Asymmetric synthesis of amines using a chiral, non-racemic, benzylidene sulfinamide derived from a recoverable precursor

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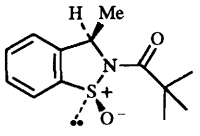
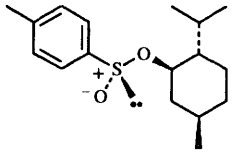
The homochiral cyclic sulfinamide $S_{(S)}R$-(+)-1 has been employed for the asymmetric synthesis of α-substituted benzylamines *via* the benzylidene sulfinamides $R_{(S)}R$-(−)-4. Following diastereoselective reduction and hydrolysis $S_{(S)}R$-(+)-1 can be recycled in one step from the sulfinic acid 11. The addition of zinc(II) bromide reverses the diastereoselectivity of the diisobutylaluminium hydride (DIBAL) reduction of the substrates 4. The same reversal is not observed in the reactions of analogues lacking an amide side chain. In one case the required benzylidene sulfinamide exists in the form of an enamine 15, the X-ray crystallographic structure of which is also featured. A second approach to chiral amines, *via* the addition of Grignard reagents to sulfinylamines derived from $S_{(S)}R$-(+)-1, is also described.

Introduction

We have recently described the preparation and synthetic applications of the chiral, non-racemic, cyclic sulfinamide $S_{(S)}R$-(+)-**1**.[1] This reagent may be converted into chiral sulfoxides *via* reactions with nucleophiles such as Grignard reagents or the enolates of esters or ketones. In all cases inversion of configuration at sulfur is observed. Sulfinamide $S_{(S)}R$-(+)-**1** has several advantages over many other sulfoxide sources such as 1*R*,2*S*,5*R*-(−)-menthyl-(*S*)toluene-*p*-sulfinate **2**.[2] It may be prepared in homochiral form from inexpensive starting materials and is not prone to epimerisation at sulfur during use or in storage and, most significantly, it has been demonstrated to be recyclable after use.[1c] In this paper we report in detail the results of our studies of the application of $S_{(S)}R$-(+)-**1** to the asymmetric synthesis of amines.[3]



$S_{(S)}R$-(+)-**1**



S-**2**

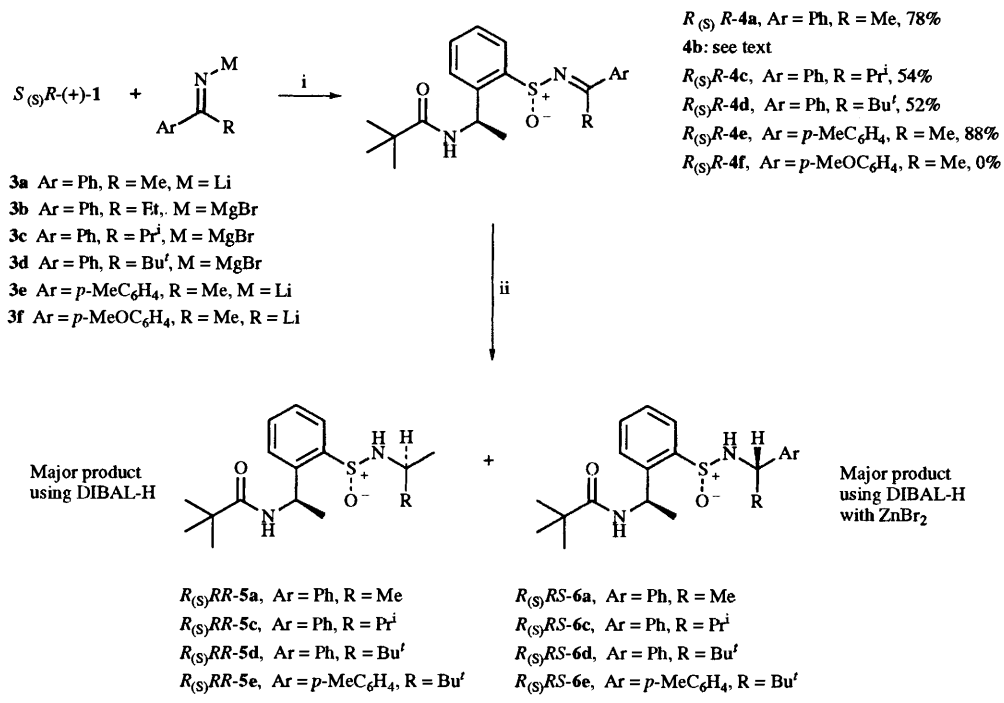
Results and discussion

Addition of the lithiated imine **3a**, generated by the reaction of methyllithium with benzonitrile, to sulfinamide $S_{(S)}R$-(+)-**1** resulted in clean formation of the benzylidene sulfinamide $R_{(S)}R$-(−)-**4a** as a single diastereoisomer (Scheme 1). Benzylidene sulfinamides have been reported in racemic[4,5] and enantiomerically enriched form.[6–9] In the latter case, these have usually, but not exclusively,[10] been prepared from the reaction of lithiated imines with *S*-**2** in which case inversion of configuration at sulfur is observed. On this basis we have been able to assign the configuration at the sulfur atom in $R_{(S)}R$-(−)-**4a**. It should be noted that although we have illustrated $R_{(S)}R$-(−)-**4a** as the *E*-isomer with respect to the C=N bond geometry, we have no direct evidence for this. However it is known that the energy barrier to isomerisation about this double bond is *ca.* 85 kJ mol^{-1}, and have therefore assumed that the isomer with the sulfur atom and large phenyl rings opposite each other will predominate.[11] Reduction of $R_{(S)}R$-(−)-**4a** to the diastereoisomeric products $R_{(S)}RR$-(−)-**5a** and $R_{(S)}RS$-(−)-**6a** with a variety of hydride transfer reagents has been examined (Scheme 1, Table 1). The highest selectivity was obtained using diisobutylaluminium hydride (DIBAL) in THF at −23 °C. This appears to be the optimum temperature; the de was observed to decrease at higher and lower reaction temperatures. The same reaction gave much lower des in dichloromethane as solvent. The diastereoselectivity of this reaction was assessed by the use of 270 and 400 MHz ^{1}H NMR and HPLC. It is important to note that two equivalents of DIBAL are required since deprotonation of the amide side chain is observed.

In order to determine the configuration of the new stereogenic centre in the reduction products we reacted sulfinamide $S_{(S)}R$-(+)-**1** with the lithio-anions of each pure enantiomer of 1-phenylethylamine. The product from the *R*-enantiomer of amine gave a product (92%) which by 270 MHz ^{1}H NMR and TLC was identical to the major diastereoisomer of the DIBAL reduction product $R_{(S)}RR$-(−)-**5a** described above. The adduct from the *S*-amine (94%) was identical to the minor diastereoisomer $R_{(S)}RS$-(−)-**6a**. Amines are known to react with chiral sulfinate esters with inversion of configuration at sulfur,[12] hence this serves to confirm that our earlier assignment of the sulfur configuration in **4a** was correct.

The use of chelating agents to change or enhance the selectivity of a reduction is well known.[13] For instance, zinc(II) bromide has been used to reverse the selectivity in the DIBAL reduction of β-ketosulfoxides.[14] Treatment of $R_{(S)}R$-(−)-**4a** with 1 equiv. of zinc(II) bromide at room temperature, followed by two equiv. of DIBAL, resulted in the formation of the diastereoisomeric products $R_{(S)}RR$-(−)-**5a** and $R_{(S)}RS$-(−)-**6a**. The selectivity of the reduction, compared to the DIBAL reduction, was completely reversed yielding $R_{(S)}RS$-(−)-**6a** as the predominate isomer, as assessed by HPLC and high field ^{1}H NMR analysis (Table 1). Unlike the reduction using DIBAL alone, room temperature was optimal for the zinc(II) mediated process. The addition of incremental quantities (units of 0.25 equiv.) of zinc(II) bromide to the DIBAL reduction results in an inversion of selectivity that is related in a linear fashion to the quantity of salt, and then plateaus at 1.0 equiv.

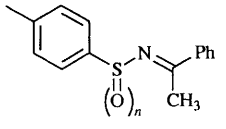
Such an effect, to our knowledge, has not been reported for a



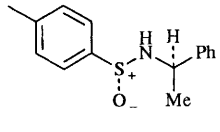
Scheme 1 *Reagents and conditions:* i, THF, −78 °C, 10 mol % CuCl in cases of **3c** and **3d**; ii, see Table 2

Table 1 Reduction reactions of $R_{(S)}R$-**4**

Compound	Reducing agent/conditions	Yield (%)	de (%)	Major diastereoisomer
4a	$LiAlH_4$, THF, rt	80	34	$R_{(S)}RR$-**5a**
4a	$NaBH_4$, EtOH, 0 °C	87	0	—
4a	L-Selectride, THF, −78 °C	52	40	$R_{(S)}RS$-**6a**
4a	L-Selectride, ether, −78 °C	53	40	$R_{(S)}RS$-**6a**
4a	LS-Selectride, THF, −78 °C	20	60	$R_{(S)}RS$-**6a**
4a	LS-Selectride, ether, −78 °C	56	60	$R_{(S)}RS$-**6a**
4a	Red-Al, THF, −78 °C	63	77	$R_{(S)}RR$-**5a**
4a	$[(MeO)_2AlH_2]Li$, THF, −78 °C	47	0	—
4a	$[(Bu^tO)_2AlH_2]Li$, THF, −78 °C	43	25	$R_{(S)}RS$-**6a**
4a	DIBAL, THF, −78 °C	22	34	$R_{(S)}RR$-**5a**
4a	DIBAL, CH_2Cl_2, −78 °C	69	60	$R_{(S)}RR$-**5a**
4a	DIBAL, toluene, −78 °C	78	0	—
4a	DIBAL, THF, −40 °C	90	83	$R_{(S)}RR$-**5a**
4a	DIBAL, THF, −23 °C	98	86	$R_{(S)}RR$-**5a**
4a	$ZnBr_2$–DIBAL, THF, rt	94	92	$R_{(S)}RS$-**6a**
4c	DIBAL, THF, −23 °C	85	71	$R_{(S)}RR$-**6c**
4c	$ZnBr_2$–DIBAL, THF, rt	62	86	$R_{(S)}RS$-**6c**
4d	DIBAL, THF, −23 °C	82	85	$R_{(S)}RR$-**6d**
4d	$ZnBr_2$–DIBAL, THF, rt	56	62	$R_{(S)}RS$-**6d**
4e	DIBAL, THF, −23 °C	85	83	$R_{(S)}RR$-**6e**
4e	$ZnBr_2$–DIBAL, THF, rt	85	80	$R_{(S)}RS$-**6e**
8	DIBAL, THF, −23 °C	89	66	**9**
8	$ZnBr_2$–DIBAL, THF, rt	81	14	**9**

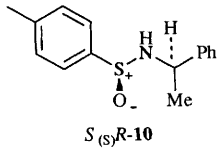


(+)-**7** (*n* = 0)
(+)-**8** (*n* = 1)



$R_{(S)}R$-**9**

Major product using DIBAL-H or DIBAL-H with $ZnBr_2$



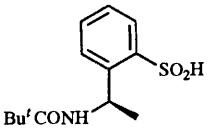
$S_{(S)}R$-**10**

benzylidene sulfinamide. To examine whether this reversal of the selectivity is general for the reduction of such compounds, the racemic *p*-tolyl derivative (±)-**7** was prepared *via* published procedures. The sulfenylimine (68%) was prepared from *p*-tolyl disulfide, acetophenone and ammonia using the method of Davis[15] and was subsequently oxidised with MCPBA to give (±)-**8** (50%).[16]

The DIBAL-H reduction of (±)-**8**, at room temperature, resulted in the formation of a diastereoisomeric mixture of (±)-**9** and (±)-**10** in 89% yield and 65% diastereoisomeric excess (de) in favour of (±)-**9**.[9] The zinc(II) bromide mediated DIBAL reduction resulted in a decrease in the diastereoselectivity of formation of (±)-**9** to just 14% de (81%). One must assume that the amide side chain of $R_{(S)}R$-(−)-**4a** is important in controlling the stereochemical outcome of the zinc(II) bromide–DIBAL-H reduction.

In order to complete the synthesis of amines we required a method for the hydrolysis of the imine reduction products. This was achieved simply by treating the 13:1 mixture of $R_{(S)}RR$-

(−)-**5a** and $R_{(S)}RS$-(−)-**6a** (from reduction with DIBAL) with methanolic trifluoroacetic acid. The products were isolated by the addition of hydrochloric acid (2 mol dm^{-3}) followed by extraction with dichloromethane. This procedure gave the sulfinic acid **11**, *via* the methyl sulfinate ester which was hydrolysed on workup with acid (96%). Neutralisation of the acidic aqueous layer followed by extraction with dichloromethane gave 1-phenylethylamine **12**. Conversion of the amine mixture into the (*R*)-MTPA amide derivatives **13** and **14**[17,18] revealed that the ratio of enantiomers from the hydrolysis was 13:1 (92%) and therefore confirmed that no epimerisation had taken place during the hydrolysis process. Standard samples of each (*R*)-MTPA amide were independently produced from reactions of (*R*)- and (*S*)-1-phenylethylamine to confirm our stereochemical assignment. In view of the possibility of diastereoisomeric enhancement during MTPA derivative formation we also confirmed this result using chiral HPLC to analyse the amine directly, the result of which exactly matched the above figure. The conversion of sulfinic acid **11** into diastereoisomerically pure cyclic sulfinamide $S_{(S)}R$-(+)-**1** in one step has been reported.[1c]



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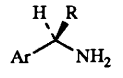


R-**12a** Ar = Ph, R = Me
R-**12b** Ar = Ph, R = Et
R-**12c** Ar = Ph, R = Pr^i
R-**12d** Ar = Ph, R = Bu^t
R-**12e** Ar = *p*-MeC_6H_4, R = Me
R-**12f** Ar = *p*-$MeOC_6H_4$, R = Me

13 **14**

Explanation of selectivity observed

The high diastereoselectivity of the imine reduction process achieved with DIBAL compared to the much lower selectivities with anionic hydride sources suggests that the coordination of $R_{(S)}R$-(−)-**4a** to the reducing agent is essential. We propose that the reduction takes place through the chelated species illustrated in Fig. 1 in which the groups on the sulfur atom and the larger group on the imine are in pseudo-equatorial positions (Fig. 1). Similar models have been proposed for related systems, and the action of the DIBAL is not regarded as novel in this example.[9] It has been assumed that the imine exists in the configuration in which the sulfoxide moiety is *trans* to the phenyl rather than the smaller methyl group. It has further been assumed that the amide side chain (which is deprotonated), does not participate in the reaction.

