar-H), 8.20 ppm (br. s, 1 H, 1-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.9 (C-3′), 23.0 (C-3″), 24.4 (C-2′), 67.5 (C-1′), 120.0, 124.6 (C-1), 127.4, 127.8, 128.2, 128.6, 129.6, 133.0, 134.6, 142.0 ppm (C-2). IR ($CDCl_3$): $\tilde{\nu}$ = 3470, 3055, 2960, 2930, 2900, 2870, 1430, 2035, 1625, 1590, 1505, 1465, 1390, 1385, 1370, 1345, 1265, 1235, 1195, 1170, 1135, 1110, 1080, 1035, 945, 905, 860, 810, 765, 750 cm^{-1}. HRMS (CI, NH_4Cl): $C_{14}H_{17}SO$ ($M + H^+$), calculated: 233.10001, found: 233.10000 (Δ = −0.1 ppm). Elemental analysis: calculated (%) for $C_{14}H_{16}SO$ (232.3 g/mol): C 72.37, H 6.94, S 13.80; found: C 72.24, H 6.79, S 13.63. The *ee* was determined by chiral HPLC (Chiralcel OD-3, *n*-heptane/EtOH 97:3, 1 mL/min, $\lambda_{detector}$ = 209 nm): $t_r(1)$ = 7.97 min, $t_r(2)$ = 8.64 min. $[\alpha]^{20}_{365} = -344.3$, $[\alpha]^{20}_{436} = -204.1$, $[\alpha]^{20}_{546} = -103.5$, $[\alpha]^{20}_{578} = -89.3$, $[\alpha]^{20}_{589} = -73.7$ (c = 1.78 in EtOH; the respective sample had 42% *ee*).

*(2-Bromophenyl) Ethyl Sulfoxide (**52**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2-bromophenyl) sulfoxide (53.2 mg, 0.148 mmol) with Et_2Mg (0.16 M in Et_2O, 0.51 mL, 0.081 mmol, 0.55 equiv) within 1.25 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 18−27) delivered *rac*-**52** (17.0 mg, 49%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2-bromophenyl) sulfoxide (70.9 mg, 0.197 mmol). After 10 s, this delivered (*S*)-(−)-**52** (31.9 mg, 69%; 89% *ee*) as a colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 1.25 (dd, $J_{2',1'\text{-A}} = J_{2',1'\text{-B}}$ = 7.3 Hz, 3 H, 3′-H_3), AB signal (δ_A = 2.85, δ_B = 3.13, $J_{A,B}$ = 13.6 Hz, A part additionally split by q, $J_{1'\text{-A},2'}$ = 7.4 Hz, 1′-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 7.4 Hz, 1′-H_B), 7.36 (ddd, ^3J = 8.8 Hz, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 4- or 5-H), 7.53−7.58 (m, 2 H, 2 × Ar-H), 7.86 ppm (dd, ^3J = 8.1 Hz, ^4J = 1.8 Hz, 3- or 6-H). The preceding data are consistent with those reported in the literature.[60] The *ee* was determined by chiral HPLC (Chiralcel OJ-H, *n*-heptane/EtOH 300:1, 1.0 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(S)$ = 29.23 min, $t_r(R)$ = 33.41 min. $[\alpha]^{20}_{365} = -1090.0$, $[\alpha]^{20}_{436} = -562.9$, $[\alpha]^{20}_{546} = -290.6$, $[\alpha]^{20}_{578} = -250.8$, $[\alpha]^{20}_{589} = -239.5$ (c = 0.62 in EtOH; the respective sample had 89% *ee*). The absolute configuration was determined by chemical correlation (cf. Supporting Information).

