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Stereoselective addition reactions to chiral *N*-benzylidene-*p*-toluenesulfinamides. Application to the synthesis of optically active 1,2-diphenylethylamines

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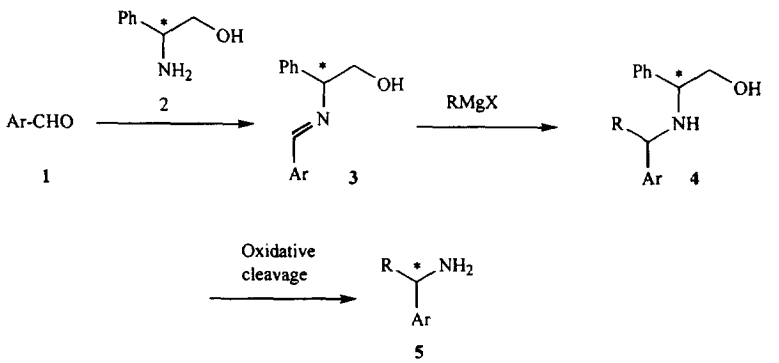
Abstract: An efficient and enantiospecific synthesis of substituted 1,2-diphenylethylamines **5** from benzaldehydes is described using a recyclable chiral auxiliary. © 1997 Elsevier Science Ltd. All rights reserved.

Many biologically important compounds contain chiral amine functionalities.[1] Consequently, the preparation of chiral primary amines is of synthetic significance, and their access by asymmetric synthesis is desirable. Only a few examples of the preparation of optically active 1,2-diphenylethylamines are reported in the literature.[2] An attractive approach makes use of the diastereoselective addition of organometallic reagents to the C=N bonds of imines and their derivatives containing removable chiral auxiliaries.[3]

As part of our ongoing studies concerning the preparation of substituted 1,2-diphenylethylamines **5**, we first used the phenyl glycinol **2** as the chiral auxiliary according to a procedure described by Pridgen[4] (Scheme 1).



Scheme 1.

Our preliminary studies showed that with benzylmagnesium chloride as a Grignard reagent, addition to the imines occurred with good diastereoselectivity (de=70±2%); however, the major drawback of this method is the loss of the expensive chiral inductor **2** during the last step to give the desired chiral amines **5**.

This paper describes the preparation of optically active 1,2-diphenylethylamines **5** using the commercially available Andersen reagent (+)-(1S)-menthyl-(R)-toluene-4-sulfinate **6**, a recyclable chiral auxiliary which affords many advantages.[5]

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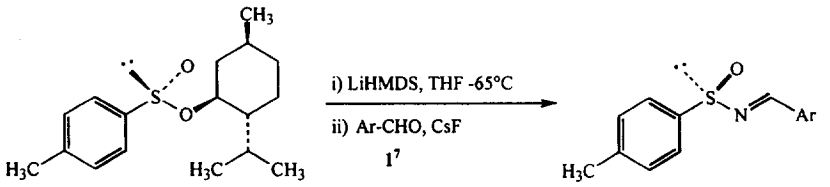
The enantiopure sulfinimines **7** were prepared in 53 to 80% yields according to Davis' procedure[6] by treatment of the (+)-Andersen reagent **6** with 1.5 equiv. of lithium bis(trimethylsilyl)amide at −65°C followed by reaction with 2 equivalents of aromatic aldehydes **1** bearing both electron donor and acceptor substituents in the presence of 1.5 equivalent of cesium fluoride (Scheme 2).

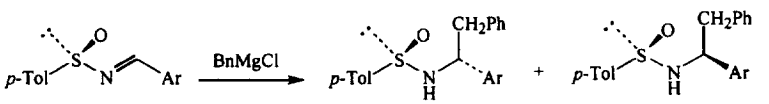


(+)-(1S,2R,5S)-6 (R)-7

	Ar	Yield(%)
7a	4-Methoxyphenyl	80
7b	Phenyl	57
7c	1-Naphthyl	53
7d	4-Dimethylaminophenyl	76
7e	4-Chlorophenyl	57
7f	2-Benzyloxyphenyl	79
7g	4-Nitrophenyl	31

Scheme 2.

The key step in this synthetic sequence is the addition of benzylmagnesium chloride to the sulfinimines **7**. The diastereoselectivity of the asymmetric addition is influenced by several factors, particularly the order of addition and the polarity of the solvent (Scheme 3).



(R)-7 Major isomer (S_r, R)-8 Minor isomer (S_r, S)-8

Scheme 3.