In the case of the zinc(II) mediated reduction the situation is rather less clear due to the large number of sites to which the metal can bind. However it has been proven conclusively that the amide side chain is important to the control of this selectivity. In view of our observations we tentatively propose the transition state shown in Fig. 2 to explain the control in this situation. A seven-membered chelate in which the zinc(II) ion bridges amide and sulfinamide nitrogen atoms is formed, leaving the sulfoxide oxygen atom to direct the DIBAL reduction as shown. In order to achieve the observed selectivity however, it is necessary for the larger group in the 'imine' unit to adopt an axial position within the six membered ring. Although this appears unfavourable at first sight, we would expect that the location of the larger group in the equatorial position would

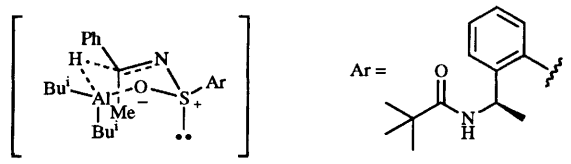


Fig. 1 Proposed transition state for benzylidene sulfinamide reduction by DIBAL

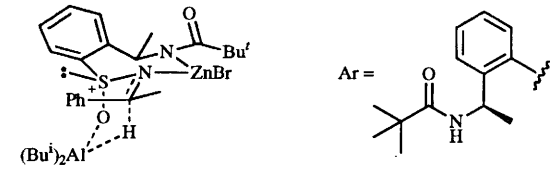


Fig. 2 Proposed transition state for benzylidene sulfinamide reduction by DIBAL–$ZnBr_2$

be disfavoured due to its close proximity to the large zinc(II) bromide unit, which presents a significant steric obstacle.

Further studies

To investigate the versatility of the new methodology we wished to demonstrate that a number of different amines could be prepared. However, unlike 1-phenylethylamine, few related amines are commercially available in enantiomerically pure form for comparison. We therefore chose to first prepare a series of derivatives which would allow us to assign absolute configurations and de values. This was achieved following the protocol outlined in Scheme 2. Racemic amides **12b** to **12f** were prepared from the reaction of the appropriate nitrile with a Grignard reagent followed by reduction. A sample of derivative **12f** was also prepared by reductive amination of 4-methoxyphenylethanone (90%). The racemic amines were then reacted with $S_{(S)}R$-(+)-**1** to give, in each case, a 1:1 mixture of diastereoisomeric adducts **5b–f** and **6b–f** which were separated by flash chromatography. The spectroscopic data of each adduct **5** was subsequently found to be identical to that of the major products of DIBAL reduction of the precursor imines (described below). Hydrolytic cleavage of the S–N bond in each diastereoisomer **5b–f** resulted in formation of the chiral amines **12b–f** with the exception of **5d**, from which no hydrolysis products were obtained. Comparison of the signs and magnitudes of the optical rotations of **12b,c,e** and **f** with published values permitted accurate assignment of the configurations in each case as *R* (Table 2).[19] The configuration of the benzylic centre in **5d** is therefore inferred only by comparison with the related compounds.

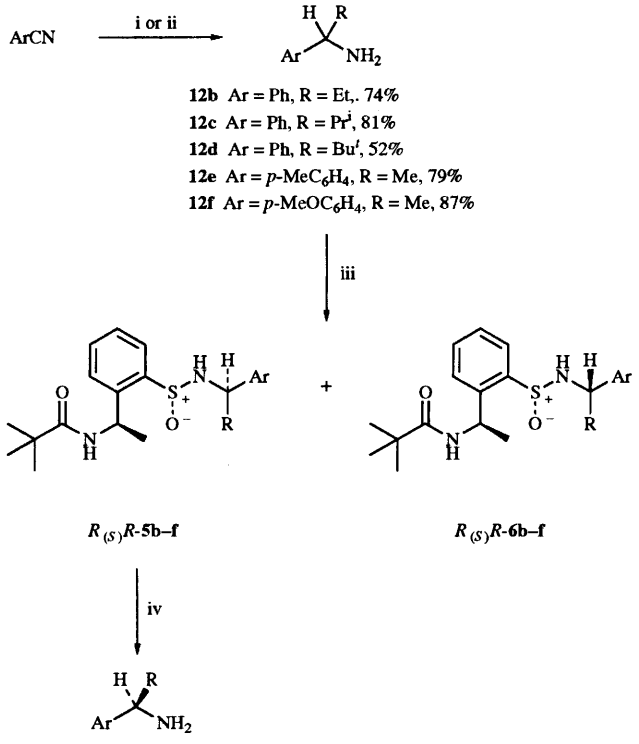
Reaction of metallo-imines **3c** to **3e** with $R_{(S)}S$-(+)-**1** gave the expected imines **4c** to **4e** respectively. In the cases of **4c** and **4d** it was necessary to add a small amount (10 mol %) of CuCl to promote the reaction. Reduction with either DIBAL or DIBAL–zinc(II) bromide gave products, identified by comparison to the standards described above, in which the same pattern of selectivity was observed as for the reductions of **4a** (Scheme 1). Lithio-imine **3b** gave the enamine **15** in 88% yield. An X-ray crystallographic study of this product confirmed that the new double bond possessed *Z* stereochemistry (Fig. 3). Presumably, in contrast to **4a** the extra methyl group must lend sufficient extra stabilisation to favour this isomer over the imine. In **4c** the enamine will be destabilised by the necessity for the phenyl and a methyl group to be oriented *cis* to each other. Further stabilisation is afforded to the sulfinamide enamine **15** by an intramolecular hydrogen bond between the enamine proton and the carbonyl oxygen of the amide side-chain. No adduct could be obtained from the reaction of **3f** with $S_{(S)}R$-(+)-**1**, despite several attempts.

A number of attempts were made to form amines *via* the addition of carbon nucleophiles to **4a**, however no success was achieved in the use of representative examples **16** to **18**.[20,21]

Table 2 Preparation of standards of **5b–f** and **6b–f**

Racemic amine	**5** (%)	**6** (%)	% amine from hydrolysis of **5**	$[\alpha]_D$ (c, $CHCl_3$)	lit. $[\alpha]_D$ (c, $CHCl_3$)
12b	41	42	92	+36.6 (1.0)	+36.2 (1.2) [a]
12c	36	38	78	+14.0 (1.0)	+5.9 (1.5) [b]
12d	33	34	trace	—	—
12e	45	46	86	+28.1 (1.0)	−25 (1.0) [c]
12f	45	47	93	+24.8 (1.0)	+24.6 (1.0) [d]

[a] 95% ee, ref. 19*a*. [b] 41.8% ee, ref. 19*b*. [c] *S*-configuration, 87% ee, ref. 19*c*. [d] 96% ee, ref. 19*d*,*e*.



Scheme 2 *Reagents and conditions:* i, RMgX (with 10 mol % CuCl in case of **12b–12d**), THF, reflux, then rt, $LiAlH_4$, rt to reflux; ii, (for **12f** only) $NH_4{\cdot}HCO_2$, heat, then NaOH, reflux; iii, BuLi, THF, 0 °C, then **1**, −78 °C, THF; iv, HCl/MeOH, then aq. work-up

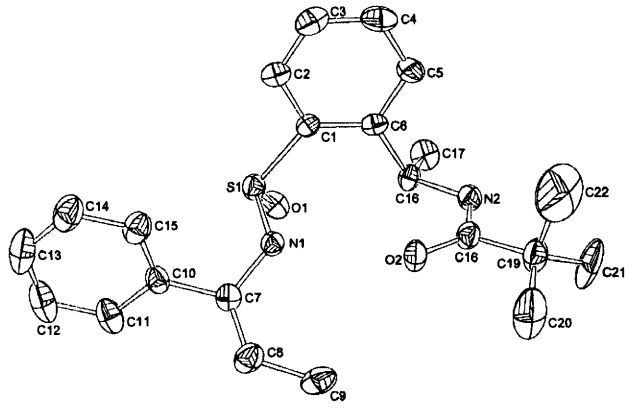
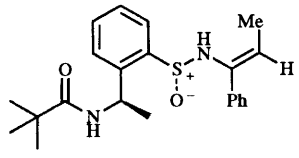


Fig. 3 X-Ray crystal structure of **15**

Simple enolates of esters also failed to react in the expected manner. This was disappointing in view of the known viability of related reactions;[10,22] however it may reflect the hindered nature of these electrophiles due to the amide side chain.



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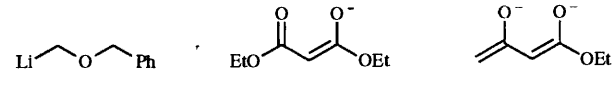


16 **17** **18**

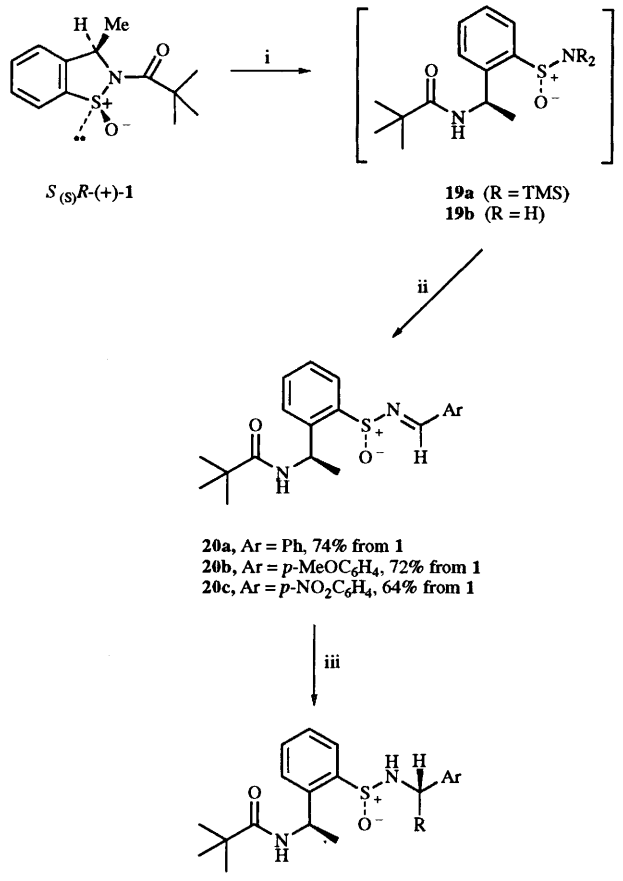
As a complementary approach to the synthesis of chiral amines *via* benzylidene sulfinamides we wished to study the control of the addition of Grignard reagents and other nucleophiles to sulfinylamines of type **20**. Following a literature precedent[23] we were able to prepare the bis(trimethylsilyl)-sulfinamide **19a** and condense this, in the presence of dry caesium fluoride (2 equiv.) with aldehydes to prepare the representative compounds **20a** to **c**. Although it was not possible to fully characterise **19a**, hydrolysis by stirring overnight with silica gel gave desilylated **19b** in 73% yield. The reaction of **20a** with methylmagnesium bromide at −78 °C gave **6a** in 83% de and 92% yield, thereby completing an alternative, and complementary, synthesis of amine precursors (Scheme 3). By analogy to the DIBAL reduction work we would expect that the transition state involved in the control of this process is similar to that shown in Fig. 4, in which the carbanion is directed to one face of the imine *via* coordination to the sulfinamide oxygen atom.[10,22] Reaction of **20a** with ethylmagnesium bromide resulted in formation of **6b**, which had been inaccessible through the reduction protocol. Another previously inaccessible compound, **6f**, was also prepared *via* the addition of methylmagnesium bromide to **20b**. However attempts to add nucleophiles to **20c** failed, possibly due to reactions with the nitro group.

Conclusions

In conclusion, we have demonstrated that zinc(II) bromide–DIBAL-H is a complementary method to the DIBAL reduction of benzylidene sulfinamides of the type $R_{(S)}R$-(−)-**4**. The reactions are high yielding with good diastereoselectivity. A complementary process, involving addition of Grignard reagents to benzylidene sulfinamides derived from aldehydes, has also been described. We have also demonstrated that this chemistry provides the basis of a new and useful synthesis of homochiral benzylamines.

Experimental

Tetrahydrofuran (THF) and diethyl ether ('ether') were freshly distilled from sodium under a nitrogen atmosphere using benzophenone as an indicator. Toluene was freshly distilled from sodium under a nitrogen atmosphere. All solvents were



Scheme 3 *Reagents and conditions:* i, NaHMDS, THF, −78–0 °C; ii, ArCHO, 2.0 equiv. CsF, THF; iii, RMgBr or RMgl, THF, −78 °C

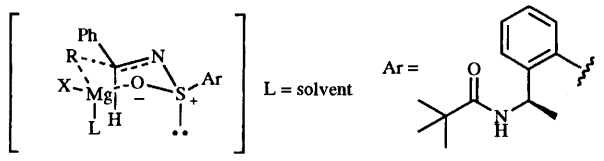


Fig. 4 Proposed transition state for Grignard reagent addition to benzylidene sulfinamide **20a**

distilled prior to use. Reagents were either used as received from commercial sources or purified by recognised methods. Light petroleum refers to that fraction which boils in the range 60–80 °C. All reactions were carried out in flame dried Schlenk tubes under an argon atmosphere, unless otherwise stated.

Flash chromatography [24] was performed using either Merck 9835 (70–230 mesh) or Sorbsil C60 40/60 Å flash silica gel, unless otherwise stated. All reactions were monitored by thin-layer chromatography (TLC) and carried out on aluminium sheets precoated with $60F_{254}$ silica gel, unless otherwise stated, and were visualised by UV light and then by potassium permanganate solution, phosphomolybdic acid solution, ninhydrin solution or anisaldehyde solution.

^{1}H NMR were recorded on a JEOL GX270 FT instrument operating at 270.2 MHz, or a JEOL EX400, or a Bruker AMX400 instrument operating at 399.7 MHz. Chemical shifts (δ_H) were recorded relative to tetramethylsilane as an internal standard; all coupling constants, J, are reported in Hz. ^{13}C NMR spectra were recorded on a JEOL GX270 FT instrument operating at 67.8 MHz, a JEOL EX400, or a Bruker AMX400 instrument operating at 100.4 MHz. The chemical shifts (δ_C) were recorded relative to deuteriochloroform (or relative solvent peak) as internal standard in a broad band decoupled mode; the multiplicities were obtained by using 135° and 90° Distortionless Enhancement by Polarization Transfer (DEPT) or Off-Resonance Decoupling experiments to aid in assignments (q, methyl; t, methylene; d, methine; s, quaternary). Homonuclear J Correlated Spectroscopy (^{1}H–^{1}H COSY) and Heteronuclear J Correlated Spectroscopy (^{1}H–^{13}C COSY) were conducted on a JEOL EX400 instrument to aid assignments if required. All spectra were recorded for solutions in $CDCl_3$ unless otherwise stated.

