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Asymmetric Synthesis of 1,3-Diamines. II: Diastereoselective Reduction of Atropisomeric *N-tert*-Butanesulfinylketimines

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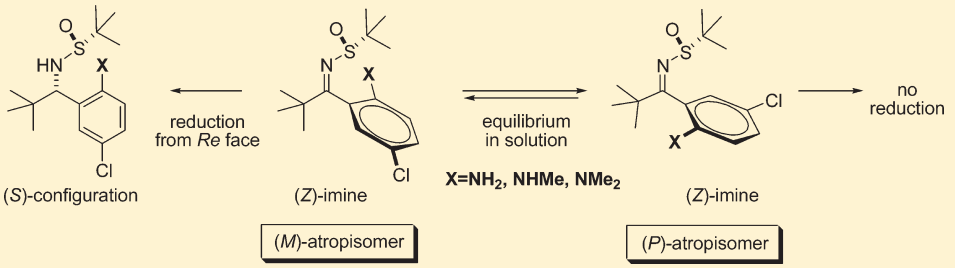
Supporting Information

ABSTRACT:



Chiral, nonracemic *o*-aminobenzylamines were prepared in a highly diastereoselective reduction of atropisomeric *N-tert*-butanesulfinylketimines. The ortho-substituent ensures the distinct reactivity of atropisomers **4d**−**f**. The free energy of activation for atropisomerization of sulfinylimines **4d**−**f** in THF-d_8 was determined by NMR methods to range from 70.8 to 97.9 kJ/mol.

INTRODUCTION

Chiral, nonracemic α-methylbenzylamines have found numerous applications in asymmetric synthesis.[1] Introduction of an ortho-substituent often enhances enantioselectivity and endows this chiral entity with 1,3-bidentate properties, thus considerably expanding the scope of potential applications. Thus, enantiopure *o*-hydroxybenzylamines[2] have been employed as chiral ligands for asymmetric addition of dialkyl zinc reagents to aldehydes[3] and in the enantioselective reduction of ketones,[4] whereas *o*-methoxybenzylamines have been used in the design of highly efficient phosphoramidite ligands for Ir-catalyzed asymmetric allylic substitution reaction.[5] Furthermore, chiral *o*-phosphinobenzylamines are useful bidentate ligands for enantioselective hydrogenation.[6] Finally, *o*-aminobenzylamines have also been employed as efficient chiral catalysts[7] and chiral reagents.[8] However, even broader application of *o*-aminobenzylamines in asymmetric synthesis has been hampered by lack of convenient methods for their preparation.

Herein we report an efficient approach toward chiral, nonracemic *o*-aminobenzylamines **1**, **2** (Figure 1) via the diastereoselective reduction of *N-tert*-butanesulfinylketimines.[9,10] This study was stimulated by our recent demonstration of unusual directing effects by the ortho-substituent in the diastereoselective reduction of *N-tert*-butanesulfinylketimines.[11] Thus, we showed that the ortho-substituent controls the *E*/*Z* geometry of diaryl *N-tert*-butanesulfinylketimines and established that there is a correlation between facial selectivity of the reduction and the *E*/*Z* geometry of the starting ketimines. Our new investigation reinforces the observed correlation by increasing the structural diversity of ketimines as well as provides additional insights into the relationship between the reactivity and structure of *N-tert*-butanesulfinylketimines. In particular, we demonstrate herein the distinct reactivity of configurationally stable atropisomers of *N-tert*-butanesulfinylketimines in the diastereoselective reduction with representative hydride reducing agents.

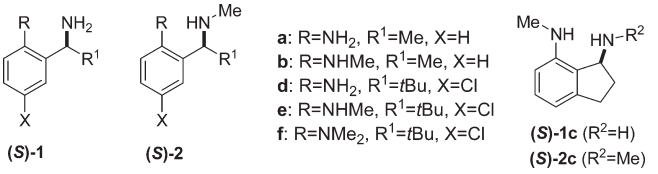


Figure 1. Target diamines **1** and **2**.

RESULTS AND DISCUSSION

Synthesis and Structural Analysis of Sulfinylimines 4a−f. Following the procedure reported in the literature,[12] heating of ketones **3a**−**e**[13] with (R_S)-*tert*-butanesulfinamide at 75 °C in the presence of Ti(OEt)$_4$ (Scheme 1) afforded sulfinylimines **4a**−**e**. Sulfinylimine **4f** could not be synthesized in the reaction of ketone **3f** with (R_S)-*tert*-butanesulfinamide even under forcing conditions (heating at 120 °C in Ti(OEt)$_4$ without solvent). Therefore, **4f** was obtained from (*Z*)-**4e** by a deprotonation−alkylation sequence (Scheme 1).

Sulfinylimines **4a**,**b** were formed as *E*-isomers (entries 1 and 2, Table 1) as evidenced by the X-ray crystallographic analysis. The

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formation of *E*-sulfinylimines **4a,b** is noteworthy because structurally related ortho-substituted acetophenone imines favor the opposite, i.e. *Z*-geometry.[14] The preference for *E*-isomers of sulfinylimines **4a,b** was attributed to stabilization by an intramolecular hydrogen bond between the nitrogen of the aniline and that of the imino group, as evidenced by the 2.66−2.68 Å distance[15] between the two nitrogens in crystal lattices of sulfinylimines **4a,b** (see N1−N2 distances in entries 1 and2, Table 1). The intramolecular hydrogen bond enforces a *syn*-periplanar relationship between the aniline ring and the C=N bond of the imines **4a,b** (see C1−C2−C3−N2 torsion angles, Table 1), and places the sulfoxide moiety in the trans position.[16] As anticipated, sulfinylimine **4c** was obtained as *E*-isomer. *Z*-geometry is unfavorable because of nonbonded steric interactions between the ortho-substituent and the sulfinylimine moiety in the conformationally fixed 2,3-dihydro-1*H*-indene scaffold.

Surprisingly, the structurally related sulfinylimines **4d−f** exist as *Z*-isomers in the crystalline form as evidenced by X-ray analysis (entries 3−5, Table 1). Apparently, the *E* geometry of sulfinylimines **4d−f** is unfavorable due to the nonbonded steric interactions between the bulky chiral auxiliary and the *tert*-butyl group of the imine moiety. Hence, the stabilization by the intramolecular hydrogen bond between the nitrogen of the aniline and that of the sulfinyl group is overriden by steric interactions in sulfinylimines (*Z*)-**4d−e**. In the observed *Z* geometry, *tert*-butyl groups are positioned mutually trans with respect to the C=N bond, and the ortho-substituted phenyl moieties of imines **4d−f** are twisted out of the C=N plane (see C1−C2−C3−N2 torsion angles, Table 1). Furthermore, sulfinylimine (Z)-**4e** exists as a 1:1 mixture of (*M*) and (*P*) atropisomers in the crystal lattice, apparently because of a hindered rotation about the aryl-imine axis. By intriguing contrast, individual crystals of sulfinylimines (*Z*)-**4d** and (*Z*)-**4f** were obtained exclusively as the (*M*)-atropisomers (see Table 1).

(*E*)-Sulfinylimines **4a,b** were the only species observed in THF-d_8 and $CDCl_3$ solutions at ambient temperature. The absence of (*Z*)-**4a,b** isomers (within NMR detection limits) suggests a high configurational stability of the *E*-isomers in various solvents, apparently owing to the stabilizing effect of the intramolecular hydrogen bond. On the other hand, sterically hindered sulfinylimines **4d−f** existed solely as the (*Z*)-isomers in THF-d_8 solution. Furthermore, each of the sulfinylimines (*Z*)-**4d−f** appeared as a mixture of (*M*) and (*P*) atropisomers. Thus, when a single crystalline atropisomer (*Z*)-(*M*)-**4d** was dissolved in THF-d_8 at room temperature, the ^{1}H NMR spectrum of the resulting suspension showed two sets of signals in a ratio of 78:22.[17] Likewise, a 79:21 ratio of isomers was formed when the crystalline 1:1 mixture of (*Z*)-**4e** atropisomers was dissolved in THF-d_8.

Crystalline atropisomer (*Z*)-(*M*)-**4f** displayed high configurational stability in THF-d_8 solution at −15 °C, and none of the isomeric (*Z*)-(*P*)-**4f** was observed after 24 h. However, isomerization to a 1:1 equilibrium mixture of atropisomers (*Z*)-(*M*)-**4f** and (*Z*)-(*P*)-**4f** occurred within 6 h at room temperature.[18] Remarkably, the atropisomers of (*Z*)-**4f** could be easily separated by chromatography on silica gel. The individual atropisomers (*Z*)-(*M*)-**4f** and (*Z*)-(*P*)-**4f** are stable in the crystalline form at −18 °C for more than three weeks.

Scheme 1. Preparation of Sulfinylimines 4a−f

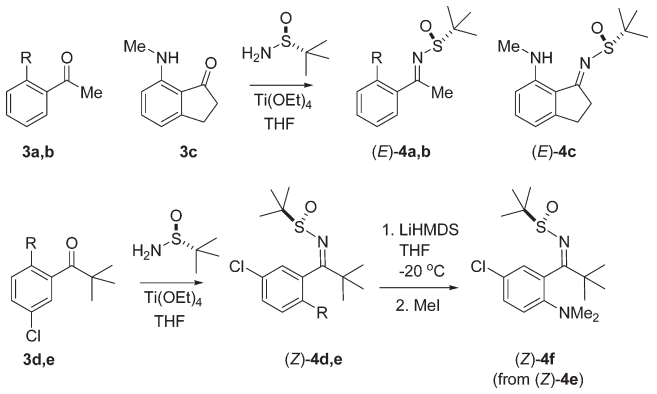
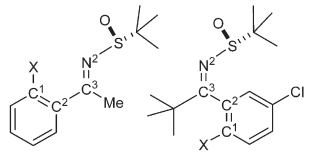


Table 1. Selected Crystallographic Parameters for Sulfinylketimines 4a,b,d−f



(*E*)-**4a**: X=NH_2 (*Z*)-**4d**: X=NH_2
(*E*)-**4b**: X=NHMe (*Z*)-**4e**: X=NHMe
(*Z*)-**4f**: X=NMe_2

entry	imine (R_S)-**4**	N^1-N^2 (Å)	$C^1-C^2-C^3-N^2$ torsion angle	C^3-N^2-S-O torsion angle
1	(*E*)-**4a**	2.683	−10.9	−138.9
2	(*E*)-**4b**	2.658	6.3	−140.6
3	(*Z*)-**4d**[a]		−77.9	−82.5
4	(*Z*)-**4e**[b]		79.7 (*P*)	−95.5 (*P*)
			−84.1 (*M*)	−102.0 (*M*)
5	(*Z*)-**4f**[a]		−111.2[c]	−93.5[c]

[a] Crystallized as individual (*M*)-atropisomer. [b] Crystallized as 1:1 mixture of (*M*):(*P*) atropisomers in the unit cell. [c] Average values of two molecules crystallized in a unit cell.

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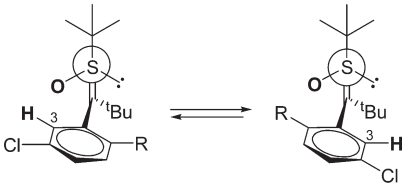
Table 2. Rate Constants and Free Energy of Activation for Atropisomerization of Sulfonylketimines (*Z*)-4d−f in THF-d_8



(*Z*)-(*M*, R_S)-**4d-f** (*Z*)-(*P*, R_S)-**4d-f**

				(*P*) → (*M*)		(*M*) → (*P*)		
entry	imine	R	(*M*):(*P*) ratio, %	*k*, s^{-1}	$\Delta G^{\ddagger}_{258}$ (kJ/mol)	k_{-1}, s^{-1}	$\Delta(\Delta G^{\ddagger}_{258})$, kJ/mol	$\Delta G^{\ddagger}_{258}$ (kJ/mol)
1	(*Z*)-**4d**	NH_2	22:78[a]	62×10^{-4}	73.8	221×10^{-4}	71.1	2.7
2	(*Z*)-**4e**	NHMe	21:79[a]	66×10^{-4}	73.7	247×10^{-4}	70.8	2.9
3	(*Z*)-**4f**	NMe_2	1:1[b]	0.45×10^{-4}	97.9[c]	0.45×10^{-4}	97.9[c]	0

[a] Determined in THF-d_8 at 258 K by NMR. [b] Determined in THF-d_8 at 298 °C by NMR. [c] Corresponds to $\Delta G^{\ddagger}_{298}$ (kJ/mol).