The results of our preliminary studies show that the best diastereoselectivity and chemical yields are observed when sulfinimines **7** are added to a BnMgCl solution using non-polar solvents such as toluene and that there was no significant difference in the diastereoselectivity of the addition as a function of the temperature of the reaction. The diastereomeric excess (de) of the addition was much lower when the BnMgCl solution was added to the sulfinimides **7** as well as when the reaction was conducted in more polar solvents (Et_2O, THF, TBME, anisole). With the mixture of solvents such as THF–heptane or toluene–heptane, no improvement in the diastereoselectivity was observed. The use of excess BnMgCl or the presence of chelating agents such as $MgBr_2$ and $CeCl_3$ seemed to have no effect on the diastereoselectivity of the reaction.

In order to study the electronic and steric effects governing the diastereoselectivity, we submitted the various substituted sulfinimines **7** previously prepared to this addition reaction. Accordingly, the sulfinamides **8** were prepared in good yields by treatment of the sulfinimines **7** with 2 equiv. of a solution of benzyl magnesium chloride in toluene at −30°C (Table 1).

Despite several attempts, the reaction conducted with the sulfinimine **7g** never allowed the preparation of the corresponding pure sulfinamide but gave a complex mixture probably resulting from the presence of the nitro group in the 4-position.

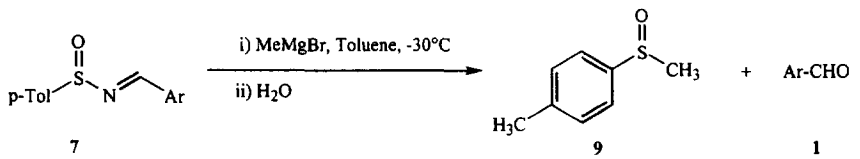
As shown in Table 1, no significant difference in the diastereoselectivity of the reaction was encountered whatever the nature of the aromatic substituent.

Table 1. Alkylation of sulfinimines **7** with BnMgCl to sulfonamides **8**

Compounds	Ar	% de [a]	% de[b]	% Yield [c]
8a	4-methoxyphenyl	74	84	76
8b	phenyl	64	94	61
8c	1-naphthyl	70	80	55
8d	4-dimethylaminophenyl	68	80	73
8e	4-chlorophenyl	60	80	61
8f	2-benzyloxyphenyl	60	60	72

Diastereomeric ratios were determined by integration of the 500-MHz ^{1}H NMR spectra. a) de observed for the condensation reaction, b) de after recrystallization of the diastereomeric mixture, c) chemical yield (not optimized) after recrystallization.

We also investigated the influence of the nature of the Grignard reagent on the diastereoselectivity of the reaction. Surprisingly, the reaction with methylmagnesium bromide conducted under the same conditions as used with BnMgCl gave, after hydrolysis, a mixture of the starting aromatic aldehydes **1** and the (S)-(−) methyl *p*-tolyl sulfoxide **9** ($[\alpha]_D^{20}$ −135.1, acetone, ee=93.2%) (Scheme 4).



7 9 1

Scheme 4.

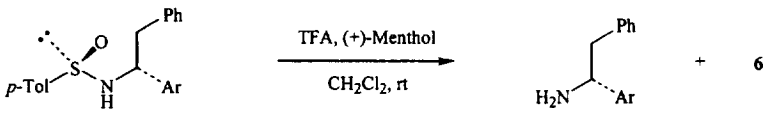
The position of the addition seems dependent on the nature of the Grignard reagent used, occurring in the 1,4 position with allylmagnesium bromide[8] and benzylmagnesium chloride, and in the 1,2 position with methylmagnesium bromide.

The last step is the hydrolysis of the sulfinamides **8**. In order to optimize the recycling of the (+)-Andersen reagent **6**, we tried to reduce the racemization occurring during the hydrolysis–transesterification step. Whichever conditions were used (lower temperatures, lower excess of TFA, various acidic conditions (HCl, (+)-camphorsulfonic acid, Montmorillonite K-10) or basic conditions (NaH, (+)-menthol)) we could never increase the diastereomeric excess of the mixture of the recovered (+)- and (−)-Andersen reagent, which was in the range of 8 and 28%. The best results for this step were obtained using the method described by Davis[4] by treatment of the sulfinamides **8** with 3 equivalents of TFA and 1.2 equivalents of (+)-menthol in CH_2Cl_2 to give simultaneously the recycled enantiomeircally pure (+)-Andersen reagent **6** in 50% yield and the chiral 1,2 diphenylethylamines **5** in 65 to 90% yield with 75 to 94% ee (Scheme 5, Table 2). It was shown that the ee of the amines **5** may be optimized by formation of the corresponding mandelate salt and recrystallization from a mixture of heptane/isopropanol; for example, an enantiomeric mixture of **5f** (ee=75%, $[\alpha]_D$ −43.5) treated according to this procedure led to the (R)-enantiomer (ee>99%, $[\alpha]_D$ −94.0.

