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PAPER

Scope of the organocatalysed asymmetric reductive amination of ketones with trichlorosilane†

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A highly active organocatalyst has been shown to affect the asymmetric reductive amination of ketones producing both aromatic and aliphatic amines. At 1 mol% catalyst loading, a series of structurally diverse chiral amines were quickly and economically prepared with good enantioselectivity and generally useful yield. The efficient synthesis of the calcimimetic (+)-NPS R-568 (67%, 89% *ee*) demonstrated the synthetic applicability of this methodology.

Introduction

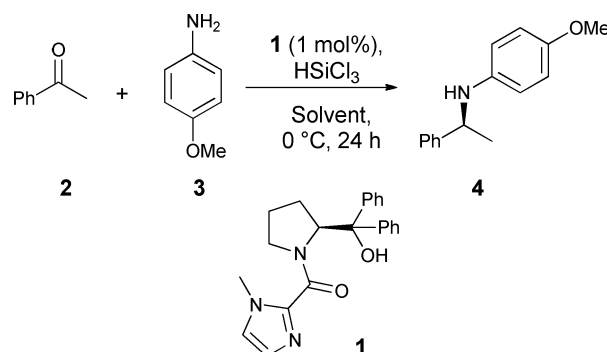
Chiral amines are found in a vast array of natural products and pharmaceutically active molecules.¹ The asymmetric reduction of imines has proved to be an efficient route to access such compounds,^{2,3} but can be hampered by the sometimes non-trivial preparation and stability of the imine precursors, resulting in low overall yields. An alternative strategy using asymmetric reductive amination provides a convenient alternative that circumvents this problem. It is not surprising that the development of such a reaction has been a sought-after goal, and a few groups have reported breakthroughs using both transition-metal catalysed hydrogenation⁴ and organocatalysed reduction with Hantzsch esters as the hydride source.^{3b,5} In contrast, the organocatalysed asymmetric reduction of imines employing trichlorosilane has been less studied in this respect.⁶ In 2007, Malkov *et al.* described a process for the direct synthesis of chiral α -chloroamines from chloroketones and an aromatic amine, where the ketimine was prepared *in situ* before addition of the catalyst and reductant.⁷ More recently, the first example of direct asymmetric reductive amination using trichlorosilane activated by an organic catalyst at 10 mol% catalyst loading was reported by Benaglia's group.⁸ They reported three examples of this process; two benchmark reactions produced *N*-phenyl-1-phenylethylamine in 98% yield and 87% *ee* after 40 h, and *N*-4-methoxyphenyl-1-phenylethylamine in 80% yield and 87% *ee* after 90 h. Their final example demonstrated the synthesis of the herbicide metolachlor, providing the product in 86% yield and 70% *ee*.

We recently reported the development of the imidazole based organocatalyst **1** that facilitates the asymmetric reduction of a

variety of imines in excellent yields and enantioselectivities at very low catalyst loading.⁹ We also found that catalyst **1** did not reduce ketones with trichlorosilane, and with this in mind, envisioned developing a quick and cost effective process for the asymmetric reductive amination of ketones. Herein, we describe our efforts towards this goal using an array of ketones employing trichlorosilane with catalyst **1** at unprecedented low catalyst loading.

Results and discussion

Acetophenone **2** and *p*-anisidine **3** were used as standard substrates for optimization of the reaction conditions, starting with previously optimized conditions for the direct imine reduction (Scheme 1, Table 1, entry 1).⁹ Although the product was obtained in good *ee*, the yield was significantly reduced. Increasing the equivalents of acetophenone or *p*-anisidine increased the yield slightly (Table 1, entries 2–3), although increasing the equivalents of trichlorosilane from 2 eq. to 4 eq. gave no benefit (Table 1, entries 4–5). Reaction in toluene gave the desired amine **4** in a lower yield compared with that performed in dichloromethane (Table 1, entries 3 and 6). Although good enantioselectivities were obtained, the yield was unsatisfactory. Lewis acid catalysts have been successfully used in

Scheme 1 Optimisation of reductive amination of ketone **2**.