The structural assignment of atropisomers (*Z*)-**4d,e** in *solution* was based on the differences in chemical shifts of H-3 and C-3 between the (*M*) and (*P*) atropisomeric series. Thus, the corresponding signals in the case of stable atropisomer (*Z*)-(*M*)-**4f**[19] appeared downfield compared with those in the isomeric (*Z*)-(*P*)-**4f**, apparently due to the deshielding of the ortho-position by the sulfoxide oxygen (see Newman projections in the graphic of Table 2).[20] Similar differences between the chemical shifts of H-3 and C-3 were observed also for all atropisomeric sulfinylimines (*Z*)-**4d**−**f** ($\Delta\delta[^1H]$ = 0.03−0.05 ppm, $\Delta\delta[^{13}C]$ = 1.5−2.6 ppm).[21] Consequently, the major atropisomers (*Z*)-**4d,e** in solution were assigned (*P*) geometry. The predominance of (*P*) atropisomers of (*Z*)-**4d,e** in solution was further supported by DFT calculations by using a B3LYP/6-31G(d,p) basis set.[22] Accordingly, (*Z*)-(*P*)-**4e** was calculated to be more stable by 4.7 kJ/mol than the isomeric (*Z*)-(*M*)-**4e**.

To account for the observed fast interconversion of sulfinylimines (*Z*)-**4d,e** in solutions, the free energy of activation and rate constants for the atropisomerization of (*Z*)-**4d**−**f** were determined in THF-d_8 by NMR methods.[23] Barriers to the rotation around the aryl-imine bond of (*Z*)-**4d,e** isomers in THF-d_8 varied from 70.8 to 73.8 kJ/mol (see Table 2), values that are comparable to the isomerization barriers of related aryl ketimines.[24] The observed ground-state energy differences ($\Delta\Delta G^{\ddagger}_{258}$) correlate well with the equilibrium ratio of atropisomers in THF-d_8 (Table 2). The atropisomerization barrier for (*Z*)-**4f** in THF-d_8 was determined to be 97.9 kJ/mol (see Table 2), which is considerably higher than the interconversion barriers for (*Z*)-**4d,e** and comparable to the atropisomerization barriers of the most hindered (*Z*)-ketimines.[25]

Diastereoselective Reduction of Sulfinylimines 4a−f. The reduction of imines **4a**−**f** was carried out by using BH_3·THF or DIBAL at −78 °C in THF (Table 3, conditions A and B, respectively). Both reducing agents ensured excellent levels of diastereoselectivity. Furthermore, the purity of the major diastereomers **5a**−**f** could be readily increased to >99:1 dr by flash column chromatography.

The relative configuration at the newly created asymmetric carbon was determined for reduction products **5a,b,d,e** as well as for derivatives **6c** and **7f** by X-ray crystallographic analysis. Sulfinylamides **5a**−**c** were formed with the *R* absolute configuration at the newly created asymmetric center, whereas reduction products **5d**−**f** possessed the *S* configuration. These results reinforced previously reported correlation between the sense of asymmetric induction and the favored *E* or *Z* configuration of the starting imines **4a**−**f**.[11] Accordingly, the reduction of (*E*)-**4a**−**c** resulted in formation of (R_S,*R*)-**5a**−**c** whereas (*Z*)-**4d**−**f** afforded sulfinylamides (R_S,*S*)-**5d**−**f**.

The correlation between the facial selectivity of the reduction and *E* or *Z* geometry of the starting ketimines implies the involvement of a cyclic transition state for the reduction. Consequently, a chelation-controlled reduction mechanism[26] is proposed, where borane or DIBAL forms an "ate" complex with sulfinyl oxygen,[27] ensuring the internal sulfoxide-mediated delivery of hydride from the *Si* face (for (*E*)-**4a**−**c**) or from the *Re* face (for imines (*Z*)-**4d**−**f**) of the C═N bond (Figure 2, TS-1). Less likely is an alternative mechanism, where the NMe_2 group of the aniline controls the diastereoselectivity by forming a covalent N−B bond with the BH_3−THF or N−Al bond with DIBAL. In the latter case, the internal hydride transfer from (*Z*)-(*M*)-**4f** derived amidometallohydrides must occur from the *Si* face and afford the reduction products with (*R*) configuration at the newly created stereogenic center. In fact, (*Z*)-(*M*)-**4f** was reduced with DIBAL to (R_S,*S*)-**5f** with (*S*) configuration (99% conversion, 99:1 dr), and the outcome is consistent with the involvement of sulfinyl oxygen in the transient "ate" complex (Figure 2, TS-1).

Notably, the isomeric sulfinylimine (*Z*)-(*P*)-**4f** was completely unreactive in the reduction with DIBAL (Table 3, entries 16 vs 13). Thus, (*Z*)-(*P*)-**4f** did not react with BH_3·THF at −15 °C within 3 h, whereas (*Z*)-(*M*)-**4f** was reduced in 47% yield (dr = 99:1) (Table 3, entries 12 vs 15). After 22 h at −15 °C the conversion of (*Z*)-(*M*)-**4f** increased to 88%, but (*Z*)-(*P*)-**4f** still was not reduced.[28] The reluctance of (*Z*)-(*P*)-**4f** to undergo reduction by BH_3·THF or DIBAL presumably results from steric shielding of the sulfinylimine *Re* face by the *o*-dimethylamino group (TS-2, Figure 2) together with high configurational stability of (*Z*)-**4f** atropisomers under the reduction conditions.[29] Eventually, sulfinylimine (*Z*)-(*P*)-**4f** could be reduced with BH_3·THF at room temperature (2 h, 75% conversion, 99:1 dr). In the latter case, however, isomerization of (*Z*)-(*P*)-**4f** to the more reactive atropisomer (*Z*)-(*M*)-**4f** apparently took place.[30]

Steric hindrance of the *Re*-face presumably would also occur in the structurally closely related sulfinylimines (*Z*)-(*P*)-**4d,e** (see TS-2, Figure 2), rendering them unreactive under the reduction

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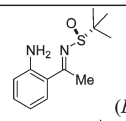
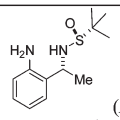
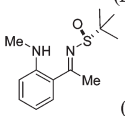
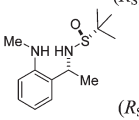
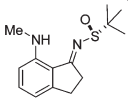
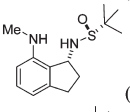
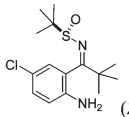
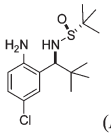
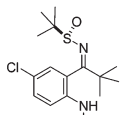
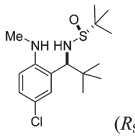
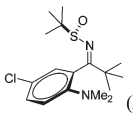
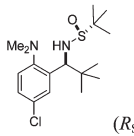
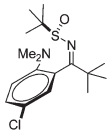
Table 3. Diastereoselective Reduction of *tert*-Butanesulfinylimines 4a−f

Entry	Imine (R_S)-4[a]	*Z*:*E* ratio in THF[b] (%)	Reduction conditions[c]	d.r.[d]	Major diastereomer 5[e]	Yield,[f] %
1	 (*E*)-**4a**	1:99	A	97:3	 (R_S,*R*)-**5a**	(99)
2			B	93:7		88 (99)
3	 (*E*)-**4b**	1:99	A	99:1	 (R_S,*R*)-**5b**	(99)
4			B	99:1		97 (99)
5	 (*E*)-**4c**	1:99	A	99:1	 (R_S,*R*)-**5c**[g]	(99)
6			B	99:1		94 (99)
7	 (*Z*)-**4d**	99:1	A	99:1	 (R_S,*S*)-**5d**	(99)
8			B	99:1		99
9	 (*Z*)-**4e**	99:1	A	89:11	 (R_S,*S*)-**5e**[h]	90
10			B	99:1		(47)[i]
11	 (*Z*)-(*M*)-**4f**	99:1	A	-		0
12			A1	99:1	 (R_S,*S*)-**5f**[j]	(47)
13			B	99:1		97 (99)
14	 (*Z*)-(*P*)-**4f**	99:1	A	-		(0)
15			A1	-		(0)
16			B	-		(0)

[a] Geometry of the C=N bond in crystalline material was determined by X-ray crystallographic analysis. [b] The *E*/*Z* ratio in THF-d_8 was determined at −15 °C by NOESY experiments. [c] Conditions A: BH_3·THF (1.6 equiv), −78 °C, THF, 3 h. Conditions A1: BH_3·THF (1.6 equiv), −15 °C, THF, 3 h. Conditions B: DIBAL (3 equiv), −78 °C, THF, 3 h. [d] Determined by ^{1}H NMR and HPLC assay for the crude reduction mixture. [e] Relative configuration of the major diastereomer **5** was determined by X-ray crystallographic analysis. [f] Yield of major diastereomer. In parentheses: conversion of imines **4a**−**f**. [g] Relative configuration was determined by X-ray crystallographic analysis of (R_S,*R*)-**6c**. [h] X-ray analysis was performed for the minor diastereomer (R_S,*R*)-**5e**. [i] 96% yield and 99:1 dr was obtained in the reduction with DIBAL at room temperature. [j] Relative configuration was determined by X-ray crystallographic analysis of *S*-methyl sulfoximine (R_S,*S*)-**7f**.

conditions. However, the differences in the reduction rates of atropisomers (*Z*)-(*M*)-**4d,e** and (*Z*)-(*P*)-**4d,e** cannot be determined because fast atropisomerization occurs under the reduction conditions.[31] The fast isomerization of sulfinylimines (*Z*)-**4d,e** apparently accounts for the excellent diastereoselectivities of the reduction. Thus, the 99:1 diastereomer ratio of (R_S,*S*)-**5d,e** (Table 3, entries 7−10) exceeds the ∼4:1 equilibrium ratio of (*Z*)-(*P*)-**4d,e** and (*Z*)-(*M*)-**4f** in solution (see Table 2).

The isomeric (*E*)-sulfinylimines **4a**−**c** afforded sulfinylamides (R_S,*R*)-**5a**−**c** with the opposite, i.e. (*R*) absolute configuration (Table 3). On the basis of our previous observations a cyclic transition state involving internal sulfoxide-mediated delivery of borane is proposed. The intramolecular hydrogen bond between the aniline N−H and nitrogen of the imine stabilizes the favored *E* conformation of sulfinylimines **4a,b** in the transition state (TS-3).

Elaboration of Sulfinamides 5a−f To Target Diamines 1, 2. Following the procedure reported previously,[11] sulfinamides **5a**−**c** were treated with 4 N HCl in dioxane to obtain (*R*)-**1a**−**c** in excellent yields (see Scheme 2). The cleavage of the chiral auxiliary occurred without racemization of the newly created stereogenic center. To access the corresponding *N*-methyl derivatives (*R*)-**2a**−**c**, introduction of an *N*-methyl group at the benzylic nitrogen was performed before the removal of the chiral auxiliary from (R_S,*R*)-**5a**−**c**. This allowed regioselective *N*-lithiation of sulfonamide N−H in (R_S,*R*)-**5a**−**c** with LiHMDS without interference by aniline N−H, and subsequent addition of iodomethane gave the desired (R_S,*R*)-**6a**−**c**. On the other hand, a similar lithiation/methylation sequence from sulfinamides (R_S,*S*)-**5d**−**f** afforded the *S*-methyl sulfoximines (R_S,*S*)-**7e**−**f** instead of the anticipated *N*-methyl sulfinamides (Scheme 2).[32] This change from *N*- to *S*-methylation was attributed to considerable steric hindrance near the sulfinyl nitrogen in sulfinamides (R_S,*S*)-**5d**−**f**. Therefore, the desired (*S*)-**2d**−**f** were synthesized by an alternative sequence starting with the desulfinylation of (R_S,*S*)-**5d**−**f** to benzylamines (*S*)-**1d**−**f**, followed by an *N*-formylation−reduction sequence (Scheme 2).

