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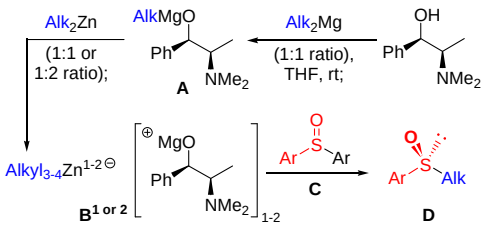

Dialkylmagnesium compounds deprotonate β-aminoalcohols, e. g. *N*-methyl-(–)-ephedrine. Plausibly, this renders β-aminoalkoxide analogs of Grignard reagents, e. g. compound **A**. One or two equivalents of the latter activate dialkylzinc compounds – perhaps as zincates **B^1 or B^2** – such that their alkyl moiety is sulfinylated by symmetric diaryl sulfoxides **C**. This provides alkyl aryl sulfoxides **D** in up to 100% yield with *ee*´s reaching the mid-80s.

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FULL PAPER

Asymmetric Sulfinylations of *N*-Methylephedrine-Modified Tri- or Tetraalkyl Zincates by Symmetric Diaryl Sulfoxides

Simon Ruppenthal[a] and Reinhard Brückner*[a]

Abstract: Diethylzinc was treated with 1 or 2 equiv. of AlkMgCl or PhMgBr (preferably) or with 1 equiv. of *n*BuLi (less efficiently) for forming species – plausibly zincates – which were sulfinylated by diaryl sulfoxides to give racemic alkyl aryl sulfoxides in yields reaching 100%. Dialkylzinc reagents were also activated by treatments with 1 or 2 equiv. of an enantiomerically pure alkylmagnesium β-aminoalkoxide. This worked best when the alkoxide stemmed from a dialkylmagnesium reagent and an equimolar amount of *N*-methyl-(–)-ephedrine. This second activation mode allowed sulfinylations of what was originally the dialkylzinc reagent with diaryl sulfoxides. This generated alkyl aryl sulfoxides with enantiomeric ratios up to 93:7 in up to 100% yield.

Literature Sulfinylations of Organozinc Compounds

The S-atom in sulfoxides is pyramidalized which makes unsymmetric sulfoxides chiral. The respective stereocenter remains stable unless the compound is heated excessively[1] or stereorandomizes by an EVANS-MISLOW rearrangement. Synthesizing sulfoxides enantioselectively is possible in many ways.[2] Probably, the most versatile access is by the enantioselective oxidation of unsymmetric sulfides.[2] Alternatively, enantiomerically pure sulfoxides result from the asymmetric sulfinylation of an organometallic. The latter access was pioneered by the *para*-toluenesufinylation of ethylmagnesium iodide by (−)-menthyl (−)-*p*-toluenesulfinate.[3] Methyl lithium[4] and Gilman cuprates react analogously.[5] Organozinc compounds[6] tolerate more functional groups than analogous organomagnesium, -lithium or -copper compounds. This reflects the lower nucleophilicity of the former compounds. Accordingly, very few organozinc compounds seem to have been sulfinylated giving a sulfoxide at all. The only examples of this approach of which we are aware are summarized in Scheme 1.

According to the top of Scheme 1 *tert*-adamantylzinc bromide and the enantiomerically pure sulfurous *N*-tosylamide **1** gave the sulfinate **2** with an inversion of configuration at the S-atom.[7] The second reaction of Scheme 1 – between a picolylzinc chloride and the sulfinate **5** – demonstrates that sulfinates may sulfinylate organozinc compounds, too;[8] however, such a possibility was not explored engaging the sulfinate **2** and adamantylzinc bromide.[7] The mentioned sulfinylation with the sulfinate **5** led to the sulfoxide **7** ("esomeprazole®") with complete inversion of configuration at the S-atom.[8] The third organozinc sulfinylation of Scheme 1[9] affects the mixed trialkyl zincates $n\text{BuEt}_2\text{Zn}^{\ominus}\,^{\oplus}\text{Li}$[10] which are more nucleophilic than alkylzinc halides or dialkylzinc compounds.[6] In this case the sulfinylating agent was the α-cyanoalkyl phenyl sulfoxide **8**.[9] It was the first sulfoxide to sulfinylate an organozinc compound.[9] At 0°C in THF this sulfinylation delivered ethyl phenyl sulfoxide (**9a**) and butyl phenyl sulfoxide (**9b**).[9] Both compounds were barely looked at, though.[9] This was because the focus was on follow-up reactions of the leaving group, that is of the α-zincated nitrile **10**[11] (e. g. by Mander´s reagent, which reacted to give the cyano ester **11**[9]). The sulfinylating sulfoxides **8** of the respective study[9] were racemic. They must have given the sulfoxides **9a** and **b** as *racemic mixtures* accordingly.

In contrast, we prepared alkyl aryl sulfoxides[12] – including ethyl phenyl sulfoxide (**9a**) – and alkyl heteroaryl sulfoxides[12c] *asymmetrically*: by sulfinylating **dialkylmagnesium compounds** with symmetric (!) diaryl[12a-b] or diheteroaryl sulfoxides.[12c] Asymmetry arose from adding Li_2-(*S*)-BINOLate.[12] Its involvement led to the transfer of *uniquely configured arylsulfinyl groups or heteroarylsulfinyl groups* from the respective sulfoxides. This was (1) in spite of their symmetry and thus (2) by desymmetrizing them[11]). Being the first reactions of their kind these sulfinylations succeeded in up to 100% yield with up to 97% *ee*.[12]

The latter route to sulfoxides, our previous endeavors into asymmetric synthesis by desymmetrization approaches,[13] and the feasibility of sulfoxide-mediated sulfinylations[9] **8** + $n\text{BuEt}_2\text{Zn}^{\ominus}\,^{\oplus}\text{Li} \rightarrow$ **9** + **10** (Scheme 1) were an incentive to identify the first asymmetric sulfinylations of **alkylzinc compounds** with symmetric diaryl sulfoxides. This intention and our respective results are sketched at the bottom of Scheme 1: Tri- or tetraalkyl zincate anions juxtaposed by (*S,S*)-configured β-amino(magnesioalkoxide) cations **12** picked up arylsulfinyl groups from diaryl sulfoxides **11** with up to 86% *ee*. Usually this gave sulfoxides **13** with an (*S*)-configuration.

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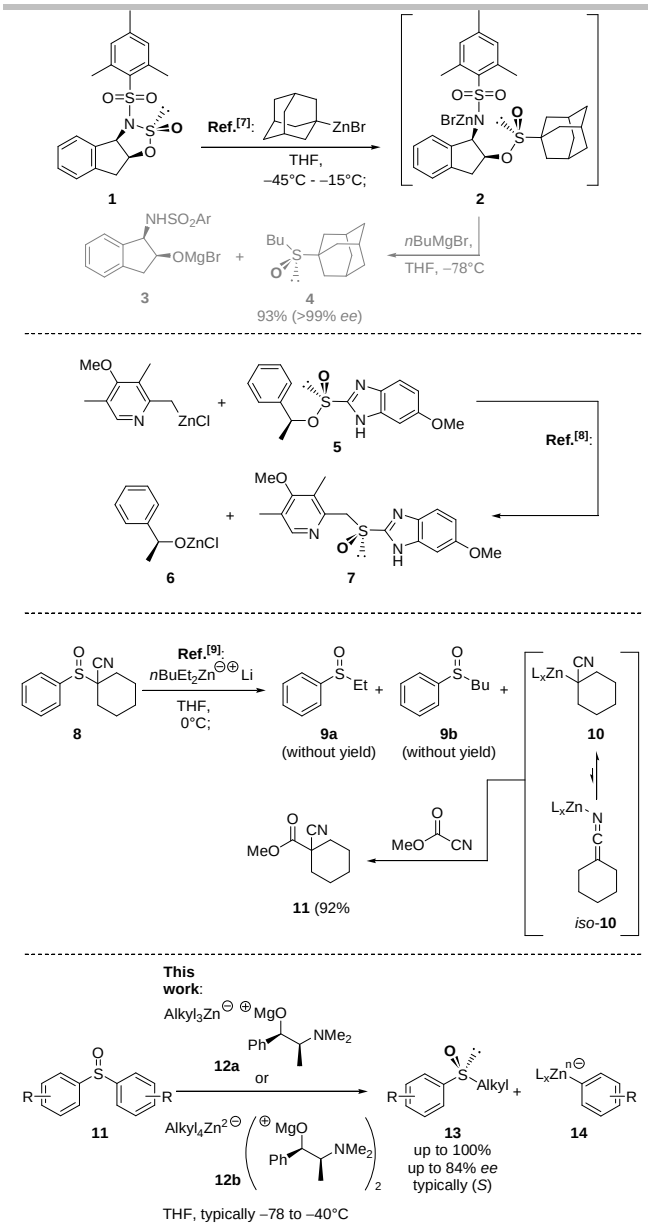
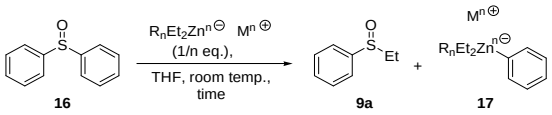


Scheme 1. Sulfoxide formation from organozinc reagents. The functionalization of adamantylzinc bromide provided the sulfinate **3**, not a sulfoxide (at top). However, a related sulfinate **5** converted a benzylzinc chloride into the sulfoxide **7** (underneath). Combining both findings suggests that compound **1** would suit as a linchpin for incorporating two different alkylzinc halides into a single(-configured) sulfoxide.