IR spectra were recorded on a Perkin-Elmer 1600 FT-IR, either as liquid films, or as Nujol mulls, between sodium chloride plates. Mass spectra were recorded on a VG analytical 7070E instrument with VG2000 data system using either an ionising potential of 70 eV (EI), or by chemical ionisation (isobutane) (CI), or fast atom bombardment (FAB) in 3-nitrobenzylalcohol matrix, unless otherwise stated. Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 141 Polarimeter at ambient temperature and are given in units of 10^{-1} deg cm^2 g^{-1}. High and low resolution FAB (thioglycolic) and TSP (0.1 mol dm^{-3} NH_4OAc in 80% MeOH–water, Thermospray) mass spectrometry were performed in the Physical Methods Department at Roche Products Ltd or by the EPSRC Mass Spectrometry Service at Swansea University. Microanalytic data were obtained on a Carlo Erba 1106 Elemental Analyser. HPLC analysis was carried out using a Waters 501 HPLC pump, Waters 486 Tuneable Absorbance Detector and a Waters 746 Data Module.

Preparation of (±)-1-phenylpropylamine 12b

A solution of benzonitrile (1.03 g, 10 mmol) and anhydrous copper(I) chloride (20 mg, 200 μmol) in THF (20 cm^3) was treated with ethylmagnesium bromide (2.5 mol dm^{-3} in THF; 4.4 cm^3, 11 mmol). After refluxing for 2 h, a slurry of lithium aluminium hydride (380 mg, 10 mmol) in THF (10 cm^3) was slowly added to the cool magnesioketimine. The mixture was refluxed for 3 h, then stirred at room temp. for a further 16 h after which the reaction was quenched by the careful addition of water (0. 38 cm^3), followed by sodium hydroxide (15% w/v, 0.38 cm^3) and water (1.14 cm^3). The precipitated aluminium residues were filtered off through a Celite pad which was washed with ethyl acetate (30 cm^3). The amine was extracted with hydrochloric acid (2 mol dm^{-3}; 3 × 20 cm^3). The combined extracts were basified with sodium hydroxide pellets (pH > 12) and extracted with ethyl acetate (3 × 20 cm^3). The organic extracts were dried (Na_2SO_4), filtered and concentrated and the residue was distilled under, reduced pressure to give the amine **12b** as a clear oil (998 mg, 74%); bp 90 °C (1 mmHg), ν_{max}(film)/cm^{-1} 3397, 3294, 3060, 2961, 2929, 1603, 1492, 1452 and 897; δ_H(270.2 MHz) 7.34–7.18 (5 H, m, ArH), 3.77 (1 H, t, J 7.0, C*H*NH$_2$), 1.67 (2 H, p, J 7.9, CHC*H*$_2$CH$_3$), 1.55 (2 H, br s, N*H*$_2$) and 0.85 (3 H, t, J 7.3, CH$_2$C*H*$_3$); δ_C(67.8 MHz) 145.8 (s), 127.7 (d), 126.2 (d), 125.7 (d), 57.2 (d), 31.8 (t) and 10.3 (q); m/z (EI) 134 (M − H$^+$, 2%), 106 (100), 91 (4), 79 (20) and 28 (15); m/z (CI) 136 (M + H$^+$, 31%), 119 (100), 106 (63), 91 (7) and 79 (5). The amine (250 mg, 1.85 mmol) was dissolved in ether (4 cm^3) and anhydrous hydrogen chloride was bubbled through for 10 min. The salt was filtered off and recrystallised from acetonitrile to give the product as a white solid (310 mg, 98%) (Found: C, 63.1; H, 8.2; N, 8.1. $C_9H_{14}ClN$ requires C, 63.0; H, 8.22; N, 8.16%).

Preparation of (±)-2-methyl-1-phenylpropylamine 12c

A solution of benzonitrile (1.03 g, 10 mmol) and anhydrous copper(I) chloride (20 mg, 200 μmol) in THF (20 cm^3) was treated with isopropylmagnesium bromide (2.0 mol dm^{-3} in THF; 5.5 cm^3, 11 mmol). After refluxing for 3 h, a slurry of lithium aluminium hydride (380 mg, 10 mmol) in THF (10 cm^3)

was slowly added to the cool magnesioketimine. The mixture was refluxed for 3 h and stirred at room temp. for a further 16 h, after which the reaction was quenched by the careful addition of water (0.38 cm^3), followed by sodium hydroxide (15% w/v, 0.38 cm^3), and water (1.14 cm^3). The precipitated aluminium residues were filtered off through a Celite pad which was washed with ethyl acetate (30 cm^3). The amine was extracted with hydrochloric acid (2 mol dm^{-3}; 3 × 20 cm^3). The combined extracts were basified with sodium hydroxide pellets (pH > 12) and extracted with ethyl acetate (3 × 20 cm^3). The organic extracts were dried (Na_2SO_4), filtered and concentrated and the residue was distilled under reduced pressure (120–122 °C, 0.5 mmHg) to give the amine **12c** as a clear oil (986 mg, 81%); ν_{max}(film)/cm^{-1} 3371, 3297, 3026, 2988, 1602, 1493, 1452, 1384 and 1365; δ_H(270.2 MHz) 7.35–7.17 (5 H, m, ArH), 3.57 (1 H, d, *J* 7.3, C*H*NH_2), 1.84 [1 H, apparent hextet, *J* 6.8, C*H*$(CH_3)_2$], 1.59 (2 H, br s, NH_2), 0.97 (3 H, d, *J* 6.6, CH_3) and 0.76 (3 H, d, *J* 6.8, CH_3); δ_C(67.8 MHz) 145.3 (s), 128.3 (d), 127.9 (d), 126.9 (d), 126.8 (d), 126.6 (d), 62.3 (d), 35.3 (d), 19.6 (q) and 18.7 (q); *m/z* (CI) 150 (M + H^+, 21%), 133 (100), 106 (100), 91 (45), 79 (11) and 22 (10). The amine (250 mg, 1.67 mmol) was dissolved in ether (4 cm^3) and anhydrous hydrogen chloride was bubbled through for 10 min. The salt was filtered off and recrystallised from acetonitrile to give the product as a white solid (285 mg, 92%) (Found: C, 64.9; H, 8.5; N, 7.7. $C_{10}H_{16}ClN$ requires C, 64.7; H, 8.68; N, 7.54%).

Preparation of (±)-2,2-dimethyl-1-phenylpropylamine 12d

A solution of benzonitrile (1.03 g, 10 mmol) and anhydrous copper(I) chloride (20 mg, 200 μmol) in THF (20 cm^3) was treated with *tert*-butylmagnesium bromide (2.0 mol dm^{-3} in THF; 5.5 cm^3, 11 mmol). After refluxing for 6 h, a slurry of lithium aluminium hydride (380 mg, 10 mmol) in THF (10 cm^3) was slowly added to the cool magnesioketimine. The mixture was refluxed for 3 h and stirred at room temp. for a further 15 h after which the reaction was quenched by the careful addition of water (0.38 cm^3), followed by sodium hydroxide (15% w/v, 0.38 cm^3) and water (1.14 cm^3). The precipitated aluminium residues were filtered off through a Celite pad which was washed with ethyl acetate (30 cm^3). The amine was extracted with hydrochloric acid (2 mol dm^{-3}; 3 × 20 cm^3). The combined extracts were basified with sodium hydroxide pellets (pH > 12) and extracted with ethyl acetate (3 × 20 cm^3). The organic extracts were dried (Na_2SO_4), filtered and concentrated and the residue was distilled under reduced pressure (103–105 °C, 0.2 mmHg) to give the amine **12d** as a clear oil (849 mg, 52%); ν_{max}(film)/cm^{-1} 3385, 3316, 3027, 2952, 1606, 1492, 1452, 1391 and 1361; δ_H(270.2 MHz), 7.26–7.16 (5 H, m, ArH), 3.35 (1 H, s, C*H*NH_2), 1.44 (2 H, br s, NH_2) and 0.88 [9 H, s, $C(CH_3)_3$]; δ_C(67.8 MHz) 143.5 (s), 129.7 (d), 127.2 (d), 126.4 (d), 65.0 (d), 34.7 (s) and 26.2 (q); *m/z* (CI) 164 (M + H^+, 28%), 147 (98), 133 (6), 106 (100) and 86 (10) (Found: C, 80.6; H, 10.8; N, 8.5. $C_{11}H_{17}N$ requires C, 80.9; H, 10.5; N, 8.58%). The amine (100 mg, 613 μmol) was dissolved in ether (4 cm^3) and anhydrous hydrogen chloride was bubbled through for 10 min. The salt was filtered off and recrystallised from acetonitrile to give the product as a white solid (115 mg, 94%) (Found: C, 66.0; H, 9.2; N, 7.0. $C_{11}H_{18}ClN$ requires C, 66.1; H, 9.08; N, 7.01%).

Preparation of racemic (±)-1-(*p*-tolyl)ethylamine 12e

A solution of 4-tolylnitrile (2.00 g, 17.1 mmol) in THF (4 cm^3) was treated with methyllithium (1.4 mol dm^{-3} in ether; 17.4 mmol) at −78 °C. The lithioketimine rapidly formed on warming to room temp. (red colouration). After 45 min lithium aluminium hydride (650 mg, 17.1 mmol) was added in small portions at −78 °C to the mixture, which was slowly warmed and refluxed for 3 h. The mixture was cooled and water (0.65 cm^3) was carefully added, followed by sodium hydroxide (15% w/v, 0.65 cm^3) and water (1.95 cm^3). The precipitated aluminium residues were filtered off through a Celite pad which was then washed with ethyl acetate (10 cm^3). The amine was extracted with hydrochloric acid (2 mol dm^{-3}; 3 × 10 cm^3). The combined extracts were basified with sodium hydroxide pellets (pH > 12) and extracted with ethyl acetate (3 × 10 cm^3). The organic extracts were dried (Na_2SO_4), filtered and concentrated and the residue was distilled under reduced pressure to give **12e** as a clear oil (2.22 g, 79%); bp 69 °C (1 mmHg); ν_{max}(film)/cm^{-1} 3363, 3290, 3018, 2960, 1598, 1598, 1514, 1450, 1368 and 1100; δ_H(270.2 MHz) 7.21 (2 H, d, *J* 8.1, AA′BB′ ArH), 7.12 (2 H, d, *J* 8.1, AA′BB′ ArH), 4.19 (1 H, q, *J* 6.6, C*H*NH_2), 2.31 (3 H, s, CH_3Ar), 1.52 (2 H, br s, NH_2) and 1.35 (3 H, d, *J* 6.6, CHCH_3); δ_C(67.8 MHz) 144.7 (s), 136.0 (s), 128.9 (d), 125.4 (d), 50.8 (d), 25.5 (q) and 20.8 (q); *m/z* (EI) 134 (M^+, 5%), 120 (100), 93 (20), 77 (10), 42 (12) and 28 (10). The amine (500 mg, 3.7 mmol) was dissolved in ether (5 cm^3) and anhydrous hydrogen chloride was bubbled through for 10 min. The salt was filtered off and recrystallised from acetonitrile to give the product as a white solid (607 mg, 96%); mp 170–171 °C (Found: C, 62.8; H, 8.3; N, 8.1. $C_9H_{14}ClN$ requires C, 63.0; H, 8.22; N, 8.16%).

Preparation of racemic (±)-1-(4-methoxyphenyl)ethylamine 12f

A solution of 4-methoxybenzonitrile (2.28 g, 17.1 mmol) in THF (4 cm^3) was treated with methyllithium (1.4 mol dm^{-3} in ether; 17.4 mmol) at −78 °C. The lithioketimine rapidly formed on warming to room temp. (red colouration). After 30 min lithium aluminium hydride (650 mg, 17.1 mmol) was added in small portions at 0 °C to the mixture, which was slowly warmed and refluxed for 3 h. The mixture was cooled and water (0.65 cm^3) was carefully added, followed by sodium hydroxide (15% w/v, 0.65 cm^3) and water (1.95 cm^3). The precipitated aluminium residues were filtered off through a Celite pad which was washed with ethyl acetate (30 cm^3). The amine was extracted with hydrochloric acid (2 mol dm^{-3}; 3 × 30 cm^3). The combined extracts were basified with sodium hydroxide pellets (pH > 12) and extracted with ethyl acetate (3 × 30 cm^3). The organic extracts were dried (Na_2SO_4), filtered and concentrated and the residue was distilled under reduced pressure (113 °C, 0.7 mmHg) to give **12f** as a clear oil (2.58 g, 87%); ν_{max}(film)/cm^{-1} 3365, 2960, 1610, 1512, 1463, 1237, 1100 and 1032; δ_H(270.2 MHz) 7.26 (2 H, d, *J* 8.6, AA′BB′ ArH), 6.86 (2 H, d, *J* 8.6, AA′BB′ ArH), 4.07 (1 H, q, *J* 6.6, C*H*NH_2), 3.79 (3 H, s, CH_3O), 1.58 (2 H, br s, NH_2) and 1.35 (3 H, d, *J* 6.6, CHCH_3); δ_C(60.7 MHz) 158.3 (s), 139.8 (s), 126.6 (d), 123.7 (d), 55.1 (q), 50.2 (d) and 25.6 (q); *m/z* (EI) 151 (M^+, 7%), 150 (6), 136 (100), 121 (6), 109 (16), 94 (8), 77 (8), 42 (7) and 28 (6). The amine (250 mg, 1.65 mmol) was dissolved in ether (5 cm^3) and anhydrous hydrogen chloride was bubbled through for 10 min. The salt was filtered off and recrystallised from isopropyl alcohol to give the product as a white solid (241 mg, 85%); mp > 200 °C (Found: C, 57.7; H, 7.6; N, 7.5. $C_9H_{14}ClNO$ requires C, 57.6; H, 7.52; N, 7.50%).

Preparation of racemic (±)-1-(4-methoxyphenyl)ethylamine 12f *via* reductive amination[25]

Ammonium formate (25.2 g, 400 mmol) was heated to 165 °C until no further water distilled off and then 4-methoxyphenylethanone (15 g, 100 mmol) was carefully added to the hot reaction mixture, allowing the frothing to subside between each addition. The temperature was maintained between 160–185 °C for 5 h and any sublimed reaction material was periodically scraped back into the mixture. After the mixture had cooled, water (50 cm^3) was added, the whole was vigorously stirred and the aqueous layer was discarded. The organic layer was treated with concentrated hydrochloric acid and refluxed for 1 h. The reaction mixture was diluted with hydrochloric acid (2 mol

dm^{-3}; 50 cm^3) and the unreacted ketone was extracted with ethyl acetate (3 × 20 cm^3). The aqueous layer was then carefully treated with solid sodium hydroxide pellets (pH > 12) and the crude amine was then extracted with ethyl acetate (3 × 50 cm^3). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. Distillation under reduced pressure gave the product amine **12f** as a clear oil (13.6 g, 90%). The product was identical to an authentic sample.