CONCLUSIONS

Synthesis of chiral, nonracemic *o*-aminobenzylamines **1** and **2** employed highly diastereoselective reduction of

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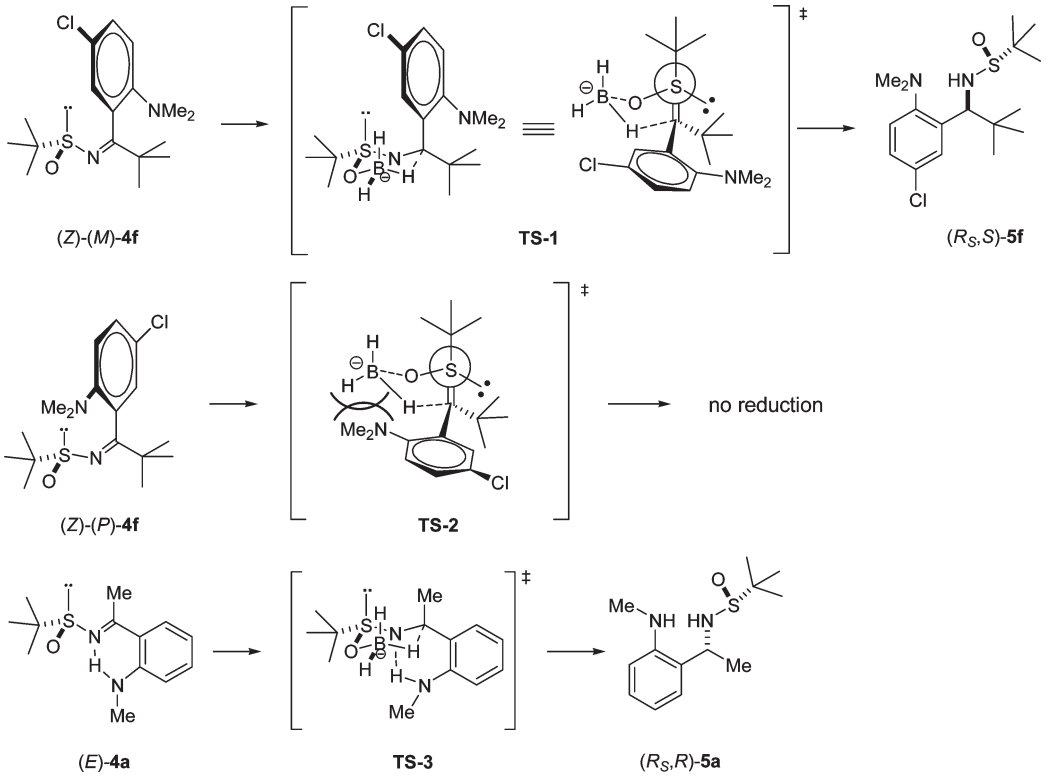
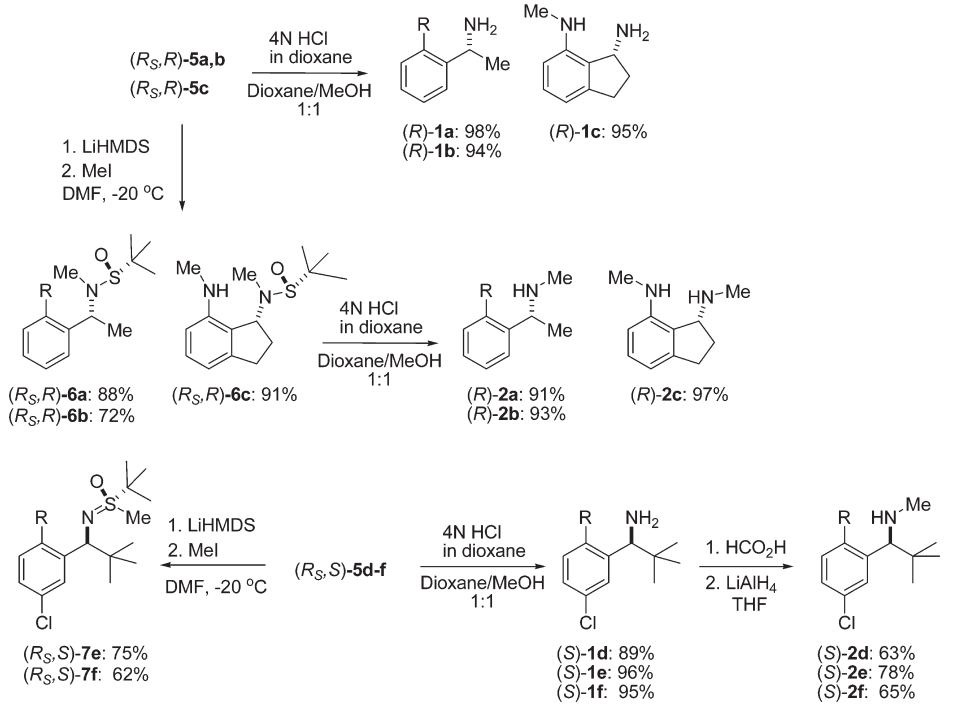


Figure 2. Transition states for the reduction of imines **4a,f**.

Scheme 2. Elaboration of the Reduction Products 5a−f



tert-butanesulfinylimines as the key step. The configuration of the newly created stereogenic center in the reduction products depended on *E* or *Z* geometry of the starting *tert*-butanesulfinylketimines. Thus, reduction of (*E*)-imines **4a−c** afforded (*R*$_S$,*R*)-**5a−c** with the *R* configuration at the newly created stereogenic center, whereas (Z)-**4d−f** were

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converted to sulfinylamides (R_S,S)-**5d**−**f** with the *S* configuration. These results reinforce the previously reported correlation between the sense of asymmetric induction and *E*/*Z* geometry of the sulfinylimines.[11]

Sulfinylimines (*Z*)-**4d,e** exist in solution as rapidly equilibrating mixtures of atropisomers. An individual atropisomer (*Z*)-(*M*)-**4f** could be reduced with DIBAL and BH_3·THF under conditions where the isomeric (*Z*)-(*P*)-**4f** was completely unreactive. The reluctance of (*Z*)-(*P*)-**4f** to undergo reduction presumably results from steric shielding of the sulfinylimine *Re* face by the ortho-substituent in a cyclic transition state for the reduction. The distinct reactivity of atropisomers together with the observed correlation between the sense of asymmetric induction and *E*/*Z* geometry of the sulfinylimines supports the hypothesis that sulfoxide oxygen plays a major role in control of reduction diastereoselectivity.

EXPERIMENTAL SECTION

Experimental Procedure for Synthesis of Ketones 3

1-[2-(Methylamino)phenyl]-1-ethanone (3b): To a solution of 2′-aminoacetophenone **3a** (5.0 g, 37.0 mmol) in anhydrous DMF (25 mL) was added K_2CO_3 (5.11 g, 37.0 mmol), followed by a solution of MeI (5.25 g, 37.0 mmol) in anhydrous DMF (5 mL). After being stirred for 48 h at room temperature the solution was diluted with water (100 mL) and extracted with MeO*t*Bu (3 × 75 mL). Combined organic extracts were washed with water (50 mL) and brine (30 mL) and dried over Na_2SO_4. Purification of the crude product by column chromatography with gradient elution from 3% EtOAc/petroleum ether to 15% EtOAc/petroleum ether afforded **3b** as a yellow solid (2.7 g, 49% yield); analytical TLC on silica gel, 1:10 EtOAc/petroleum ether, R_f 0.36. Pure material was obtained by crystallization from petroleum ether: mp 37−39 °C. IR (film, cm^{-1}) 3325 (NH), 1635 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.77 (1H, s), 7.74 (1H, dd, J = 8.0, 1.2 Hz), 7.38 (1H, dd, J = 7.5, 1.2 Hz), 6.69 (1H, d, J = 8.5 Hz), 6.59 (1H, t, J = 7.5, 1.2 Hz), 2.91 (3H, d, J = 5.1 Hz), 2.58 (3H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 200.7, 151.9, 135.0, 132.6, 117.5, 113.8, 111.2, 29.2, 27.8. Anal. Calcd for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.29; H, 7.49; N, 9.34.

2,3-Dihydro-7-(methylamino)-1*H*-inden-1-one (3c): To a solution of 7-amino-2,3-dihydro-1*H*-inden-1-one[33] (3.19 g, 21.7 mmol) in anhydrous DMF (25 mL) was added K_2CO_3 (3.0. g, 21.7 mmol), followed by a solution of MeI (3.08 g, 21.7 mmol) in anhydrous DMF (5 mL). After being stirred for 48 h at room temperature the solution was diluted with water (100 mL) and extracted with MeO*t*Bu (3 × 75 mL). Combined organic extracts were washed with water (50 mL) and brine (30 mL) and dried over Na_2SO_4. Purification of the crude product by column chromatography with use of gradient elution from from 3% EtOAc/petroleum ether to 20% EtOAc/petroleum ether afforded product as a yellow solid (1.75 g, 50% yield); analytical TLC on silica gel, 1:10 EtOAc/petroleum ether, R_f 0.20. Pure material was obtained by crystallization from hexane: mp 96−98 °C. IR (film, cm^{-1}) 3365 (NH), 1680 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.37 (1H, dd, J = 7.8, 7.8 Hz), 7.18 (1H, s), 6.60 (1H, dd, J = 7.3, 1.0 Hz), 6.41 (1H, d, J = 8.2 Hz), 3.03−2.98 (2H, m), 2.92 (3H, d, J = 5.2 Hz), 2.65−2.60 (2H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 207.9, 156.7, 149.5, 136.8, 119.9, 112.1, 106.6, 36.1, 29.0, 25.5. Anal. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.44; H, 6.92; N, 8.68.

1-(2-Amino-5-chlorophenyl)-2,2-dimethyl-1-propanone (3d): TMEDA (2.74 g, 23.6 mmol) was added to a cooled solution (−10 °C) of *N*-(4-chlorophenyl)-2,2-dimethylpropanamide[34] (5.0 g, 23.6 mmol) in anhydrous THF (45 mL) under an argon atmosphere, followed by dropwise addition of *n*-BuLi (2.2 M solution in hexane, 6.0 mL, 13.23 mmol). After stirring at −10 °C for 2 h, the yellow suspension was cooled to −78 °C, a solution of pivaloyl chloride (3.98 g, 33.04 mmol) in THF (5 mL) was rapidly added, and the mixture was allowed to warm to room temperature. After the solution was stirring for 2 h, aqueous saturated 1 N HCl (150 mL) was added and product was extracted with EtOAc (3 × 100 mL). Combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4, and concentrated (rotary evaporator). Purification of the solid reside by column chromatography on silica gel with gradient elution from 2% EtOAc/petroleum ether to 10% EtOAc/petroleum ether yielded 6.05 g of *N*-[4-chloro-2-(2,2-dimethyl-1-oxopropyl)phenyl]-2,2-dimethyl propanamide as a white solid (87% yield); analytical TLC on silica gel, 1:10 EtOAc/petroleum ether, R_f 0.52. Pure material was obtained by crystallization from EtOAc/petroleum ether: mp 50−52 °C. IR (film, cm^{-1}) 3362 (NH), 1690 (C═O), 1507 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 9.80 (1H, s), 8.37 (1H, d, J = 9.0 Hz), 7.65 (1H, d, J = 2.4 Hz), 7.38 (1H, dd, J = 9.0, 2.4 Hz), 1.33 (9H, s), 1.27 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 211.0, 177.3, 136.5, 131.8, 127.8, 127.6, 127.41, 127.39, 127.3, 127.21, 127.19, 45.5, 39.9, 28.3, 27.4. Anal. Calcd for $C_{16}H_{22}ClNO_2$: C, 64.97; H, 7.50; N, 4.73. Found: C, 65.04; H, 7.64; N, 4.52.

A suspension of *N*-[4-chloro-2-(2,2-dimethyl-1-oxopropyl)phenyl]-2,2-dimethyl propanamide (4.36 g, 14.74 mmol; from above) in aqueous 6 N HCl (150 mL) was heated at 90 °C for 12 h. The resulting clear solution was basified to pH 8 with aqueous saturated NH_4OH and extracted with EtOAc (3 × 75 mL). Combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4, and concentrated to afford 2.93 g of **3d** as a yellow solid (94% yield); analytical TLC on silica gel, 1:10 EtOAc/petroleum ether, R_f 0.26. Pure material was obtained by crystallization from hexane: mp 65−67 °C. IR (film, cm^{-1}) 3478 (NH_2), 3357 (NH_2), 1643 (C═O). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.71 (1H, d, J = 2.4 Hz), 7.14 (1H, dd, J = 8.8, 2.4 Hz), 6.63 (1H, d, J = 8.8 Hz), 5.58 (2H, s), 1.38 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 208.7, 147.8, 132.4, 129.5, 119.8, 119.5, 119.0, 44.8, 28.7, 28.6, 28.5. Anal. Calcd for $C_{11}H_{14}ClNO$: C, 62.41; H, 6.67; N, 6.62. Found: C, 62.61; H, 6.66; N, 6.49.