*(2-Bromophenyl) Butyl Sulfoxide (**53**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2-bromophenyl) sulfoxide (70.9 mg, 0.197 mmol) with Bu_2Mg (0.69 M in Et_2O, 0.14 mL, 0.10 mmol, 0.51 equiv) within 30 min. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 13−20) delivered *rac*-**53** (25.5 mg, 50%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2-bromophenyl) sulfoxide (70.8 mg, 0.197 mmol). After 10 s, this delivered (*S*)-(−)-**53** (40.4 mg, 79%; 86% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.95 (t, $J_{4',3'}$ = 7.3 Hz, 3 H, 4′-H_3), 1.39−1.50 (m, 2 H, 3′-H_2), 1.51−1.67 (m, 1 H, 2′-H_A), 1.85−1.91 (m, 1 H, 2′-H_B), AB signal (δ_A = 2.76, δ_B = 3.09, $J_{A,B}$ = 14.5 Hz, A part additionally split by dd, $J_{1'\text{-A},2'\text{-A}}$ = 9.5 Hz, $J_{1'\text{-A},2'\text{-B}}$ = 5.0 Hz, 1′-H_A; B part additionally split by dd, $J_{1'\text{-B},2'\text{-A}}$ = 9.6 Hz, $J_{1'\text{-B},2'\text{-B}}$ = 6.7 Hz, 1′-H_B), 7.36 (ddd, ^3J = 7.8 Hz, ^3J = 7.5 Hz, ^4J = 1.8 Hz, 1 H, 4-or 5-H), 7.54−7.58 (m, 2 H, 2 × Ar-H), 7.88 ppm (dd, ^3J = 8.1 Hz, ^4J = 1.8 Hz, 1 H, 3- or 6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 13.8 (C-4′), 21.9 (C-3′), 24.3 (C-2′), 54.7 (C-1′), 118.7 (C-2*), 126.7 (C-3 or C-6), 128.5, 132.2 (C-4 or C-5), 133.0, 143.9 ppm (C-1*); *assignments interchangeable. IR ($CDCl_3$): $\tilde{\nu}$ = 3555, 3060, 2960, 2930, 2870, 2385, 1965, 1565, 1445, 1430, 1380, 1245, 1160, 1095, 1045, 1015, 755, 715 cm^{-1}. HRMS (CI, NH_4Cl): $C_{10}H_{14}SOBr$ ($M + H^+$), calculated: 260.99487, found: 260.99480 (Δ = −0.3 ppm). The *ee* was determined by chiral HPLC (Chiralcel OJ-H, *n*-heptane/EtOH 98:2, 1 mL/min, $\lambda_{detector}$ = 250 nm): $t_r(S)$ = 7.96 min, $t_r(R)$ = 9.00 min. $[\alpha]^{20}_{365} = -1207.1$, $[\alpha]^{20}_{436} = -632.3$, $[\alpha]^{20}_{546} = -330.6$,

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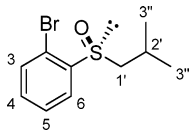
$[\alpha]_{578}^{20}$ = −284.5, $[\alpha]_{589}^{20}$ = −270.0 (*c* = 0.31 in EtOH; the respective sample had 86% *ee*). The absolute configuration was assigned by chemical correlation (cf. Supporting Information).

*(2-Bromophenyl) Isobutyl Sulfoxide (**54**): (S)-(−)-Enantiomer and Racemic.*[45]