Preparation of the Mosher's amides of 1-phenylethylamine 12a, (*R*,*R*)-(−)-2-methoxy-2-phenyl-*N*-(1-phenylethyl)-2-trifluoromethylacetamide 13 and (*R*,*S*)-(−)-2-methoxy-2-phenyl-*N*-(1-phenylethyl)-2-trifluoromethylacetamide 14

(*R*)-1-Phenylethylamine **12a** (33 mg, 273 μmol), 4-dimethylaminopyridine (52 mg, 427 μmol), (*R*)-(+)-2-methoxy-2-phenyl-2-trifluoromethylacetic acid (100 mg, 427 μmol) and dicyclohexylcarbodiimide (88 mg, 427 μmol) were dissolved in CH_2Cl_2 (1.2 cm^3). The reaction mixture was stirred for 24 h, after which it was diluted with ethyl acetate (10 cm^3) and washed with hydrochloric acid (2 mol dm^{-3}, 5 cm^3), saturated aq. sodium hydrogen carbonate (5 cm^3) and brine (5 cm^3). The mixture was dried (Na_2SO_4), filtered and evaporated and the crude product was isolated by flash chromatography (7:3, hexane–ethyl acetate) and recrystallised (CH_2Cl_2–hexane). (R,R)-(−)-2-*methoxy*-2-*phenyl*-N-(1-*phenylethyl*)-2-*trifluoromethylacetamide* **13** (87 mg, 82%); mp 108–9 °C; $[\alpha]_D^{20}$ −20.4 (*c* 0.25, chloroform); δ_H(399.7 MHz) 7.50–7.20 (10 H, m, ArH), 6.94 (1 H, br d, *J* 6.9, NH), 5.19 (1 H, p, *J* 6.9, C*H*NH), 3.30 (3 H, q, *J* 1.5, CH_3O) and 1.44 (3 H, d, *J* 6.9, C*H*CH_3); δ_C(100.4 MHz) 165.4 (s), 142.3 (s), 132.7 (s), 129.4 (d), 128.7 (d), 128.5 (d), 127.53 (d), 127.49 (d), 126.1 (d), 123.8 (q, $^1J_{C,F}$ 290), 83.9 (q, $^2J_{C,F}$ 26.0), 54.9 (qq, $^3J_{C,F}$ 1.8), 48.8 (q) and 21.2 (q); *m*/*z* (FAB, thioglycolic) 338 (M + H^+, 61%), 234 (9), 202 (25), 189 (22) and 105 (100) (Found: C, 64.2; H, 5.2; N, 4.1. $C_{18}H_{18}F_3NO_2$ requires C, 64.09; H, 5.38; N, 4.15%) (Found: M + H^+, 338.1371. $C_{18}H_{18}F_3NO_2$ requires *M*, 338.1368). (R,S)-(−)-2-*methoxy*-2-*phenyl*-N-(1-*phenylethyl*)-2-*trifluoromethylacetamide* **14** (100 mg, 94%); mp 86–87 °C; $[\alpha]_D^{20}$ −78.8 (*c* 0.49, chloroform); ν_{max}(chloroform film)/cm^{-1} 3300 and 1672; δ_H(399.7 MHz) 7.44–7.25 (10 H, m, ArH), 7.02 (1 H, br d, *J* 6.9, NH), 5.18 (1 H, p, *J* 6.9, C*H*NH), 3.42 (3 H, q, *J* 1.5, CH_3O) and 1.54 (3 H, d, *J* 6.9, CHCH_3); δ_C(100.4 MHz) 165.2 (s), 142.4 (s), 132.4 (s), 129.3 (d), 128.6 (d), 128.4 (d), 127.6 (d), 127.4 (d), 126.1 (d), 120.9 (q, $^1J_{C,F}$ 290), 83.9 (q, $^2J_{C,F}$ 26.1), 54.8 (qq, $^3J_{C,F}$ 1.6), 47.8 (q) and 21.3 (q) (Found: C, 64.2; H, 5.3; N, 4.2. $C_{18}H_{18}F_3NO_2$ requires C, 64.09; H, 5.38; N, 4.15%).

Chiral HPLC separation of the enantiomers of 1-phenylethylamine 12a

Conditions; CHIRAL CEL OD column, 8% isopropyl alcohol–hexane–0.1% diethylamine, 0.5 cm^3 min^{-1}, λ = 215 nm, −10 °C. Retention times: (*R*)-(+)-1-phenylethylamine *R*-**12a**, 14.20 min; (*S*)-(−)-1-phenylethylamine *S*-**12a**, 17.06 min.

Preparation of ($R_{(S)}$,*R*,*R*)-(−)-2-[1-(*tert*-butylcarbonylamino)ethyl]-*N*-(1-phenylethyl)benzenesulfinamide 5a and ($R_{(S)}$,*R*,*R*)-(−)-2-[1-(*tert*-butylcarbonylamino)ethyl]-*N*-(1-phenylethyl)-benzenesulfinamide 6a

(*R*)-1-Phenylethylamine *R*-**12a** (101 mg, 836 μmol) in THF (4 cm^3) was treated with butyllithium (1.0 mol dm^{-3} in hexanes; 0.836 cm^3, 836 μmol) at −78 °C. After stirring at room temp. for 30 min, the cyclic sulfinamide $S_{(S)}$*R*-(+)-**1** (200 mg, 836 μmol) in THF (2 cm^3) was added dropwise at −78 °C. The reaction was warmed to 0 °C and quenched with saturated aq. ammonium chloride (4 cm^3) after 30 min. The crude product was extracted with ethyl acetate (3 × 4 cm^3) and the extracts were dried (Na_2SO_4), filtered and evaporated under reduced pressure. The product was isolated by flash chromatography (1:1, ethyl acetate–light petroleum) and recrystallised (carbon tetrachloride) to give the product as a white solid. ($R_{(S)}$,R,R)-(−)-2-[1-(tert-*butylcarbonylamino*)*ethyl*]-N-(1-*phenylethyl*)-*benzenesulfinamide* **5a** (286 mg, 92%); mp 93–4 °C; $[\alpha]_D^{20}$ −90.6 (*c* 0.51, chloroform); ν_{max}(Nujol)/cm^{-1} 3327, 3186, 1641 and 1458; δ_H([$^2H_6$]acetone, 399.7 MHz) 7.83 (1 H, dd, *J* 7.7, 1.4, ArH), 7.56 (1 H, dd, *J* 7.8, 1.2, ArH), 7.45 (1 H, td, *J* 7.4 and 1.3, ArH), 7.40–7.36 (2 H, m, ArH and NHCO), 7.27–7.14 (5 H, m, ArH), 6.61 (1 H, br d, *J* 6.3, NHSO), 5.65 (1 H, p, *J* 6.9, C*H*NHCO), 4.52 (1 H, p, *J* 6.7, C*H*NHSO), 1.56 (3 H, d, *J* 6.8, CH_3CHNHSO), 1.31 (3 H, d, *J* 6.9, CH_3CHNHCO) and 1.12 [9 H, s, C$(CH_3)_3$]; δ_C([$^2H_6$]acetone, 100.4 MHz) 177.8 (s), 145.7 (s), 144.6 (s), 144.3 (s), 131.6 (d), 128.9 (d), 127.65 (d), 127.63 (d), 127.4 (d), 127.3 (d), 125.0 (d), 54.1 (d), 45.1 (d), 38.7 (s), 27.7 (q), 24.8 (q) and 21.6 (q); *m*/*z* (FAB) 373 (M + H^+, 12%), 252 (41), 168 (60), 150 (88), 105 (39) and 57 (100) (Found: M + H^+, 373.1961. $C_{21}H_{29}N_2O_2S$ requires *M*, 373.1950). ($R_{(S)}$,R,S)-(−)-2-[1-(tert-*butylcarbonylamino*)*ethyl*]-N-(1-*phenylethyl*)*benzenesulfinamide* **6a** (292 mg, 94%); mp 117 °C; $[\alpha]_D^{20}$ −95.5 (*c* 0.50, chloroform); δ_H[$^2H_6$]acetone, 399.7 MHz) 7.64 (1 H, dd, *J* 7.6 and 1.4, ArH), 7.58 (1 H, br d, *J* 7.6, NHCO), 7.55 (1 H, dd, *J* 7.6 and 1.0, ArH), 7.49–7.42 (3 H, m, ArH and NHCO), 7.36–7.28 (3 H, m, ArH), 7.25 (1 H, tt, *J* 7.3 and 1.4, *p*-ArH), 7.04 (1 H, br d, *J* 4.9, NHSO), 5.83 (1 H, p, *J* 6.9, C*H*NHCO), 4.61 (1 H, p, *J* 6.7, C*H*NHSO), 1.52 (3 H, d, *J* 6.7, CH_3CHNHSO), 1.42 (3 H, d, *J* 6.8, CH_3CHNHCO) and 1.16 [9 H, s, C$(CH_3)_3$]; δ_C([$^2H_6$]acetone, 100.4 MHz) 178.4 (s), 145.4 (s), 145.3 (s), 144.6 (s), 131.8 (d), 129.1 (d), 127.93 (d), 127.90 (d), 127.8 (d), 55.3 (d), 45.5 (d), 38.8 (s), 27.6 (q), 25.2 (q) and 22.3 (q).

($R_{(S)}$,*R*)-2-[1-(*tert*-butylcarbonylamino)ethyl]-*N*-(1-phenylethylidene)benzenesulfinamide 4a

Methyllithium (1.31 mol dm^{-3} in ether; 0.77 cm^3, 1.0 mmol) was added dropwise to a solution of benzonitrile (103 mg, 1.0 mmol) in THF (2 cm^3) at −78 °C. The solution was warmed to 0 °C and stirred for 30 min to give the orange coloured lithioketimine. The cyclic sulfinamide $S_{(S)}$*R*-(+)-**1** (251 mg, 1.0 mmol) in THF (3 cm^3) was added slowly at −78 °C. Rapid decolourisation occurred and was complete within 30 min at 0 °C. Saturated aq. ammonium chloride (5 cm^3) was added and the product extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were dried (Na_2SO_4), filtered and evaporated under reduced pressure to give a pale yellow oil. The title compound $S_{(S)}$*R*-(−)-**4a** was isolated by flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) to give a pale yellow foam (288 mg, 78%); $[\alpha]_D^{20}$ −36.0 (*c* 0.63, chloroform); ν_{max}(chloroform film)/cm^{-1} 3349, 1647, 1589 and 1522; δ_H(270.2 MHz) 8.08–8.02 (1 H, m, ArH), 7.75 (1 H, d, *J* 7.3, ArH), 7.46–7.26 (7 H, m, ArH), 6.04 (1 H, d, *J* 6.8, NH), 5.42 (1 H, p, *J* 6.8, C*H*NH), 2.80 (3 H, s, CCH_3), 1.44 (3 H, d, *J* 6.8, CH_3CH) and 1.11 [9 H, s, C$(CH_3)_3$]; δ_C(100.4 MHz) 177.4 (s), 144.3 (s), 141.2 (s), 138.4 (s), 131.5 (d), 128.3 (d), 128.2 (d), 127.9 (d), 127.4 (d), 125.9 (d), 125.0 (d), 46.1 (d), 45.3 (q), 38.2 (s), 27.3 (q) and 21.5 (q); *m*/*z* (TSP) 371 (M^+, 100%), 248 (27), 269 (53), 254 (26), 238 (51), 223 (30), 206 (26) and 150 (19) (Found: M^+, 371.1790. $C_{21}H_{27}N_2O_2S$ requires *M*, 371.1793).

General procedures for the reduction of the sulfinylimine 4a

Unless otherwise indicated, routine work-up was as follows: The crude mixtures resulting from hydrolysis were extracted with ethyl acetate, dried (Na_2SO_4) and concentrated under reduced pressure. Diastereoisomeric excesses (de) were determined by ^1H NMR and HPLC.

With lithium aluminium hydride. A solution of **4a** (50 mg, 135 μmol) in THF (2 cm^3) was treated with lithium aluminium hydride (5.1 mg, 135 μmol) at room temp. Water (2 cm^3) was added followed by ethyl acetate (5 cm^3) and the mixture was filtered through a Celite pad.

With sodium borohydride.† A solution of **4a** (50 mg, 135 μmol) in methanol (2 cm^3) was treated with sodium borohydride (5.1 mg, 135 μmol) at 0 °C. The reaction was quenched with saturated aq. ammonium chloride (2 cm^3).

With the Selectrides®. A solution of **4a** (50 mg, 135 μmol) in either ether or THF (1 cm^3) was treated with either L- or LS-Selectride (1.0 mol dm^{-3} in THF; 0.270 cm^3, 270 μmol) at −78 °C. The reaction was quenched with saturated aq. ammonium chloride (1 cm^3) and worked up as above. Methanol (5 cm^3) was added to the white solid and heated for a few min after which the remaining solid was filtered off and the filtrate evaporated.

With Red-Al®. A solution of **4a** (50 mg, 135 μmol) in THF (1 cm^3) was treated with Red-Al (3.4 mol dm^{-3} in toluene; 0.079 cm^3, 270 μmol) at −78 °C and then quenched with saturated aq. ammonium chloride (1 cm^3).

With bis(alkoxy)lithium aluminium hydride. Lithium aluminium hydride (1.0 mol dm^{-3} in THF; 0.162 cm^3, 162 μmol) was treated with either methanol or *tert*-butyl alcohol (324 μmol) with rapid stirring at room temp. A solution of **4a** (30 mg, 810 μmol) in THF (0.25 cm^3) was added at −78 °C. Methanol (1 cm^3) was added to the mixture, which was then evaporated under reduced pressure. Aqueous sodium hydroxide (2 mol dm^{-3}; 1 cm^3) was added to the residue, which was worked up as above, with ethyl acetate (3 × 3 cm^3).

With DIBAL. A solution of **4a** (50 mg, 135 μmol) in THF (0.5 cm^3) was added to DIBAL (1.0 mol dm^{-3} in hexanes; 0.30 cm^3, 300 μmol) in THF (0.5 cm^3) at the required temp. (see Table 1). Methanol (1 cm^3) was added to the mixture, which was then evaporated under reduced pressure. Aqueous sodium hydroxide (15% w/v, 1 cm^3) was added to the residue, which was worked up as above, with ethyl acetate (3 × 3 cm^3).

With $ZnBr_2$–DIBAL. A solution of **4a** (50 mg, 135 μmol) in THF (1 cm^3) was treated with zinc bromide (1.0 mol dm^{-3} in THF; 0.135 cm^3, 135 μmol) and stirred at room temp. for 30 min. The mixture was cooled to the required temp. and DIBAL (1.0 mol dm^{-3} in hexanes; 0.30 cm^3, 300 μmol) was slowly added. Methanol (1 cm^3) was added to the mixture, which was evaporated under reduced pressure. Aqueous sodium hydroxide (15% w/v, 1 cm^3) was added to the residue, which was worked up as above, with ethyl acetate (3 × 3 cm^3).