In conclusion, the methodology described in this paper offers an efficient and enantioselective route to various substituted 1,2-diphenylethylamines using a recyclable chiral auxiliary.

Experimental

Unless otherwise noted, starting materials were obtained from commercial suppliers and were used without further purification. Melting points were taken on a Büchi 510 capillary apparatus and are



(S_r,R)-**8** (R)-**5**

Scheme 5.

Table 2. Hydrolysis of sulfinamides **8** with TFA–(+)-menthol in CH_2Cl_2 to amines **5**

Compounds	Ar	Yields[a] (%)	ee[b,c] (%)	$[\alpha]_D$[c]
5a	4-methoxyphenyl	90	85	-91.9
5b	phenyl	84	94	-118.1[d]
5c	1-naphthyl	65	88	-4.4
5d	4-dimethylaminophenyl	77	84	-95.0
5e	4-chlorophenyl	85	77	-117.0
5f	2-benzyloxyphenyl	84	75	-43.5

a) Chemical yields were not optimized. b) Determined by chiral HPLC analysis. c) in MeOH/0.1N HCL:50/50. For details see Experimental section. d) $[\alpha]_D$: -10.1°, $CHCl_3$. Lit.[2a] $[\alpha]_D$: -10.1°, $CHCl_3$.

uncorrected. ^{1}H NMR spectra were recorded in DMSO-d_6 solutions on a Bruker ARX 500 spectrometer at 500 MHz. The ^{1}H chemical shifts are reported in ppm relative to internal DMSO. Infra-red spectra were recorded on a Nicolet FT-IR SXC spectrophotometer. Optical rotations were measured in a 1-dm cell with a Perkin–Elmer model 241 polarimeter. Concentrations are given in g/100mL. Positive electrospray ionization mass spectra were obtained using a Fisons VG-Quattro equipped with a quadrapole analyzer. Merck silica gel 60 was used for the chromatographic purifications of all specified products. For the chiral HPLC analysis of compound **5e**, the chromatographic system consisted of a Hewlett Packard 1040 HPLC system. A Daicel Chiralcel 0J 250×4.6 mM column was used. The mobile phase consisted of *n*-hexane/isopropanol/diethylamine (90/10/0.1, v/v), and a flow rate of 1.0 mL/min was maintained. Chiral HPLC analysis for the other 1,2-diphenylethylamines **5** was performed using a Daicel Chiralcel OD 250×4.6 mM column. The mobile phase consisted of *n*-hexane–isopropanol (95/5, v/v) at a flow rate of 1.0 mL/min. The diode array detector was set to 220 nm.

General procedure for the preparation of the sulfinimines 7 (e.g., (R)-(4-methoxy)-benzylidene-p-toluenesulfinimine 7a)[6]

Into a 250-mL, dry, two-necked, round-bottomed flask equipped with a magnetic stir bar, thermometer, rubber septum and argon inlet was placed 5 g (17.0 mmol) of (+)-(1S)-menthyl (R)-toluene-4-sulfinate **6** dissolved in 85 mL of THF, and the solution was cooled to −65°C. A solution of 25.5 mL of LiHMDS (1.0 M solution in THF) was added dropwise via syringe, and after 15 min the reaction mixture was allowed to warm to room temperature with stirring. After 5 h the reaction mixture was cooled to 0°C, and 4.13 mL (34 mmol) of 4-anisaldehyde **1a** was added via syringe followed by 3.870 g (25.5 mmol) of powdered CsF (99.9%). After stirring overnight at room temperature, the reaction was quenched with saturated NH_4Cl, and the mixture was diluted with ethyl acetate and water. The organic layer was separated and the aqueous layer was extracted twice with ethyl acetate. The combined organic extracts were washed with brine. After drying ($MgSO_4$), concentration in vacuo afforded a yellow solid which was purified by recrystallization from a mixture of *n*-hexane and ethyl acetate to give 3.732 g of yellow crystals in 80% yield: mp 153°C; $[\alpha]_D^{20}$ −39.3 (c 1.0, $CHCl_3$); IR

(KBr) 3014, 1592, 1511, 1460, 1262, 1096, 1065, 809 cm^{-1}; ^1H NMR (DMSO) d 2.40 (s, 3H, CH_3), 3.87 (s, 3H, OCH_3), 7.10 (d, 2H, J=8.8 Hz, ArH), 7.42 (d, 2H, J=8.1 Hz, ArH), 7.64 (d, 2H, J=8.1 Hz, ArH), 7.91 (d, 2H, J=8.8 Hz, ArH), 8.71 (s, 1H, N=CH) ppm; MS m/z 274 (MH^+).