The **racemic synthesis**[44] followed the *General Procedure for the Preparation of Racemic Alkyl Aryl Sulfoxides* using bis(2-bromophenyl) sulfoxide (100 mg, 0.278 mmol) with *i*-Bu_2Mg (0.80 M in Et_2O, 0.19 mL, 0.15 mmol, 0.55 equiv) within 2 h. Flash chromatography on silica gel[40] (*c*-C_6H_{12}:EtOAc 80:20, F. 10−15) delivered *rac*-**54** (58.9 mg, 81%) as a colorless oil. The **asymmetric synthesis** followed the *Procedure for the Asymmetric Sulfinylations of Dialkylmagnesium Compounds by Symmetric Diarylsulfoxides* using bis(2-bromophenyl) sulfoxide (70.9 mg, 0.197 mmol). After 1 h, this delivered (*S*)-(−)-**54** (42.9 mg, 83%; 53% *ee*) as a colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.07 (d, $J_{3',2'}$ = 7.3 Hz, 3 H, 3′-H_3), 1.23 (d, $J_{3'',2'}$ = 8.0 Hz, 3 H, 3″-H_3), 2.39 (m_c, 1 H, 2′-H), 2.60 (dd, $J_{1'\text{-A},1'\text{-B}}$ = 12.8 Hz, $J_{1'\text{-A},2'}$ = 4.2 Hz, 1 H, 1′-H_A), 2.91 (dd, $J_{1'\text{-B},1'\text{-A}}$ = 12.9 Hz, $J_{1'\text{-B},2'}$ = 10.4 Hz, 1 H, 1′-H_B), 7.35 (ddd, ^3J = 9.6 Hz, ^3J = 7.4 Hz, ^4J = 1.6 Hz, 1 H, 4- or 5-H), 7.54−7.58 (m, 2 H, 2 × Ar-H), 7.91 ppm (dd, ^3J = 7.6 Hz, ^4J = 1.8 Hz, 1 H, 3- or 6-H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.4 (C-3″), 23.0 (C-3′), 24.5 (C-2′), 65.6 (C-1′), 118.6 (C-2*), 126.3 (C-3 or C-6), 128.7, 132.2 (C-4 or C-6), 133.0, 144.7 ppm (C-1*); *assignments interchangeable. IR ($CDCl_3$): $\tilde{\nu}$ = 3665, 3260, 2960, 2925, 2870, 2405, 195, 1565, 1465, 1445, 1400, 1385, 1370, 1145, 1095, 1070, 1050, 1015, 755, 715 cm^{-1}. HRMS (CI, NH_4Cl): $C_{10}H_{14}SOBr$ ($M + H^+$), calculated: 260.99487, found: 260.99490 (Δ = +0.1 ppm). The *ee* was determined by chiral HPLC (Chiralcel OD-H, *n*-heptane/EtOH 97:3, 1 mL/min, $\lambda_{detector}$ = 210 nm): $t_r(R)$ = 8.32 min, $t_r(S)$ = 9.49 min. $[\alpha]_{365}^{20}$ = −888.8, $[\alpha]_{436}^{20}$ = −466.2, $[\alpha]_{546}^{20}$ = −243.8, $[\alpha]_{578}^{20}$ = −210.5, $[\alpha]_{589}^{20}$ = −200.1 (*c* = 1.06 in EtOH; the respective sample had 53% *ee*). The absolute configuration was assigned by chemical correlation (cf. Supporting Information).

■ ASSOCIATED CONTENT

Supporting Information

Detailed procedures for the configurational assignments, copies of NMR spectra, copies of HPLC traces, and X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) In this paper, sulfoxides are depicted with an S═O double bond. When this S═O bond starts from the sulfur atom of a *symmetric* sulfoxide, this representation needs no refinement. When the S═O bond starts from a sulfur atom of an *asymmetric* sulfoxide, we depict it with two heavy lines if the O atom is above the drawing plane; for reinforcing the 3D impression, we attach a hatched bond to the sulfur atom of such a sulfoxide for indicating that there is a lone pair below the drawing plane. When the S═O bond of an *asymmetric* sulfoxide is oppositely configured, we depict the S═O bond by one bond and a parallel hatched bond for making clear that the O atom lies below the drawing plane; for reinforcing the 3D impression, we attach a wedged bond to such a sulfur atom for emphasizing that there is a lone pair above the drawing plane.

(2) Reviews: (a) Carreño, M. C.; Hernández-Torres, G.; Ribagorda, M.; Urbano, A. *Chem. Commun.* **2009**, 6129−6144. (b) Pellissier, H. *Tetrahedron* **2006**, *62*, 5559−5601. (c) Senanayake, C. H.; Krishnamurthy, D.; Lu, Z.-H.; Han, Z.; Gallou, I. *Aldrichimica Acta* **2005**, *38*, 93−104. (d) Fernández, I.; Khiar, N. *Chem. Rev.* **2003**, *103*, 3651−3708. (e) Hanquet, G.; Colobert, F.; Lanners, S.; Solladié, G. *ARKIVOC* **2003**, *Part vii*, 328−401. (f) Wang, C.-C.; Huang, H.-C.; Reitz, D. B. *Org. Prep. Proced. Int.* **2002**, *34*, 271−319. (g) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717−1760.