Hydrolysis of the reduction products of $R_{(S)}R$-(−)-4a

A mixture of the sulfinamides $R_{(S)}RR$-(−)-**5a** and $R_{(S)}RS$-(−)-**6a** (86% de in favour of **5a**, 50 mg, 134 μmol) in methanol (0.5 cm^3) was treated with trifluoroacetic acid (30 mg, 0.021 cm^3, 268 μmol). After 2 h, hydrochloric acid (2 mol dm^{-3}, 1.0 cm^3) was added and the mixture extracted with CH_2Cl_2 (3 × 2 cm^3). The combined organic extracts were dried (Na_2SO_4), filtered and evaporated under reduced pressure to give the sulfinic acid *R*-(−)-**11** (36 mg, 96%); mp 66 °C; $[\alpha]_D^{20}$ −70 (*c* 0.43, chloroform); ν_{max}(Nujol)/cm^{-1} 3316, 2485, 1660, 1102 and 805; δ_H 270.2 MHz) 7.61 (1 H, d, *J* 6.4, ArH), 7.49 (3 H, m, ArH), 6.53 (1 H, br d, *J* 6.8, NH), 6.10 (1 H, p, *J* 6.8, CH), 1.55 (3 H, d, *J* 6.8, $CHCH_3$) and 1.16 [9 H, s, $C(CH_3)_3$]; δ_C(67.8 MHz) 176.9 (s), 145.2 (s), 141.1 (s), 131.7 (d), 127.2 (d), 126.0 (d), 122.3 (d), 43.98 (d), 37.95 (s), 27.37 (q) and 22.21 (q); *m/z* (FAB) 270 (M + H^+, 100%), 252 (7), 205 (21) and 150 (93) (Found: M + H^+, 270.1160. $C_{13}H_{19}NO_3S$ requires *M*, 270.1164). A solution of **11** in water was treated with aq. sodium hydroxide (2 mol dm^{-3}; *ca.* 3 cm^3; pH > 12) and extracted with CH_2Cl_2 (3 × 2 cm^3). The combined extracts were dried (Na_2SO_4), filtered and evaporated to give the enantiomerically enriched amine **12a** (15.5 mg, 92%) which was subsequently converted into the corresponding Mosher's amide. ^1H NMR analysis of the Mosher's amide indicated that the major diastereoisomer was *R,R*-(−)-**13** (de 86%). Chiral HPLC confirmed that the enantiomeric purity of the amine was 86% ee.

Examination of the effect of $ZnBr_2$ concentration on the diastereoselectivity for the reduction of the sulfinylimine 4a using DIBAL in THF

A solution of **4a** (50 mg, 135 μmol) in THF (1 cm^3) was treated with zinc bromide (1.0 mol dm^{-3} in THF: 25 mol % ⇒ 0.34 cm^3, 34 μmol; 50 mol % ⇒ 0.0675 cm^3, 67.5 μmol; 75 mol % ⇒ 0.101 cm^3, 101 μmol; 100 mol % ⇒ 0.135 cm^3, 135 μmol; 150 mol% ⇒ 0.202 cm^3, 202 μmol) and stirred at room temp. for 30 min. DIBAL (1.0 mol dm^{-3} in hexanes; 0.30 cm^3, 300 μmol) was slowly added to the mixture at room temp. and after 30 min, methanol (1 cm^3) was added to the reaction, which was vigorously stirred. After 5 min the mixture was evaporated under reduced pressure. Aqueous sodium hydroxide (15% w/v, 1 cm^3) was added to the residue and the mixture was then extracted with ethyl acetate (2 × 1 cm^3). The combined extracts were dried (Na_2SO_4), filtered and evaporated. The residue was dissolved in deuteriochloroform (*ca.* 0.6 cm^3) and the de of the reaction was determined by ^1H NMR. Results: Amount of $ZnBr_2$ (mol %)/% de of $R_{(S)}RS$-(−)-**6a**; 0/−70.0; 0.25/−29.8; 0.50/11.1; 0.75/51.4; 1.00/91.9; 1.50/92.1 (minus sign denotes $R_{(S)}RR$-**5a** major product).

Preparation of (±)-(*S,E*)-*N*-(1-phenylethylidene)toluene-*p*-sulfinamide 8

To a solution of silver nitrate (4.5 g, 27 mmol) in methanol (300 cm^3) at 0 °C was added *p*-tolyl disulfide (6.82 g, 27 mmol). Anhydrous ammonia was passed through the mixture for 15 min until the formation of a white precipitate was observed and acetophenone was added in a fast dropwise fashion. The reaction mixture was allowed to warm to room temp. and mechanically stirred for 16 h. The precipitated silver salt was filtered off and washed with methanol (100 cm^3). The filtrate was concentrated under reduced pressure and the crude sulfenylimine was distilled under reduced pressure (198–200 °C, 1 mmHg) to give the product **7** as a pale yellow oil (4.20 g, 68%); ν_{max}(film)/cm^{-1} 3018, 2919, 1893, 1597, 1489, 1366, 1287, 1091 and 1019; δ_H(270.2 MHz) 7.79–7.75 (2 H, m, ArH), 7.51 (2 H, d, *J* 8.3, ArH), 7.34 (2 H, dd, *J* 8.4 and 8.3, ArH), 7.17 (2 H, d, *J* 8.4, ArH), 2.41 (3 H, s, CH_3) and 2.32 (3 H, s, CH_3); δ_C(60.7 MHz) 161.0 (s), 139.3 (s), 135.9 (s), 129.5 (d), 129.1 (d), 128.5 (d), 126.0 (d), 125.6 (d), 21.0 (q) and 19.8 (q). The sulfenylimine **7** (1.0 g, 4.36 mmol) was dissolved in chloroform (6 cm^3) and sodium hydrogen carbonate (550 mg, 6.55 mmol) in water (5 cm^3) was added. The biphasic mixture was cooled to 0 °C and vigorously stirred. *m*-Chloroperbenzoic acid (MCPBA; 60% dispersion, 1.63 g, 5.65 mmol) in chloroform (16 cm^3) was added dropwise and the solution was stirred for 30 min at 0 °C then at room temp. for a further 30 min. The organic layer was separated, washed with saturated aq. sodium hydrogen carbonate (2 × 10 cm^3), dried (Na_2SO_4), filtered and evaporated under reduced pressure. The product **8** was isolated by flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) to give a white solid (535 mg, 50%); δ_H(270.2 MHz) 7.87 (2 H, d, *J* 7.3, ArH), 7.72 (2 H, d, *J* 8.1, ArH), 7.48–7.29 (5 H, m, ArH), 2.75 (3 H, s, CH_3) and 2.38 (3 H, s, CH_3); δ_C(60.7 MHz) 174.9 (s), 143.2 (s), 141.6 (s), 138.0 (s), 131.7 (d), 128.3 (d), 127.3 (d), 125.0 (d), 21.3 (q) and 20.1 (q); *m/z* (FAB) 258 (M + H^+, 37%), 241 (13), 209 (12), 154 (23), 139 (100), 120 (63) and 77 (20) (Found: M + H^+, 258.0955. $C_{15}H_{16}NOS$ requires *M*, 258.0953).

Preparation of ($R_{(S)}$,*R*)- and ($S_{(S)}$,*R*)-*N*-(1-phenylethyl)toluene-*p*-sulfinamide 9 and 10

To a stirred solution of toluene-*p*-thiol (2 g, 16.12 mmol) in 10% aq. methanol (68 cm^3) was added in one portion sodium periodate (6.88 g, 32.24 mmol). The resultant dark brown reaction mixture was stirred at ambient temperature for 16 h

† The recommended IUPAC name for the BH_4^- ion or 'borohydride' is boranuide.

and then poured into ethyl acetate (200 cm^3). The organic phase was washed with water (200 cm^3) and saturated aq. sodium thiosulfate (200 cm^3), dried (Na_2SO_4), filtered and evaporated under reduced pressure. The crude mixture was chromatographed on a silica column (0 ⟶ 25%, ethyl acetate–light petroleum). The second eluted compound was the required racemic methyl toluene-*p*-sulfinate (1.85 g, 68%); δ_H(270.2 MHz) 7.59 (2 H, d, *J* 8.6, ArH), 7.35 (2 H, d, *J* 8.6, ArH), 3.44 (3 H, s, OCH_3) and 2.42 (3 H, s, CH_3). In a separate flask (*R*)-(+)-1-phenylethylamine **12a** (182 mg, 1.50 mmol) in THF (2 cm^3) was treated with butyllithium (1.6 mol dm^{-3} in hexanes; 0.94 cm^3, 1.50 mmol) at −78 °C. After 5 min it was warmed to room temp. and stirred for 30 min. The racemic methyl toluene-*p*-sulfinate (281 mg, 1.65 mmol) was added dropwise, neat, at −78 °C. The mixture was stirred at room temp. for 30 min after which it was quenched with saturated aq. ammonium chloride (3 cm^3). The product was extracted with ethyl acetate (3 × 5 cm^3) and the solution was dried (Na_2SO_4), filtered and evaporated. The product was isolated by flash chromatography (3:7, ethyl acetate–hexane), which consisted of a 1:1 mixture of diastereoisomers (331 mg, 87%); $R_{(S)}R$-**9** had δ_H(270.2 MHz) 7.48 (2 H, d, *J* 8.2, ArH), 7.37–7.11 (7 H, m, ArH), 4.49 (1 H, dq, *J* 6.8 and 6.7, C*H*NH), 4.18 (1 H, br d, *J* 4.3, NH), 2.30 (3 H, s, CH_3Ar) and 1.55 (3 H, d, *J* 6.7, CHCH_3). $S_{(S)}R$-**10** had δ_H(270.2 MHz) 7.53 (2 H, d, *J* 8.2, ArH), 7.37–7.11 (7 H, m, ArH), 4.60 (1 H, dq, *J* 6.8 and 6.7, C*H*NH), 4.07 (1 H, br d, *J* 4.3, NH), 2.34 (3 H, s, CH_3Ar) and 1.39 (3 H, d, *J* 6.7, CHCH_3).[16,9]

DIBAL reduction of the sulfinylimine 8

A solution of the sulfinylimine **8** (100 mg, 389 μmol) in THF (1.0 cm^3) was added to a solution of DIBAL (1.0 mol dm^{-3} in hexanes; 0.43 cm^3, 430 μmol) in THF (1.0 cm^3) at room temp. After 30 min, methanol (1.0 cm^3) was added to the mixture, which was evaporated under reduced pressure after 5 min. The residue was treated with aq. sodium hydroxide (15% w/v, 1 cm^3) and then extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were dried (Na_2SO_4), filtered and evaporated. A small portion of the residue was dissolved in methanol (*ca.* 0.5 cm^3) and the diastereoisomeric excess of the crude sulfinamides **9** and **10** was determined by HPLC to be 65% de in favour of isomer **9**. The remainder was purified by flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) to give the required product as a white solid (90 mg, 89%).

$ZnBr_2$ mediated DIBAL reduction of the sulfinylimine 8

A solution of the sulfinylimine **8** (100 mg, 389 μmol) in THF (1.0 cm^3) was treated with zinc bromide (1.0 mol dm^{-3} in THF; 0.389 cm^3, 389 μmol) and stirred at room temp. for 30 min. A solution of DIBAL (1.0 mol dm^{-3} in hexanes; 0.43 cm^3, 430 μmol) was slowly added at room temp. After 30 min methanol (1.0 cm^3) was added to the mixture, which was evaporated under reduced pressure after 5 min. The residue was treated with aq. sodium hydroxide (15% w/v, 1 cm^3) and then extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were dried (Na_2SO_4), filtered and evaporated. A small portion of the residue was dissolved in methanol (*ca.* 0.5 cm^3) and the diastereoisomeric excess of the crude sulfinamides **9** and **10** was determined by HPLC to be 14% de in favour of isomer **9**. The remainder was purified by flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) to give the required product as a white solid (82 mg, 81%).

Attempted preparation of ($R_{(S)}$,*R*)-2-[1-(*tert*-butylcarbonylamino)ethyl]-*N*-(1-phenylpropylidene)benzenesulfinamide 4b; preparation of enamine 15

Benzonitrile (206 mg, 2.0 mmol) in THF (4 cm^3) was treated with ethyl magnesium bromide (2.0 mol dm^{-3} in THF; 1.05 cm^3, 2.1 mmol) at −78 °C. The solution was warmed to room temp. and stirred for 30 min. The blood red solution was recooled to −78 °C and the cyclic sulfinamide $S_{(S)}R$-(+)-**1** (500 mg, 2.0 mmol) in THF (4 cm^3) was added dropwise. The solution rapidly decolourised to give a pale yellow solution. After 30 min saturated aq. ammonium chloride (10 cm^3) was added and the product was extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The product was isolated by flash chromatography (3:7, ethyl acetate–hexane) and recrystallised (CH_2Cl_2–hexane) to give $R_{(S)}R$-(−)-(*Z*)-**15** as a white crystalline solid (677 mg, 88%); mp >200 °C; $[\alpha]_D^{17}$ −35.5 (*c* 0.56, chloroform); ν_{max}(chloroform film)/cm^{-1} 3683, 3025, 1649, 1521, 1476, 1423 and 1216; δ_H(399.7 MHz) 8.80 (1 H, s, NHSO), 7.56 (2 H, d, *J* 6.8), 7.52 (1 H, d, *J* 7.3), 7.45–7.22 (6 H, m), 6.25 (1 H, d, *J* 5.4, NHCO), 6.12 (1 H, p, *J* 6.8, ArC*H*CH_3), 5.37 (1 H, q, *J* 7.3, C=C*H*CH_3), 1.79 (3 H, d, *J* 7.3, C=CHCH_3), 1.53 (3 H, d, *J* 6.8, ArCHCH_3) and 1.16 (9 H, s); δ_C([$^2H_6$]acetone, 100.4 MHz) 178.1 (s), 144.0 (s), 143.3 (s), 138.8 (s), 131.3 (s), 128.6 (d), 128.2 (d), 127.9 (d), 127.8 (d), 127.5 (d), 126.6 (d), 125.5 (d), 113.1 (d), 45.5 (d), 38.3 (s), 27.4 (q), 22.5 (q) and 12.9 (q); *m/z* (FAB) 385 (M + H^+, 6), 328 (29), 282 (4), 204 (20), 150 (100), 135 (33), 105 (15) and 57 (43) (Found: C, 68.4; H, 7.3; N, 7.1. $C_{22}H_{28}N_2O_2S$ requires C, 68.6; H, 7.33; N, 7.27%) (Found: M + H^+, 385.1948. $C_{22}H_{29}N_2O_2S$ requires *M*, 385.1950).