(R)-(−)-Benzylidene-p-*toluenesulfinimine 7b*[6]

Using the procedure described above for **7a**, the reaction of 3.45 mL (34 mmol) of benzaldehyde (**1**) afforded a brown oil which was purified by crystallization from *n*-hexane to give 2.341 g of yellow crystals in 57% yield: mp 79–80°C; $[\alpha]_D^{20}$ −111.2 (c 0.26, $CHCl_3$); IR (KBr) 3056, 1604, 1572, 1448, 1100, 1068, 810, 759, 717, 689 cm^{-1}; ^1H NMR (DMSO) d 2.41 (s, 3H, CH_3), 7.44 (d, 2H, J=8.0 Hz, ArH), 7.56 (dd, 2H, J_1=7.7 Hz, J_2=6.5 Hz, ArH), 7.62 (t, 1H, J=7.7 Hz, ArH), 7.66 (d, 2H, J=6.5 Hz, ArH), 7.96 (d, 2H, J=8.0 Hz, ArH), 8.80 (s, 1H, N=CH) ppm; MS m/z 244 (MH^+).

(R)-Naphthylidene-p-*toluenesulfinimine 7c*

Using the procedure described above for **7a**, the reaction of 4.6 mL (34 mmol) of 1-naphthaldehyde **1c** afforded a brownish oil which was purified by silica gel column chromatography (5%, then 20% ethyl acetate/*n*-hexane) to give 2.603 g of yellow crystals in 53% yield: mp 85°C; $[\alpha]_D^{20}$ 0.0 (c 1.01, $CHCl_3$); IR (KBr) 3048, 1597, 1564, 1444, 1092, 1056, 801, 773, 687 cm^{-1}; ^1H NMR (DMSO) d 2.40 (s, 3H, CH_3), 7.45 (d, 2H, J=8.0 Hz, ArH), 7.66 (t, 1H, J=7.0 Hz, ArH), 7.73 (d, 2H, J=8.0 Hz, ArH), 7.73–7.68 (m, 2H, ArH), 8.09 (d, 1H, J=7.6 Hz, ArH), 8.18 (d, 1H, J=7.3 Hz, ArH), 8.22 (d, 1H, J=8.3 Hz, ArH), 9.04 (d, 1H, J=8.3 Hz, ArH)), 9.28 (s, 1H, N=CH) ppm; MS m/z 294 (MH^+).

(R)-(+)-(4-Dimethylamino)-benzylidene-p-*toluenesulfinimine 7d*

Using the same procedure described above for **7a**, the reaction of 5.067 g (34 mmol) of 4-dimethylaminobenzaldehyde **1d** afforded a slightly orange solid which was purified by recrystallization from a mixture of *n*-hexane and ethyl acetate to give 3.669 g of yellow crystals in 76% yield: mp 128°C; $[\alpha]_D^{20}$ +147.9 (c 0.27, $CHCl_3$); IR (KBr) 3017, 1609, 1577, 1432, 1368, 1177, 1097, 1070, 809, 744, 701 cm^{-1}; ^1H NMR (DMSO) d 2.40 (s, 3H, CH_3), 3.05 (s, 6H, $N(CH_3)_2$), 6.79 (d, 2H, J=8.9 Hz, ArH), 7.41 (d, 2H, J=8.0, ArH), 7.62 (d, 2H, J=8.0 Hz, ArH), 7.74 (d, 2H, J=8.9 Hz, ArH), 8.57 (s, 1H, N=CH) ppm; MS m/z 287 (MH^+).

(R)-(−)-(4-Chloro)-benzylidene-p-*toluenesulfinimine 7e*

Using the same procedure described above for **7a**, the reaction of 4.774 g (34 mmol) of 4-chlorobenzaldehyde (**1e**) afforded a yellow solid which was purified by recrystallization from a mixture of *n*-hexane and ethyl acetate to give 2.464 g of yellow crystals in 57% yield: mp 120°C; $[\alpha]_D^{20}$ −51.1 (c 1.01, $CHCl_3$); IR (KBr) 3050, 1587, 1564, 1486, 1107, 1074, 809, 733, 666 cm^{-1}; ^1H NMR (DMSO) d 2.40 (s, 3H, CH_3), 7.44 (d, 2H, J=8.0 Hz, ArH), 7.63 (d, 2H, J=8.5 Hz, ArH), 7.66 (d, 2H, J=8.0 Hz, ArH), 7.98 (d, 2H, J=8.5 Hz, ArH), 8.80 (s, 1H, N=CH) ppm; MS m/z 278/280 (MH^+).