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Table 1 Optimization of reductive amination of ketone **2** according to Scheme 1

Entry	Molar ratio		HSiCl ₃	Additive (equiv.)	Solvent (mL)	Yield (%) ^a	ee (%)
	2	3					
1	1.2	1	2	—	CH ₂ Cl ₂ (1)	39	85
2	2	1	2	—	CH ₂ Cl ₂ (1)	47	84
3	1	2	2	—	CH ₂ Cl ₂ (1)	53	84
4	1	2	3	—	CH ₂ Cl ₂ (1)	52	85
5	1	2	4	—	CH ₂ Cl ₂ (1)	46	86
6	1	2	2	—	Toluene (1)	39	84
7	1	2	2	TMSOTf (0.1)	CH ₂ Cl ₂ (1)	75	77
8	1	2	2	TMSOTf (0.05)	CH ₂ Cl ₂ (1)	58	80
9	1	2	2	TMSOTf (0.1)	Toluene (1)	52	76
10 ^b	1	2	2	TMSOTf (0.1)	CH ₂ Cl ₂ (1)	78	77
11	1	2	2	TMSCl (0.1)	CH ₂ Cl ₂ (1)	52	84
12	1	2	2	TMSCl (1.0)	CH ₂ Cl ₂ (1)	40	71
13	1	2	2	—	CH ₂ Cl ₂ (5)	43 ^c	79
14	1	2	2	—	CH ₂ Cl ₂ (0.5)	66	84
15	1	1.5	2	—	CH ₂ Cl ₂ (0.5)	71	84

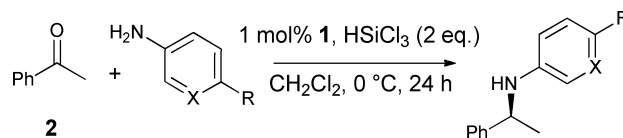
^a Based on isolated product. ^b 5 mol% of catalyst **1**; ^c Refers to conversion calculated from the integrals of appropriate signals in the ¹H NMR spectrum.

the three component Strecker reactions for the preparation of α -aminonitriles.¹⁰ It was envisioned that use of these could increase the rate of imine formation and thus improve the yield of reductive amination. This was indeed the case; the yield of amine **4** could be increased to 75% employing 0.1 eq. of TMSOTf as an additive, but the enantioselectivity decreased (Table 1, entries 7–9) and could not be recovered by increasing catalyst loading from 1 mol% to 5 mol% (Table 1, entry 10). TMSCl also failed to offer any improvements (Table 1, entries 11 and 12). It was reasoned that increasing the concentration of the substrate and reagents may also lead to a similar effect (Table 1, entries 13–15) which gave a much more satisfactory result, the optimum conditions thus being use of ketone, *p*-anisidine and HSiCl₃ in a molar ratio of 1 : 1.5 : 2, providing amine **4** in 71% yield and 84% *ee* at 1 mol% catalyst loading (Table 1, entry 15). These conditions offer an order of magnitude difference in catalyst loading, with considerable time savings (24 h *vs.* 90 h) to deliver a product with almost identical yield and *ee* to the best competitive related catalyst system reported by Benaglia.⁸ Indeed, if one calculates the Asymmetric Catalytic Efficiency (ACE) and Asymmetric Catalytic Efficiency Speed (ACES),¹¹ catalyst **1** provides amine **4** with an ACE of 37.5 and an ACES of 1.6. These compare very well next to the competitor catalyst with an ACE of 5.2 and ACES of 0.1,⁸ and illustrate the cost and time savings associated with using the cheap, low molecular weight catalyst **1**.

With the optimal conditions in hand, the generality of the process was explored. Both electron rich and electron poor aryl methyl ketones afforded the corresponding amines in good enantioselectivities (70%–84% *ee*, Table 2, entries 1–7), although slightly lower yields were observed when using electron poor aryl methyl ketones as substrates (Table 2, entries 4–5). Surprisingly, the asymmetric amination of *o*-methylphenyl methyl ketone afforded the amine in low yield (12%), but use of *o*-methoxyphenyl methyl ketone led to a good yield despite a small drop in enantioselectivity (Table 2, entries 6 *vs.* 7). This small change in the steric requirements of the substrate adjacent to the reaction site can also be seen when contrasting the 1-naphthyl substrate with the 2-naphthyl (Table 2, entries 8 and 9). 2-Acetyl thiophene is reasonably well tolerated, while in contrast the furyl analogue is a poor substrate