Racemic Phenylsulfinylations of "Activated Diethylzinc"

First we investigated the racemic phenylsulfinylation of Et_2Zn-containing organometallics testing diphenyl sulfoxide (**16**) as the sulfinylating reagent. It is known that alkylzinc halides and dialkylzinc reagents are unreactive towards sulfoxides.[14] We verified the latter fact (Table 1, entry 1) by mixing Et_2Zn and **16** in THF at room temperature (entry 1). No reaction occurred. The same was true for two related experiments. Employing the same reagents we tried to activate one of them either by adding a stoichiometric amount of lithium 2-(dimethylamino)ethanolate to the Et_2Zn (entry 2) or by adding 1.0 equiv. $BF_3{\cdot}OEt_2$ to the sulfoxide[15] (entry 3).

Table 1. Towards a racemic phenylsulfinylation of diethylzinc-containing reagents[a,b] by diphenyl sulfoxide (**16**).



#	R	n	M	Additive (1.0 eq.)	Time	Yield 9a	Other sulfoxides
1	—	0	—	—	1.5 h	no conversion	—
2					3 h		
3				$BF_3 \cdot OEt_2$	5 h		
4	Bu	1	Li	—	3.5 h	22%	8% PhS(=O)Bu
5	Et		MgCl		20 min	87%	—
6	Me_3SiCH_2					91%	
7	*i*Pr					18%	17% PhS(=O)*i*Pr
8	*t*Bu					65%	—
9	Ph		MgBr			100%	
10	Et	2	$(MgCl)_2$			84%	

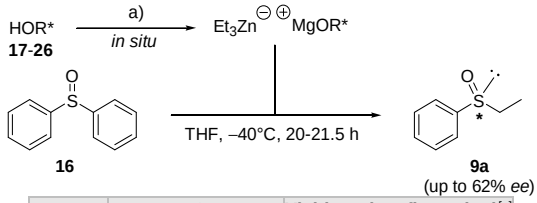
[a]The triorganozincates were prepared by mixing $ZnEt_2$ and 1.0 equiv. of an organolithium or Grignard reagent in THF at room temp. (10 min).– [b]The tetraethyl zincate stemmed from mixing $ZnEt_2$ and 2.0 equiv. of EtMgCl in THF at room temp. (10 min).

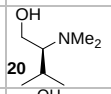
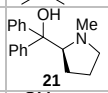
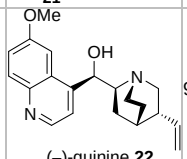
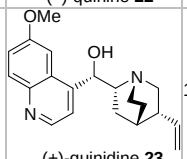
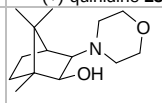
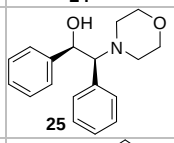
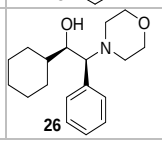
The mixed triorganozincate *n*BuEt$_2$Zn$^{\ominus}$ $^{\oplus}$Li had been phenylsulfinylated by the (activated) sulfoxide **8** of Scheme 1.[9] This suggested to combine the same zincate with diphenyl sulfoxide (**16**). This provided ethyl phenyl sulfoxide (**9a**) in 22% yield and butyl phenyl sulfoxide in 8% yield (Table 1, entry 4). Thereupon other organo diethyl zincates were tested similarly. Therein we replaced Li by MgHal and *n*Bu by Et, Me_3SiCH_2[16], *i*Pr[17], *t*Bu[18], and Ph (entries 5-9). At room temp. the respective phenylsulfinylations were over within 20 min. The homo-zincate $Et_3Zn^{\ominus}$ $^{\oplus}$MgCl rendered ethyl phenyl sulfoxide (**9a**) in 87% yield (entry 5). The mixed zincates $(Me_3SiCH_2)Et_2Zn^{\ominus}$ $^{\oplus}$MgCl (entry 6, 91% yield), *t*BuEt$_2$Zn$^{\ominus}$ $^{\oplus}$MgCl (entry 8, 65% yield), and PhEt$_2$Zn$^{\ominus}$ $^{\oplus}$MgBr (entry 9, quantitative yield) reacted analogously; their phenylsulfinylations affected the ethyl moiety exclusively. In contrast, the mixed zincate *i*PrEt$_2$Zn$^{\ominus}$ $^{\oplus}$MgCl (entry 7) reacted with the ethyl (→ 18% **9a**) and with the isopropyl moiety (→ 17% isopropyl phenyl sulfoxide). Finally, the tetraethyl zincate $Et_4Zn^{2\ominus}$ $^{\oplus}(MgCl)_2$ was phenylsulfinylated; it performed almost as well (→ 84% **9a**, entry 10) as the triethyl zincate $Et_3Zn^{\ominus}$ $^{\oplus}$MgCl (→ 87% **9a**, entry 5).

Asymmetric Arylsulfinylations of "Activated Diethylzinc"

Having established, inter alia, the suitability of magnesium triorganozincates for undergoing racemic phenylsulfinylations by diphenyl sulfoxide (**16**) (Table 1) we wondered whether changing their cation moiety $^{\oplus}$MgHal into $^{\oplus}$MgOR* allows to perform such

Table 2. The first asymmetric ("desymmetrizing"[11]) phenylsulfinylations of triethyl zincates containing enantiopure magnesium β-aminoalkoxide counterions using diphenyl sulfoxide (**16**) as the sulfinylating agent I: first counterion variations.



entry	R*OH	Yield; *ee* (configuration)[a]
1[b],[23]		70%; 16% *ee* (+)-(*R*)
2[b],[24]		76%; 57% *ee* (−)-(*S*)
3[c]		93%; 62% *ee* (−)-(*S*)
4[c]		66%; 13% *ee* (+)-(*R*)
5[c]	 **20**	85%; 15% *ee* (+)-(*R*)
6[c],[25]	 **21**	trace; *ee* not measured
7[c],[26]	 (–)-quinine **22**	98%; 29% *ee* (−)-(*S*)
8[c],[26]	 (+)-quinidine **23**	100%; 3% *ee* (+)-(*R*)
9[c],[27]	 **24**	93%; 29% *ee* (+)-(*R*)
10[c],[28]	 **25**	93%; 7% *ee* (+)-(*R*)
11[c],[28]	 **26**	73%; 11% *ee* (+)-(*R*)

Reagents and conditions: a) Et_2Mg (1.0 equiv.), THF, room temp., 30 min; $ZnEt_2$ (1.0 equiv.), 10 min.– [a]Sulfoxide (–)-**9a** is (*S*)-configured according to a previous study.[12b] As a consequence, sulfoxide (+)-**9a** must be (*R*)-configured. The configuration of the major enantiomer of all specimens of sulfoxide **9a** resulting from the experiments tabulated here was deduced from its migratory aptitude on a Chiralcel OD-3 column in *n*-heptane/*i*PrOH 96:4 (cf. Experimental Section): (−)-(*S*)-**9a** eluted slower than (+)-(*R*)-**9a**.– [b]A solution of sulfoxide **16** was added dropwise to a solution of "organozincate" precooled to −40°C; the reaction was quenched with MeOH after TLC showed complete conversion of the starting material (except for entry 6 where only a trace amount of starting material was consumed) and worked up with aqueous sat. NH_4Cl-solution and *t*BuOMe.– [c]We proceeded as in footnote [b] but added the solution of the "zincate" to a solution of the sulfoxide **16** which had been precooled to −40°C.

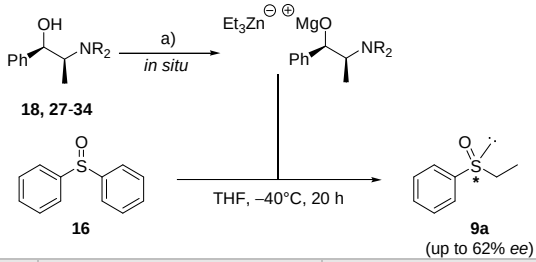
phenyl- or analogous arylsulfinylations still using the symmetric diphenyl sulfoxide (**16**) or other symmetric diaryl sulfoxides as sulfinylating agents. We determined that the OR* moiety of the envisaged cations ⊕MgOR* should originate from homochiral β-aminoalcohols. This choice was mainly based on the plausibility of being chelating ligands. Obviously, we could have tested homochiral glycols – or TADDOLs or BINOLs – with similar hopes. Focusing instead on β-aminoalcohols was inspired to some extent by their potential of making diethylzinc additions to aldehydes enantioselective.[19] Of course, these additions rely on *catalytic* amounts of a β-amino*alcohol* while our arylsulfinylations utilize *stoichiometric* amounts of the respective β-amino*alkoxides*. This difference is quite basic. Nonetheless, studying triorganozincates $R_3Zn^{\ominus}$ ⊕MgOR* at least formally would concern novel kinds of organozincates. Whatever they would really be,[20] the potential of their O- and N-atoms for binding not only to magnesium but also to zinc appeared likely to define such species spatially precisely. This might lead to good asymmetric inductions.