X-Ray crystallographic data for 15. A crystal of approximate dimensions 0.3 × 0.1 × 0.4 mm was used for data collection. $C_{22}H_{28}N_2O_2S$, *M* = 384.5, orthorhombic, *a* = 9.964(3), *b* = 10.933(2), *c* = 20.297(3) Å, *U* = 2211.2 $Å^3$, space group $P2_12_12_1$, D_c = 1.16 g cm^{-3}, μ(Mo-Kα) = 10.8 cm^{-1}, *F*(000) = 1464. Data were measured at room temp. on a CAD4 automatic four-circle diffractometer in the range $2 \leqslant \theta \leqslant 24°$. 2015 Reflections were collected of which 1053 were unique with $I \geqslant 2\sigma(I)$. Data were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by direct methods and refined using the SHELX suite of programs.[26] In the final least squares cycles all non-hydrogen atoms were allowed to vibrate anisotropically. Hydrogen atoms were included at calculated positions except in the instances of the protons attached to N1, N2 and C8. In these cases the hydrogens were located in an advanced difference Fourier and refined at a distance of 0.98 Å and 1.08 Å from the relevant parent nitrogen and carbon atoms respectively. Final residuals after 14 cycles of least squares were *R* = 0.0459 and R_w = 0.0351, for a weighting system of $w = 2.3424/[\sigma^2(F) + 0.000\,071(F)^2]$. Max. final shift/esd was 0.004. The max. and min. residual densities were 0.11 and −0.13 e $Å^{-3}$ respectively.

Preparation of ($R_{(S)}$,*R*)-2-[1-(*tert*-butylcarbonylamino)ethyl]-*N*-(2-methyl-1-phenylpropylidene)benzenesulfinamide 4c

Benzonitrile (206 mg, 2.0 mmol) and copper(I) chloride (19.8 mg, 200 μmol) in THF (4 cm^3) were treated with isopropylmagnesium iodide (2.0 mol dm^{-3} in THF; 1.05 cm^3, 2.1 mmol) at 0 °C. The solution was gently warmed to reflux and heated for 3 h. The reddish-brown solution was cooled to 0 °C and the cyclic sulfinamide $S_{(S)}R$-(+)-**1** (500 mg, 2.0 mmol) in THF (4 cm^3) was added dropwise. The solution decolourised to give a pale yellow solution which was allowed to warm to room temp. After 30 min saturated aq. ammonium chloride (10 cm^3) was added and the product was extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The product was isolated by flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) to give $R_{(S)}R$-(−)-**4c** as a pale yellow foam (430 mg, 54%); $[\alpha]_D^{18}$ +127.4 (*c* 1.14, chloroform); ν_{max}(chloroform film)/cm^{-1} 3347, 2970, 1644, 1521, 1210 and 1080; δ_H(270.2 MHz) 7.90 (1 H, dd, *J* 7.6 and 1.5, ArH), 7.50–7.35 (6 H, m, ArH), 7.24–7.18 (2 H, m, ArH), 6.04 (1 H, br d, *J* 6.7, CHN*H*CO), 5.05 (1 H, p, *J* 6.7, C*H*NHCO), 3.12–2.94 [1 H, m, C*H*$(CH_3)_2$], 1.45 (3 H, d, *J* 6.8, CH_3CHNH), 1.17 [3 H, d, *J* 6.8, CH$(CH_3)_2$], 1.15 [3 H, d, *J* 6.8, CH$(CH_3)_2$] and 1.10

[9 H, s, C(CH_3)$_3$]; δ_C(100.4 MHz) 178.3 (s), 146.4 (s), 143.7 (s), 141.2 (s), 132.6 (d), 129.8 (d), 129.3 (d), 128.9 (d), 128.0 (d), 126.9 (d), 125.2 (d), 45.6 (d), 32.7 (s), 27.4 (q), 20.6 (d), 24.5 (q) and 15.5 (q); *m/z* (FAB) 399 (M + H$^+$, 25), 252 (30), 236 (5), 204 (5), 168 (28), 150 (100), 135 (5), 120 (7), 104 (7) and 90 (11); *m/z* (EI) 356 (4), 303 (4), 288 (4), 268 (12), 253 (8), 251 (7), 236 (23), 204 (100), 193 (8), 168 (15), 150 (86), 135 (43),121 (10), 105 (62), 91 (16), 77 (34) and 57 (92) (Found: M$^+$, 204.1390. $C_{13}H_{18}NO$ requires *M*, 204.1388. Found: M$^+$, 193.0557. $C_{10}H_{11}NOS$ requires *M*, 193.0561).

Preparation of ($R_{(S)}$,*R*)-2-[1-(*tert*-butylcarbonylamino)ethyl]-*N*-(2,2-dimethyl-1-phenylpropylidene)benzenesulfinamide 4d

Benzonitrile (206 mg, 2.0 mmol) and copper(I) chloride (19.8 mg, 200 μmol) in THF (4 cm^3) were treated with *tert*-butylmagnesium iodide (2.0 mol dm^{-3} in THF; 1.05 cm^3, 2.1 mmol) at 0 °C. The solution was gently warmed to reflux, and heated for 5 h. The reddish-brown solution was cooled to 0 °C and the cyclic sulfinamide $S_{(S)}R$-(+)-**1** (500 mg, 2.0 mmol) in THF (4 cm^3) was added dropwise. The solution decolourised to give a pale yellow solution which was allowed to warm to room temp. After 30 min saturated aq. ammonium chloride (10 cm^3) was added and the product was extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were dried (Na_2SO_4), filtered and evaporated under reduced pressure. The product was isolated by flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) to give $R_{(S)}$-(−)-**4d** as a pale yellow foam (429 mg, 52%); $[\alpha]_D^{20}$ −105.2 (*c* 1.24, chloroform); ν_{max}(chloroform film)/cm^{-1} 3515, 2999, 1652, 1520, 1424, 1215 and 1004; δ_H(399.7 MHz) 7.83 (1 H, dd, *J* 7.6 and 1.5, ArH), 7.50–7.35 (8 H, m, ArH), 6.01 (1 H, br d, *J* 6.7, CHN*H*CO), 4.84 (1 H, p, *J* 6.7, C*H*NHCO), 1.44 (3 H, d, *J* 6.8, CH_3CHNH), 1.19 [9 H, s, C(CH_3)$_3$] and 1.11 [9 H, s, C(CH$_3$)$_3$]; δ_C(100.4 MHz) 178.6 (s), 147.2 (s), 141.5 (s), 136.5 (s), 131.7 (d), 128.7 (d), 128.6 (d), 128.1 (d), 126.6 (d), 126.2 (d), 126.1 (d), 45.6 (d), 28.2 (s), 27.9 (q), 27.4 (s), 27.4 (q) and 20.8 (q); *m/z* (FAB) 413 (M + H$^+$, 16), 328 (34), 252 (2), 204 (5), 162 (100), 91 (5) and 57 (25) (Found: M + H$^+$, 413.2253. $C_{24}H_{33}N_2O_2S$ requires *M*, 413.2263).

Preparation of ($R_{(S)}$,*R*)-2-[1-(*tert*-butylcarbonylamino)ethyl]-*N*-[1-(*p*-tolyl)ethylidene]benzenesulfinamide 4e

p-Tolyl cyanide (234 mg, 2.0 mmol) in THF (4 cm^3) was treated with methyllithium (1.4 mol dm^{-3} in ether; 1.5 cm^3, 2.1 mmol) at −78 °C. The solution was warmed to room temp. and stirred for 30 min. The blood red solution was re-cooled to −78 °C and the cyclic sulfinamide $S_{(S)}R$-(+)-**1** (500 mg, 2.0 mmol) in THF (4 cm^3) was added dropwise. The solution rapidly decolourised to give a pale yellow solution. After 30 min saturated aq. ammonium chloride (10 cm^3) was added and the product was extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The product was isolated by flash chromatography (3:7, ethyl acetate–hexane) to give $R_{(S)}$-(−)-**4e** as a pale yellow foam (677 mg, 88%); $[\alpha]_D^{18}$ −106.1 (*c* 1.13, chloroform); ν_{max}(chloroform film)/cm^{-1} 3683, 3027, 1659, 1518, 1424, 1220 and 928; δ_H([$^2H_6$]acetone, 270.2 MHz) 8.18–8.14 (1 H, m, ArH), 7.91 (2 H, d, *J* 8.2, ArH), 7.77–7.56 (3 H, m, ArH), 7.51 (1 H, br d, *J* 6.8, NH), 7.35 (2 H, d, *J* 8.1, ArH), 5.63 (1 H, quintet, *J* 7.0, C*H*NH), 3.01 (3 H, s, CCH_3), 2.46 (3 H, s, CH_3Ar), 1.54 (3 H, d, *J* 7.0, C*H*CH$_3$) and 1.26 [9 H, s, C(CH$_3$)$_3$]; δ_C([$^2H_6$]acetone, 67.8 MHz) 181.1 (s), 179.4 (s), 149.3 (s), 148.0 (s), 147.0 (s), 140.8 (s), 135.9 (d), 133.8 (d), 132.4 (d), 132.2 (d), 130.7 (d), 128.4 (d), 49.5 (d), 42.8 (q), 31.6 (q), 26.0 (q), 25.2 (q) and 23.5 (s); *m/z* (FAB) 385 (M$^+$, 30), 252 (25), 168 (28), 150 (78) and 134 (100) (Found: M$^+$, 385.1949. $C_{22}H_{29}N_2O_2S$ requires *M*, 385.1950).

Preparation of ($R_{(S)}$,*R*)-2-[1-(*tert*-butylcarbonylamino)ethyl]-*N*-[1-(4′-methoxyphenyl)ethylidene]benzenesulfinamide 4f

4-Methoxybenzonitrile (266 mg, 2.0 mmol) in THF (4 cm^3) was treated with methyllithium (1.4 mol dm^{-3} in ether; 1.5 cm^3, 2.1 mmol) at − 78 °C. The solution was warmed to room temp. and stirred for 30 min. The dark brown solution was re-cooled to −78 °C and the cyclic sulfinamide $S_{(S)}R$-(+)-**1** (500 mg, 2.0 mmol) in THF (4 cm^3) was added dropwise. After 30 min saturated aq. ammonium chloride (10 cm^3) was added and the product was extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. Flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) failed to isolate any of the required product $R_{(S)}R$-**4f**, instead the cyclic sulfinamide (460 mg, 92%) was recovered with 4-methoxyphenylethanone (240 mg, 80%) along with a trace of 4-methoxybenzonitrile.

Preparation of the standard reduction products 5b–f and 6b–f from the corresponding racemic amines

A solution of required amine (1.0 mmol) in THF (2 cm^3) was treated with butyllithium (2.5 mol dm^{-3} in hexanes; 0.4 cm^3, 1.0 mmol) at −78 °C and the solution was stirred at room temp. for 30 min. The mixture was re-cooled to −78 °C and the cyclic sulfinamide $S_{(S)}R$-(+)-**1** (251 mg, 1.0 mmol) in THF (2 cm^3) was added in a fast dropwise manner. After stirring at room temp. for 30 min, saturated aq. ammonium chloride (5 cm^3) was added and the product extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were dried (Na_2SO_4), filtered and evaporated. The two diastereoisomers were separated by flash chromatography (1:1, ethyl acetate–hexane) to give white foams.

For (±)-1-phenylpropylamine 12b. $R_{(S)}RR$-(−)-**5b** (158 mg, 41%); $[\alpha]_D^{20}$ −198.2 (*c* 1.01, chloroform); ν_{max}(chloroform film)/cm^{-1} 3016, 2981, 1646, 1511, 1418 and 1210; δ_H(399.7 MHz) 7.51 (1 H, d, *J* 8.3, ArH), 7.41–7.06 (8 H, m, ArH), 6.65 (1 H, br s, CHN*H*CO), 6.44 (1 H, br s, CHN*H*), 5.80 (1 H, p, *J* 6.7, C*H*NHCO), 4.37 (1 H, dt, *J* 8.2 and 5.2, C*H*CH$_2$), 2.00–1.92 (1 H, m, CHCH_2), 1.88–1.76 (1 H, m, CHCH_2), 1.43 (3 H, d, *J* 6.7, CH_3CHNH), 1.15 [9 H, s, C(CH_3)$_3$] and 0.81 (3 H, t, *J* 7.3, CH$_2$CH_3]; δ_C(100.4 MHz) 177.8 (s), 143.3 (s), 142.8 (s), 141.6 (s), 131.0 (d), 128.2 (d), 127.6 (d), 127.2 (d), 127.1 (d), 126.4 (d), 124.9 (d), 60.7 (d), 44.8 (d), 38.2 (s), 30.9 (t), 27.2 (q), 21.9 (q) and 10.4 (q); *m/z* (EI) 386 (M$^+$, 4), 357 (3), 309 (2), 251 (49), 234 (25), 204 (7), 190 (6), 168 (28), 166 (14), 150 (100), 136 (32), 119 (28), 105 (20), 91 (34) and 57 (52) (Found: M$^+$, 386.2016. $C_{22}H_{30}N_2O_2S$ requires *M*, 386.2028). $R_{(S)}RS$-(−)-**6b** (162 mg, 42%); $[\alpha]_D^{20}$ −217.6 (*c* 0.99, chloroform); δ_H(399.7 MHz) 7.91 (1 H, dd, *J* 5.8 and 3.7, ArH), 7.50–7.05 (8 H, m, ArH), 5.94 (1 H, d, *J* 7.0, CHN*H*CO), 5.54 (1 H, p, *J* 7.0, C*H*NHCO), 5.33 (1 H, d, *J* 5.0, CHN*H*), 4.22 (1 H, dt, *J* 7.3 and 5.0, C*H*CH$_2$), 1.86–1.74 (2 H, m, CHCH_2), 1.30 (3 H, d, *J* 6.7, CH_3CHNH), 1.15 [9 H, s, C(CH$_3$)$_3$] and 0.81 (3 H, t, *J* 7.3, CH$_2$CH_3); δ_C(100.4 MHz) 177.8 (s), 142.9 (s), 142.5 (s), 141.85 (s), 131.4 (d), 128.5 (d), 127.9 (d), 127.3 (d), 126.2 (d), 125.2 (d), 125.1 (d), 59.0 (d), 44.4 (d), 38.7 (s), 30.6 (t), 27.7 (q), 20.9 (q) and 10.8 (q).