(Table 2, entries 10 and 11). Propiophenone afforded the corresponding amine in high enantioselectivity but low yield (Table 2, entry 12). This illustrates the limitations of this methodology, since ketones with further substitution at the aliphatic centre fail to afford the amine and return only the starting materials after workup (Table 2, entries 13–14). Further elongation of the aliphatic chain, using benzyl ketones, or conjugated cinnamyl ketones provided the products in high yields but low enantioselectivities (Table 2, entries 15–17). Trifluoromethyl ketones did not react, presumably because the strongly electron withdrawing trifluoromethyl group stabilizes the tetrahedral hemi-aminal intermediate, disfavoring imine formation.

Various aromatic amines can also be used and afforded the corresponding products in synthetically useful yield and good enantioselectivity (Scheme 2, Table 3, entries 1–3). However, reductive amination employing 3-aminopyridine gave the product in low enantioselectivity (10% *ee*), albeit good yield (Table 3, entry 4).

**Scheme 2** Reductive amination of ketone **2** with aryl amines.

Reductive amination of acetophenone with aliphatic amines provided only recovered starting materials, presumably due to the formation of an initial amino-silane complex that inhibited subsequent reactions. With this in mind, a two step-one pot procedure was developed by microwave-assisted imine formation immediately prior to reduction. Ketone **2** and aliphatic amine were heated at 150 °C for 40 min with 4 Å molecular sieves using microwave irradiation and the crude product immediately submitted to standard reduction conditions. Using this process, several *N*-alkyl amines were successfully obtained in good yield and *ee* (Scheme 3, Table 4, entries 1–7). It was notable that sterically hindered ketones were also transformed under these

Table 2 Asymmetric reductive amination with *p*-anisidine^a

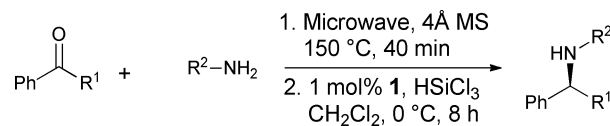
Entry	Ketone	Product	Yield (%) ^b	ee (%)
1			71	84
2			76	81
3			66	83
4			61	83
5			46	83
6			71	70
7			12	81
8			11	77
9			63	85
10			61	79
11			72	44
12			15	85
13			— ^c	N.A
14			— ^c	N.A
15			82	14
16 ^d			81	15
17			77	0

^a A mixture of ketone (1 mmol), *p*-anisidine **3** (1.5 mmol), catalyst **1** (0.01 mmol) and HSiCl₃ (2 mmol) in CH₂Cl₂ (0.5 mL) were stirred for 24 h at 0 °C. ^b Refers to isolated product. ^c No reaction or < 5% conversion. ^d Reaction performed in 1 mL of CH₂Cl₂.

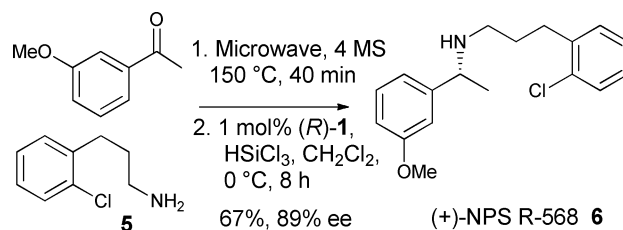
Table 3 Reductive amination of ketone **2** with aryl amines according to Scheme 2^a

Entry	X	R	Product	Yield (%) ^b	ee (%)
1	CH	H		56	82
2	CH	Me		64	84
3	CH	F		65	81
4 ^c	N	H		58	10

^a A mixture of **2** (1 mmol), amine (1.5 mmol), **1** (0.01 mmol) and HSiCl₃ (2 mmol) in CH₂Cl₂ (0.5 mL) stirred for 24 h at 0 °C. ^b Refers to isolated product. ^c Reaction was performed in 2 mL of CH₂Cl₂.