Table 2 - Table 5 summarize our results. Each experiment began with preparing a solution of what, we hypothesized, was an enantiomerically pure "zincate".[20] Its overall composition was $Et_3Zn^{\ominus}$ ⊕MgOR* or $REt_2Zn^{\ominus}$ ⊕MgOR* or $Et_4Zn^{2\ominus}$ $(⊕MgOR^*)_2$. Their OR* moiety was a β-aminoalkoxide. The respective aminoalcohol was dissolved in THF and combined with an Et_2O solution of Et_2Mg (Table 2, Table 3, Table 5) or $Alkyl_2Mg$ (Table 4) (room temp., 30 min). This was supposed to give the alkylmagnesium aminoalkoxide. The latter was carried on to the (surmised) zincate by treatment with 1.0 or 0.5 equiv. of Et_2Zn at room temp.[21]. That reagent was cooled to typically −40°C.[22] A THF solution of our benchmark sulfoxide **16** was added dropwise. The respective sulfinylation was allowed to progress at −40°C overnight. Usually, this ensured complete conversions.

The β-aminoalcohol precursors of our ethylmagnesium β-aminoalkoxide cation moieties ⊕MgOR* (cf. above) were varied extensively in rounds 1 (Table 2) and 2 (Table 3) of our study. Most of them had a history of having been employed as successful chiral promoters other kinds of organozinc reactions. The β-aminoalcohols allowing the phenylsulfinylations of Table 2 stemmed from ephedra alkaloids (**17**[23] and **18**[24]), amino acids (**19**, **20**, and **21**[25]) or chinchona alkaloids (**22**[26] and **23**[26]) or were synthetic materials introduced by Nugent (**24**[27], **25**[28], and **26**[28]). The sulfinylations of Table 3 leaned on *N*-alkylated (−)-ephedrines (**18**[24], **27**[23], **28**[29], **29**[30], and **30**[29,31]) and *N*,*N*-dialkylated (−)-norephedrines (**31**[29], **32**[29], **33**[29], and **34**[29]).

The best *ee* values of the phenylsulfinylations summarized in Table 2 were due to the cation ⊕MgOR* derived from *N*-methyl-(−)-ephedrine (**17**; entries 2 and 3): adding diphenyl sulfoxide (**16**) to the precooled organozincate[20] delivered sulfoxide (−)-(*S*)-**9a** in 76% yield with 57% *ee* (entry 2). The inverse addition mode was more satisfactory, though (entry 3). It increased both yield (93%) and enantioselectivity (62% *ee*). Therefore, the second procedure was adopted for all remaining arylsulfinylations – with a single exception, namely the phenylsulfinylation in the presence of the magnesium alkoxide of *N*-methyl-(+)-pseudoephedrine (**17**, entry 1). In Table 2 these reactions proceeded with low to modest enantioselectivities (3-29% *ee*) in good to excellent yields (66-100%).

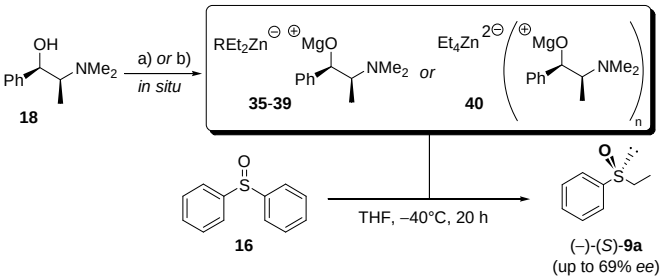
Table 3. Asymmetric ("desymmetrizing"[11]) phenylsulfinylations of triethyl zincates containing enantiopure magnesium β-aminoalkoxide counterions using diphenyl sulfoxide (**16**) as the sulfinylating agent II: fine-tuning the (−)-ephedrine (→ **18** and **27**-**29**) and (−)-norephedrine (→ **30**-**34**) substituents.



entry		Yield; *ee* (configuration)[a]
1[24]	**18**	93%; 62% *ee* (−)-(*S*) (= Table 2; entry 3)
2[23]	**27**	87%; 31% *ee* (−)-(*S*)
3[29]	**28**	96%; 5% *ee* (−)-(*S*)
4[30]	**29**	100%; 20% *ee* (−)-(*S*)
5[29,31]	**30**	34%; 3% *ee* (−)-(*S*)
6[29]	**31**	92%; 5% *ee* (−)-(*S*)
7[29]	**32**	62%; 13% *ee* (+)-(*R*)
8[29]	**33**	34%; 8% *ee* (+)-(*R*)
9[29]	**34**	90%; 7% *ee* (+)-(*R*)

[a]The predominant configuration of sulfoxide **9a** was determined as detailed in footnote [a] of Table 2.– *Reagents and conditions:* a) Et_2Mg (1.0 equiv.), THF, room temp., 30 min; $ZnEt_2$ (1.0 equiv.), 10 min; thereafter we proceeded as described in footnote [c] of Table 2.

Table 4. Optimizing the asymmetric ("desymmetrizing"[11]) phenylsulfinylation of ethyl-containing zincates juxtaposed by an *N*-methyl-(−)-ephedrine-based magnesium β-aminoalkoxide counterion using diphenyl sulfoxide (**16**) as the sulfinylating agent.



entry	Organozincate	Solvent	Yield; *ee* (configuration)[a]
1	**35**	THF	93%; 62% *ee* (= Table 2, entry 3)
2		Et_2O	45%; 2% *ee*
3		DME	no conversion
4		toluene	53%; 2% *ee*
5[b]		THF	72%; 63% *ee*
6	**36**		89%; 62% *ee*
7	**37**		66%; 3% *ee*
8	**38**		69%; 28% *ee*
9	**39**		49%; 37% *ee*
10	**40**		86%; 69% *ee*

[a]The predominant configuration of sulfoxide **9a** was determined as detailed in footnote [a] of Table 2.– [b]2.0 equiv. of the "organozincate" were used.– *Reagents and conditions:* a) Et_2Mg or $Alkyl_{non\text{-}transferable,2}Mg$ (1.0 equiv.), THF, room temp., 30 min; $ZnEt_2$ (1.0 equiv.), 10 min; thereafter we proceeded as described in footnote [c] of Table 2.– b) Same as a) except for using Et_2Mg (2.0 equiv.).

The triethyl zincate of Table 2 which was phenysulfinylated with the highest enantioselectivity (62% *ee*) was derived from "*N*,*N*-dimethylated (−)-norephedrine" [= *N*-monomethylated (−)-ephedrine; **18**]. This led us to examine the enantiocontrol exerted by eight other *N*,*N*-dialkylated ephedra alkaloids (Table 3). None of them topped the result of *N*-methyl-(−)-ephedrine (**18**, entry 1), however. On the contrary, low *ee*'s (5%-31%) resulted. The increased sterical demand at the nitrogen seems to affect enantiocontrol adversely – to the point of inverting it from a weak (*S*)-(entries 1-6) to a weak (*R*)-preference (entries 7-9).

The phenylsulfinylations recorded in Table 4 maintained *N*-methylated (−)-ephedrine (**18**) as the chiral auxiliary but varied the reaction conditions; the resulting sulfoxide (**9a**) was always (*S*)-configured:

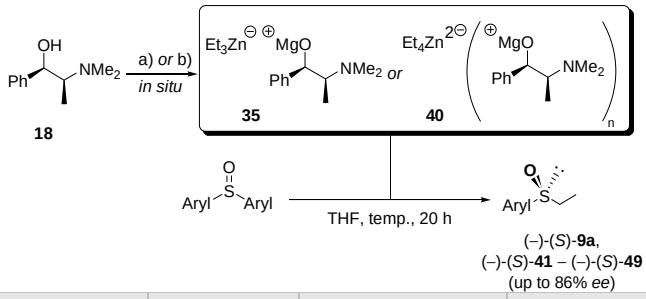
1) We moved from THF as the solvent to Et_2O, dimethoxyethane ("DME") or toluene (entries 2-4). Using Et_2O and toluene decreased yield (45% or 53%, respectively) and uplifted enantiocontrol (2% *ee*). DME stopped the phenylsulfinylation altogether.

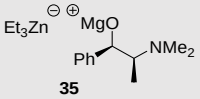
2) We increased the proportion of "$Et^{\ominus}$" in the reaction mixture: either by using twice as much triethyl zincate **35** (entry 5; → 72% yield and 63% *ee*) or by using an equimolar amount of the analogous tetraethyl zincate (**40**, entry 10; → 86% and 69% *ee*). The

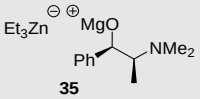
second result was tantamount to a small yield decrease (86% instead of 93% in entry 1) and *ee* increase (69% instead of 62% in entry 1).