(3) Reviews: (a) García Ruano, J. L.; Alemán, J.; Cid, M. B.; Fernández-Ibáñez, M. Á.; Maestro, M. C.; Rosario Martín, M.; Martín-Castro, A. M. In *Organosulfur Chemistry in Asymmetric Synthesis*; Toru, T., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2008; pp 55−160. (b) Nenajdenko, V. G.; Krasovskiy, A. L.; Balenkova, E. S. *Tetrahedron* **2007**, *63*, 12481−12539. (c) Ruano, J. L. G.; Castro, A. M. M. *Heteroat. Chem.* **2007**, *18*, 537−548. (d) Ferber, B.; Kagan, H. B. *Adv. Synth. Catal.* **2007**, *349*, 493−507. (e) Rivero, M. R.; Adrio, J.; Carretero, J. C. *Synlett* **2005**, 26−41.

(4) Reviews: (a) Fernández, I.; Khiar, N. In *Organosulfur Chemistry in Asymmetric Synthesis*; Toru, T., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2008; pp 265−290. (b) Mellah, M.; Voituriez, A.; Schulz, E. *Chem. Rev.* **2007**, *107*, 5133−5209. (c) Pellissier, H. *Tetrahedron* **2007**, *63*, 1297−1330.

(5) Reviews: (a) Solladié, G. *Heteroat. Chem.* **2002**, *13*, 443−452. (b) Prilezhaeva, E. N. *Russ. Chem. Rev.* **2000**, *69*, 403−446. (c) Solladié, G. *Enantiomer* **1999**, *4*, 183−193. (d) Matsuyama, H. *Sulfur Rep.* **1999**, *22*, 85−121.

(6) Reviews: (a) O'Mahony, G. E.; Kelly, P.; Lawrence, S. E.; Maguire, A. R. *ARKIVOC* **2011**, *Part i*, 1−110. (b) Wojaczyńska, E.; Wojaczyński, J. *Chem. Rev.* **2010**, *110*, 4303−4356.

(7) Reviews: (a) Bryliakov, K. P.; Talsi, E. P. *Curr. Org. Chem.* **2012**, *16*, 1215−1242. (b) Volcho, K. P.; Salakhutdinov, N. F. *Russ. Chem. Rev.* **2009**, *78*, 457−464. (c) Bryliakov, K. P.; Talsi, E. P. *Curr. Org. Chem.* **2008**, *12*, 386−404. (d) Legros, J.; Dehli, J. R.; Bolm, C. *Adv. Synth. Catal.* **2005**, *347*, 19−31. (e) Volcho, K. P.; Salakhutdinov, N. F.; Tolstikov, A. G. *Russ. J. Org. Chem.* **2003**, *39*, 1537−1552.

(8) (a) Cotton, H.; Elebring, T.; Larsson, M.; Li, L.; Sörensen, H.; von Unge, S. *Tetrahedron: Asymmetry* **2000**, *11*, 3819−3825. (b) Li, Z.; Kong, X.; Mai, W.; Sun, G.; Zhao, S. *Adv. Mater. Res.* **2014**, *881*−*883*, 351−355 and references cited therein.

(9) Capozzi, M. A. M.; Cardellicchio, C.; Naso, F.; Rosito, V. *Eur. J. Org. Chem.* **2004**, 1855−1863.

(10) (a) Sandrinelli, F.; Perrio, S.; Averbuch-Pouchot, M.-T. *Org. Lett.* **2002**, *4*, 3619−3622. (b) Maitro, G.; Vogel, S.; Sadaoui, M.; Prestat, G.; Madec, D.; Poli, G. *Org. Lett.* **2007**, *9*, 5493−5496.