**Scheme 3** Two-step-one pot reductive amination.

conditions, and that the iso-propyl ketone led to a reversal of the sense of stereoselectivity (Table 4, entry 7). The origins of this latter observation are currently being investigated. The two-step procedure can also be used with aromatic amines, the products being isolated in approximately the same yield and *ee* compared to the one pot procedure (Table 2 entry 1 vs. Table 4, entry 8). However, the two-step-one pot procedure offers considerable time savings (4 h 40 min vs. 24 h), increasing the ACES from 1.6 to 7.6. The synthetic utility of this two-step-one pot procedure was demonstrated by synthesis of the calcimimetic (*R*)-(+)-NPS R-568 in 67% yield and 89% *ee* (Scheme 4).¹²

**Scheme 4** Synthesis of calcimimetic (*R*)-(+)-NPS R-568.

From the studies outlined in Table 1, it is very likely that the optimized reaction conditions promote formation of the imine that then undergoes reduction mediated by the catalyst. The microwave-assisted reactions for the aliphatic amines are also likely to act in this manner. What is less clear at the moment are the mechanistic origins for some of the more surprising results obtained (for example, Table 2, entries 10 & 11, and Table 4, entry 7). These may be a result of the optimized reaction conditions outlined herein, or be a more general feature associated with the

Table 4 Two-step-one pot reductive amination according to Scheme 3^a

Entry	R ¹	R ²	Product	Yield (%) ^b	ee (%)
1	Me	PhCH ₂		63	80
2 ^c	Me	Ph(CH ₂) ₂		65	86
3	Me	Ph(CH ₂) ₃		76	84
4	Me	2-methylfuryl		65	86
5	Me	2-methylthienyl		64	83
6	Et	PhCH ₂		66	73
7	<i>i</i> -Pr	PhCH ₂		62	76
8 ^d	Me	<i>p</i> -anisidine		68	84

^a A mixture of ketone (1 mmol), amine (1.5 mmol) and 4 Å MS (200 mg) was irradiated under microwave for 40 min at 150 °C, then cooled to RT. Catalyst **1** (0.01 mmol) and CH₂Cl₂ (0.5 mL) were added, the reaction cooled to 0 °C, HSiCl₃ (2 mmol) added and left to stir for 8 h; ^b Refers to isolated product; ^c Reaction was performed in 2 mL of CH₂Cl₂. ^d Conducted for 4 h 40 min.

mechanism of action of catalyst **1** in comparison with related species. Mechanistic studies which aim to address these issues are currently in progress and will be reported in due course.

Conclusions

In conclusion, methods for the asymmetric reductive amination of ketones with aromatic and aliphatic amines were successfully developed employing organocatalyst **1** at 1 mol% catalyst loading. Sterically hindered ketones are also transformed in good yield and ee, highlighted in the asymmetric synthesis of (+)-NPS R-568. For a number of substrates, this offers quick access to chiral amines of good enantiomeric purity at a low cost.

Experimental

General information

Unless stated otherwise, all solvents were obtained from a Grubbs dry solvent system and glassware was flame dried and cooled under vacuum before use. All chemicals were used as received without further purification unless otherwise stated. Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plate. Subsequent to elution, plates were visualized using UV radiation (254 nm); further visualization was possible by staining with basic solution of potassium permanganate. Flash chromatography was performed using silica gel 40–63 μm 60 Å (Fluorochem Limited). Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use. ¹H and ¹³C NMR spectra were recorded on

Bruker 400 MHz spectrometer at ambient temperature. Chemical shifts for ¹H NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-d (δ 7.26, singlet). Coupling constants are reported as a *J* value in Hz. Data for ¹³C NMR are reported as δ in ppm downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-d (δ 77.0, triplet). Enantioselectivities were determined by high performance liquid chromatography (HPLC) analysis employing a Gilson HPLC chain with an ABI Analytical Spectroflow 783 UV detector (λ 254 nm), using a mixture of hexane and propan-2-ol as mobile phase and Chiralcel OD-H, Chiralcel OJ, Kromasil 3-Cellucoat OD or Phenomenex Lux 3u cellulose-2 column as stationary phase. Mobile phase flow, unless specified otherwise, was 1.0 mL min⁻¹. Absolute configuration of the products was determined by comparison with compounds previously published.