For (±)-2-methyl-1-phenylpropylamine 12c. $R_{(S)}RR$-(−)-**5c** (144 mg, 36%); $[\alpha]_D^{18}$ −202.8 (*c* 1.17, chloroform); ν_{max}(chloroform film)/cm^{-1} 4213, 3683, 3014, 2968, 2399, 1652, 1503, 1424, 1216, 1069 and 1035; δ_H([$^2H_6$]acetone, 399.7 MHz) 7.99 (1 H, dd, *J* 7.9 and 1.3), 7.88–7.54 (10 H, m, ArH and 2 × NH), 6.18 (1 H, p, *J* 6.8), 4.72 (1 H, dd, *J* 8.4 and 3.3, SONHC*H*), 2.16–2.06 [1 H, m, C*H*(CH$_3$)$_2$], 1.75 (3 H, d, *J* 7.0, CONHCHCH_3), 1.50 [9 H, s, C(CH$_3$)$_3$], 1.20 [3 H, d, *J* 10.3, (CHCH_3)$_2$] and 1.15 [3 H, d, *J* 7.5, (CHCH_3)$_2$]; δ_C([$^2H_6$]acetone, 100.4 MHz) 177.8 (s), 144.8 (s), 144.0 (s), 142.9 (s), 131.1 (d), 128.4 (d), 127.9 (d), 127.3 (d), 127.3 (d), 127.1 (d), 124.6 (d), 61.2 (d), 45.0 (q), 31.6 (s), 27.0 (q), 21.6 (q), 13.7 (d) and 10.2 (q); *m/z* (EI) 400 (M$^+$, 5), 357 (64), 341 (2), 279 (2), 252 (86), 251 (57), 234 (33), 204 (15), 168 (88), 150 (100), 135 (68), 106 (72), 91 (66), 77 (24) and 57 (92) (Found: M$^+$, 400.2188. $C_{23}H_{32}N_2O_2S$ requires *M*, 400.2184). $R_{(S)}RS$-(−)-**6c** (152 mg, 38%); $[\alpha]_D^{18}$ −202.8 (*c* 1.17, chloroform); δ_H([$^2H_6$]acetone, 399.7 MHz) 7.92 (1 H, dd, *J* 7.1 and 1.1), 7.63 (1 H, dd, *J* 7.7 and 1.7), 7.51–7.45 (2 H, m), 7.35–

7.25 (3 H, m), 6.96 (1 H, d, *J* 7.1, CONH), 5.77 (1 H, p, *J* 7.0, CONHC*H*), 4.35 (1 H, q, *J* 7.3, SONHC*H*), 3.12 (1 H, br s, SONH), 2.20–2.05 [1 H, m, C*H*$(CH_3)_2$], 1.36 (3 H, d, *J* 7.0, CONHCHCH_3), 1.25 [9 H, s, C$(CH_3)_3$], 0.98 [3 H, d, *J* 10.7, $(CHCH_3)_2$] and 0.91 [3 H, d, *J* 7.3, $(CHCH_3)_2$]; δ_C([$^2H_6$]acetone, 100.4 MHz) 177.3 (s), 143.8 (s), 143.7 (s), 143.6 (s), 130.9 (d), 128.2 (d), 127.3 (d), 127.0 (d), 126.9 (d), 124.5 (d), 59.6 (d), 44.5 (q), 38.1 (s), 27.0 (q), 20.8 (q), 13.7 (d) and 10.4 (q).

For (±)-2,2-dimethyl-1-phenylpropylamine 12d. $R_{(S)}RR$-(−)-**5d** (137 mg, 33%); $[\alpha]_D^{18}$ −165.3 (*c* 1.89, chloroform); δ_H(270.2 MHz) 7.45–7.20 (9 H, m, ArH), 6.48 [1 H, br d, *J* 4.6, C$(CH_3)_3$CHN*H*], 6.08 (1 H, br d, *J* 6.2, CHN*H*CO), 5.75 (1 H, p, *J* 6.2, C*H*NHCO), 4.22 (3 H, d, *J* 4.8), 3.70 [1 H, s, C$(CH_3)_3$C*H*NH] 1.44 (3 H, d, *J* 6.8, CH_3CHNH), 1.15 [9 H, s, C$(CH_3)_3$] and 0.90 [9 H, s, C$(CH_3)_3$]; δ_C(67.8 MHz) 177.6 (s), 143.6 (s), 143.1 (s), 140.1 (s), 130.9 (d), 129.2 (d), 128.2 (d), 127.5 (d), 126.7 (d), 126.0 (d), 125.0 (d), 65.3 (d), 45.2 (d), 38.2 (s), 35.1 (s), 27.3 (q), 26.5 (q) and 22.0 (q); *m*/*z* (FAB) 415 (M + H^+, 8), 399 (2), 341 (5), 314 (2), 252 (35), 204 (2), 168 (35), 162 (12), 150 (100), 147 (12), 135 (18), 106 (21), 91 (20) and 57 (38) (Found: M + H^+, 415.2419. $C_{24}H_{35}N_2O_2S$ requires *M*, 415.2419). $R_{(S)}RS$-(−)-**6d** (141 mg, 34%); $[\alpha]_D^{18}$ −212.7 (*c* 0.734, chloroform); ν_{max}(chloroform film)/cm^{-1} 3365, 3198, 2967, 1636, 1526, 1211 and 1064; δ_H(270.2 MHz) 7.80 (1 H, dd, *J* 7.5 and 2.0, ArH), 7.42–7.00 (8 H, m, ArH), 6.39 [1 H, br d, *J* 8.4, C$(CH_3)_3$CHN*H*], 5.91 (1 H, br d, *J* 7.0, CHN*H*CO), 5.61 (1 H, p, *J* 7.0, C*H*NHCO), 3.97 [3 H, d, *J* 8.2, C$(CH_3)_3$CHNH], 1.22 (3 H, d, *J* 6.8, CH_3CHNH), 1.16 [9 H, s, C$(CH_3)_3$] and 0.88 [9 H, s, C$(CH_3)_3$]; δ_C(67.8 MHz) 177.6 (s), 142.8 (s), 140.9 (s), 130.6 (s), 128.2 (d), 127.4 (d), 127.42 (d), 127.37 (d), 126.3 (d), 125.9 (d), 125.4 (d), 66.4 (d), 44.0 (d), 38.3 (s), 35.1 (s), 27.4 (q), 26.8 (q) and 20.2 (q).

For (±)-1-(*p*-tolyl)ethylamine 12e. $R_{(S)}RR$-(−)-**5e** (174 mg, 45%); $[\alpha]_D^{18}$ −86.6 (*c* 2.90, chloroform); ν_{max}(chloroform film)/cm^{-1} 4213, 3016, 2300, 1650, 1505, 1420 and 1216; δ_H([$^2H_6$]acetone, 399.7 MHz) 7.82 (1 H, d, *J* 7.6), 7.56 (1 H, d, *J* 7.6), 7.37–7.47 (4 H, m), 7.13 (1 H, dd, *J* 8.2 and 1.8), 7.03 (1 H, d, *J* 8.0), 6.44 (1 H, br d, *J* 6.4), 5.61 (1 H, dp, *J* 7.0 and 1.8), 4.46 (1 H, p, *J* 6.7), 2.97 (1 H, br d, *J* 11.9), 2.24 (3 H, s), 1.54 (3 H, d, *J* 7.0), 1.32 (3 H, d, *J* 6.7) and 1.11 (9 H, s); *m*/*z* (FAB) 387 (M + H^+, 39), 252 (74), 168 (48), 150 (100), 136 (42) and 119 (100) (Found: M + H^+, 387.2097. $C_{22}H_{31}N_2O_2S$ requires *M*, 387.2106). $R_{(S)}RS$-(−)-**6e** (178 mg, 46%); $[\alpha]_D^{18}$ −76.6 (*c* 1.66, $CHCl_3$); δ_H([$^2H_6$]acetone, 399.7 MHz) 7.64 (1 H, dd, *J* 7.9 and 1.2), 7.61 (1 H, br d, *J* 7.0), 7.56 (1 H, dd, *J* 7.6 and 1.2), 7.45 (1 H, dt, *J* 7.3 and 1.2), 7.29–7.36 (2 H, m), 7.14 (1 H, d, *J* 7.9), 6.99 (1 H, d, *J* 4.9), 5.81 (1 H, p, *J* 7.0), 4.57 (1 H, dq, *J* 4.9 and 6.7), 2.30 (3 H, s), 1.50 (3 H, d, *J* 6.8), 1.42 (3 H, d, *J* 7.0) and 1.15 (9 H, s); δ_C([$^2H_6$]acetone, 100.4 MHz) 177.7 (s), 144.8 (s), 143.8 (s), 141.4 (s), 136.7 (s), 131.1 (d), 129.1 (d), 127.2 (d), 127.1 (d), 124.6 (d), 54.3 (d), 44.8 (d), 38.1 (s), 27.0 (q), 24.6 (q), 21.6 (q) and 20.4 (q).

For (±)-1-(*p*-methoxyphenyl)ethylamine 12f. $R_{(S)}RR$-(−)-**5f** (181 mg, 45%); $[\alpha]_D^{22}$ −238.5 (*c* 1.03, chloroform); ν_{max}(chloroform film)/cm^{-1} 3334, 3162, 2969, 1733, 1639, 1514, 1456, 1247, 1208, 1179 and 1036; δ_H(399.7 MHz) 7.61 (1 H, d, *J* 7.6, ArH), 7.44–7.27 (5 H, m, ArH), 6.87 (2 H, d, *J* 8.5, ArH), 6.26 (1 H, d, *J* 3.7, CHN*H*SO), 6.14 (1 H, d, *J* 6.1, CHN*H*), 5.78 (1 H, p, *J* 6.1, C*H*NHCO), 4.62 (1 H, dt, *J* 10.7 and 6.1, C*H*NHSO), 3.80 (3 H, s, OCH_3), 1.51 (3 H, d, *J* 6.7, CH_3CHNH), 1.46 (3 H, t, *J* 7.3, CH_2CH_3) and 1.16 [9 H, s, C$(CH_3)_3$]; δ_C(100.4 MHz) 177.8 (s), 158.9 (s), 143.1 (s), 135.2 (s), 131.2 (s), 128.3 (d), 127.5 (d), 126.4 (d), 125.1 (d), 113.8 (d), 55.2 (q), 53.6 (d), 44.8 (d), 38.2 (s), 27.4 (q), 24.3 (q) and 22.0 (q); *m*/*z* (EI) 402 (M^+, 4), 279 (2), 251, (23), 234 (14), 204 (5), 190 (4), 168 (9), 166 (9), 150 (92), 135 (100), 132 (100), 105 (27) and 57 (36); *m*/*z* (FAB) 403 (M + H^+, 4), 328 (2), 269 (6), 252 (15), 204 (4), 168 (10), 150 (44), 135 (100) and 57 (22) (Found: M^+, 402.1965. $C_{22}H_{30}N_2O_3S$ requires *M*, 402.1977). $R_{(S)}RS$-(−)-**6f** (189 mg, 47%); $[\alpha]_D^{24}$ −208.7 (*c* 1.38, chloroform); δ_H(399.7 MHz) 7.92 (1 H, dd, *J* 7.9 and 1.2, ArH), 7.44–7.37 (2 H, m, ArH), 7.21 (1 H, dd, *J* 7.3 and 2.1, ArH), 7.11 (2 H, d, *J* 8.6, AA′BB′ CH_3O–aromatic), 6.76 (2 H, d, *J* 8.6, AA′BB′ CH_3O–aromatic), 5.99 (1 H, s, NH), 5.57 (1 H, p, *J* 6.7, C*H*NHCO), 5.00 (1 H, s, NH), 4.52 (1 H, dt, *J* 11.0 and 6.4, C*H*NHSO), 3.74 (3 H, s, OCH_3), 1.60 (3 H, d, *J* 6.7, CH_3CHNH), 1.41 (3 H, t, *J* 7.0, CHCH_3) and 1.16 [9 H, s, C$(CH_3)_3$]; δ_C(100.4 MHz) 177.7 (s), 159.0 (s), 143.0 (s), 142.0 (s), 136.1 (s), 131.5 (d), 128.0 (d), 126.2 (d), 124.8 (d), 114.0 (d), 55.5 (q), 52.8 (d), 44.4 (d), 38.7 (s), 27.7 (q), 23.5 (q) and 21.4 (q).

Hydrolysis of sulfinamides $R_{(S)}RR$-(−)-5b–f

The pure sulfinamide $R_{(S)}RR$-(−)-**5b–f** (260 μmol) in methanol (1.0 cm^3) was treated with trifluoroacetic acid (58 mg, 0.041 cm^3, 520 μmol). Once the reaction was judged to be complete by TLC (2 ⟶ 4 h), hydrochloric acid (2 mol dm^{-3}; 2 cm^3) was added to the mixture, which was then extracted with CH_2Cl_2 (3 × 5 cm^3). The combined organic extracts were dried (Na_2SO_4), filtered and evaporated to give the sulfinic acid *R*-(−)-**11**. The solution was treated with aq. sodium hydroxide (2 mol dm^{-3}; *ca.* 6 cm^3; pH > 12) and extracted with CH_2Cl_2 (3 × 5 cm^3). The combined extracts were dried (Na_2SO_4), filtered and evaporated to give the optically enriched amine **5b–f**. Enantiomeric excesses were obtained by comparison with published rotation values. Results: Amine isolated/yield of **11**/yield of amine/$[\alpha]_D$ (*c* 1.00, $CHCl_3$); **12b** /96/92/+36.6; **12c**/80/78/+14.0; **12d** no product isolated; **12e**/87/86/+28.1; **12f**/98/93/+24.8.

Attempted addition of lithiomethyl benzyl ether 16 to the sulfinylimine 4a

Anionic method. A solution of the sulfinylimine **4a** (100 mg, 270 μmol) in THF (1 cm^3) was added dropwise to a solution of lithiomethyl benzyl ether **16** (567 μmol) in THF (2.5 cm^3) prepared by the method of Still,[20] at −100 °C. The solution was allowed to warm to 0 °C over 30 min. Saturated aq. ammonium chloride (3 cm^3) was added and the solution was extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were washed with brine (5 cm^3) and dried (Na_2SO_4), filtered and concentrated under reduced pressure. The starting sulfinylimine **4a** (97 mg, 97%) was recovered by flash chromatography (0 ⟶ 50%, ethyl acetate–hexane).

Reductive method. Lithium powder (9.4 mg, 1.35 mmol) and naphthalene (3.5 mg, 27 μmol) in THF (5 cm^3) was stirred at room temp. until a greenish-gray suspension was formed.[26] A solution of chloromethyl benzyl ether (89 mg, 567 μmol) and the sulfinylimine **4a** (100 mg, 270 μmol) in THF (3 cm^3) was added dropwise (*ca.* 40 min) at 0 °C to the former solution. After an additional 30 min, saturated aq. ammonium chloride (10 cm^3) was added to the mixture, which was then extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were dried (Na_2SO_4), filtered and concentrated. Flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) gave benzyl alcohol (54 mg, 88%) and the starting sulfinylimine **4a** (96 mg, 96%) was recovered.