1-[5-Chloro-2-(methylamino)phenyl]-2,2-dimethyl-1-propanone (3e): NaH (60% suspension in mineral oil, 389 mg, 16.22 mmol) was washed under an argon atmosphere with anhydrous Et_2O (2 × 10 mL) to remove the mineral oil, then suspended in anhydrous DMF (5 mL) and cooled to 1−2 °C in an ice bath. A solution of *N*-[4-chloro-2-(2,2-dimethyl-1-oxopropyl)phenyl]-2,2-dimethyl propanamide (4.0 g, 13.52 mmol; synthesized as described in the experimental for **3d**) in anhydrous DMF (15 mL) was added dropwise. When gas evolution ceased, the ice bath was removed. After the mixture was stirred at ambient temperature for 1 h, a solution of MeI (3.81 g, 27.04 mmol) in anhydrous DMF (5 mL) was added. After being stirred for 5 h the solution was diluted with water (75 mL) and extracted with MeO*t*Bu (3 × 50 mL). Combined organic extracts were washed with water (30 mL) and brine (20 mL) and dried over Na_2SO_4. Purification by column chromatography by using gradient elution from 10% EtOAc/petroleum ether to 20% EtOAc/petroleum ether afforded *N*-[4-chloro-2-(2,2-dimethyl-1-oxopropyl)phenyl]-*N*,2,2-trimethyl propanamide as a white solid (3.59 g, 86% yield); analytical TLC on silica gel, 2:5 EtOAc/petroleum ether, R_f 0.20. Pure material was obtained by crystallization from EtOAc/petroleum ether: mp 83−85 °C. IR (film, cm^{-1}) 1689 (C═O), 1636 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.40−7.35 (2H, m), 7.12−7.08 (1H, m), 3.34 (3H, s), 1.30−1.23 (18H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 209.5, 177.8, 141.9, 139.8, 131.6, 130.4, 130.1, 126.2, 44.4, 41.1, 39.2, 28.2, 28.0. Anal. Calcd for $C_{17}H_{24}ClNO_2$: C, 65.90; H, 7.81; N 4.52. Found C, 66.24; H, 7.89; N, 4.37.

A suspension of *N*-[4-chloro-2-(2,2-dimethyl-1-oxopropyl)phenyl]-*N*,2,2-trimethyl propanamide (6.7 g, 21.6 mmol; from above) in aqueous 6 N HCl (75 mL) was heated at 90 °C for 12 h. The resulting clear solution was basified to pH 8 with aqueous saturated NH_4OH and

extracted with EtOAc (3 × 75 mL). Combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4, and concentrated to afford product **3e** as a yellow solid (4.58 g, 94% yield); analytical TLC on silica gel, 1:10 EtOAc/petroleum ether, R_f 0.48. Pure material was obtained by crystallization from EtOAc/petroleum ether: mp 57−59 °C. IR (film, cm^{-1}) 3365 (NH), 1635 (C═O). ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.97 (1H, s), 7.81 (1H, d, J = 2.5 Hz), 7.26 (1H, dd, J = 9.0, 2.5 Hz), 6.65 (1H, d, J = 9.0 Hz), 2.85 (3H, s), 1.39 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 208.6, 150.1, 133.1, 130.4, 117.81, 117.79, 113.1, 44.8, 29.7, 29.0. Anal. Calcd for $C_{12}H_{16}ClNO$: C, 63.85; H, 7.15; N, 6.21. Found: C, 63.94; H, 7.21; N, 6.11.

1-[5-Chloro-2-(dimethylamino)phenyl]-2,2-dimethyl-1-propanone (3f): To a solution of ketone **3e** (1.0 g, 4.43 mmol) in anhydrous DMF (25 mL) was added K_2CO_3 (1.22 g, 8.86 mmol), followed by a solution of MeI (1.26 g, 8.86 mmol) in anhydrous DMF (5 mL). After being stirred at room temperature for 48 h the solution was diluted with water (100 mL) and extracted with MeO*t*Bu (3 × 75 mL). Combined organic extracts were washed with water (50 mL) and brine (30 mL) and dried over Na_2SO_4. Purification of the crude product by column chromatography by using gradient elution from 5% CH_2Cl_2/petroleum ether to 15% CH_2Cl_2/petroleum ether afforded product as a yellow oil (754 mg, 71% yield); analytical TLC on silica gel, 1:10 EtOAc/petroleum ether, R_f 0.60. IR (film, cm^{-1}) 1690 (C═O); ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.25 (1H, dd, J = 8.6, 2.5 Hz), 7.01 (1H, dd, J = 8.6 Hz), 6.92 (1H, d, J = 2.5 Hz), 2.63 (6H, s), 1.19 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 215.5, 149.1, 139.0, 129.2, 127.9, 125.9, 120.5, 44.9, 29.0, 27.4. HRMS-ESI (m/z) calcd for $C_{13}H_{18}ClNO$ $[M + H]^+$ 240.1155, found 240.1169.

General Procedure for the Condensation of Ketones with (R_S)-*tert*-Butanesulfinamide. A mixture of appropriate ketone **3** (1.0 equiv), (R_S)-*tert*-butanesulfinamide (1.0 equiv), and neat $Ti(OEt)_4$ (Alfa Aesar, Vertec, 99+%, 2.0 equiv) in a sealed Ace pressure tube was stirred and heated for 12 h at 75 °C (ketones **3a,b,d,e**) or 125 °C (ketone **3c**) under an argon atmosphere. After cooling to room temperature, the reaction mixture was poured into a mixture of brine (20 mL/mmol of ketone **3**) and EtOAc (20 mL/mmol of ketone **3**). The resulting slurry was stirred for 10 min and filtered throught a plug of Celite (3 × 5 cm), then the filter cake was washed with EtOAc (50 mL/mmol of ketone **3**). The organic layer from the filtrate was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel.

***N*-[(*E*)-1-(2-Aminophenyl)ethylidene]-2-methyl-(R_S)-2-propanesulfinamide (4a):** Following the general procedure, ketone **3a** (500 mg, 3.7 mmol) was converted into sulfinylimine **4a**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 100% EtOAc afforded product as a yellow solid (776 mg, 88% yield); analytical TLC on silica gel, 1:1 EtOAc/petroleum ether, R_f 0.24. Pure material was obtained by crystallization from EtOH: mp 189−191 °C. IR (film, cm^{-1}) 3400 (NH_2), 3283 (NH_2), 1457 (C═N), 1066 (S═O). ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.57 (1H, dd, J = 8.3, 1.1 Hz), 7.23−7.18 (1H, m), 6.69−6.63 (2H, m), 6.49 (2H, s), 2.91 (3H, s), 1.28 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 179.6, 149.5, 132.9, 130.5, 118.3, 117.4, 116.1, 56.3, 22.3, 21.6. Anal. Calcd for $C_{12}H_{18}N_2OS$: C 60.47; H 7.61; N 11.75. Found: C 60.51; H 7.60; N 11.63. $[\alpha]^{20}_D$ −76.4 (c 0.97, EtOH).

***N*-[(*E*)-1-[2-(Methylamino)phenyl]ethylidene]-2-methyl-(R_S)-2-propanesulfinamide (4b):** Following the general procedure, ketone **3b** (200 mg, 1.6 mmol) was converted into sulfinylimine **4b**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 38% EtOAc/petroleum ether afforded product as a yellow solid (241 mg, 60% yield); analytical TLC on silica gel, 1:1 EtOAc/petroleum ether, R_f 0.39. Pure material was obtained by crystallization from Et_2O: mp 81−83 °C. IR (film, cm^{-1}) 3223 (NH), 1543 (C═N), 1071 (S═O). ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 9.23 (1H, s), 7.63 (1H, dd, J = 8.0, 1.0 Hz), 7.37−7.31 (1H, m), 6.69 (1H, d, J = 8.5 Hz), 6.65−6.59 (1H, m), 2.92 (3H, d, J = 5.0 Hz), 2.77 (3H, s), 1.29 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 179.6, 151.3, 113.7, 131.1, 117.5, 114.2, 111.2, 56.2, 29.5, 22.2, 21.4. Anal. Calcd for $C_{13}H_{20}N_2OS$: C, 61.87; H, 7.99; N, 11.10. Found: C, 62.02; H, 7.83; N, 11.09. $[\alpha]^{20}_D$ −164.5 (c 2.58, EtOH).

***N*-[2,3-Dihydro-7-(methylamino)-1*H*-inden-1-yliden]-2-methyl-(R_S)-2-propanesulfinamide (4c):** Following the general procedure, ketone **3c** (837 mg, 5.19 mmol) was converted into sulfinylimine **4c**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 37% EtOAc/petroleum ether afforded product as a yellow solid (471 mg, 34% yield); analytical TLC on silica gel, 2:5 EtOAc/petroleum ether, R_f 0.36. Pure material was obtained by crystallization from hexane: mp 100−102 °C. IR (film, cm^{-1}) 3325 (NH), 1604 (C═N), 1068 (S═O). ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.64 (1H, s), 7.33 (1H, dd, J = 8.2, 7.4 Hz), 6.58 (1H, dd, J = 7.4, 0.8 Hz), 6.44 (1H, d, J = 8.2 Hz), 3.41−3.32 (1H, m), 3.06−2.95 (3H, m), 2.93 (3H, s), 1.29 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 187.7, 153.6, 149.6, 135.6, 120.4, 111.5, 106.8, 56.1, 32.2, 29.3, 28.5, 22.2. Anal. Calcd for $C_{14}H_{20}N_2OS$: C, 63.60; H, 7.62; N, 10.60. Found: C, 63.64; H, 7.54; N, 10.44. $[\alpha]^{20}_D$ −16.3 (c 0.93, EtOH).

***N*-[(*Z*)-1-(2-Amino-5-chlorophenyl)-2,2-dimethylpropylidene]-2-methyl-(R_S)-2-propanesulfinamide (4d):** Following the general procedure, ketone **3d** (500 mg, 2.36 mmol) was converted into sulfinylimine **4d**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 30% EtOAc/petroleum ether afforded product as a white solid (520 mg, 75% yield); analytical TLC on silica gel, 2:5 EtOAc/petroleum ether, R_f 0.20. Pure material was obtained by crystallization from petroleum ether: mp 116−118 °C. IR (film, cm^{-1}) 3442 (NH_2), 3339 (NH_2), 1586 (C═N), 1069 (S═O). ^1H NMR for a mixture of atropisomers (*Z*)-(*M*)-**4d** and (*Z*)-(*P*)-**4d** (400 MHz, $CDCl_3$, ppm) δ 7.14−7.08 (1H, m), 6.93 (0.16H, d, J = 2.2 Hz), 6.73 (0.84H, d, J = 2.2 Hz), 6.65 (0.84H, d, J = 8.6 Hz), 6.62 (0.16H, d, J = 8.6 Hz), 3.74 (2H, s), 1.26−1.21 (18H, m). ^{13}C NMR for a mixture of atropisomers (*Z*)-(*M*)-**4d** and (*Z*)-(*P*)-**4d** (100.6 MHz, $CDCl_3$, ppm) δ 193.0, 142.1, 129.5, 129.4, 127.2, 126.3, 125.5, 122.7, 118.2, 116.2, 55.8, 43.3, 28.2, 28.0, 22.3, 21.7. Anal. Calcd for $C_{15}H_{23}ClN_2OS$: C, 57.22; H, 7.36; N, 8.90. Found: C, 57.28; H, 7.30; N, 8.81. $[\alpha]^{20}_D$ −56.6 (c 0.69, EtOH; determined for a mixture of atropisomers (*Z*)-(*M*)-**4d** and (*Z*)-(*P*)-**4d**).