(11) (a) Andersen, K. K. *Tetrahedron Lett.* **1962**, *3*, 93−95. (b) Andersen, K. K. *J. Org. Chem.* **1964**, *29*, 1953−1956.

(12) Evans, D. A.; Faul, M. M.; Colombo, L.; Bisaha, J. J.; Clardy, J.; Cherry, D. *J. Am. Chem. Soc.* **1992**, *114*, 5977−5985.

(13) Cogan, D. A.; Liu, G.; Kim, K.; Backes, B. J.; Ellman, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 8011−8019.

(14) Cardellicchio, C.; Fiandese, V.; Naso, F.; Scilimati, A. *Tetrahedron Lett.* **1992**, *33*, 5121−5124.

(15) Capozzi, M. A. M.; Cardellicchio, C.; Fracchiola, G.; Naso, F.; Tortorella, P. *J. Am. Chem. Soc.* **1999**, *121*, 4708−4709.

(16) Cardellicchio, C.; Iacuone, A.; Naso, F.; Tortorella, P. *Tetrahedron Lett.* **1996**, *37*, 6017−6020.

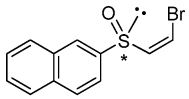
(17) Capozzi, M. A. M.; Cardellicchio, C.; Naso, F.; Tortorella, P. *J. Org. Chem.* **2000**, *65*, 2843−2846.

(18) Capozzi, M. A. M.; Cardellicchio, C.; Naso, F.; Rosito, V. *J. Org. Chem.* **2002**, *67*, 7289−7294.

(19) Hoffmann, R. W.; Nell, P. G. *Angew. Chem.* **1999**, *111*, 354−355; *Angew. Chem., Int. Ed.* **1999**, *38*, 338−340.

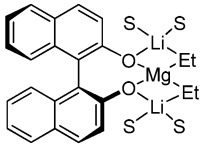
(20) (a) Hoffmann, R. W.; Hölzer, B.; Knopff, O.; Harms, K. *Angew. Chem.* **2000**, *112*, 3206−3207; *Angew. Chem., Int. Ed.* **2000**, *39*,

3072−3074. (b) Hoffmann, R. W.; Nell, P. G.; Leo, R.; Harms, K. *Chem.—Eur. J.* **2000**, *6*, 3359−3365.
(21) Rayner, P. J.; O'Brien, P.; Horan, R. A. J. *J. Am. Chem. Soc.* **2013**, *135*, 8071−8077.
(22)



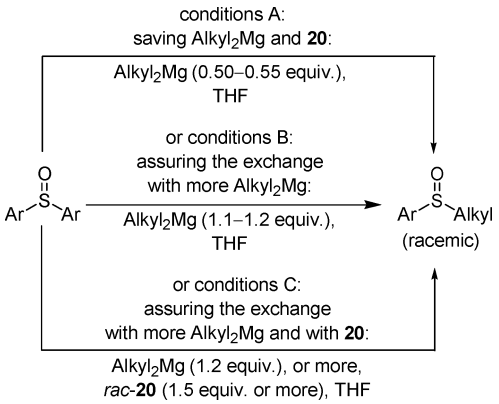
56 (80% *ee*)