Attempted addition of the lithium enolate of methyl acetate to the sulfinylimine 4a

A solution of diisopropylamine (57 mg, 567 μmol) in THF (1 cm^3) was treated with butyllithium (1.6 mol dm^{-3} in hexanes; 0.354 cm^3, 567 μmol) at −78 °C. The solution was allowed to warm to 0 °C and stirred for 30 min. The reaction mixture was re-cooled to −78 °C, and methyl acetate (42 mg, 567 μmol) in THF (0.5 cm^3) was added dropwise. The solution was allowed to warm to 0 °C and stirred for 30 min. The reaction mixture was re-cooled to −78 °C, and the sulfinylimine **4a** (100 mg, 270 μmol) in THF (1.0 cm^3) was added dropwise. The reaction mixture was allowed to warm to room temp. over 30 min and stirred at this temp. for a further 30 min. The reaction was

quenched with saturated aq. ammonium chloride (3 cm^3) and the mixture extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were washed with hydrochloric acid (1 mol dm^{-3}; 5 cm^3), saturated aq. $NaHCO_3$ (5 cm^3) and brine (5 cm^3), dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the starting sulfinylimine **4a** (93 mg, 93%).

Attempted addition of the lithium enolate of *tert*-butyl acetate to the sulfinylimine 4a

A solution of diisopropylamine (57 mg, 567 μmol) in THF (1 cm^3) was treated with butyllithium (1.6 mol dm^{-3} in hexanes; 0.354 cm^3, 567 μmol) at −78 °C. The solution was allowed to warm to 0 °C and stirred for 30 min. The mixture was re-cooled to −78 °C, and *tert*-butyl acetate (65.9 mg, 567 μmol) in THF (0.5 cm^3) was added dropwise. The solution was allowed to warm to 0 °C and stirred for 30 min. The mixture was re-cooled to −78 °C, and the sulfinylimine **4a** (100 mg, 270 μmol) in THF (1.0 cm^3) was added dropwise. The reaction mixture was allowed to warm to room temp. over 30 min and stirred at this temp. for a further 30 min. The reaction was quenched with saturated aq. ammonium chloride (3 cm^3) and the mixture extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were washed with hydrochloric acid (1 mol dm^{-3}, 5 cm^3) saturated aq. $NaHCO_3$ (5 cm^3) and brine (5 cm^3), dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the starting sulfinylimine **4a** (95 mg, 95%).

Attempted addition of the sodium enolate of diethyl malonate 17 to the sulfinylimine 4a

A solution of diethyl malonate (90.8 mg, 567 μmol) in THF (1.0 cm^3) was treated with sodium hydride (60% dispersion in mineral oil; 22.7 mg, 567 μmol) at 0 °C. Once all the hydrogen gas had evolved and the solution was transparent (< 10 min), the mixture was cooled to −78 °C, and the sulfinylimine **4a** (100 mg, 270 μmol) in THF (1.0 cm^3) was added dropwise. The reaction mixture was allowed to warm to room temp. over 30 min and stirred at this temp. for a further 30 min. The reaction was quenched with saturated aq. ammonium chloride (3 cm^3) and the mixture extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the starting sulfinylimine **4a** (91 mg, 91%).

Attempted addition of the dianion of ethyl acetoacetate 17 to the sulfinylimine 4a

Ethyl acetoacetate (74 mg, 567 μmol) in THF (1.0 cm^3) was added dropwise to a suspension of sodium hydride (60% dispersion in mineral oil; 24.9 mg, 624 μmol) in THF (0.5 cm^3) at 0 °C. The colourless solution was stirred for 10 min and then cooled to −78 °C. Butyllithium (2.2 mol dm^{-3} in hexanes; 0.27 cm^3, 595 μmol) was added in a dropwise fashion. The solution was warmed to 0 °C and the yellow–orange solution was stirred for 10 min after which a solution of sulfinylimine **4a** (100 mg, 270 μmol) in THF (1.0 cm^3) was added. No decolourisation of the solution was observed over 1 h at 0 °C. After a further 1 h at room temp., saturated aq. ammonium chloride (5 cm^3) was added to the mixture, which was then extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The sulfinylimine **4a** (98 mg, 98%) was recovered by flash chromatography (0 ⟶ 50%, ethyl acetate–hexane).

Preparation of ($R_{(S)}$,*R*)-(−)-2-[1-(*tert*-butylcarbonylamino)-ethyl]phenylsulfinamide 19b

Cyclic sulfinamide $S_{(S)}R$-(+)-**1** (503 mg, 2.0 mmol) in THF (10 cm^3) was treated with sodium bis(trimethylsilyl)amide (1.0 mol dm^{-3} in THF; 2.1 cm^3, 2.1 mmol) at −78 °C. The mixture was allowed to warm to room temp. over 1 h. Silica gel (flash chromatography grade, 2 g) was slowly added to the solution and the resulting suspension was stirred overnight. Saturated aq. ammonium chloride (10 cm^3) was added to the solution, which was then extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were washed with hydrochloric acid (10 cm^3), saturated aq. $NaHCO_3$ (10 cm^3) and brine (10 cm^3), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The product sulfinamide **19b** was isolated by flash chromatography (0⟶ 75%, ethyl acetate–hexane) to give a white solid which was recrystallised (CH_2Cl_2–hexane) (392 mg, 73%); mp > 200 °C; $[\alpha]_D^{17}$ −188.1 (*c* 1.21, acetonitrile); ν_{max}(chloroform film)/cm^{-1} 3336, 2969, 1638, 1526, 1367, 1210 and 1035; δ_H(270.2 MHz) 7.73 (1 H, dd, *J* 9.3 and 1.7, ArH), 7.50–7.30 (3 H, m, ArH), 6.20 (1 H, br d, *J* 6.8, CHN*H*CO), 5.87 (1 H, p, *J* 6.8, C*H*NHCO), 5.37 (2 H, s, NH_2), 1.51 (3 H, d, *J* 6.8, CH_3CHNH) and 1.18 [9 H, s, $C(CH_3)_3$]; δ_C(100.4 MHz) 178.6 (s), 144.2 (s), 142.7 (s), 131.4 (d), 127.7 (d), 126.8 (d), 124.8 (d), 45.4 (d), 38.6 (s), 27.9 (q) and 22.1 (q); *m*/*z* (FAB) 269 (M + H^+, 25), 252 (32), 236 (10), 227 (14), 204 (20), 168 (43), 150 (100), 135 (46), 102 (17) and 57 (96) (Found: C, 58.2; H, 7.6; N, 10.3. $C_{13}H_{20}N_2O_2S$ requires C, 58.18; H, 7.51; N, 10.44%).

Preparation of the sulfinylimines 20a–c

Finely ground, dry caesium fluoride (638 mg, 4.2 mmol) was placed into a flame dried Schlenk tube and dried at 130 °C under reduced pressure (*ca.* 1 mmHg) overnight. THF (5 cm^3) was added to the cooled tube and stirred for 10 min. The aldehyde (4.2 mmol) in THF (5 cm^3) was added and the mixture was cooled to 0 °C. To this suspension was added a solution of the *N*,*N*-bis(trimethylsilyl)sulfinamide **19a** generated by the treatment of the cyclic sulfinamide $S_{(S)}R$-(+)-**1** (503 mg, 2.0 mmol) in THF (10 cm^3) with sodium bis(trimethylsilyl)amide (1.0 mol dm^{-3} in THF; 2.1 cm^3, 2.1 mmol) at −78 °C, then allowed to warm to 0 °C and stirred for 1 h. The reaction was stirred at 0 °C for 1 h then at room temp. for a further 6 h. The reaction was quenched with saturated aq. ammonium chloride (20 cm^3) and the mixture rapidly extracted with ethyl acetate (3 × 20 cm^3). The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The product sulfinylimines **20a–c** were isolated by rapid flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) on neutral alumina to give foams.

Adduct of benzaldehyde 20a. (527 mg, 74%); $[\alpha]_D^{21}$ −108.6 (*c* 1.10, chloroform); ν_{max}(film)/cm^{-1} 3342, 2971, 1659, 1585, 1563, 1516, 1302, 1263, 1175 and 1077; δ_H(270.1 MHz) 8.54 (1 H, s, N=CH), 7.76 (1 H, dd, *J* 8.8 and 1.7, ArH), 7.68–7.38 (8 H, m, ArH), 6.16 (1 H, br d, *J* 6.8, CHN*H*CO), 5.45 (1 H, p, *J* 6.8, C*H*NHCO), 1.64 (3 H, d, *J* 6.8, CH_3CHNH) and 1.19 [9 H, s, $C(CH_3)_3$]; δ_C(100.4 MHz) 177.3 (s), 154.1 (s), 141.7 (s), 139.9 (s), 131.6 (d), 130.0 (d), 128.3 (d), 127.3 (d), 126.5 (d), 125.2 (d), 121.2 (d), 46.8 (d), 38.3 (s), 27.5 (q) and 21.5 (q); *m*/*z* (EI) 356 (M^+, 10), 303 (7), 228 (7), 268 (16), 253 (18), 236 (56), 204 (100), 193 (18), 178 (18), 168 (24), 150 (98), 91 (33), 85 (15), 77 (73) and 57 (94); *m*/*z* (FAB) 357 (M + H^+, 45), 252 (20), 236 (46), 204 (30), 181 (25), 168 (42), 150 (100), 135 (62), 105 (38) and 57 (9) (Found: M^+, 356.1564. $C_{20}H_{24}N_2O_2S$ requires *M*, 356.1559).

Adduct of 4-methoxybenzaldehyde 20b. (556 mg, 72%); $[\alpha]_D^{21}$ −499.4 (*c* 1.13, chloroform); ν_{max}(film)/cm^{-1} 3346, 2967, 1652, 1595, 1567, 1512, 1309, 1258, 1167 and 1093; δ_H(270.2 MHz) 8.65 (1 H, s, N=CH), 7.78–7.72 (3 H, m, ArH), 7.46–7.38 (3 H, m, ArH), 6.93 (2 H, d, *J* 8.8, CH_3O–aromatic), 6.16 (1 H, br d, *J* 6.8, CHN*H*CO), 5.60 (1 H, p, *J* 6.8, C*H*NHCO), 3.84 (3 H, s, OCH_3), 1.68 (3 H, d, *J* 6.8, CH_3CHNH) and 1.21 [9 H, s, $C(CH_3)_3$]; δ_C(100.4 MHz) 177.5 (s), 163.1 (s), 159.2 (s), 142.9 (s), 142.1 (s), 131.5 (s), 131.4 (d), 128.4 (d), 127.0 (d), 126.0 (d), 122.8 (d), 114.3 (d), 55.5 (q), 46.1 (d), 38.5 (s), 27.5 (q) and 22.4 (q); *m*/*z* (EI) 386 (M^+, 32), 235 (5), 220 (4), 204 (90), 193 (4), 178 (16), 150 (70), 135 (100), 77 (18) and 57 (41) (Found: M^+, 386.1654. $C_{21}H_{26}N_2O_3S$ requires *M*, 386.1664).

Adduct of 4-nitrobenzaldehyde 20c. (514 mg, 64%); $[\alpha]_D^{25}$ −133.1 (*c* 1.72, chloroform); ν_{max}(film)/cm^{-1} 3356, 2970, 1644, 1523, 1346, 1214 and 1100; δ_H(270.2 MHz, at ambient temp.

1:1 mixture of rotamers) 8.82 ($\frac{1}{2}$ H, s, N=CH), 8.40–8.22 ($\frac{3}{2}$ H, m, ArH and N=CH), 7.97 (1 H, d, *J* 9.0, ArH), 7.75–7.38 (4 H, m, ArH), 6.45 ($\frac{1}{2}$ H, br d, *J* 6.8, CHN*H*CO), 6.12 ($\frac{1}{2}$ H, br d, *J* 6.8, CHN*H*CO), 5.95 ($\frac{1}{2}$ H, p, *J* 6.8, C*H*NHCO), 5.59 ($\frac{1}{2}$ H, p, *J* 6.8, C*H*NHCO), 1.65 ($\frac{3}{2}$ H, d, *J* 6.8, CH_3CHNH), 1.55 ($\frac{3}{2}$ H, d, *J* 6.8, CH_3CHNH), 1.22 [$\frac{9}{2}$ H, s, C$(CH_3)_3$] and 1.20 [$\frac{9}{2}$ H, s, C$(CH_3)_3$]; δ_C(100.4 MHz, at −100 °C) 177.1 (s), 162.2 (s), 158.7 (s), 140.9 (s), 139.1 (s), 131.9 (s), 130.4 (d), 128.4 (d), 127.0 (d), 126.0 (d), 126.8 (d), 124.3 (d), 48.1 (d), 38.3 (s), 27.7 (q) and 20.7 (q); *m/z* (FAB) 402 (M + H^+, 2), 328 (3), 385 (6), 271 (6), 268 (5), 252 (20), 236 (20), 204 (22), 168 (32), 150 (100), 135 (38), 102 (18) and 57 (97) (Found: M + H^+, 402.1492. $C_{20}H_{24}N_3O_4S$ requires *M*, 402.1488).

Addition of methylmagnesium iodide to the sulfinylimines 20a–c

The sulfinylimine **20a–c** (500 μmol) in THF (3.6 cm^3) was treated with methylmagnesium iodide (2.0 mol dm^{-3} in THF; 0.55 cm^3, 1.1 mmol) at −78 °C. After 30 min the creamy-white suspension was warmed to ambient temp. and saturated aq. ammonium chloride (10 cm^3) was added. The clear solution was extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were washed with brine (10 cm^3), dried (Na_2SO_4), filtered and concentrated under reduced pressure and the residue was dissolved in $CDCl_3$ (*ca.* 0.6 cm^3) and the diastereoisomeric excess of the reaction was determined by ^1H NMR. The combined diastereoisomeric products were isolated by flash chromatography (0 ⟶ 10%, methanol–CH_2Cl_2). Each product was identified by comparison with authentic samples already described. Compound **20c** failed to give any addition products, and no other products were identified.

Addition of ethylmagnesium bromide to the sulfinylimine 20a

The sulfinylimine **20a** (178 mg, 500 μmol) in THF (3.6 cm^3) was treated with ethylmagnesium bromide (2.0 mol dm^{-3} in THF; 0.55 cm^3, 1.1 mmol) at −78 °C. After 30 min the creamy-white suspension was warmed to ambient temp. and saturated aq. ammonium chloride (10 cm^3) was added. The clear solution was extracted with ethyl acetate (3 × 10 cm^3). The combined extracts were washed with brine (10 cm^3) and dried (Na_2SO_4), filtered and concentrated under reduced pressure and the residue was dissolved in $CDCl_3$ (*ca.* 0.6 cm^3) and the diastereoisomeric excess of the reaction was determined by ^1H NMR to be 85% de in favour of $R_{(S)}RS$-(−)-**6b**. The combined diastereoisomeric products were isolated by flash chromatography (0 ⟶ 50%, ethyl acetate–hexane) to give a white foam (168 mg, 87%).

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