3) Similarly as recorded in Table 1, we compared the phenylsulfinylation of the triethyl zincate **35** with phenylsulfinylations of the mixed alkyl or phenyl diethyl zincates **36**-**39** (entries 6-9). The latter contained a non-transferable group which, other than in Table 1 (cf. entry 7 there and entry 7 here), included the *i*Pr group. The *i*Pr-, *t*Bu-, and Ph-modified zincates (**37**-**39**) were inferior (entries 7-9; → 49-69% yield and 3-37% *ee*) to the triethyl zincate **35** (entry 5; → 72% yield and 63% *ee*), the Me_3SiCH_2-modified zincate **36** slightly superior (entry 6; → 89% yield and 62% *ee*). However, this left **36** inferior compared to the tetaethyl zincate **40** (entry 10; → 86% and 69% *ee*). Accordingly, we continued our sulfinylations employing only the tri- and the tetraethyl zincate.

Table 5. Asymmetric ("desymmetrizing"[11]) aryl- rather than phenylsulfinylations of ethyl-containing zincates juxtaposed by an *N*-methyl-(−)-ephedrine-based magnesium β-aminoalkoxide counterion using symmetric diaryl rather than diphenyl sulfoxides as sulfinylating agents. The absolute configuration of the resulting sulfoxides emerged from their levorotation; it correlates with their stereostructure as previously established.[12b]



Reagent ↓ / Aryl, Nr. of product, and temp. →	**9a** at −40°C	**41** at −40°C	**42** at −40°C	**43** at room temp.	**44** at −78°C
(1.0 equiv.)  **35** (2.0 equiv.)	93%; 62% *ee*	35%; 45% *ee*	no conversion	28%; 0% *ee*	14%; 86% *ee*
	72%; 63% *ee*	94%; 68% *ee*	trace; *ee* not measured	62%; 0% *ee*	70%; 79% *ee*
(1.0 equiv.)	86%; 69% *ee*	100%; 65% *ee*	50%; 69% *ee*	71%; 0% *ee*	90%; 82% *ee*

Reagent ↓ / Aryl, Nr. of product, and temp. →	**45** at −78°C	**46** at −78°C	**47** at −40°C	**48** at −78°C	**49** at −78°C
(1.0 equiv.)  **35** (2.0 equiv.)	trace; *ee* not measured	11%; 33% *ee*	trace; *ee* not measured	71%; 80% *ee*	trace; *ee* not measured
	trace; *ee* not measured	7%; 46% *ee*	58%; 78% *ee*	100%; 82% *ee*	58% Ph−S(=O)−Et (**9a**), which includes hydrodebromination; 51% *ee*
(1.0 equiv.)	50%; 78% *ee*	65%; 46% *ee*	79%; 57% *ee*	87%; 84% *ee*	47%; 47% *ee* + 31% Ph−S(=O)−Et (**9a**), which includes hydrodebromination; 53% *ee*[a]

[a] The two sulfoxides were isolated separately after flash chromatography on silica gel[33].– *Reagents and conditions:* a), b): Same as a) and b), respectively, in the caption of Table 4.

According to Table 5 the best conditions of our asymmetric phenylsulfinylation of the ethyl-containing zincates **35** (Table 2, entry 3 and Table 4, entry 5) and **40** (Table 4, entry 10) suited for undertaking analogous arylsulfinylations, too. Each reaction was tested using either 1.0 or 2.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[MgO-*N*-methyl-(−)-ephedrinate] (**35**) or, alternatively, 1.0 equiv. of $Et_4Zn^{\ominus}$ [$^{\oplus}$MgO-*N*-methyl-(−)-ephedrinate]$_2$ (**40**) in THF. The respective results are repeated in Table 5 at top and left.

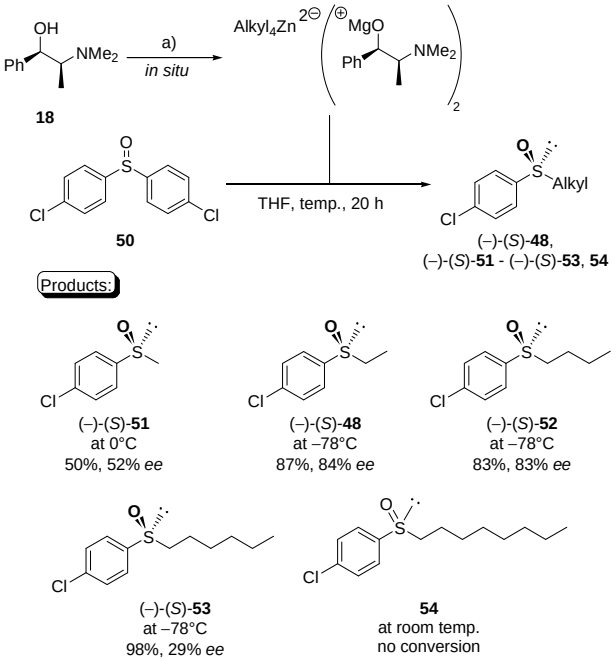
The arylsulfinylations of Table 5 provided (*S*)-configured aryl ethyl sulfoxides unexceptionally. They were realized at the lowest temperature possible:[22] The relatively electron-poor diaryl sulfoxides – containing chloro, bromo or aryl substituents – reacted at −78°C. The relatively electron-rich diaryl sulfoxides – with methyl or methoxy substituents – reacted at −40°C and the sterically demanding dimesityl sulfoxide **43** at room temperature. These arylsulfinylations proceeded with considerable substrate and nucleophile dependencies:

1) Sulfinylating 1.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[MgO-*N*-methyl-(−)-ephedrinate] (**35**) there was only one good result: (−)-(*S*)-4-chlorophenyl ethyl sulfoxide (**48**) was obtained in 71% yield with 80% *ee*. The seemingly analogous aryl ethyl sulfoxides (−)-(*S*)-**41** (35%, 45% *ee*), **43** (28%, *rac*), (−)-(*S*)-**44** (14%, 86% *ee*), and (−)-(*S*)-**46** (11%, 33% *ee*) resulted in low yields and their *ee* values were mediocre – except for (−)-(*S*)-**44** (86% *ee*). The aryl ethyl sulfoxides **43**, **45**, **47**, and **49** emerged at most in trace amounts, even if their preparation was attempted at 22°C.

2) Sulfinylating 2.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[MgO-*N*-methyl-(−)-ephedrinate] (**35**) brought major improvements: The aryl ethyl sulfoxides (−)-(*S*)-**41**, (−)-(*S*)-**44**, (−)-(*S*)-**47**, and (−)-(*S*)-**48** were obtained in good yields (50-100%) and good enantioselectivities (68-82% *ee*). Sulfoxide **43** was obtained in 62% yield (yet once more racemic). The yield of sulfoxide (−)-(*S*)-**46** was low again (7%) and the sulfoxides **42** and **45** still not obtained. Bis(2-bromophenyl) sulfoxide was a viable arylating reagent, too. However, a hydrodebromination of the expected sulfoxide ensued under the reaction conditions. Overall, this afforded the bromine-free sulfoxide **9a** in 58% yield with 51% *ee*.

3) Sulfinylating 1.0 equiv. of the tetraorganozincate $Et_4Zn^{2\ominus}$ [$^{\oplus}$MgO-*N*-methyl-(−)-ephedrinate]$_2$ (**40**) with the diaryl sulfoxides of Table 5 was our best procedure both in terms of yield (47-100%) and enantiocontrol. The highest enantiomeric excesses were 84% for (−)-(*S*)-**48** and 82% for (−)-(S)-**44**. They were unmatched by the remaining sulfoxides (46-78% *ee*). Only ethyl mesityl sulfoxide (**43**) arose as a racemic mixture. Bis(2-bromophenyl) sulfoxide was partly a bromophenylating agent (→ brominated sulfoxide **49**; isolated in 47% yield with 47% *ee*) and partly a phenylating agent (→ bromine-free sulfoxide **9a**; isolated in 31% yield with 53% *ee*) because of some in-situ dehydrodebromination **46** → **9a** (cf. above).

Arylsulfinylations of Activated Dialkylzinc Compounds Other Than Diethylzinc



Scheme 2. Asymmetric ("desymmetrizing"[11]) 4-chlorophenylations of tetraalkyl rather than tetraethyl zincates juxtaposed by an *N*-methyl-(−)-ephedrine-based magnesium β-aminoalkoxide counterion employing the symmetric bis(4-chlorophenyl) sulfoxide (**50**) as a sulfinylating agent. The absolute configuration of the resulting sulfoxides emerges from their levorotation. It correlates with previously determined 3D structures [for (−)-**51**: ref.[42]; for (−)-**48** and (−)-**52**: ref.[12b]]. The absolute configuration of 4-chlorophenyl hexyl sulfoxide [(−)-**53**] was determined after converting it through sulfoxide-magnesium exchange with PhMgBr[44] – with inversion of configuration – into *dextrorotatory* hexyl phenyl sulfoxide. The latter is (*R*)-configured according to ref.[46].– *Reagents and conditions:* a) **18** (2.0 equiv.), $Alkyl_2Mg$ (2.0 equiv.), THF, room temp., 30 min; $Alkyl_2Zn$ (1.0 equiv.), 10 min; this solution was added to a (precooled) solution of **50** (−78°C for Alkyl = Et, Bu, and Hex; 0°C for Alkyl = Me, or room temp. for Alkyl = Oct) and stirred for 20 h. The reaction was worked up with aqueous sat. NH_4Cl-solution and *t*BuOMe.