Complete chirality transfer was described for the sulfinylation of methyl- and propylmagnesium halide by sulfoxide **56**: ref 14.
(23) (a) First sulfoxide/Mg exchange: Nokami, J.; Kunieda, N.; Kinoshita, M. *Chem. Lett.* **1977**, 249−252. (b) First sulfoxide/Mg exchange in a racemic alkyl aryl sulfoxide: Hojo, M.; Masuda, R.; Saeki, T.; Fujimoi, K.; Tsutsumi, S. *Synthesis* **1977**, 789−791. (c) First sulfoxide/Mg exchange in aryl heteroaryl sulfoxides: Furukawa, N.; Shibutani, T.; Matsumura, K.; Fujihara, H.; Oae, S. *Tetrahedron Lett.* **1986**, *27*, 3899−3902. (d) First sulfoxide/Mg exchange in diarylsulfoxides with RMgHal: Furukawa, N.; Shibutani, T.; Fujihara, H. *Tetrahedron Lett.* **1987**, *28*, 2727−2730. (e) First sulfoxide/Mg exchanges in diarylsulfoxides with *i*-PrMgCl·LiCl for making functionalized arylmagnesium reagents: Rauhut, C. B.; Melzig, L.; Knochel, P. *Org. Lett.* **2008**, *10*, 3891−3894.
(24) Boymond, L.; Rottländer, M.; Cahiez, G.; Knochel, P. *Angew. Chem.* **1998**, *110*, 1801−1803; *Angew. Chem., Int. Ed.* **1998**, *37*, 1701−1703.
(25) Hampel, T.; Ruppenthal, S.; Sälinger, D.; Brückner, R. *Chem.—Eur. J.* **2012**, *18*, 3136−3140.
(26)



57 ("S" = THF or DME)