(R)-(−)-(2-Benzyloxy)-benzylidene-p-*toluenesulfinimine 7f*

Using the same procedure described above for **7a**, the reaction of 7.208 g (34 mmol) of 2-benzyloxy benzaldehyde **1f** afforded a brown oil which was purified by silica gel column chromatography (5%, 10%, 15% and 25% ethyl acetate/ *n*-hexane) to give 4.693 g of a yellow gum in 79% yield: $[\alpha]_D^{20}$ 291.2 (c 0.22, $CHCl_3$); IR (neat) 3034, 1597, 1556, 1487, 1453, 1249, 1161, 1099, 811, 757, 699 cm^{-1}; ^1H NMR (DMSO) d 2.40 (s, 3H, CH_3), 5.32 (s, 2H, OCH_2Ph), 7.09 (t, 1H, J=7.7 Hz, ArH), 7.32 (d, 1H, J=8.4 Hz, ArH), 7.40 (t, 1H, J=7.3 Hz, ArH), 7.42 (d, 2H, J=8.5 Hz, ArH), 7.46 (t, 2H, J=7.3 Hz, ArH), 7.52 (d, 2H, J=7.3 Hz, ArH), 7.58 (dt, 1H, J_1=8.4 Hz, J_2=1.6 Hz, ArH), 7.63 (d, 2H, J=8.5 Hz, ArH), 7.90 (dd, 1H, J_1=7.7 Hz, J_2=1.6 Hz, ArH), 9.17 (s, 1H, N=CH) ppm; MS m/z 350 (MH^+).

(R)-(−)-(4-Nitro)-benzylidene-p-*toluenesulfinimine 7g*

Using the same procedure described above for **7a**, the reaction of 5.132 g (34 mmol) of 4-nitrobenzaldehyde **1g** afforded a red gum which was purified by silica gel column chromatography (5

to 40% ethyl acetate/ *n*-hexane) to give 1.523 g of red–orange crystals in 31% yield: mp 164–165°C; $[\alpha]_D^{20}$ 0.0 (c 0.50, $CHCl_3$); IR (KBr) 3108, 1589, 1522, 1343, 1102, 1056, 806, 748, 720, 685 cm^{-1}; ^1H NMR (DMSO) d 2.41 (s, 3H, CH_3), 7.45 (d, 2H, J=8.2 Hz, ArH), 7.69 (d, 2H, J=8.2 Hz, ArH), 8.22 (d, 2H, J=8.9 Hz, ArH), 8.37 (d, 2H, J=8.9 Hz, ArH), 8.95 (s, 1H, N=CH) ppm.

*General procedure for the preparation of the sulfinamides 8 (e.g. (S_r,R)-(−)-*N*-[1-(4-methoxyphenyl)-2-phenylethyl]-*p*-toluenesulfinamide 8a)*

Into a 250-mL, dry, two-necked, round-bottomed flask fitted with a magnetic stir bar, thermometer, argon inlet, and rubber septum was placed 8.2 mL (16.4 mmol) of benzylmagnesium chloride (2.0 M solution in THF) and the solution was cooled to −30°C. A solution of 2.242 g (8.2 mmol) of sulfinimine **7a** in toluene (110 mL) was then added dropwise via a dried, 250-mL, pressure-equalizing addition funnel. After stirring 15 min at −30°C, the reaction mixture was diluted with a mixture of H_2O and ethyl acetate. The resulting mixture was filtered through celite. The organic layer was separated and the aqueous layer was extracted twice with ethyl acetate. The combined organic extracts were dried over $MgSO_4$ and concentrated to afford a yellow solid which was purified by recrystallization from a mixture of heptane/TBME to give 2.271 g of yellow crystals in 76% yield and 84% de: mp 68–69°C; $[\alpha]_D^{20}$ −66.0 (c 1.00, $CHCl_3$); IR (KBr) 3196, 3021, 1611, 1514, 1453, 1247, 1030, 807, 700 cm^{-1}; ^1H NMR (DMSO) d 2.36 (s, 3H, CH_3), 3.05 (dd, 1H, J_1=13.5 Hz, J_2=7.8 Hz, CH_2Ph), 3.17 (dd, 1H, J_1=13.5 Hz, J_2=7.3 Hz, CH_2Ph), 3.73 (s, 3H, OCH_3), 4.43 (dd, 1H, J_1=7.8 Hz, J_2=7.3 Hz, NH–CH), 6.79 (d, 2H, J=8.7 Hz, ArH), 7.09 (m, 4H, ArH), 7.19 (m, 1H, ArH), 7.23–7.26 (m, 6H, ArH) ppm; MS m/z 366 (MH^+).