The final variation of the asymmetric arylsulfinylations of our investigation altered the alkyl group of the tetraethylzincate **40** studied hitherto to Me, Bu, Hex, and Oct. That is, we studied the asymmetric sulfinylation of the corresponding zincates $Alkyl_4Zn^{2\ominus}$ [$^{\oplus}$MgO-*N*-methyl-(−)-ephedrinate]$_2$.[32] The respective sulfinylating agent was bis(4-chlorophenyl) sulfoxide (**50**; Scheme 2), not diphenyl sulfoxide (**9a**; cf. Table 2 - Table 4) because the former sulfoxide was associated with the highest *ee* values of Table 5.

The highest-yielding sulfinylations of Table 5 occurred at −78°C and furnished the aryl hexyl sulfoxide (−)-(*S*)-**53** (98% yield) and the aryl butyl sulfoxide (−)-(*S*)-**52** (83% yield). Surprisingly, the respective *ee* values differed widely, being 29% and 83%. In

accordance with the lower nucleophilicity of Zn-bound Me vs. higher alkyl groups,[18] the 4-chlorophenylsulfinylation of $Me_4Zn^{2\ominus}$ [$^{\oplus}$MgO-*N*-methyl-(−)-ephedrinate]$_2$ had be performed at 0°C. It provided the sulfoxide (−)-(*S*)-**51** in 50% yield with 52% *ee*. In stark contrast to the ease of sulfinylation both of the tetrabutyl zincate and the tetrahexyl zincate – at −78°C! – the tetraoctyl zincate was not even sulfinylated at room temperature.

Conclusions

We prepared – at least formally – trialkyl zincates containing one equivalent of a $Mg^{2\oplus}$-bound enantiomerically pure β-aminoalkoxide ligand; preferably, the latter was *N*-methyl-(−)-ephedrinate. Likewise, we prepared – at least formally – tetraalkyl zincates which contain two equivalents of $Mg^{2\oplus}$-bound *N*-methyl-(−)-ephedrinate. Both kinds of zincates reacted with symmetric diaryl sulfoxides such that one Zn-bound alkyl group was arylsulfinylated asymmetrically. From a different vantage point the starting diaryl sulfoxide was "desymmetrized" thereby.[11] The mentioned arylsulfinylations rendered alkyl aryl sulfoxides in yields up to 86% and with *ee* values up to 86%. This route to enantiomerically enriched sulfoxides is novel and conceptionally interesting. Developing it from needing stoichiometric amounts of a homochiral additive at present to needing perhaps just catalytic amounts thereof is an intriguing challenge for the future.

Experimental Section

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, hexane and toluene were distilled over sodium or potassium under an atmosphere of N_2. 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, fractions 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.*[33] **Nuclear magnetic resonance spectra:** Spectra were obtained on a NMR spectrometer (400 MHz, and 300 MHz for ^{1}H, 100 MHz for ^{13}C, respectively); 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. For AB signals the high-field part was named A and the low-field part B. NMR Assignments were made using a combination of 1D and 2D techniques (DQF-COSY and ed-HSQC). **High-resolution mass spectra:** These spectra were obtained in CI/NH_3 (110 eV) or ESI (spray voltage: 4-5 kV) mode, using an orbitrap analyzer. **Elemental analyses:** Analyses were obtained on a CHNS analysator. **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 589 nm at 20°C and were calculated by the Drude equation {[α] = (α_{exp} × 100)/(c × d)}; rotational values are the average of five measurements of α_{exp} in a given solution of the respective sample.

Preparation of Reactants

Me_2Zn, Et_2Zn, EtMgCl, *i*PrMgMgCl, *t*BuMgCl, and PhMgBr were purchased. The concentration of $Alkyl_2Zn$ was determined by titration with iodine in a THF-solution of lithium chloride.[34] The concentration of organomagnesium compounds was determined by titration with salicylic aldehyde phenylhydrazone.[35]

Preparation of Me_3SiCH_2MgCl

(Chloromethyl)trimethylsilan (2.80 ml, 2.45 g, 20.0 mmol) was added dropwise to Mg turnings (535 mg, 22.0 mmol, 1.1 equiv.) in THF (20 ml). Afterwards the mixture was refluxed for 3 h. Then, the solution of the Grignard reagent was separated from residual Mg turnings with a canula. The resulting solution of the Grignard reagent could be stored at 4°C for several weeks. Its concentration was determined by titration with salicylic aldehyde phenylhydrazone.[35]

Preparation of Et_2Mg, $(Me_3SiCH_2)_2Mg$, and Bu_2Mg solutions in Et_2O

At room temperature the appropriate alkyl bromide or chloride (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 grey 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 under 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 $Alkyl_2Mg$ could be stored at 4°C for several weeks. Its concentration was determined by titration with salicylic aldehyde phenylhydrazone.[35]

Preparation of $Alkyl_2Mg$ solutions in Et_2O (Alkyl = Me, Hex, Ph)[36]

At room temperature AlkylLi (solution in THF, 12.0 mmol, 1.0 equiv.) was added dropwise to a solution of 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.[35] At 4°C such solutions could be stored for several weeks.

Preparation of Bu_2Zn and Hex_2Zn[37]

At 0°C *n*BuLi or *n*HexLi (solutions in hexane, 18.7 mmol, 2.0 equiv.) was added dropwise to dry $ZnCl_2$ (1.28 g, 9.35 mmol) in Et_2O (10 ml). After 4 h at 0°C the solvent was evaporated in a stream of nitrogen. The residue was taken up in dry hexane (10 ml). The clear supernatant was separated from the precipitate with a canula and transferred into a dry Schlenk flask. The solution was stored at 4°C for several weeks. Its concenctration was determined by titration with iodine in a THF-solution of lithium chloride.[34]

Preparation of Oct_2Zn[38]

At room temp. BEt_3 (1.0 M in THF, 2.0 ml, 2.0 mmol, 0.66 equiv.) and $BH_3 \cdot THF$ (1.0 M in THF, 1.0 ml, 1.0 mmol, 0.33 equiv.) were premixed for 5 min. 1-Octene (0.47 ml, 337 mg, 3.0 mmol) was added dropwise to the resulting solution of $HBEt_2$ (1.0 M in THF, 3.0 ml, 3.0 mmol, 1.0 equiv.) at 0°C and stirred for 3 h at 0°C. Then, the solvent was evaporated in high vacuo at room temp. before $ZnEt_2$ (0.76 M in hexane, 7.9 ml, 6.0 mmol, 2.0 equiv.) was added dropwise. This mixture was stirred for 30 min and

the solvent was evaporated once again in high vacuo. The residue was taken up in THF (3 ml). The solution (quantitative yield) was stored at 4°C for several weeks. Its concenctration was determined by titration with iodine in a THF solution of lithium chloride.[34]

Preparation of Substrates and Alkyl Aryl Sulfoxides

The symmetric diaryl sulfoxides and the racemic alkyl aryl sulfoxides except *rac*-**51** and *rac*-**53** were materials from our previous study.[12b] The synthesis of the enantiopure aminoalcohols is disclosed in the Supporting Information.

General Procedure for the Racemic Phenylsulfinylation of $R_nEt_2Zn^{n\ominus}M^{n\oplus}$ (cf. Table 1)

At room temp. R−M (in THF or Et_2O; 0.223 mmol, 1.0 equiv. for n = 1 or 0.446 mmol, 2.0 equiv. for n = 2) was added to a solution of $ZnEt_2$ (0.93 M in hexane, 0.24 ml, 0.223 mmol, 1.0 equiv.) in THF (1 ml). After 10 min diphenyl sulfoxide (**9a**, 45.1 mg, 0.223 mmol) was added in one portion. After the time indicated in Table 1 the reaction was stopped by the addition of MeOH (1 ml) and aqueous sat. NH_4Cl-solution (1 ml). The layers were separated and 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[33] to yield the title compound (for details on flash chromatography, yields, *ee*, and deviations from this procedure: cf. individual descriptions).

General Procedure for the Asymmetric Arylsulfinylation of 1.0 equiv. of $Et_3Zn^{\ominus}{}^{\oplus}$[Magnesio *N*-Methyl-(−)-ephedrinate] – "Treatment A"

At room temp. Et_2Mg (0.54 M in Et_2O, 0.41 ml, 0.223 mmol, 1.0 equiv) was added dropwise to a solution of *N*-methyl-(−)-ephedrine (**18**, 40.0 mg, 0.223 mmol, 1.0 equiv.) in THF (1 ml). After 30 min Et_2Zn (0.93 M in hexane, 0.24 ml, 0.223 mmol, 1.0 equiv.) was added and stirred for another 10 min. This freshly prepared solution was added dropwise to a precooled (for temperature cf. individual descriptions) solution of the diaryl sulfoxide (0.223 mmol) in THF (1.0 ml). When the reaction was finished (typically 20 h), the reaction was stopped by the addition of MeOH (1 ml) and aqueous sat. NH_4Cl-solution (1 ml). The layers were separated and 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[33] (details: cf. individual descriptions) to yield the title compound.