General procedure A for preparation of amines

Ketone (1 mmol), amine (1.5 mmol), catalyst (*S*)-**1** (0.01 mmol) and dry CH₂Cl₂ (0.5 mL) were introduced into an oven-dried 25 mL two-necked flask or an oven-dried carousel tube. The mixture was stirred until complete dissolution, then cooled to 0 °C and trichlorosilane (2 mmol, 0.2 mL) was added by syringe. A suspension was formed immediately upon addition of trichlorosilane. The resulting reaction mixture was left to stir for 24 h at 0 °C. The reaction was diluted by CH₂Cl₂ (20 mL), quenched by water (2 mL) and followed by addition of aqueous sodium hydroxide (1 M, 20 mL). This mixture was stirred until the precipitate was completely dissolved and no gas was emitted. The organic phase was separated and the aqueous phase was extracted with CH₂Cl₂ (2 × 20 mL). The combined organic phase was wash with brine (20 mL) and dried over MgSO₄. Filtration and concentration gave crude product, which was purified by chromatography column on silica gel using 2% ~ 10% solution of diethyl ether in petroleum ether.

General procedure B for preparation of amines

Ketone (1 mmol), amine (1.5 mmol), and 4 Å molecular sieves (200 mg) was introduced into a microwave tube (10 mL) and the mixture was heated at 150 °C for 40 min under microwave irradiation. After the reaction mixture was cooled to room temperature, catalyst (*S*)-**1** (0.01 mmol) and dry CH₂Cl₂ (0.5 mL or as mentioned) were added, the vessel cooled to 0 °C and trichlorosilane (2 mmol, 0.2 mL) added by syringe. The resulting reaction mixture was left to stir at 0 °C for 8 h. The reaction was diluted by CH₂Cl₂ (20 mL), quenched by water (2 mL) and followed by addition of aqueous sodium hydroxide (1 M, 20 mL). This mixture was stirred until the precipitate was completely dissolved and no gas was emitted. The organic phase was separated and the aqueous phase was extracted with CH₂Cl₂ (2 × 20 mL). The combined organic phase was wash with brine (20 mL) and dried over MgSO₄. Filtration and concentration gave crude product, which was purified by chromatography column on silica gel using 2% ~ 20% solution of diethyl ether in petroleum ether.

Analytical data of amines

For ease of identification, a numbering system for these compounds has been devised relating to the ketone and amine that

Table 5 Numbering system for condensation of ketones and amines.

Ketone	Amine
a Acetophenone	a <i>p</i> -Methoxyaniline
b 4-Methoxyacetophenone	b Aniline
c 4-Methylacetophenone	c <i>p</i> -Methylaniline
d 4-Chloroacetophenone	d <i>p</i> -Fluoroaniline
e 4-Nitroacetophenone	e 3-Aminopyridine
f 2-Methoxyacetophenone	f Benzylamine
g 2-Methylacetophenone	g 2-Phenylethylamine
h 1-Acetylnaphthalene	h 3-Phenylpropylamine
i 2-Acetylnaphthalene	i 2-(Aminomethyl)furan
j 2-Acetylthiophene	j 2-(Aminomethyl)thiophene
k 2-Acetylfuran	
l Propiophenone	
m 4-Phenyl-2-butanone	
n 3',4'-Dimethoxyphenyl-propanone	
o (<i>E</i>)-4-Phenyl-3-buten-2-one	
p Isobutyrophenone	

have been condensed (see Table 5). Thus product **aa** comes from the imine formed by condensing ketone **a** with amine **a**.