***N*-[(*Z*)-1-[5-Chloro-2-(methylamino)phenyl]-2,2-dimethylpropylidene]-2-methyl-(R_S)-2-propanesulfinamide (4e):** Following the general procedure, ketone **3e** (3.36 g, 14.90 mmol) was converted into sulfinylimine **4e**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 20% EtOAc/petroleum ether afforded product as a white solid (3.66 g, 75% yield); analytical TLC on silica gel, 1:1 EtOAc/petroleum ether, R_f 0.48. Pure material was obtained by crystallization from Et_2O: mp 154−156 °C. IR (film, cm^{-1}) 3375 (NH), 1458 (C═N), 1053 (S═O). ^1H NMR for a mixture of atropisomers (*Z*)-(*M*)-**4e** and (*Z*)-(*P*)-**4e** (400 MHz, $CDCl_3$, ppm) δ 7.24−7.18 (1H, m), 6.90 (0.13H, d, J = 2.2 Hz), 6.70 (0.87H, d, J = 2.2 Hz), 6.63 (0.87H, d, J = 8.8 Hz), 6.57 (0.13H, d, J = 8.8 Hz), 3.79 (0.87H, q, J = 5.0 Hz), 3.17 (0.13H, q, J = 5.0 Hz), 2.84 (0.44H, d, J = 5.0 Hz), 2.77 (2.56H, d, J = 5.0 Hz), 1.24−1.19 (18H, m). ^{13}C NMR for a mixture of atropisomers (*Z*)-(*M*)-**4e** and (*Z*)-(*P*)-**4e** (100.6 MHz, $CDCl_3$, ppm) δ 193.3, 144.4, 129.6, 129.5, 126.8, 125.9, 125.3, 121.2, 112.3, 111.2, 55.7, 43.2, 30.9, 28.3, 28.1, 22.3, 21.7. Anal. Calcd for $C_{16}H_{25}ClN_2OS$: C, 58.43; H, 7.66; N, 8.52. Found: C, 58.39; H, 7.64; N, 8.44. $[\alpha]^{20}_D$ −33.4 (c 2.07, EtOH).

***N*-[(*Z*)-1-[5-Chloro-2-(dimethylamino)phenyl]-2,2-dimethylpropylidene]-2-methyl-(R_S)-2-propanesulfinamide (4f):** Sulfinyl imine **4e** (500 mg, 1.52 mmol) was dissolved in anhydrous DMF (5 mL) and cooled to −20 °C under argon atmosphere. A solution of LiHMDS in THF (1 M solution in THF, 1.67 mmol) was added dropwise and the colorless solution was stirred at −20 °C for 1 h whereupon neat MeI (258 mg, 1.82 mmol) was added. After warming to room temperature and stirring for 2 h, the mixture was diluted with water (30 mL) and extracted with MeO*t*Bu (3 × 50 mL). Combined organic extracts were dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 38% EtOAc/petroleum ether afforded individual atropisomers[35] (*Z*)-(*M*)-**4f** and (*Z*)-(*P*)-**4f** as white solids (totally 476 mg, 91% yield); analytical TLC on silica gel, 2:5 EtOAc/petroleum ether R_f 0.56 (for (*Z*)-(*M*)-**4f**) and R_f 0.48 (for (*Z*)-(*P*)-**4f**). Pure material was obtained by crystallization from hexane: mp 76−78 °C. IR (film, cm^{-1}) 1489 (C═N), 1084(S═O). Anal. Calcd for $C_{17}H_{27}ClN_2OS$: C, 59.54; H, 7.94; N, 8.17. Found: C, 59.77; H, 7.99; N, 8.08. $[\alpha]^{20}_D$ −122.4 (*c* 0.96, EtOH; determined for the mixture of atropisomers (*Z*)-(*M*)-**4f** and (*Z*)-(*P*)-**4f**).

(*Z*)-(*M*)-4f: ^{1}H NMR (400 MHz, THF-d_8, ppm) δ 7.35 (1H, dd, *J* = 8.7, 2.2 Hz), 7.18 (1H, d, *J* = 8.7 Hz), 7.08 (1H, d, *J* = 2.2 Hz), 2.63 (6H, s), 1.21 (9H, s), 1.19 (9H, s). ^{13}C NMR (100.6 MHz, THF-d_8, ppm) δ 190.8, 149.2, 133.2, 129.2, 128.2, 128.9, 126.3, 120.7, 56,0 43.7, 42.4, 28.9, 21.7.

(*Z*)-(*P*)-4f: ^{1}H NMR (400 MHz, THF-d_8, ppm) δ 7.28 (1H, dd, *J* = 8.7, 2.5 Hz), 7.10 (1H, d, *J* = 8.7 Hz), 6.92 (1H, d, *J* = 2.5 Hz), 2.72 (6H, s), 1.22 (9H, s), 1.21 (9H, s). ^{13}C NMR (100.6 MHz, THF-d_8, ppm) δ 191.6, 149.2, 135.6, 129.0, 126.5, 126.3, 120.8, 55.7, 43.6, 42.4, 28.9, 21.5.

General Procedure A for the Reduction of *N*-*tert*-Butanesulfinyl Imines 4a−f with BH_3·THF. Sulfinylimine **4** (1.0 equiv) was dissolved in anhydrous THF (10 mL/mmol of imine **4**) and cooled to −78 °C under argon atmosphere. Borane·THF complex (1.0 M solution in THF, 1.6 equiv) was added dropwise and the resulting solution was stirred at −78 °C for 3 h whereupon it was quenched at −78 °C with brine (50 mL/mmol of imine **4**). After the solution was warmed to room temperature, EtOAc (50 mL/mmol of imine **4**) was added and the layers were separated. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated. An aliquot of the crude product was submitted to ^{1}H NMR and HPLC analysis to determine the diastereoselectivity of the reduction. Diastereomerically pure product was obtained after purification by column chromatography on silica gel.

General Procedure B for the Reduction of *N*-*tert*-Butanesulfinyl Imines 4a−f with DIBAL. Sulfinylimine **4** (1.0 equiv) was dissolved in anhydrous THF (5.0 mL/mmol of imine **4**) and the mixture was cooled to −78 °C under argon atmosphere. Diisobutylaluminium hydride (1.0 M solution in hexanes, 3.0 equiv) was added dropwise and the resulting solution was stirred at −78 °C for 3 h whereupon it was quenched at −78 °C with brine (12 mL/mmol of imine **4**). After the solution was warmed to room temperature, EtOAc (15 mL/mmol of imine **4**) was added and the layers were separated. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated. An aliquot of the crude product was submitted to ^{1}H NMR and HPLC analysis to determine th diastereoselectivity of the reduction. Diastereomerically pure product was obtained after purification by column chromatography on silica gel.

(R_S)-*N*-(*R*)-[1-(2-Aminophenyl)ethyl]-2-methyl-2-propanesulfinamide (5a): Following general procedure B for the reduction, sulfinylimine **4a** (839 mg, 3.52 mmol) was converted into **5a**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 100% EtOAc afforded product as a white solid (745 mg, 88% yield); analytical TLC on silica gel, 1:1 EtOAc/petroleum ether, R_f 0.20. Pure material was obtained by crystallization from Et_2O: mp 126−128 °C. IR (film, cm^{-1}) 3459 (NH_2), 3369 (NH_2), 3205 (NH), 1038 (S═O). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.22 (1H, d, *J* = 7.8 Hz), 7.13 (1H, dd, *J* = 7.8, 1.0 Hz), 6.75 (1H, dd, *J* = 7.8, 7.8 Hz), 6.69 (1H, d, *J* = 7.8 Hz), 4.55 (1H, dq, *J* = 6.6, 2.1 Hz), 4.27 (2H, s), 3.40 (1H, s), 1.59 (3H, d, *J* = 6.6 Hz), 1.22 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 144.6, 128.9, 126.8, 125.7, 118,0 116.6, 55.2, 49.8, 22.5, 19.8. Anal. Calcd for $C_{12}H_{20}N_2OS$: C, 59.96; H, 8.39; N, 11.65. Found: C, 60.0; H, 8.32; N, 11.63. Optical rotation (99% de, HPLC/csp) $[\alpha]^{20}_D$ −147.7 (*c* 2.2, EtOH). HPLC/csp assay: Daicel CHIRALPAK IB, 25 cm × 4.6 mm i.d., mobile phase 20% IPA/80% Hex, flow rate 0.7 mL/min, detector UV 210 nm, retention time 8.5 min ((R_S,*R*)-**5a**), major and 9.2 min ((R_S,*S*)-**5a**), minor.

(R_S)-*N*-(*R*)-1-[2-(Methylamino)phenyl]ethyl-2-methyl-2-propanesulfinamide (5b): Following general procedure B for the reduction, sulfinylimine **4b** (767 mg, 3.04 mmol) was converted into **5b**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 42% EtOAc/petroleum ether afforded product as a white solid (750 mg, 97% yield); analytical TLC on silica gel, 1:1 EtOAc/petroleum ether, R_f 0.20. Pure material was obtained by crystallization from Et_2O: mp 81−83 °C. IR (film, cm^{-1}) 3380 (NH), 1046 (S═O); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.29−7.20 (2H, m), 6.75−6.64 (2H, m), 4.89 (1H, s), 4.51 (1H, dq, *J* = 6.5, 2.1 Hz), 3.34 (1H, s), 2.87 (3H, s), 1.59 (3H, d, *J* = 6.5 Hz), 1.20 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 146.8, 129.2, 126.5, 125.0, 116.1, 110.5, 55.2, 49.6, 30.3, 22.5, 19.9. Anal. Calcd for $C_{13}H_{22}N_2OS$: C, 61.38; H, 8.72; N, 11.01. Found: C, 61.39; H, 8.80; N, 10.97. Optical rotation (99% de, HPLC/csp) $[\alpha]^{20}_D$ −164.5 (*c* 2.58, EtOH). HPLC/csp assay: Daicel CHIRALPAK IA, 25 cm × 4.6 mm i.d., mobile phase 10% IPA/90% Hex, flow rate 0.9 mL/min, detector UV 254 nm, retention time 5.8 min ((R_S,*R*)-**5b**), major and 6.3 min ((R_S,*S*)-**5b**), minor.

(R_S)-*N*-[(*R*)-7-(Methylamino)-2,3-dihydro-1*H*-inden-1-yl]-2-methyl-2-propanesulfinamide (5c): Following general procedure B for the reduction, sulfinylimine **4c** (420 mg, 1.59 mmol) was converted into **5c**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 20% EtOAc/petroleum ether afforded product as a white solid (398 mg, 94% yield); analytical TLC on silica gel, 2:5 EtOAc/petroleum ether, R_f 0.26. Pure material was obtained by crystallization from hexane: mp 127−129 °C. IR (film, cm^{-1}) 3365 (NH), 3220 (NH), 1046 (S═O). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.19 (1H, dd, *J* = 7.8, 7.8 Hz), 6.58 (1H, d, *J* = 7.4 Hz), 6.45 (1H, d, *J* = 8.0 Hz), 5.07−5.02 (1H, m), 4.80 (1H, ddd, *J* = 8.0, 5.6, 2.7 Hz), 3.41 (1H, d, *J* = 5.6 Hz), 3.05 (1H, dt, *J* = 16.0, 8.0 Hz), 2.84 (3H, d, *J* = 4.3 Hz), 2.76 (1H, ddd, *J* = 16.0, 9.0, 3.6 Hz), 2.46−2.35 (1H, m), 2.07−1.98 (1H, m), 1.21 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 146.1, 145.2, 130.3, 125.5, 112.4, 107.5, 59.1, 55.3, 35.0, 30.5, 30.0, 22.6. Anal. Calcd for $C_{14}H_{22}N_2OS$: C, 63.12; H, 8.32; N, 10.52. Found: C, 62.78; H, 8.32; N, 10.41. Optical rotation (measured for a batch with 86% de, HPLC/csp) $[\alpha]^{20}_D$ −3.3 (*c* 1.0, EtOH). HPLC/csp assay: Daicel CHIRALPAK IA, 25 cm × 4.6 mm i.d., mobile phase 5% IPA/95% Hex, flow rate 0.9 mL/min, detector UV 254 nm, retention time 6.2 min ((R_S,*R*)-**5c**), major and 10.1 min ((R_S,*S*)-**5c**), minor.