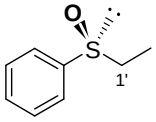
General Procedure for the Asymmetric Arylsulfinylation of 2.0 equiv. of $Et_3Zn^{\ominus}{}^{\oplus}$[Magnesio *N*-Methyl-(−)-ephedrinate] – "Treatment B"

At room temp. Et_2Mg (0.54 M in Et_2O, 0.82 ml, 0.446 mmol, 2.0 equiv.) was added dropwise to a solution of *N*-methyl-(−)-ephedrine (**18**, 80.0 mg, 0.446 mmol, 2.0 equiv.) in THF (1 ml). After 30 min Et_2Zn (0.93 M in hexane, 0.48 ml, 0.446 mmol, 2.0 equiv.) was added and stirred for another 10 min. This freshly prepared solution was added dropwise to a precooled (for temperature cf. individual descriptions) solution of the diaryl sulfoxide (0.223 mmol) in THF (1.0 ml). When the reaction was finished (typically 20 h), the reaction was stopped by the addition of MeOH (1 ml) and aqueous sat. NH_4Cl-solution (1 ml). The layers were separated and 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[33] to yield the title compound (for details on flash chromatography, yields, *ee*, and deviations from this procedure: cf. individual descriptions).

General Procedure for the Asymmetric Arylsulfinylation of 1.0 equiv. of $Alkyl_4Zn^{2\ominus}{}^{\oplus}$[Magnesio *N*-Methyl-(−)-ephedrinate]$_2$ – "Treatment C"

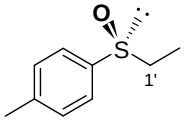
At room temp. $Alkyl_2Mg$ (solution in Et_2O, 0.82 ml, 0.446 mmol, 2.0 equiv.) was added dropwise to a solution of *N*-methyl-(−)-ephedrine (**18**, 80.0 mg, 0.446 mmol, 2.0 equiv.) in THF (1 ml). After 30 min $Alkyl_2Zn$ (solution in hexane, 0.24 ml, 0.223 mmol, 1.0 equiv.) was added and stirred for another 10 min. This freshly prepared solution was added dropwise to a precooled (for temperature cf. individual descriptions) solution of the diaryl sulfoxide (0.223 mmol) in THF (1.0 ml). When the reaction was finished (typically 20 h), the reaction was stopped by the addition of MeOH (1 ml) and aqueous sat. NH_4Cl-solution (1 ml). The layers were separated and 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[33] to yield the title compound (for details on flash chromatography, yields, *ee*, and deviations from this procedure: cf. individual descriptions).

(−)-(*S*)-Ethyl Phenyl Sulfoxide (9a)



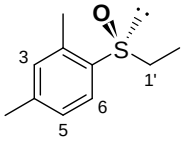
The asymmetric synthesis was accomplished at −40°C over 20 h either using 1.0 equiv. of $Et_3Zn^{\ominus}{}^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment A"** [except for using more sulfoxide (namely 80.0 mg, 0.396 mmol); which delivered (−)-(*S*)-**9a** (57.0 mg, 0.370 mmol, 93%, 62% *ee*)] or using 2.0 equiv. of $Et_3Zn^{\ominus}{}^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment B"** [except for using more sulfoxide (namely 80.0 mg, 0.396 mmol); which delivered (−)-(*S*)-**9a** (43.8 mg, 0.284 mmol, 72%, 63% *ee*)] or using 1.0 equiv. of $Et_4Zn^{2\ominus}{}^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**9a** (29.6 mg, 0.192 mmol, 86%, 69% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 55:45, fractions 27-42) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 1.20 (dd, $J_{2',1'-A} = J_{2',1'-B}$ = 7.4 Hz, 3H, 2'-H_3), AB signal (δ_A = 2.77, δ_B = 2.90, $J_{A,B}$ = 13.2 Hz, A part additionally split by q, $J_{1'-A,2'}$ = 7.4 Hz, 1'-H_A; B part additionally split by q, $J_{1'-B,2'}$ = 7.4 Hz, 1'-H_B), 7.48-7.56 (m, 3H, 3 × Ar-H), 7.59-7.65 ppm (m, 2H, 2 × Ar-H). The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralcel OD-3, *n*-heptane/*i*PrOH 96:4, 1 mL/min, $\lambda_{detector}$ = 208 nm): t_r(*R*) = 11.79 min, t_r(*S*) = 15.59 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = –125.3 (c = 1.32 in $CHCl_3$; a sample with 69% *ee* was used); ref.[39]: $[\alpha]_{589}^{20}$ = –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.[39]

(−)-(*S*)-Ethyl *p*Tolyl Sulfoxide (41)



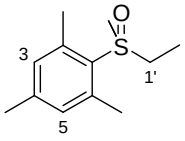
The asymmetric synthesis was accomplished at −40°C over 20 h either using 1.0 equiv. of $Et_3Zn^{\ominus}{}^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment A"** [which delivered (−)-(*S*)-**41** (13.0 mg, 77.0 µmol, 35%, 45% *ee*)], or using 2.0 equiv. of $Et_3Zn^{\ominus}{}^{\oplus}$[magnesio N-methyl-(−)-ephedrinate] under the conditions of **"Treatment B"** [which delivered (−)-(*S*)-**41** (35.3 mg, 0.210 mmol, 94%, 68% *ee*)], or using 1.0 equiv. of $Et_4Zn^{2\ominus}{}^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**41** (37.5 mg, 0.223 mmol, 100%, 65% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 50:50, fractions 18-29) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 1.19 (dd, $J_{2',1'-A} = J_{2',1'-B}$ = 7.4 Hz, 3H, 2'-H_3), AB signal (δ_A = 2.76, δ_B = 2.87, $J_{A,B}$ = 13.2 Hz, A part additionally split by q, $J_{1'-A,2'}$ = 7.4 Hz, 1'-H_A; B part additionally split by q, $J_{1'-B,2'}$ = 7.5 Hz, 1'-H_B), AA'BB' signal with signal centers at δ_A = 7.32 and δ_B = 7.50 ppm (4H, 2 × 2-H and 2 × 3-H). The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralcel OJ-H, *n*-heptane/EtOH 98:2, 1 mL/min, $\lambda_{detector}$ = 232 nm): t_r(*R*) = 17.13 min, t_r(*S*) = 20.26 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = –153.1 (c = 1.04 in $CHCl_3$; a sample with 68% *ee* was used); ref.[40]: $[\alpha]_{589}^{20}$ = –247 [*c* = 2.6 in $CHCl_3$, a sample of the (*S*)-enantiomer with 94% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[12b],[39]

(−)-(*S*)-(2,4-Dimethylphenyl) Ethyl Sulfoxide (42)



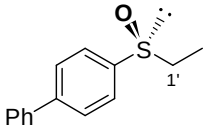
The asymmetric synthesis was accomplished at −40°C over 20 h using 1.0 equiv. of $Et_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**42** (20.4 mg, 0.112 mmol, 50%, 69% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 55:45, fractions 18-30) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 1.23 (dd, $J_{2',1'\text{-A}} = J_{2',1'\text{-B}}$ = 7.5 Hz, 3H, 2'-H_3), 2.34 (s, 3H, Ar-CH_3), 2.36 (s, 3H, Ar-CH_3), AB signal (δ_A = 2.71, δ_B = 2.86, $J_{A,B}$ = 13.3 Hz, A part additionally split by q, $J_{1'\text{-A},2'}$ = 7.4 Hz, 1'-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 7.5 Hz, 1'-H_B), 7.01 (m_c, 1H, 3-H), 7.22 (m_c, $J_{5,6}$ = 7.9 Hz, 1H, 5-H), 7.75 ppm (d, $J_{6',5'}$ = 8.1 Hz, 1H, 6-H). The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralpak AD-3, *n*-heptane/EtOH 90:10, 1 mL/min, $\lambda_{detector}$ = 204 nm): t_r(*R*) = 8.46 min, t_r(*S*) = 11.79 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = −193.6 (c = 0.55 in $CHCl_3$; a sample with 69% *ee* was used); ref.[12b]: $[\alpha]_{589}^{20}$ = −248.7 [*c* = 1.64 in EtOH, a sample of the (*S*)-enantiomer with 96% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[12b]

***rac*-Ethyl (2,4,6-Trimethylphenyl) Sulfoxide (43)**



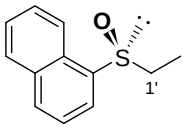
The synthesis was accomplished at room temp. over 20 h either using 1.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment A"** [which delivered rac-**43** (12.3 mg, 63.0 µmol, 28%)], or using 2.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment B"** [which delivered *rac*-**43** (27.1 mg, 0.138 mmol, 62%)], or using 1.0 equiv. of $Et_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered *rac*-**43** (31.2 mg, 0.159 mmol, 71%)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 55:45, fractions 21-31) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 1.28 (dd, $J_{2',1'\text{-A}} = J_{2',1\text{-B}}$ = 7.5 Hz, 3H, 2'-H_3), 2.28 (s, 3H, Ar-CH_3), 2.54 (s, 6H, 2 × Ar-CH_3), AB signal (δ_A = 2.94, δ_B = 3.22, $J_{A,B}$ = 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, $J_{1'\text{-B},2'}$ = 7.6 Hz, 1'-H_B), 6.86 ppm (s, 2H, 2 × Ar-H). The preceding data were reported by us earlier.[12b] 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(1) = 11.86 min, t_r(2) =19.57 min.