(*S*)-*N*-[1-(1-Phenylethyl)-4-methoxyaniline **4** (**aa**)]⁹

Obtained using general procedure A as a brown oil (71% yield); $[\alpha]_D -2.5$ (*c* 3.0 in CHCl₃, 84% *ee*; Lit.⁹ $[\alpha]_D -5.6$, *c* 0.54 in CHCl₃, 87% *ee*); δ_H (400 MHz; CDCl₃) 1.52 (3 H, d, *J* 6.8, CH₃), 3.72 (3 H, s, OCH₃), 3.81 (1 H, br, *NH*), 4.43 (1 H, q, *J* 6.8, *NCH*), 6.49 [2 H, (AX)₂, ArCH], 6.71 [2 H, (AX)₂, ArCH] and 7.23–7.40 (5 H, m, ArH); δ_C (100 MHz; CDCl₃) 25.2 (CH₃), 54.3 (NCH), 55.8 (CH₃O), 114.6 (ArCH), 114.8 (ArCH), 125.9 (ArCH), 126.9 (ArCH), 128.7 (ArCH), 141.6 (ArC), 145.5 (ArC) and 151.9 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μ m Cellulose-1) 2% ipa in hexane @ 1 mL min⁻¹, *t_R* = 16.5 min (minor), 19.2 min (major). Data was in accordance with the literature.

(*S*)-*N*-[1-(4'-Methoxyphenyl)ethyl]-4-methoxyaniline (**ba**)]⁹

Obtained using general procedure A as a white solid (76% yield); mp 93–95 °C (not reported in literature); $[\alpha]_D -14.5$ (*c* 0.96 in CHCl₃, 81% *ee*, lit.⁹ $[\alpha]_D -15.5$, *c* 1.1 in CHCl₃, 85% *ee*); δ_H (250 MHz; CDCl₃) 1.49 (3 H, d, *J* 6.6, CH₃), 3.72 (3 H, s, OCH₃), 3.76 (1 H, br, *NH*), 3.80 (3 H, s, OCH₃), 4.39 (1 H, q, *J* 6.6, *NCH*), 6.49 [2 H, (AX)₂, ArCH], 6.71 [2 H, (AX)₂, ArCH], 6.87 [2 H, (AX)₂, ArCH] and 7.29 [2 H, (AX)₂, ArCH]; δ_C (63 MHz; CDCl₃) 25.1 (CH₃), 53.7 (NCH), 55.3 (OCH₃), 55.8 (OCH₃), 114.0 (ArCH), 114.6 (ArCH), 114.8 (ArCH), 127.0 (ArCH), 137.6 (ArC), 141.7 (ArC), 151.9 (ArC) and 158.5 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μ m Cellulose-1) 10% ipa in hexane @ 1 mL min⁻¹, *t_R* = 9.1 min (minor), *t_R* = 10.1 min (major). Data was in accordance with the literature.

(*S*)-*N*-[1-(4'-Methylphenyl)ethyl]-4-methoxyaniline (**ca**)]¹³

Obtained using general procedure A as a yellow solid (66% yield); mp 50–52 °C (not reported in literature); $[\alpha]_D -17.8$ (*c* 1.05 in CHCl₃, 83% *ee*, lit.¹³ $[\alpha]_D +13.3$, *c* 2 in CHCl₃, 79% *ee*); δ_H (250 MHz; CDCl₃) 1.50 (3 H, d, *J* 6.6, CH₃), 2.34 (3 H, s, CH₃), 3.72 (3 H, s, OCH₃), 3.78 (1 H, br, *NH*), 4.41 (1 H, q, *J* 6.6, *NCH*), 6.49 [2 H, (AX)₂, ArCH], 6.71 [2 H, (AX)₂, ArCH], 7.13–7.16 (2

H, m, ArH) and 7.26–7.29 (2 H, m, ArH); δ_C (63 MHz; CDCl₃) 21.2 (CH₃), 25.2 (CH₃), 54.0 (NCH), 55.8 (OCH₃), 114.7 (ArCH), 114.9 (ArCH), 125.9 (ArCH), 129.4 (ArCH), 136.4 (ArC), 141.8 (ArC), 142.6 (ArC) and 152.0 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Chiralcel OD-H) 5% ipa in hexane @ 1 mL min⁻¹, *t_R* = 7.5 min (minor), *t_R* = 8.6 min (major). Data was in accordance with the literature.