(R_S)-*N*-(*S*)-[1-(2-Amino-5-chlorophenyl)-2,2-dimethylpropyl]-2-methyl-2-propanesulfinamide (5d): Following general procedure B for the reduction, sulfinylimine **4d** (1.80 g, 5.71 mmol) was converted into **5d**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 100% EtOAc/petroleum ether afforded product as a white solid (1.79 g, 99% yield); analytical TLC on silica gel, 1:1 EtOAc/petroleum ether, R_f 0.19. Pure material was obtained by crystallization from hexane: mp 147−149 °C. IR (film, cm^{-1}) 3459 (NH), 3355 (NH_2), 3245 (NH_2), 1055 (S═O); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.17−7.13 (0.81H, m), 7.05−6.95 (1.19H, m), 6.62−6.48 (1H, m), 4.23 (0.78H, s), 4.04 (0.22H, s), 3.68 (0.25H, s), 3.66 (2H, s), 3.52 (0.75H, s), 1.27−1.18 (9H, m), 1.05−0.97 (9H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 144.3, 133,0 129.6, 128.5, 127.9, 125.3, 122.9, 118.4, 117.8, 68.7, 58.8, 55.5, 55.3, 37.4, 36.6, 28.0, 26.5, 22.5. Anal. Calcd for $C_{15}H_{25}ClN_2OS$: C, 56.85; H, 7.95; N, 8.84. Found: C, 56.91; H, 8.12; N, 8.78. Optical rotation (99% de,

HPLC/csp) $[\alpha]^{20}_{D}$ −97.9 (*c* 1.07, EtOH). HPLC/csp assay: Daicel CHIRALPAK IB, 25 cm × 4.6 mm i.d., mobile phase 10% IPA/90% Hex, flow rate 0.9 mL/min, detector UV 254 nm, retention time 6.4 min ((*R*$_S$,*S*)-**5d**), major and 7.8 min ((*R*$_S$,*R*)-**5d**), minor.

(*R*$_S$)-*N*-(*S*)-[1-[5-Chloro-2-(methylamino)phenyl]-2,2-dimethylpropyl]-2-methyl-2-propanesulfinamide (5e): Following general procedure B for the reduction, sulfinylimine **4e** (658 mg, 2.0 mmol) was converted into **5e**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 80% EtOAc/petroleum ether afforded product as a white solid (636 mg, 96% yield); analytical TLC on silica gel, 1:1 EtOAc/petroleum ether, R_f 0.40. Pure material was obtained by crystallization from Et_2O: mp 101−103 °C. IR (film, cm^{-1}) 3390 (NH), 1057 (S═O); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.17−7.10 (1.7H, m), 6.97−6.95 (0.3H, m), 6.56 (0.7H, d, *J* = 8.7 Hz), 6.49 (0.3H, d, *J* = 8.7 Hz), 5.35 (1H, s), 4.23 (0.7H, s), 4.06 (0.3H, s), 3.58 (0.3H, s), 3.51 (0.7H, s), 2.82 (2H, s), 2.73 (1H, s), 1.26−1.19 (9H, m), 1.02−0.97 (9H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 147.4, 146.8, 132.8, 129.4, 128.6, 128.0 124.9, 121.3, 120.7, 111.7, 111.6, 69.0, 58.1, 55.5, 55.3, 37.1, 36.6, 31.2, 30.1, 28.1, 26.5, 22.6, 22.5. Anal. Calcd for $C_{16}H_{27}ClN_2OS$: C, 58.07; H, 8.22; N, 8.47. Found: C, 58.15; H, 8.22; N, 8.33. Optical rotation (99% de, HPLC/csp) $[\alpha]^{20}_{D}$ −96.0 (*c* 1.01, EtOH). HPLC/csp assay: Daicel CHIRALPAK IB, 25 cm × 4.6 mm i.d., mobile phase 5% IPA/95% Hex, flow rate 0.9 mL/min, detector UV 254 nm, retention time 10.4 min ((*R*$_S$,*S*)-**5e**), major and 8.2 min ((*R*$_S$,*R*)-**5e**), minor.

(*R*$_S$)-*N*-(*S*)-[1-[5-Chloro-2-(dimethylamino)phenyl]-2,2-dimethylpropyl]-2-methyl-2-propanesulfinamide (5f): Following general procedure B for the reduction, the individual (*M*)-atropisomer of sulfinylimine **4f** (737 mg, 2.15 mmol) was converted into **5f**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 40% EtOAc/petroleum ether afforded product as a white solid (719 mg, 97% yield); analytical TLC on silica gel, 2:5 EtOAc/petroleum ether, R_f 0.32. Pure material was obtained by crystallization from hexane: mp 75−77 °C. IR (film, cm^{-1}) 3443 (NH), 3335 (NH); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.22−7.16 (2H, m), 7.13−7.10 (1H, m), 4.98 (1H, d, *J* = 2.0 Hz), 3.51 (1H, s), 2.64 (6H, s), 1.22 (9H, s), 0.93 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 153.2, 137.4, 129.7, 128.8, 127.9, 122.1, 59.1, 55.6, 45.4, 35.9, 26.4, 22.6. Anal. Calcd for $C_{17}H_{29}ClN_2OS$: C, 59.19; H, 8.47; N, 8.12. Found: C, 59.23; H, 8.09; N, 8.05. Optical rotation (99% de, HPLC/csp) $[\alpha]^{20}_{D}$ −8.8 (*c* 0.95, EtOH). HPLC/csp assay: Daicel CHIRALPAK IB, 25 cm × 4.6 mm i.d., mobile phase 5% IPA/95% Hex, flow rate 0.9 mL/min, detector UV 254 nm, retention time 9.2 min ((*R*$_S$,*S*)-**5f**), major and 12.3 min ((*R*$_S$,*R*)-**5f**), minor.

General Procedure for the Alkylation of *N*-*tert*-Butanesulfinyl Amides 5a−c. Sulfinyl amide **5** (1.0 equiv) was dissolved in anhydrous DMF (3 mL/mmol of amide **5**) and cooled to −20 °C under argon atmosphere. A solution of LiHMDS in THF (1 M solution in THF, 1.0 equiv) was added dropwise and the yellow solution was stirred at −20 °C for 1 h whereupon neat MeI (2.0 equiv) was added. After being warmed to room temperature and stirred for 2 h, the mixture was diluted with water (30 mL/mmol of amide **5**) and extracted with MeO*t*Bu. Combined organic extracts were dried (Na_2SO_4) and concentrated and the residue was purified by column chromatography on silica gel.

(*R*$_S$)-*N*-(*R*)-[1-(2-Aminophenyl)ethyl]-*N*,2-dimethyl-2-propanesulfinamide (6a): Following the general procedure for the alkylation, sulfinyl amide **5a** (1.00 g, 4.17 mmol) was converted into **6a**. Purification of the crude product by column chromatography by using gradient elution from 10% EtOAc/petroleum ether to 100% EtOAc/petroleum ether afforded product as a white solid (936 mg, 88% yield); analytical TLC on silica gel, 1:1 EtOAc/petroleum ether, R_f 0.12. Pure material was obtained by crystallization from Et_2O: mp 93−95 °C. IR (film, cm^{-1}) 3433 (NH_2), 3343 (NH_2), 1054 (S═O). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.20 (1H, dd, *J* = 7.0, 1.5 Hz), 7.10 (1H, ddd, *J* = 7.8, 7.8, 1.5 Hz), 6.77 (1H, ddd, *J* = 7.8, 7.8, 1.5 Hz), 6.68 (1H, dd, *J* = 7.8, 1.0 Hz), 4.32 (1H, q, *J* = 7.0 Hz), 4.01 (2H, s), 2.56 (3H, s), 1.63 (3H, d, *J* = 7.0 Hz), 1.10 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 145.1, 128.5, 127.8, 125.9, 118.4, 116.6, 59.9, 57.5, 29.3, 23.6, 16.6. Anal. Calcd for $C_{13}H_{22}N_2OS$: C, 61.38; H, 8.72; N, 11.01. Found: C, 61.41; H, 8.84; N, 10.93. Optical rotation $[\alpha]^{20}_{D}$ −14.9 (*c* 1.14, EtOH).

(*R*$_S$)-*N*-(*R*)-[1-[2-(Methylamino)phenyl]ethyl]-*N*,2-dimethyl-2-propanesulfinamide (6b): Following the general procedure for the alkylation, sulfinyl amide **5b** (572 mg, 2.25 mmol) was converted into **6b**. Purification of the crude product by column chromatography by using gradient elution from 6% EtOAc/petroleum ether to 60% EtOAc/petroleum ether afforded product as a colorless oil (434 mg, 72% yield); analytical TLC on silica gel, 1:1 EtOAc/petroleum ether, R_f 0.28. IR (film, cm^{-1}) 3385 (NH), 1068 (S═O). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.25−7.17 (2H, m), 6.74 (1H, ddd, *J* = 7.5, 7.5, 1.0 Hz), 6.65 (1H, dd, *J* = 7.5, 1.0 Hz), 4.48 (1H, s), 4.25 (1H, q, *J* = 6.8 Hz), 2.86 (3H, s), 2.56 (3H, s), 1.64 (3H, d, *J* = 6.8 Hz), 1.07 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, pmm) δ 147.5, 128.7, 127.5, 125.2, 116.7, 110.4, 60.4, 57.5, 30.5, 29.7, 23.6, 22.5, 16.5. HRMS-ESI (*m*/*z*) calcd for $[M + Na]^+$ 291.1507, found 291.1518. Optical rotation $[\alpha]^{20}_{D}$ −155.2 (*c* 0.66, EtOH).

(*R*$_S$)-*N*-(*R*)-[2,3-Dihydro-7-(methylamino)-1*H*-inden-1-yl]-*N*,2-dimethyl-2-propanesulfinamide (6c): Following the general procedure for the alkylation, sulfinyl amide **5c** (321 mg, 1.21 mmol) was converted into **6c**. Purification of the crude product by column chromatography on amine-functionalized silica by using gradient elution from 6% EtOAc/petroleum ether to 60% EtOAc/petroleum ether afforded product as a white solid (309 mg, 91% yield); analytical TLC on silica gel, 2:5 EtOAc/petroleum ether, R_f 0.32. Pure material was obtained by crystallization from Et_2O: mp 107−109 °C. IR (film, cm^{-1}) 3408 (NH), 1054 (S═O). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.17 (1H, dd, *J* = 7.8, 7.8 Hz), 6.57 (1H, d, *J* = 7.8 Hz), 6.42 (1H, d, *J* = 7.8 Hz), 4.98 (1H, dd, *J* = 8.3, 6.3 Hz), 4.77 (1H, s), 2.94 (1H, ddd, *J* = 16.0, 9.4, 4.6 Hz), 2.84 (3H, s), 2.78−2.69 (1H, m), 2.44 (3H, s), 2.31 (1H, dtd, *J* = 9.0, 4.6, 4.6 Hz), 2.08−1.99 (1H, m), 1.24 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 147.1, 145.2, 129.9, 122.9, 112.7, 107.2, 69.5, 58.1, 30.3, 30.2, 30.1, 25.5, 23.9. Anal. Calcd for $C_{15}H_{24}N_2OS$: C, 64.25; H, 8.63; N, 9.99. Found: C, 64.33; H, 8.75; N, 9.83. Optical roation $[\alpha]^{20}_{D}$ −163.8 (*c* 1.71, EtOH).