(−)-(*S*)-Ethyl (4-Phenylphenyl) Sulfoxide (44)



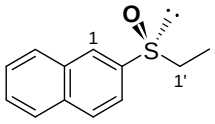
The asymmetric synthesis was accomplished at −78°C over 20 h either using 1.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment A"** [except for using more sulfoxide (namely 163.8 mg, 0.462 mmol); which delivered (−)-(*S*)-**44** (14.4 mg, 63.0 µmol, 14%, 86% *ee*)], or using 2.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment B"** [which delivered (−)-(*S*)-**44** (35.8 mg, 0.155 mmol, 70%, 79% *ee*)], or using 1.0 equiv. of $Et_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**44** (46.3 mg, 0.201 mmol, 90%, 82% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 50:50, fractions 18-30) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 1.24 (dd, $J_{2'',1''\text{-A}} = J_{2'',1''\text{-B}}$ = 7.4 Hz, 3H, 2''-H_3), AB signal (δ_A = 2.82, δ_B = 2.95, $J_{A,B}$ = 13.3 Hz, A part additionally split by q, $J_{1''\text{-A},2''}$ = 7.4 Hz, 1''-H_A; B part additionally split by q, $J_{1''\text{-B},2''}$ = 7.5 Hz, 1''-H_B), 7.37-7.42 (m, 1 H, 4'-H), 7.45-7.50 (m, 2H, 2 × 2'-H*), 7.59-7.62 (m, 2H, 2 × 3'-H*), AA'BB' signal with signal centers at δ_A = 7.68 and δ_B = 7.75 ppm (4H, 2 × 2-H and 2 × 3-H); *assignments interchangeable. The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralpak AD-3, *n*-heptane/*i*PrOH 95:5, 1 mL/min, $\lambda_{detector}$ = 269 nm): t_r(*S*) = 32.31 min, t_r(*R*) = 35.51 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = −207.3 (c = 1.59 in $CHCl_3$; a sample with 86% *ee* was used); ref.[12b]: $[\alpha]_{589}^{20}$ = −145.4 [*c* = 1.4 in EtOH, a sample of the (*S*)-enantiomer with 70% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[12b]

(−)-(*S*)-Ethyl (1-Naphthyl) Sulfoxide (45)



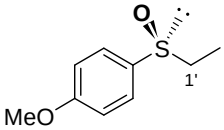
The asymmetric synthesis was accomplished at −78°C over 20 h using 1.0 equiv. of $Et_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**45** (23.0 mg, 0.113 mmol, 51%, 78% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 55:45, fractions 11-16) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$, the sample contains a trace of grease with s at 1.25 ppm): δ = 1.22 (dd, $J_{2',1'\text{-A}} = J_{2',1'\text{-B}}$ = 7.4 Hz, 3H, 2'-H_3), AB signal (δ_A = 2.85, δ_B = 3.12, $J_{A,B}$ = 13.6 Hz, A part additionally split q, $J_{1'\text{-A},2'}$ = 7.4 Hz, 1'-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 7.4 Hz, 1'-H_B), 7.58 (m_c, 2H, 2 × Ar-H), 7.67 (dd, ^3J = 8.2 Hz, ^3J = 7.0 Hz, 1H, 1 × Ar-H), 7.92-7.99 (m, 3H, 3 × Ar-H), 8.11 ppm (dd, ^3J = 7.2 Hz, ^4J = 1.2 Hz, 1H, 1 × Ar-H). The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralcel OJ-H, *n*-heptane/*i*PrOH 80:20, 1 mL/min, $\lambda_{detector}$ = 224 nm): t_r(*R*) = 6.85 min, t_r(*S*) = 7.62 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = −161.8 (c = 1.25 in $CHCl_3$; a sample with 78% *ee* was used); ref.[12b]: $[\alpha]_{589}^{20}$ = −248.7 [*c* = 1.40 in EtOH, a sample of the (*S*)-enantiomer with 93% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[12b]

(−)-(*S*)-Ethyl (2-Naphthyl) Sulfoxide (46)



The asymmetric synthesis was accomplished at −78°C over 20 h either using 1.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment A"** [which delivered (−)-(*S*)-**46** (5.0 mg, 25 µmol, 11%, 33% *ee*)], or using 2.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment B"** [which delivered (−)-(*S*)-**46** (3.5 mg, 17 µmol, 7%, 46% *ee*)], or using 1.0 equiv. of $Et_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**46** (29.4 mg, 0.144 mmol, 65%, 46% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 55:45, fractions 15-33) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 1.22 (dd, $J_{2',1'\text{-A}} = J_{2',1'\text{-B}}$ = 7.5 Hz, 3H, 2'-H_3), AB signal (δ_A = 2.84, δ_B = 3.00, $J_{A,B}$ = 13.3 Hz, A part additionally split by q, $J_{1'\text{-A},2'}$ = 7.4 Hz, 1'-H_A; B part additionally split by q, $J_{1'\text{-B},2'}$ = 7.5 Hz, 1'-H_B), 7.55-7.62 (m, 3H, 3 × Ar-H), 7.89-7.99 (m, 3H, 3 × Ar-H), 8.18 ppm (d, $J_{1,8}$ = 1.8 Hz, 1H, 1-H). The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralcel OJ-H, *n*-heptane/EtOH 95:5, 1 mL/min, $\lambda_{detector}$ = 232 nm): t_r(*R*) = 16.12 min, t_r(*S*) = 16.90 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = −75.3 (c = 0.59 in $CHCl_3$; a sample with 46% *ee* was used); ref.[12b]: $[\alpha]_{589}^{20}$ = −99.8 [*c* = 0.49 in EtOH, a sample of the (*S*)-enantiomer with 66% *ee*] or ref.[39]: $[\alpha]_{589}^{20}$ = −180.5 [*c* = 1.3 in acetone, 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.[12b],[39]

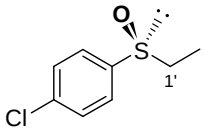
(−)-(*S*)-Ethyl (4-Methoxyphenyl) Sulfoxide (47)



The asymmetric synthesis was accomplished at −40°C over 20 h either using 2.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment B"** [which delivered (−)-(*S*)-**47** (22.3 mg, 0.131 mmol, 58%, 78% *ee*)], or using 1.0 equiv. of $Et_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**47** (29.8 mg, 0.175 mmol, 79%, 57% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 40:60,

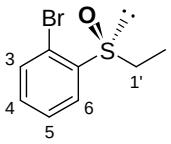
fractions 23-34) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 1.18 (dd, $J_{2',1'\text{-}A} = J_{2',1'\text{-}B}$ = 7.5 Hz, 3H, 2'-H_3), AB signal (δ_A = 2.78, δ_B = 2.84, $J_{A,B}$ = 13.1 Hz, A part additionally split q, $J_{1'\text{-}A,2'}$ = 7.5 Hz, 1'-H_A; B part additionally split by q, $J_{1'\text{-}B,2'}$ = 7.5 Hz, 1'-H_B), 3.86 (s, 3H, O-CH_3), AA'BB' signal with signal centers at δ_A = 7.03 and δ_B = 7.55 ppm (4H, 2 × 2-H and 2 × 3-H). The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralcel OD-3, *n*-heptane/*i*PrOH 96:4, 1 mL/min, $\lambda_{detector}$ = 204 nm): t_r(*R*) = 10.68 min, t_r(*S*) = 22.65 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = –139.3 (c = 0.70 in $CHCl_3$; a sample with 78% *ee* was used); ref.[12b]: $[\alpha]_{589}^{20}$ = –161.8 [*c* = 0.82 in EtOH, a sample of the (*S*)-enantiomer with 81% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[12b]

(–)-(*S*)-(4-Chlorophenyl) Ethyl Sulfoxide (48)



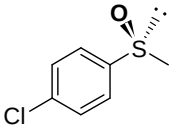
The asymmetric synthesis was accomplished at −78°C over 20 h either using 1.0 equiv. of $Et_3Zn^{\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment A"** [except for using more sulfoxide (namely 131 mg, 0.483 mmol); which delivered (−)-(*S*)-**48**(64.3 mg, 0.341 mmol, 71%, 80% *ee*)], or using 2.0 equiv. $Et_3Zn^{\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate] under the conditions of **"Treatment B"** [which delivered (−)-(*S*)-**48** (41.9 mg, 0.222 mmol, 100%, 82% *ee*)], or using 1.0 equiv. of $Et_4Zn^{2\ominus}$ $^{\oplus}$[magnesio N-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**48** (36.8 mg, 0.195 mmol, 87%, 84% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 55:45, fractions 18-33) and obtained as a colorless oil. **^{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, 3H, 2'-H_3), AB signal (δ_A = 2.74, δ_B = 2.90, $J_{A,B}$ = 13.3 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), AA'BB' signal with signal centers at δ_A = 7.50 and δ_B = 7.56 ppm (4H, 2 × 2-H and 2 × 3-H). The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralpak AD-3, *n*-heptane/EtOH 95:5, 1 mL/min, $\lambda_{detector}$ = 230 nm): t_r(*S*) = 14.96 min, t_r(*R*) = 17.64 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = –167.2 (c = 0.87 in $CHCl_3$; a sample with 84% *ee* was used); ref.[12b]: $[\alpha]_{589}^{20}$ = –161.8 [*c* = 0.82 in EtOH, a sample of the (*S*)-enantiomer with 81% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[12b]