Noyori et al. elucidated the structure of the Li_2-(*S*)-BINOLate complex **57** of Et_2Mg in THF or in DME: Noyori, R.; Suga, S.; Kawai, K.; Okada, S.; Kitamura, M. *Pure Appl. Chem.* **1988**, *60*, 1597−1606 . Since our reagents consisted of Li_2-(*S*)-BINOLate and R_2Mg (including Et_2Mg), we consider "Li_2-(*S*)-BINOLate·R_2Mg" as plausible active reagents in our sulfinylation reactions.
(27) The quotation marks shall indicate that we used a solvent mixture, in which THF was the major but not the only ingredient. This is because *n*-BuLi was used as a solution in hexane and the dialkylmagnesiums were used as solutions in Et_2O.
(28) To the best of our knowledge, these are the first sulfoxide/magnesium exchange reactions in diarylsulfoxides, which work with organomagnesium reagents containing *primary alkyl* groups. All previous sulfoxide/magnesium exchange reactions in diarylsulfoxides, of which we are aware, were effected with PhMgBr, [(a) Ref 23c. (b) Satoh, T.; Kitoh, Y.; Onda, K.; Yamakawa, K. *Tetrahedron Lett.* **1993**, *34*, 2331−2334.], with *i*-PrMgCl·LiCl [(c) Ref 23e. (d) Melzig, L.; Rauhut, C. B.; Knochel, P. *Synthesis* **2009**, 1041−1048. (e) Melzig, L.; Rauhut, C. B.; Knochel, P. *Chem. Commun.* **2009**, *24*, 3536−3538. (f) Melzig, L.; Rauhut, C. B.; Naredi-Rainer, N.; Knochel, P. *Chemistry* **2011**, *17*, 5362−5372.] or with *i*-Pr_2Mg (ref 25).
(29) The sulfinylations of *i*-Bu_2Mg giving **45** or **47** and the sulfinylation of Bn_2Mg were effected at −68 °C and +22 °C, respectively.
(30) The yield and *ee* of the 2,4-dimethylphenyl isopropyl sulfoxide (*S*)-(−)-**19** shown in Scheme 1 did not change when that compound was kept under the reaction conditions unnecessarily long (details: ref 33).[25] This means that (*S*)-(−)-**19** sulfinylated neither residual *i*-Pr_2Mg nor the stoichiometric byproduct 2,4-dimethylphenyl isopropyl magnesium (for contrasting behavior: see ref 45).
(31) The sulfinylation of Bn_2Mg had to be carried out at +22 °C in order to achieve any conversion at all.
(32) The 32 nonracemic sulfoxides, which emerged from the asymmetric sulfinylations of the present study are levorotatory. This consistency is paralleled by the consistency of attributing an (*S*)-configuration to 21 of these sulfoxides by independent evidence. Details: Supporting Information.
(33) When we sulfinylated *i*-Pr_2Mg asymmetrically under almost exactly the conditions specified in Scheme 1, the *ee* of the sulfoxide (*S*)-(−)-**19** did not change and the yield did not change more than marginally when we varied the reaction time between 10 min and 3 h.[25] In contrast, some sulfinylations of our present study revealed *ee* and yield variations with time, e.g.: • The sulfinylation of Et_2Mg delivering the sulfoxide (*S*)-(−)-**29** rendered 71% *ee* and 77% yield after 2 min (= experiment reported in Scheme 3) but 31% *ee* and 34% yield after 30 min (not mentioned elsewhere in this paper); the follow-up reaction, which occurred in between, thus consumed (*S*)-(−)-**29** faster than its (*R*)-enantiomer. • The sulfinylation of Et_2Mg delivering the sulfoxide (*S*)-(−)-**30** rendered 90% yield and 69% *ee* after 10 s (not mentioned elsewhere in this paper) and 39% yield and 94% *ee* after 30 min (= experiment reported in Scheme 3); the follow-up reaction, which occurred in between, thus consumed (*S*)-(−)-**30** more slowly than its (*R*)-enantiomer. • The sulfinylation of Et_2Mg delivering the sulfoxide (*S*)-(−)-**32** rendered 82% yield and 70% *ee* after 10 s (= experiment reported in Scheme 3) and 11% yield and 89% *ee* after 30 min (not mentioned elsewhere in this paper); the follow-up reaction, which occurred in between, thus consumed (*S*)-(−)-**32** more slowly than its (*R*)-enantiomer.
(34) (a) $H_2C{=}C(-O^{\ominus})Ph$: ref 23a. (b) $^{\ominus}CHRCl$ as well as $^{\ominus}CH_2Br$: ref 23b. $R^1HalC{=}C(-O^{\ominus})R^2$: (c) Satoh, T.; Onda, K.-i.; Itoh, N.; Yamakawa, K. *Tetrahedron Lett.* **1991**, *32*, 5599−5600. (d) Kopp, F.; Sklute, G.; Marek, I.; Knochel, P. *Org. Lett.* **2005**, *7*, 3789−3791. $R^1R^2C{=}C{=}N^{\ominus}$: (e) Nath, D.; Fleming, F. *Angew. Chem.* **2011**, *123*, 11994−11997; *Angew. Chem., Int. Ed.* **2011**, *50*, 11790−11793. (f) Nath, D.; Fleming, F. *Chem.—Eur. J.* **2013**, *19*, 2023−2029.
(35) Freeman, F.; Kim, D. S. H. L. *J. Org. Chem.* **1992**, *57*, 1722−1727.
(36) (a) Satoh, T.; Takano, K. *Tetrahedron* **1996**, *52*, 2349−2358. (b) Satoh, T.; Kurihara, T.; Fujita, K. *Tetrahedron* **2001**, *57*, 5369−5375. (c) Satoh, T.; Kondo, A.; Musashi, J. *Tetrahedron* **2004**, *60*, 5453−5460.
(37) Satoh, T.; Mizu, Y.; Kawashima, T.; Yamakawa, K. *Tetrahedron* **1995**, *51*, 703−710.
(38) Sulfoxide-lithium exchanges: (a) Lockard, J. P.; Schroeck, C. W.; Johnson, C. R. *Synthesis* **1973**, 485−486. (b) Durst, T.; LeBelle, M. J.; Van den Elzen, R.; Tin, K.-C. *Can. J. Chem.* **1974**, *52*, 761−766. (c) Satoh, T.; Kaneko, Y.; Yamakawa, K. *Tetrahedron Lett.* **1986**, *27*, 2379−2382. (d) Zhao, S. H.; Kagan, H. B. *Tetrahedron* **1987**, *43*, 5135−5144. (e) Satoh, T.; Itoh, N.; Onda, K.-i.; Kitoh, Y.; Yamakawa, K. *Tetrahedron Lett.* **1992**, *33*, 1483−1484.
(39) Sulfoxide-zinc exchanges: (a) ref 34e. (b) ref 34f.
(40) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923−2925.
(41) Sälinger, D.; Brückner, R. *Chem.—Eur. J.* **2009**, *15*, 6688−6703.
(42) Love, B. E.; Jones, E. G. *J. Org. Chem.* **1999**, *64*, 3755−3756.
(43) Screttas, C. G.; Micha-Screttas, M. *J. Organomet. Chem.* **1985**, *292*, 325−333.
(44) The racemic sulfoxides of this study were required for optimizing enantiomer separation by chiral HPLC. They were prepared by sulfinylating a given dialkylmagnesium compound with the appropriate diarylsulfoxide in the absence of enantiomerically pure Li_2-BINOLate. There was no emphasis on yield optimization because we considered any such synthesis as "accomplished" after having isolated a sufficient amount of the respective sulfoxide. We attempted each sulfinylation first under "conditions A" of the ensuing scheme. If more forcing conditions seemed to be called for, we tried "conditions B" and finally "conditions C".