(*R*$_S$)-2-((1*S*)-1-[*tert*-Butyl(methyl)oxo-λ^6-sulfanylidene]amino-2,2-dimethylpropyl)-4-chloro-*N*-methylaniline (7e): Following the general procedure for the alkylation, sulfinyl amide **5e** (200 mg, 0.61 mmol) was converted into **7e**. Purification of the crude product by column chromatography by using gradient elution from 5% EtOAc/petroleum ether to 30% EtOAc/petroleum ether afforded product as a white solid (158 mg, 75% yield); analytical TLC on silica gel, 2:5 EtOAc/EtOAc, R_f 0.44. Pure material was obtained by crystallization from hexanes: mp 134−136 °C. IR (film, cm^{-1}) 3330 (NH), 1513 (N═S), 1231 (S═O). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.32 (0.2H, d, *J* = 2.6 Hz), 7.07−7.02 (1H, m), 6.89 (0.8H, d, *J* = 2.6 Hz), 6.51 (0.2H, d, *J* = 8.6 Hz), 6.44 (0.8H, d, *J* = 8.6 Hz), 6.23 (1H, q, *J* = 4.9 Hz), 4.07 (0.2H, s), 4.05 (0.8H, s), 2.84 (0.5H, s), 2.74 (2.5H, s), 2.42 (2.5H, s), 2.19 (0.5H, s), 1.47−1.41 (9H, m), 0.93−0.90 (9H, m). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 147.9, 114.9, 130.9, 130.6, 129.4, 127.2, 127.1, 126.7, 119.4, 111.4, 111.1, 67.5, 59.4, 59.0, 56.6, 38.1, 37.4, 33.0, 31.1, 30.4, 27.8, 26.5, 23.7, 23.6. Anal. Calcd for $C_{17}H_{29}ClN_2OS$: C, 59.19; H, 8.47; N, 8.12. Found: C, 59.43; H, 8.48; N, 7.99. $[\alpha]^{20}_{D}$ −10.4 (*c* 0.92, EtOH).

(*R*$_S$)-2-((1*S*)-1-[*tert*-Butyl(methyl)oxo-λ^6-sulfanylidene]amino-2,2-dimethylpropyl)-4-chloro-*N*,*N*-dimethylaniline (7f): Following the general procedure for the alkylation, sulfinyl amide **5f** (185 mg, 0.54 mmol) was converted into **7f**. Purification of the crude product by column chromatography using gradient elution from 5% EtOAc/petroleum ether to 20% EtOAc/petroleum ether afforded product as a white foam (119 mg, 62% yield); analytical TLC on silica gel, 2:5 EtOAc/petroleum ether, R_f 0.56. IR

(film, cm^{-1}) 1479 (N═S), 1239 (S═O). ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.38 (1H, d, J = 2.2 Hz), 7.11 (1H, dd, J = 8.5, 2.2 Hz), 7.07 (1H, d, J = 8.5 Hz), 4.80 (1H, s), 2.63 (6H, s), 2.24 (3H, s), 1.44 (9H, s), 0.99 (9H, s). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ 151.5, 142.9, 129.8, 128.9, 127.0, 122.2, 59.8, 57.2, 45.5, 37.1, 34.6, 26.6, 23.7. HRMS-ESI (m/z) calcd for $C_{18}H_{32}N_2OSCl$ $[M + H]^+$ 359.1924, found 359.1918. $[\alpha]^{20}_D$ +3.9 (c 0.80, EtOH).

General Procedure for Cleavage of *N*-*tert*-Butanesulfinyl Chiral Auxiliary. Sulfinyl amide **5a**−**f** or **6a**−**c** (1.0 equiv) was dissolved in a 1:1 mixture of anhydrous 1,4-dioxane and anhydrous MeOH (6 mL/mmol of amide), and anhydrous HCl in dioxane (4 M solution in dioxane, 4.0 equiv) was added. After the mixture was stirred at room temperature for 1 h, all volatiles were removed in vacuo, and the residue was dissolved in water (20 mL/mmol of amide) and extracted with EtOAc (10 mL/mmol of amide). The water layer was basified to pH 8 with aqueous concentrated NH_4OH and extracted with EtOAc. Combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated (rotary evaporator) to afford the 1,3-diamines. The crude diamines were dissolved in anhydrous 1,4-dioxane and converted into hydrochloric acid salts by dropwise addition of anhydrous HCl in dioxane (4 M solution in dioxane, 1.0 equiv), followed by filtration of the formed precipitate.

(1*R*)-1-(2-Aminophenyl)-1-ethanamine hydrochloride (1a·HCl): Following the general procedure, cleavage of the chiral auxiliary in sulfinyl amide **5a** (250 mg, 1.04 mmol) afforded **1a·HCl** as a white solid (176 mg, 98% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.28. Pure material was obtained by crystallization from MeOH/MeCN: mp 125−127 °C. IR (free base **1a**, film, cm^{-1}) 3364 (NH_2), 3359 (NH_2), 3324 (NH_2), 3294 (NH_2). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 8.41 (2H, s), 7.33 (1H, dd, J = 7.8, 1.2 Hz), 7.06−6.99 (1H, m), 6.74−6.70 (1H, m), 6.66−6.60 (1H, m), 4.52 (1H, q, J = 6.6 Hz), 1.44 (3H, d, J = 6.6 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$, pmm) δ 145.4, 129.0, 126.3, 123.6, 117.3, 116.6, 44.9, 20.1. HRMS-ESI (m/z) calcd for $C_8H_{12}N_2$ $[M + H]^+$ 137.1079, found 137.1094. $[\alpha]^{20}_D$ −7.1 (c 1.0, MeOH).

(1*R*)-1-[2-(Methylamino)phenyl]-1-ethanamine hydrochloride (1b·HCl): Following the general procedure, cleavage of the chiral auxiliary in sulfinyl amide **5b** (250 mg, 0.98 mmol) afforded **1b·HCl** as a white solid (171 mg, 94% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.12. Pure material was obtained by crystallization from MeOH/MeCN: mp 173−175 °C. IR (free base **1b**, film, cm^{-1}) 3370 (NH), 3309 (NH), 3200 (NH); ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 8.39 (3H, s), 7.32 (1H, dd, J = 7.7, 1.4 Hz), 7.22−7.12 (1H, m), 6.70−6.63 (1H, m), 6.62−6.53 (1H, dd, J = 8.2, 0.8 Hz), 5.63 (1H, s), 4.54 (1H, s), 2.70 (3H, s), 1.43 (3H, d, J = 6.7 Hz). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 146.6, 129.5, 125.8, 123.7, 116.3, 100.6, 44.5, 30.5, 20.2. Anal. Calcd for $C_9H_{15}N_2Cl$: C, 57.90; H, 8.10; N, 15.01. Found: C, 57.88; H, 8.13; N, 14.85. Optical rotation $[\alpha]^{20}_D$ −19.1 (c 0.92, MeOH).

(1*R*)-7-(Methylamino)-2,3-dihydro-1*H*-inden-1-amine hydrochloride (1c·HCl): Following the general procedure, cleavage of the chiral auxiliary in sulfinyl amide **5c** (564 mg, 2.12 mmol) afforded **1c·HCl** as a white solid (400 mg, 95% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.20. Pure material was obtained by crystallization from MeOH/MeCN: mp 175−177 °C. IR (free base **1c**, film, cm^{-1}) 3346 (NH), 3189 (NH). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 8.22 (3H, s), 7.16 (1H, dd, J = 7.6, 7.6 Hz), 6.56 (1H, d, J = 7.4 Hz), 6.40 (1H, d, J = 8.0 Hz), 4.66 (1H, d, J = 7.0 Hz), 3.63 (1H, s), 3.16−3.06 (1H, m), 2.77−2.69 (1H, m), 2.72 (3H, s), 2.36−2.24 (1H, m), 2.14−2.06 (1H, m). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 146.6, 146.4, 131.3, 123.2, 122.7, 108.1, 53.0, 31.0, 30.5, 30.1. Anal. Calcd for $C_{10}H_{15}N_2Cl$: C, 60.45; H, 7.61; N, 14.10. Found: C, 60.45; H, 7.69; N, 13.85. Optical rotation $[\alpha]^{20}_D$ −77.7(c 0.87, MeOH).

(1*S*)-1-(2-Amino-5-chlorophenyl)-2,2-dimethyl-1-propanamine hydrochloride (1d·HCl): Following the general procedure, cleavage of the chiral auxiliary in sulfinyl amide **5d** (448 mg, 1.41 mmol) afforded **1d·HCl** as a white solid (312 mg, 89% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.28. Pure material was obtained by crystallization from MeOH/MeCN: mp 225−227 °C. IR (free base **1d**, film, cm^{-1}) 3352 (NH), 3334 (NH), 3321 (NH), 3253 (NH); ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 8.37 (3H, s), 7.25 (1H, d, J = 2.4 Hz), 7.04 (1H, dd, J = 8.6, 2.4 Hz), 6.68 (1H, d, J = 8.6 Hz), 5.51 (2H, s), 4.34 (1H, s), 0.97 (9H, s). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 146.4, 128.8, 127.7, 120.9, 119.1, 117.4, 56.0, 35.8, 26.2. Anal. Calcd for $C_{11}H_{18}Cl_2N_2$: C, 53.02; H, 7.28; N, 11.24. Found: C, 52.96; H, 7.24; N, 11.19. Optical rotation $[\alpha]^{20}_D$ −66.9 (c 1.11, MeOH).

(1*S*)-1-[5-Chloro-2-(methylamino)phenyl]-2,2-dimethyl-1-propanamine hydrochloride (1e·HCl): Following the general procedure, cleavage of the chiral auxiliary in sulfinyl amide **5e** (371 mg, 1.12 mmol) afforded **1e·HCl** as a white solid (283 mg, 96% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.32. Pure material was obtained by crystallization from MeOH/MeCN: mp 234−236 °C. IR (free base **1e**, film, cm^{-1}) 3313 (NH), 3230 (NH). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 8.45 (3H, s), 7.32 (1H, d, J = 2.4 Hz), 7.18 (1H, dd, J = 8.8, 2.4 Hz), 6.54 (1H, d, J = 8.8 Hz), 5.89 (1H, q, J = 4.3 Hz), 4.45 (1H, s), 2.69 (3H, d, J = 4.3 Hz), 0.96 (9H, s). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 146.9, 129.0, 127.7, 121.9, 118.8, 66.8, 55.5, 35.7, 30.6, 26.2. Anal. Calcd for $C_{12}H_{20}Cl_2N_2$: C, 54.76; H, 7.66; N, 10.64. Found: C, 54.87; H, 7.70; N, 10.27. Optical rotation $[\alpha]^{20}_D$ −52.7(c 1.01, MeOH).

(1*S*)-1-[5-Chloro-2-(dimethylamino)phenyl]-2,2-dimethyl-1-propanamine hydrochloride (1f·HCl): Following the general procedure, cleavage of the chiral auxiliary in sulfinyl amide **5f** (262 mg, 0.76 mmol) afforded **1f·HCl** as a white solid (200 mg, 95% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.32. Pure material was obtained by crystallization from MeOH/MeCN: mp 254−259 °C. IR (free base **1f**, film, cm^{-1}) 3355 (NH), 3163 (NH). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 8.64 (3H, s), 7.61 (1H, d, J = 2.4 Hz), 7.41 (1H, dd, J = 8.6, 2.4 Hz), 7.35 (1H, d, J = 8.6 Hz), 4.65 (1H, q, J = 5.7 Hz), 2.57 (6H, s), 0.93 (9H, s). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 152.8, 134.5, 129.5, 128.7, 128.3, 123.9, 56.8, 45.6, 35.0, 26.6. Anal. Calcd for $C_{13}H_{22}Cl_2N_2$: C, 56.32; H, 8.0; N, 10.10. Found: C, 56.33; H, 8.13; N, 9.96. Optical rotation $[\alpha]^{20}_D$ +78.7 (c 0.91, MeOH).

(1*R*)-1-(2-Aminophenyl)-*N*-methyl-1-ethanamine hydrochloride (2a·HCl). Following the general procedure, cleavage of the chiral auxiliary in sulfinyl amide **6a** (204 mg, 0.80 mmol) afforded **2a·HCl** as a white solid (165 mg, 91% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.12. Pure material was obtained by crystallization from MeOH/MeCN: mp 184−186 °C. IR (free base **2a**, film, cm^{-1}) 3339 (NH), 3180 (NH). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 8.45 (3H, s), 7.56 (1H, d, J = 7.8 Hz), 7.24−7.16 (1H, m), 7.04−6.88 (2H, m), 4.54 (1H, q, J = 6.5 Hz), 3.57 (1H, s), 2.42 (3H, s), 1.53 (3H, d, J = 6.5 Hz). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 141.4, 129.9, 124.5, 121.3, 119.3, 52.3, 30.6, 19.0. HRMS-ESI (m/z) calcd for $C_9H_{15}N_2$ $[M + H]^+$ 151.1235, found 151.1261. Optical rotation $[\alpha]^{20}_D$ −18.4 (c 0.84, MeOH).