(*S*)-*N*-[1-(4'-Chlorophenyl)ethyl]-4-methoxyaniline (**da**)]¹⁴

Obtained using general procedure A as a yellow oil (61% yield); $[\alpha]_D -10.9$ (*c* 1.1 in CHCl₃, 83% *ee*, lit.¹⁴ $[\alpha]_D +8.9$, *c* 1.16 in CHCl₃, 97% *ee*, *R* isomer); δ_H (400 MHz; CDCl₃) 1.50 (3 H, d, *J* 6.6, CH₃), 3.73 (3 H, s, OCH₃), 3.81 (1 H, br, *NH*), 4.41 (1 H, q, *J* 6.6, *NCH*), 6.47 [2 H, (AX)₂, ArCH], 6.73 [2 H, (AX)₂, ArCH] and 7.28–7.35 (4 H, m, ArH); δ_C (100 MHz; CDCl₃) 25.2 (CH₃), 53.8 (NCH), 55.8 (OCH₃), 114.6 (ArCH), 114.9 (ArCH), 127.4 (ArCH), 128.8 (ArCH), 132.4 (ArC), 141.4 (ArC), 144.2 (ArC) and 152.1 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μ m Cellulose-1) 8% ipa in hexane @ 1 mL min⁻¹, *t_R* = 10.6 min (minor), *t_R* = 12.6 min (major); Data was in accordance with the literature.

(*S*)-*N*-[1-(4'-Nitrophenyl)ethyl]-4-methoxyaniline (**ea**)]⁹

Obtained using general procedure A as a brown oil (46% yield); $[\alpha]_D -30.8$ (*c* 1.0 in CHCl₃, 83% *ee*, lit.⁹ $[\alpha]_D -25.9$, *c* 0.54 in CHCl₃, 86% *ee*); δ_H (400 MHz; CDCl₃) 1.55 (3 H, d, *J* 6.8, CH₃), 3.72 (3 H, s, OCH₃), 3.93 (1 H, br, *NH*), 4.53 (1 H, q, *J* 6.8, *NCH*), 6.43 [2 H, (AX)₂, ArCH], 6.72 [2 H, (AX)₂, ArCH], 7.57 [2 H, (AX)₂, ArCH] and 8.20 [2 H, (AX)₂, ArCH]; δ_C (100 MHz; CDCl₃) 25.0 (CH₃), 54.0 (NCH), 55.7 (OCH₃), 114.5 (ArCH), 114.8 (ArCH), 124.1 (ArCH), 126.8 (ArCH), 140.7 (ArC), 147.0 (ArC), 152.3 (ArC) and 153.6 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μ m Cellulose-1) 10% ipa in hexane @ 1 mL min⁻¹, *t_R* = 28.3 min (minor), *t_R* = 34.8 min (major); Data was in accordance with the literature.

(*S*)-*N*-[1-(2'-Methoxyphenyl)ethyl]-4-methoxyaniline (**fa**)]¹⁵

Obtained using general procedure A as a light yellow solid (71% yield), mp 56–58 °C (not reported in literature); $[\alpha]_D +11.8$ (*c* 1.5 in CHCl₃, 70% *ee*, lit.¹⁵ $[\alpha]_D +14.0$, *c* 0.25 in CDCl₃, 90% *ee*, absolute configuration assumed to be *S*); δ_H (250 MHz; CDCl₃) 1.58 (3 H, d, *J* 6.6, CH₃), 3.77 (3 H, s, OCH₃), 3.96 (3 H, s, OCH₃), 4.04 (1 H, br, *NH*), 4.90 (1 H, q, *J* 6.6, *NCH*), 6.59 [2 H, (AX)₂, ArH], 6.80 [2 H, (AX)₂, ArH], 6.99 (2 H, t, *J* 7.4, ArH), 7.29 (1 H, td, *J* 7.4 and 1.6, ArH) and 7.42 (1 H, dd, *J* 7.4 and 1.6, ArH); δ_C (63 MHz; CDCl₃) 23.0 (CH₃), 49.0 (NCH), 55.4 (OCH₃), 55.8 (OCH₃), 110.6 (ArCH), 114.7 (ArCH), 114.9 (ArCH), 120.9 (ArCH), 126.6 (ArCH), 127.7 (ArCH), 133.1 (ArC), 141.9 (ArC), 151.9 (ArC) and 156.9 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Chiralcel OD-H) 5% ipa in hexane @ 1 mL min⁻¹, *t_R* = 7.9 min (minor), *t_R* = 9.2 min (major); Data was in accordance with the literature.