*(S_r,R)-(−)-*N*-[1-Phenyl-2-phenylethyl]-*p*-toluenesulfinamide 8b*

Using the same procedure described above for **8a**, reaction of a solution of 2 g (8.2 mmol) of sulfinimine **7b** in toluene (90 mL) afforded a brown oil which was first purified by silica gel column chromatography (20%, 30% and 40% ethyl acetate/*n*-hexane) to give a yellow solid which was then purified by recrystallization from a mixture of heptane/TBME to give 1.665 g of yellow crystals in 61% yield and 94% de: mp 107–108°C; $[\alpha]_D^{20}$ −74.0 (c 1.03, $CHCl_3$); IR (KBr) 3183, 3027, 1598, 1449, 1057, 804, 699 cm^{-1}; ^1H NMR (DMSO) d 2.36 (s, 3H, CH_3), 3.07 (dd, 1H, J_1=13.5 Hz, J_2=7.5 Hz, CH_2Ph), 3.17 (dd, 1H, J_1=13.5 Hz, J_2=7.6 Hz, CH_2Ph), 4.49 (dt, 1H, J_1=7.6 Hz, J_2=7.5 Hz, NH–CH), 7.12 (m, 3H, ArH), 7.19 (m, 3H, ArH), 7.21–7.27 (m, 8H, ArH) ppm; MS m/z 336 (MH^+).

*(S_r,R)-(−)-*N*-[1-Naphthyl-2-phenylethyl]-*p*-toluenesulfinamide 8c*

Using the same procedure described above for **8a**, reaction of a solution of 2.406 g (8.2 mmol) of the sulfinimine **7c** in toluene (90 mL) afforded a yellow gum which was recrystallized from a mixture of heptane/TBME to give 1.716 g of yellow crystals in 55% yield and 84% de: mp 114–115°C; $[\alpha]_D^{20}$ −72.7 (c 1.01, $CHCl_3$); IR (KBr) 3211, 3021, 1596, 1450, 1053, 1022, 776, 702 cm^{-1}; ^1H NMR (DMSO) d 2.30 (s, 3H, CH_3), 3.29 (d, 2H, J=7.4 Hz, CH_2Ph), 5.34 (q, 1H, J=7.4 Hz, NH–CH), 7.14–7.24 (m, 10H, ArH), 7.32 (d, 1H, J=8.3 Hz, ArH), 7.42 (m, 1H, ArH), 7.47 (m, 2H, ArH), 7.79 (d, 1H, J=8.2 Hz, ArH), 7.88 (d, 1H, J=7.8 Hz, ArH) ppm; MS m/z 386 (MH^+).

*(S_r,R)-(−)-*N*-[1-(4-Dimethylaminophenyl)-2-phenylethyl]-*p*-toluenesulfinamide 8d*

Using the same procedure described above for **8a**, reaction of a solution of 3.5 g (12.2 mmol) of the sulfinimine **7d** in toluene (150 mL) afforded a brown oil which was purified by crystallization from a mixture of heptane/TBME to give 3.344 g of yellow crystals in 73% yield and 80% de: mp 106–107°C; $[\alpha]_D^{20}$ −52.1 (c 1.01, $CHCl_3$); IR (KBr) 3205, 3024, 1614, 1522, 1452, 1056, 1031, 810, 701 cm^{-1}; ^1H NMR (DMSO) d 2.37 (s, 3H, CH_3), 2.87 (s, 6H, $N(CH_3)_2$), 3.06 (dd, 1H, J_1=14 Hz, J_2=8.0 Hz, CH_2Ph), 3.20 (dd, 1H, J_1=14 Hz, J_2=7.1 Hz, CH_2Ph), 4.36 (dd 1H, J_1=8.0 Hz, J_2=7.1 Hz, NH–CH), 6.59 (d, 2H, J=8.8 Hz, ArH), 6.98 (d, 2H, J=8.8 Hz, ArH), 7.09 (d, 2H, J=6.9 Hz, ArH), 7.17–7.27 (m, 7H, ArH) ppm; MS m/z 379 (MH^+).

(S_r,R)-(−)-N-[1-(4-Chlorophenyl-2-phenylethyl]-p-toluenesulfinamide ***8e***

Using the same procedure described above for **8a**, reaction of a solution of 2.5 g (9 mmol) of the sulfinimine **7e** in toluene (100 mL) afforded a yellow solid which was purified by recrystallization from a mixture of heptane/TBME to give 1.5 g of yellow crystals in 61% yield and 80% de: mp 66–67°C; $[\alpha]_D^{20}$ −48.8 (c 1.00, $CHCl_3$); IR (KBr) 3189, 3025, 1595, 1492, 1450, 1090, 1033, 800, 701 cm^{-1}; ^1H NMR (DMSO) d 2.35 (s, 3H, CH_3), 3.04 (dd, 1H, J_1=13.6 Hz, J_2=7.6 Hz, CH_2Ph), 3.14 (dd, 1H, J_1=13.6 Hz, J_2=6.0 Hz, CH_2Ph), 4.53 (dt, 1H, J_1=7.6 Hz, J_2=6.0 Hz, NH–CH), 7.13 (m, 2H, ArH), 7.17–7.36 (m, 11H, ArH) ppm; MS m/z 370/372 (MH^+).