(–)-(*S*)-(2-Bromophenyl) EthylSulfoxide (49)



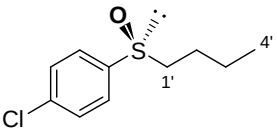
The asymmetric synthesis was accomplished at −78°C over 20 h using 1.0 equiv. of $Et_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**49** (24.5 mg, 0.105 mmol, 47%, 47% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 70:30, fractions 12-17) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 1.25 (dd, $J_{2',1'\text{-}A} = J_{2',1'\text{-}B}$ = 7.4 Hz, 3H, 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, $J_{1'\text{-}B,2'}$ = 7.5 Hz, 1'-H_B), 7.36 (ddd, ^3J = 8.8 Hz, ^3J = 7.7 Hz, ^4J = 1.7 Hz, 1H, 4- or 5-H), 7.52-7.58 (m, 2H, 2 × Ar-H), 7.86 ppm (dd, ^3J = 8.2 Hz, ^4J = 1.9 Hz, 1H, 3- or 6-H). The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralpak AD-3, *n*-heptane/EtOH 95:5, 1 mL/min, $\lambda_{detector}$ = 204 nm): t_r(*S*) = 8.90 min, t_r(*R*) = 12.18 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = –122.4 (c = 2.01 in $CHCl_3$; a sample with 47% *ee* was used); ref.[12b]: $[\alpha]_{589}^{20}$ = –239.5 [*c* = 0.62 in EtOH, a sample of the (*S*)-enantiomer with 89% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[12b]

(–)-(*S*)-(4-Chlorophenyl) Methyl Sulfoxide (51)



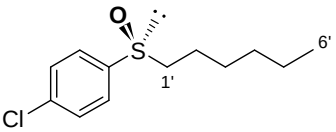
The **racemic synthesis** was accomplished by mixing MeMgCl (2.37 M in THF, 0.26 ml, 0.615 mmol, 1.0 equiv.) with bis(4-chlorophenyl) sulfoxide (167 mg, 0.615 mmol) in THF (2 ml) at room temperature. After 1 h the mixture was quenched by the addition of aqueous sat. NH_4Cl-solution (2 ml). The workup was carried out in analogy to the asymmetric synthesis (cf. general procedures above). This led to *rac*-**51** (48.7 mg, 0.279 mmol, 45%). The **asymmetric synthesis** was accomplished at 0°C over 20 h using 1.0 equiv. of $Me_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**51** (19.5 mg, 0.112 mmol, 50%, 52% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 50:50, fractions 23-39) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 2.72 (s, 3H, CH_3), AA'BB'-signal with signal centers at 7.51 and 7.60 ppm (4H, 4 × Ar-H). The preceding data are consistent with those reported in the literature.[41] The *ee* was determined by **chiral HPLC** (LC-3, *n*-heptane/EtOH 85:15, 0.8 mL/min, $\lambda_{detector}$ = 254 nm): t_r(*R*) = 8.98 min, t_r(*S*) = 10.05 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = –44.5 (c = 1.10 in $CHCl_3$; a sample with 52% *ee* was used); ref.[42]: $[\alpha]_{589}^{20}$ = –152.6 [*c* = 0.95 in $CHCl_3$, a sample of the (*S*)-enantiomer with 89% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[42]

(–)-(*S*)-Butyl (4-Chlorophenyl) Sulfoxide (52)



The asymmetric synthesis was accomplished at −78°C over 20 h using 1.0 equiv. of $Bu_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**52** (40.4 mg, 0.186 mmol, 83%, 83% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 75:25, fractions 15-27) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 0.92 (t, $J_{4',3'}$ = 7.5 Hz, 3H, 4'-H_3), 1.35-1.81 (m, 4H, 2'- and 3'-H_2), 2.74-2.80 (m, 2H, 1'-H_2), AA'BB' signal with signal centers at δ_A = 7.50 and δ_B = 7.56 ppm (4H, 2 × 2-H and 2 × 3-H). The preceding data were reported by us earlier.[12b] The *ee* was determined by **chiral HPLC** (Chiralcel OD-3, *n*-heptane/*i*PrOH 96:4, 1.0 mL/min, $\lambda_{detector}$ = 222 nm): t_r(*R*) = 8.30 min, t_r(*S*) = 9.75 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = –121.5 (c = 3.40 in $CHCl_3$; a sample with 52% *ee* was used); ref.[12b]: $[\alpha]_{589}^{20}$ = –61.1 [*c* = 0.90 in EtOH, a sample of the (*S*)-enantiomer with 29% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[12b]

(–)-(*S*)-(4-Chlorophenyl) Hexyl Sulfoxide (53)



The **racemic synthesis** was accomplished by mixing HexLi (2.54 M in hexane, 0.24 ml, 0.597 mmol, 1.0 equiv.) with bis(4-chlorophenyl) sulfoxide (162 mg, 0.597 mmol) in THF (2 ml) at room temperature. After 1 h the mixture was quenched by the addition of aqueous sat. NH_4Cl-solution (2 ml). The workup was carried out in analogy to the asymmetric synthesis (cf. general procedures above). This led to *rac*-**53** (117 mg, 0.448 mmol, 80%). The **asymmetric synthesis** was accomplished at −78°C over 20 h using 1.0 equiv. $Hex_4Zn^{2\ominus}$ $^{\oplus}$[magnesio *N*-methyl-(−)-ephedrinate]$_2$ under the conditions of **"Treatment C"** [which delivered (−)-(*S*)-**53** (53.6 mg, 0.219 mmol, 98%, 29% *ee*)]. This product was purified by flash chromatography on silica gel[33] (3 cm, 20 ml, *c*-C_6H_{12}:AcOEt 75:25, fractions 15-27) and obtained as a colorless oil. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 0.87 (m_c, 3H, 6-H_3), 1.18-1.83 (m, 8H, 2-H_2 to 5-H_2), 2.77 (m_c, 2H, 1-H_2), AA'BB'-signal with signal centers at 7.50 and 7.56 ppm (4H, 4 × Ar-H). The literature spectrum was measured in CCl_4.[43] The *ee* was determined by **chiral HPLC** (Chiralcel OD-3, *n*-heptane/*i*PrOH 96:4, 1.0 mL/min, $\lambda_{detector}$ = 222 nm): t_r(*R*) = 8.30 min, t_r(*S*) = 9.75 min. **Optical rotation:** $[\alpha]_{589}^{20}$ = –121.5

(c = 3.40 in $CHCl_3$; a sample with 52% *ee* was used). The **absolute configuration was determined by chemical correlation:**[44] PhMgBr (2.7 M in Et_2O, 80 µl, 0.21 mmol) was added dropwise to a solution of (−)-**53** (19.0 mg, 78.0 µmol) in THF (0.5 ml) at room temperature. After 3 h the reaction was quenched by the addition of aqueous sat. NH_4Cl-solution (1 ml). The layers were separated and 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[33] (1.5 cm, 8 ml, *c*-C_6H_{12}:AcOEt 92:8, fractions 34-46) to yield (+)-(*R*)-hexyl phenyl sulfoxide (5.3 mg, 25 µmol, 32%) as a colorless oil. Since such a sulfinylation is known to proceed under inversion of the configuration[44], the starting material (−)-**53** had to be (*S*)-configured. **^{1}H NMR** (300.1 MHz, $CDCl_3$): δ = 0.86 (m_c, 3H, 6'-H_3), 1.20-1.77 (m, 8H, 2'-, 3'-, 4'-, and 5'-H_2), 2.75-2.81 (m, 2H, 1'-H_2), 7.47-7.55 (m, 3H, 3 × Ar-H), 7.59-7.64 ppm (m, 2H, 2 × Ar-H). The preceding data are consistent with those reported in the literature.[45] **:** $[\alpha]_{589}^{20}$ = +38.3 (c = 0.37 in $CHCl_3$); ref.[46]: $[\alpha]_{589}^{20}$ = +37.6 [*c* = 0.25 in $CHCl_3$, a sample of the (*R*)-enantiomer with 25% *ee*]. The absolute configuration was determined by comparing the sense of the optical rotation with literature data.[45]

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Keywords: desymmetrization • enantioselectivity • ephedrine • organozincates • sulfinylation • sulfoxides • sulfoxide-zinc exchange

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[21] The β-aminoalcohols and the diaryl sulfoxides were dissolved in THF. The dialkylmagnesium reagents were used as solutions in Et_2O and the dialkylzinc reagents as solutions in *n*-hexane. As a result, our sulfinylations were performed in mixtures of THF, Et_2O, and *n*-hexane wherein THF represented the major component.

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[32] The zincates used for the study of Scheme 2 were prepared like their Et-containing antecessor **40**: 2.0 equiv. of *N*-methyl-(−)-ephedrine (**18**) were deprotonated with 2.0 equiv. of $Alkyl_2Mg$ in THF at room temperature. After 30 min 1.0 equiv. of $Alkyl_2Zn$ was added. After another 10 min, this solution was added dropwise to a precooled solution of bis(4-chlorophenyl) sulfoxide (**50**) in THF.
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