(1*R*)-*N*-Methyl-1-[2-(methylamino)phenyl]-1-ethanamine hydrochloride (2b·HCl). Following the general procedure, cleavage of the chiral auxiliary in sulfinyl amide **6b** (338 mg, 1.26 mmol) afforded **2b·HCl** as a white solid (235 mg, 93% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.20. Pure material was obtained by crystallization from MeOH/MeCN: mp 206−208 °C. IR (free base **2b**, film, cm^{-1}) 3286 (NH), 3200 (NH). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 9.78 (1H, s), 8.99 (1H, s), 7.44 (1H, d, J = 7.5 Hz), 7.24−7.16 (1H, m), 6.71 (1H, dd, J = 7.5, 7.5 Hz), 6.63 (1H, d, J = 8.0 Hz), 4.55 (1H, q, J = 6.4 Hz), 3.84−3.09 (1H, br s), 2.70 (3H, s), 2.39 (3H, s), 1.49 (3H, d, J = 6.4 Hz). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 147.0, 130.0, 126.9, 121.8, 116.9, 111.2, 51.9, 30.6, 30.6, 18.8. HRMS-ESI (m/z) calcd for $C_{10}H_{17}N_2$ $[M + H]^+$ 165.1392, found 165.1371. Optical rotation $[\alpha]^{20}_D$ −40.6(c 0.98, MeOH).

(1*R*)-*N*-Methyl-7-(methylamino)-2,3-dihydro-1*H*-inden-1-amine hydrochloride (2c·HCl). Following the general procedure, cleavage of the chiral auxiliary in sulfinyl amide **6c** (200 mg, 0.713 mmol) afforded **2c·HCl** as a white solid (148 mg, 97% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.12. Pure material was obtained by crystallization from MeOH/MeCN: mp 192−194 °C. IR (free base **2c**, film, cm^{-1}) 3298 (NH), 3274 (NH). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 9.08 (2H, s), 7.17 (1H, dd, J = 7.8, 7.8 Hz), 6.55 (1H, d, J = 7.4 Hz), 6.39 (1H, d, J = 7.8 Hz), 4.76−4.69 (1H, m), 3.33 (1H, s), 3.23−3.05 (1H, m), 2.80−2.63 (4H, m), 2.47 (3H, s), 2.30−2.16 (2H, m). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 147.3, 147.0, 131.7, 120.9, 112.5, 107.9, 60.6, 30.7, 30.3, 30.0, 28.6. Anal. Calcd for $C_{11}H_{17}N_2Cl$: C, 62.11; H, 8.06; N, 13.17. Found: C, 62.14; H, 7.98; N, 13.15. Optical rotation $[\alpha]^{20}_D$ −148.5 (c 0.91, MeOH).

General Procedure for Synthesis of Diamines 2d−f. To a solution of diamine **1d−f** (1 equiv) in CH_2Cl_2 (5 mL/mmol of diamine **1d−f**) at 0 °C under argon atmosphere was added dropwise neat DIC (1.0 equiv). The mixture was stirred at 0 °C for 15 min, whereupon neat HCOOH (1.0 equiv) was added slowly. After being stirred for 1.5 h at 0 °C, the solution was basified to pH 8 with aqueous saturated NH_4OH, extracted with EtOAc (3 × 35 mL), dried over Na_2SO_4, and evaporated. The semisolid residue was treated with CH_2Cl_2 (5 mL/mmol of diamine **1d−f**), the resulting precipitate was removed by filtration, and the filter cake was washed with CH_2Cl_2. Combined filtrates were concentrated, then the oily residue was dissolved in dry THF (5 mL/mmol of diamine **1d−f**) and cooled to 0 °C under argon atmosphere. Lithium aluminum hydride (1 M solution in THF, 3 equiv with respect to the diamine **1d−f**) was added dropwise, and the resulting solution was heated under reflux for 5 h. After the solution was cooled to 0 °C, the Fieser-type workup[36] (careful successive dropwise addition of water, 15% aqueous NaOH solution, and additional water followed by filtration of a granular inorganic precipitate) afforded the diamines **2d−f**. Diamines **2d−f** were dissolved in anhydrous 1,4-dioxane and converted into hydrochloric acid salts by dropwise addition of anhydrous HCl in dioxane (4 M solution in dioxane, 1.0 equiv), followed by filtration of the formed precipitate.

(1*S*)-1-(2-Amino-5-chlorophenyl)-*N*,2,2-trimethyl-1-propanamine hydrochloride (2d·HCl): Following the general procedure, *N*-formylation of (*S*)-**1d** (200 mg, 0.94 mmol) and subsequent reduction with $LiAlH_4$ afforded diamine **2d·HCl** as a white solid (156 mg, 63% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.32. Pure material was obtained by crystallization from MeOH/MeCN: mp 225−227 °C. IR (free base **2d**, film, cm^{-1}) 3371 (NH), 3292 (NH), 3180 (NH). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 9.19 (1H, s), 8.94 (1H, s), 7.41−7.36 (1H, m), 7.12−7.04 (1H, m), 6.77−6.69 (1H, m), 4.37 (1H, d, J = 9.8 Hz), 3.88−2.78 (2H, s), 2.35−2.25 (3H, m), 1.01 (9H, s). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 147.7, 129.3, 127.3, 119.6, 118.0, 117.9, 64.7, 35.9, 32.7, 26.6. HRMS-ESI (m/z) calcd for $C_{12}H_{20}N_2Cl$ $[M + H]^+$ 227.1315, found 227.1297. $[\alpha]^{20}_D$ −16.4 (c 0.94, MeOH).

(1*S*)-1-[5-Chloro-2-(methylamino)phenyl]-*N*,2,2-trimethyl-1-propanamine hydrochloride (2e·HCl): Following the general procedure, *N*-formylation of (*S*)-**1e** (200 mg, 0.88 mmol) and subsequent reduction with $LiAlH_4$ afforded diamine **2e·HCl** as a white solid (190 mg, 78% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f 0.40. Pure material was obtained by crystallization from MeOH/MeCN: mp 237−239 °C. IR (free base **2e**; film, cm^{-1}) 3284 (NH), 3200 (NH). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 9.05 (1H, s), 8.88 (1H, s), 7.34 (1H, d, J = 2.4 Hz), 7.20 (1H, dd, J = 8.8, 2.4 Hz), 6.57 (1H, d, J = 8.8 Hz), 5.84 (1H, s), 4.43−4.38 (1H, m), 2.66 (3H, s), 2.27 (3H, t, J = 5.0 Hz), 0.96 (9H, s). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 148.2, 129.6, 127.1, 119.3, 118.8, 112.4, 64.2, 35.9, 32.8, 30.7, 26.5. HRMS-ESI (m/z) calcd for $C_{13}H_{22}N_2Cl$ $[M + H]^+$ 241.1472, found 241.1472. $[\alpha]^{20}_D$ −52.1(c 0.83, MeOH). Anal. Calcd for salt of **2e** with picric acid, $C_{19}H_{24}ClN_5O_7$: C, 48.57; H, 5.15; N, 14.90. Found: C, 48.56; H, 5.00; N, 14.98.

(1*S*)-1-[5-Chloro-2-(dimethylamino)phenyl]-*N*,2,2-trimethyl-1-propanamine hydrochloride (2f·HCl): Following the general procedure, *N*-formylation of (*S*)-**1f** (200 mg, 0.83 mmol) and subsequent reduction with $LiAlH_4$ afforded diamine **2f·HCl** as a white solid (157 mg, 65% yield); analytical TLC on silica gel, 9:1 $CHCl_3$/MeOH, R_f = 0.48. Pure material was obtained by crystallization from MeOH/MeCN: mp 221−223 °C. IR (free base **2f**; film, cm^{-1}) 3210 (NH). ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 9.42 (1H, s), 8.90 (1H, s), 7.74 (1H, s), 7.46 (2H, s), 4.70 (1H, s), 2.55 (6H, s), 2.38 (3H, s), 0.98 (9H, s). ^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ 154.2, 132.3, 130.2, 129.6, 127.8, 125.3, 65.5, 46.0, 35.3, 33.2, 27.1. HRMS-ESI (m/z) calcd for $C_{14}H_{24}N_2Cl$ $[M + H]^+$ 255.1628, found 255.1645. $[\alpha]^{20}_D$ +4.2 (c 0.12, MeOH). Anal. Calcd for salt of **2f** with picric acid, $C_{20}H_{26}ClN_5O_7$: C, 49.64; H, 5.42; N, 14.47. Found: C, 49.63; H, 5.28; N, 14.44.

■ ASSOCIATED CONTENT

Supporting Information. Kinetics of the atropisomerization of (*Z*)-**4f**; DFT computed relative energies of (*P*)-(*Z*)-**4e** and (*M*)-(*Z*)-**4e** atropisomers; X-ray crystallographic data for imines **4a,b,d−f** and sulfinylamides **5a,b,e** and **6c** as well as sulfoximine **7f** (CIF files); and copies of ^1H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) For a list of chemical shifts see the Supporting Information (Table S1, p S9).
(22) Complete geometry optimization was carried out for aniline (*Z*)-**4e** with hydrogen bonded THF molecule using B3LYP hybrid density functional as implemented in Gaussian 03. A THF molecule was introduced to minimize the putative intramolecular hydrogen bond in (*P*)-atropisomer between N-H of aniline and oxygen of sulfinyl group. In fact, the small difference between N-H chemical shifts of (*P*) and (*M*) atropisomers in various solvents ($\Delta\delta$(THF-d_8) = 0.22 ppm; $\Delta\delta$-(CHCl$_3$-*d*) = 0.6 ppm) confirms the absence of the intramolecular hydrogen bond in solutions. A relative energy of (*P*) and (*M*) atropisomers of (*Z*)-**4e** was calculated by using the B3LYP/6-31G(d,p) basis set (see the Supporting Information for details).
(23) A series of 2D EXSY spectra were acquired by using the phase-sensitive NOESY pulse sequence to establish reasonable mixing times. A mixing time of 1 s at *T* = 258 K was subsequently chosen for all 2D EXSY experiments. The rate constants for chemical exchange were calculated from the ratio of diagonal and exchange cross peaks as described in: (a) Perrin, C. L.; Dwyer, T. G. *Chem. Rev.* **1990**, *90*, 935. (b) Gibson, K. R.; Hitzel, L.; Mortishire-Smith, R. J.; Gerhard, U.; Jelley, R. A.; Reeve, A. J.; Rowley, M.; Nadin, A.; Owens, A. P. *J. Org. Chem.* **2002**, *67*, 9354. See also the Supporting Information (pp S5−S6) for details. The exchange rate constant for (*Z*)-**4f**, however, could not be determined from the 2D EXSY (NOESY) spectra because of the very slow interconversion of (*Z*)-**4f** isomers on the time scale of the NMR experiment. Instead, isomerization kinetics of the individual pure atropisomer (*Z*)-(*P*)-**4f** was measured at three different temperatures (T_1 = 298 K, T_2 = 313 K, and T_3 = 333 K). The Gibbs free energy of activation at *T* = 298 K was calculated from the Eyring plot of the atropisomerization rate constants vs inverse temperature (see the Supporting Information, pp S3−S4, for details).
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(29) Individual atropisomers (*Z*)-(*P*)-**4f** and (*Z*)-(*M*)-**4f** did not undergo atropisomerization under the reduction conditions (BH$_3$·THF (1.6 equiv), −15 °C, THF-d_8, 3 h) as evidenced by NMR (see the Supporting Information, p S7, for details).
(30) The atropisomerization barrier of 97.9 kJ/mol at 25 °C (see Table 2) corresponds to an isomerization half-life (conversion of a pure atropisomer (*Z*)-(*P*)-**4f** to a (*P*):(*M*)=75:25 mixture) of 4.3 h. In fact, the actual (*P*)(*M*) isomerization rate is higher because the backward (*M*)(*P*) transformation is suppressed due to the rapid reduction of the more reactive atropisomer (*Z*)-(*M*)-**4f** immediate upon forming.
(31) In a control experiment pure crystalline atropisomer (*Z*)-(*M*)-**4d** was added to precooled (−78 °C) THF-d_8 and an ^{1}H NMR spectrum of the resulting suspension (at −45 °C) was acquired immediately. Two sets of signals in a ratio of 78:22 were observed for the dissolved fraction, showing that spontaneous atropisomerization occurs in THF-d_8 solution under the reduction conditions.
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