(S_r,R)-(−)-N-[1-(2-Benzyloxyphenyl)-2-phenylethyl]-p-toluenesulfinamide ***8f***

Using the same procedure described above for **8a**, reaction of a solution of 4 g (11.5 mmol) of the sulfinimine **7f** in toluene (130 mL) afforded a yellow solid which was purified by recrystallization from a mixture of heptane/TBME to give 3.627 g of white crystals in 72% yield and 60% de: mp 104–105°C; $[\alpha]_D^{20}$ −53.0 (c 1.01, $CHCl_3$); IR (KBr) 3223, 3029, 1599, 1491, 1453, 1226, 1084, 1039, 812, 753, 702 cm^{-1}; ^1H NMR (DMSO) d 2.32 (s, 3H, CH_3), 2.98 (dd, 1H, J_1=13.4 Hz, J_2=8.1 Hz, CH_2Ph), 3.05 (dd, 1H, J_1=13.4 Hz, J_2=6.4 Hz, CH_2Ph), 4.91–5.0 (m, 3H, NH–CH + OCH_2Ph), 6.93 (d, 2H, J=7.8 Hz, ArH), 7.0–7.20 (m, 10H, ArH), 7.35–7.44 (m, 6H, ArH) ppm; MS m/z 442 (MH^+).

General procedure for the hydrolysis of sulfinamides 8

Into a 250-mL, round-bottomed flask equipped with a magnetic stir bar and argon inlet were placed 5.47 mmol of sulfinamides **8**, 1.026 g (6.6 mmol) of (+)-menthol and 60 mL of CH_2Cl_2. The solution was cooled to 0°C, 1.27 mL of trifluoroacetic acid (16.4 mmol) was added, and the mixture was stirred at room temperature for 2 hours. The reaction mixture was extracted 3 times with water, and the organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by silica gel column chromatography (5–10% EtOAc/hexane) to give 75–90% of a diastereomeric mixture (de=8–28%) of Andersen reagent **6**. Crystallization of the mixture from acetone–HCl according to the literature procedure[9] afforded optically pure (+)-Andersen reagent (**1**) in 50% yield.

The aqueous layer was adjusted to pH 12 with NaOH (pellets) and extracted three times with TBME. The combined organic extracts were dried over $MgSO_4$ and concentrated to afford the 1,2 diphenyl ethylamines **5**.

(R)-(−)-1-(4-Methoxyphenyl)-2-phenylethylamine ***5a***

Colorless oil; Yield: 90%; ee: 85%; $[\alpha]_D^{20}$ −91.9 (c 1.00% MeOH/0.1N HCl: 50/50); IR (neat) 3028, 2934, 1682, 1611, 1515, 1250, 1179, 1033, 832, 731, 700 cm^{-1}; ^1H (DMSO) d 1.91 (br s, 2H, NH_2), 2.92 (d, 2H, J=7.1 Hz, CH_2), 3.76 (s, 3H, OCH_3), 4.15 (t, 1H, J=7.1 Hz, CH), 6.88 (d, 2H, J=8.7 Hz, ArH), 7.14 (m, 2H, ArH), 7.19 (m, 1H, ArH), 7.26 (t, 2H, J=7.5 Hz, ArH), 7.28 (d, 2H, J=7.8 Hz, ArH) ppm; MS m/z 228 (MH^+).

(R)-(−)-1,2-Diphenylethylamine ***5b***

Colorless oil; Yield: 84%; ee: 94%; $[\alpha]_D^{20}$ −118.1 (c 1.01, MeOH/0.1N HCl: 50/50), −10.1° (c 1.34, $CHCl_3$)[7]; IR (neat) 3061, 3027, 1603, 1494, 1452, 760, 700 cm^{-1}; ^1H NMR (DMSO) d 1.90 (br s, 2H, NH_2), 2.83 (dd, 1H, J_1=13.2 Hz, J_2=7.8 Hz, CH_2), 2.88 (dd, 1H, J_1=13.2 Hz, J_2=6.2 Hz, CH_2), 4.09 (dt, 1H, J_1=7.8 Hz, J_2=6.2 Hz, CH), 7.15–7.18 (m, 2H, ArH), 7.19 (m, 2H, ArH), 7.27 (m, 2H, ArH), 7.30 (m, 2H, ArH), 7.36 (m, 2H, ArH) ppm; MS m/z 198 (MH^+).