(45) The yield of this sulfoxide was calculated such as to account for the expected sulfinylation Ar−S(=O)−Ar + Alkyl−Mg−Alkyl → Ar−S(=O)−Alkyl + Ar−Mg−Alkyl plus, when employing only 0.50−0.55 equiv of Alkyl−Mg−Alkyl, the unexpected over-reaction Ar−S(=O)−Ar + Ar−Mg−Alkyl → Ar−S(=O)−Alkyl + Ar−Mg−Ar. The latter materialized repeatedly, as indicated, e.g., by an 87% yield of sulfoxide *rac*-**46** applying "conditions A".

(46) Malik, P.; Chakraborty, D. *Tetrahedron Lett.* **2012**, *53*, 5652−5655.

(47) Akazome, M.; Ueno, Y.; Ooiso, H.; Ogura, K. *J. Org. Chem.* **2000**, *65*, 68−76.

(48) This reaction was carried out in 20 mL of THF.

(49) This signal can be interpreted as a "d of m_c": the doublet would be caused by the coupling of 5-H to 6-H and the m_c by the coupling of 5-H to 3-H.

(50) Blakemore, P. R.; Burge, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 3068−3069.

(51) Wu, Y.; Juntao, L.; Li, X.; Chan, A. S. C. *Eur. J. Org. Chem.* **2009**, 2607−2610.

(52) Takeuchi, H.; Minato late, H.; Kobayashi, M.; Yoshida, M.; Matsuyama, H.; Kamigata, N. *Phosphorus, Sulfur Silicon Relat. Elem.* **1990**, *47*, 165−172.

(53) Gogoi, P.; Kotipalli, T.; Indukuri, K.; Bondalapati, S.; Saha, P.; Saikia, A. K. *Tetrahedron Lett.* **2012**, *53*, 2726−2729.

(54) Lindén, A. A.; Johansson, M.; Hermanns, N.; Bäckvall, J.-E. *J. Org. Chem.* **2006**, *71*, 3849−3853.

(55) Davis, F. A.; Reddy, R. T.; Han, W.; Carroll, P. J. *J. Am. Chem. Soc.* **1992**, *114*, 1428−1437.

(56) Amos, R. A. *J. Org. Chem.* **1985**, *50*, 1311−1313.

(57) (a) O'Mahony, G. E.; Ford, A.; Maguire, A. R. *J. Org. Chem.* **2012**, *77*, 3288−3296. (b) Erratum: *J. Org. Chem.* **2013**, *78*, 791.

(58) Han, Z.; Krishnamurthy, D.; Grover, P.; Fang, Q. K.; Su, X.; Wilkinson, H. S.; Lu, Z.-H.; Magiera, D.; Senanayake, C. H. *Tetrahedron* **2005**, *61*, 6386−6408.

(59) The crystallographic data of sulfoxide (−)-**46** are contained in CCDC 1016608. They can be obtained free of charge from the Cambridge Crystallographic Data Centre via the link www.ccdc.cam.ac.uk/data_request/cif.

(60) Chakraborty, D.; Malik, P.; Goda, V. K. *Appl. Organomet. Chem.* **2012**, *26*, 21−26.