(R)-(−)-1-[1]-Naphthyl-2-phenylethylamine ***5c***

Colorless oil; Yield: 65%; ee: 88%; $[\alpha]_D^{20}$ −4.4 (c 1.02, MeOH/0.1N HCl: 50/50); IR (neat) 3059, 3026, 1599, 1496, 1459, 777, 700 cm^{-1}; ^1H NMR (DMSO) d 2.19 (br s, 2H, NH_2), 2.88 (dd, 1H, J_1=13.5 Hz, J_2=8.6 Hz, CH_2), 3.14 (dd, 1H, J_1=13.5 Hz, J_2=4.9 Hz, CH_2), 4.96 (dd, 1H, J_1=8.6 Hz, J_2=4.9 Hz, CH), 7.19–7.23 (m, 1H, ArH), 7.27–7.31 (m, 4H, ArH), 7.51–7.55 (m, 2H, ArH),

7.56–7.59 (m, 1H, Ar**H**), 7.76 (d, 1H, J=7.0 Hz, Ar**H**), 7.83 (d, 1H, J=8.2 Hz, Ar**H**), 7.96 (d, 1H, J=7.6 Hz, Ar**H**), 8.29 (d, 1H, J=8.4 Hz, Ar**H**) ppm; MS m/z 248 (MH^+).

(R)-(−)-1-(4-Dimethylaminophenyl)-2-phenylethylamine ***5d***

Yellow crystals; Yield: 77%; ee: 84%; mp 51–52°C; $[\alpha]_D^{20}$ −95.0 (c 1.01, MeOH/0.1N HCl: 50/50); IR (KBr) 3062, 3024, 2893, 1614, 1522, 1452, 1337, 811, 742, 696 cm^{-1}; ^1H NMR (DMSO) d 1.75 (br s, 2H, NH_2), 2.79 (dd, 1H, J_1=13.2 Hz, J_2=7.5 Hz, CH_2), 2.85 (dd, 1H, J_1=13.2 Hz, J_2=6.2 Hz, CH_2), 2.88 (s, 6H, $N(CH_3)_2$), 3.99 (dd, 1H, J_1=7.5 Hz, J_2=6.2 Hz, C**H**), 6.68 (d, 2H, J=8.7 Hz, Ar**H**), 7.16 (d, 2H, J=8.7 Hz, Ar**H**), 7.17 (d, 2H, J=8.7 Hz, Ar**H**), 7.18 (m, 1H, Ar**H**), 7.26 (m, 2H, Ar**H**) ppm; MS m/z 241 (MH^+).

(R)-(−)-1-(4-Chlorophenyl)-2-phenylethylamine ***5e***

White crystals; Yield: 85%; ee: 77%; mp 53–54°C; $[\alpha]_D^{20}$ −117.0 (c 1.02, MeOH/0.1N HCl: 50/50); IR (KBr) 3056, 3025, 2912, 1573, 1489, 1090, 1011, 847, 817, 745, 697 cm^{-1}; ^1H NMR (DMSO) d 1.91 (br s, 2H, NH_2), 2.83 (dd, 1H, J_1=13.7 Hz, J_2=7.5 Hz, CH_2), 2.86 (dd, 1H, J_1=13.7 Hz, J_2=6.3 Hz, CH_2), 4.11 (dd, 1H, J_1=7.5 Hz, J_2=6.3 Hz, C**H**), 7.15 (m, 2H, Ar**H**), 7.19(m, 1H, Ar**H**), 7.27 (m, 2H, Ar**H**), 7.34 (d, 2H, J=8.7 Hz, Ar**H**), 7.36 (d, 2H, J=8.7 Hz, Ar**H**) ppm; MS m/z 232/234 (MH^+).

(R)-(−)-1-(2-Benzyloxyphenyl)-2-phenylethylamine ***5f***

Colorless oil; Yield: 84%; ee: 75%; $[\alpha]_D^{20}$ −43.5 (c 1.00, MeOH/0.1N HCl: 50/50); IR (neat) 3061, 3028, 1599, 1491, 1451, 1239, 1021, 750, 700 cm^{-1}; ^1H NMR (DMSO) d 1.66 (br s, 2H, NH_2), 2.64 (dd, 1H, J_1=13.1 Hz, J=8.5 Hz, CH_2), 2.99 (dd, 1H, J_1=13.1 Hz, J_2=4.7 Hz, CH_2), 4.42 (dd, 1H, J_1=8.5 Hz, J_2=4.7 Hz, C**H**), 5.14 (d, 2H, J=11.9, OCH_2Ph), 6.96 (dt, 1H, J_1=7.4 Hz, J_2=0.8 Hz, Ar**H**), 7.06–7.10 (m, 3H, Ar**H**), 7.16–7.24 (m, 4H, Ar**H**), 7.38–7.41 (m, 1H, Ar**H**), 7.44–7.49 (m, 3H, Ar**H**), 7.51–7.52 (m, 2H, Ar**H**) ppm; MS m/z 304 (MH^+).

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