(*S*)-*N*-[1-(2'-Methylphenyl)ethyl]-4-methoxyaniline (**ga**)]^{3a}

Obtained using general procedure A as a yellow oil (12% yield); $[\alpha]_D +35.4$ (*c* 0.48 in MeOH, 81% *ee*, lit.^{3a} $[\alpha]_D -33.5$, *c* 2.2 in MeOH,

78% *ee*, *R* isomer); δ_{H} (250 MHz; CDCl_3) 1.50 (3 H, d, *J* 6.6, CH_3), 2.49 (3 H, s, CH_3), 3.74 (3 H, s, OCH_3), 4.65 (1 H, q, *J* 6.6, NCH), 6.45 [2 H, (AX)₂, ArH], 6.74 [2 H, (AX)₂, ArH], 7.17–7.25 (3 H, m, ArH) and 7.46–7.50 (1 H, m, ArH); δ_{C} (63 MHz; CDCl_3) 19.0 (CH_3), 23.2 (CH_3), 50.5 (NCH), 55.8 (OCH_3), 114.3 (ArCH), 114.9 (ArCH), 124.7 (ArCH), 126.6 (ArCH), 130.6 (ArCH), 134.6 (ArC), 141.7 (ArC), 143.1 (ArC) and 151.9 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μm Cellulose-1) 10% ipa in hexane @ 1 mL min⁻¹, t_{R} = 6.3 min (minor), t_{R} = 7.7 min (major); Data was in accordance with the literature.

(S)-N-[1-(Naphthalen-1-yl)ethyl]-4-methoxyaniline (ha)⁹

Obtained using general procedure A as a yellow solid (11% yield), mp 88–89 °C (lit.⁹ 61 °C); $[\alpha]_{\text{D}}^{25} +135$ (*c* 0.4 in CHCl_3 , 77% *ee*, lit.⁹ +123.8, *c* 0.44 in CHCl_3 , 74% *ee*); δ_{H} (400 MHz; CDCl_3) 1.70 (3 H, d, *J* 6.6, CH_3), 3.73 (3 H, s, OCH_3), 4.00 (1 H, br s, NH), 5.28 (1 H, q, *J* 6.6, NCH), 6.50 [2 H, (AX)₂, ArH], 6.73 [2 H, (AX)₂, ArH], 7.48 (1 H, t, *J* 7.6, ArH), 7.56–7.65 (2 H, m, ArH), 7.73 (1 H, d, *J* 7.1, ArH), 7.81 (1 H, d, *J* 8.1, ArH), 7.97 (1 H, d, *J* 8.1, ArH) and 8.24 (1 H, d, *J* 8.3, ArH); δ_{C} (100 MHz; CDCl_3) 23.9 (CH_3), 50.2 (NCH), 55.8 (OCH_3), 114.4 (ArCH), 114.9 (ArCH), 122.4 (ArCH), 122.7 (ArCH), 125.5 (ArCH), 126.0 (ArCH), 126.1 (ArCH), 127.5 (ArCH), 129.2 (ArCH), 130.9 (ArC), 134.2 (ArC), 140.3 (ArC), 141.5 (ArC) and 151.9 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μm Cellulose-1) 5% ipa in hexane @ 1 mL min⁻¹, t_{R} = 12.9 min (minor), t_{R} = 19.0 min (major); Data was in accordance with literature.

(S)-N-[1-(Naphthalen-2-yl)ethyl]-4-methoxyaniline (ia)⁹

Obtained using general procedure A as a light yellow solid (63% yield), mp 96–98 °C (lit.⁹ 95–96 °C); $[\alpha]_{\text{D}}^{25} -24$ (*c* 1.0 in CHCl_3 , 85% *ee*, lit.⁹ -26.0, *c* 1.0 in CHCl_3 , 86% *ee*); δ_{H} (250 MHz; CDCl_3) 1.59 (3 H, d, *J* 6.9, CH_3), 3.70 (3 H, s, OCH_3), 3.90 (1 H, br s, NH), 4.59 (1 H, q, *J* 6.9, NCH), 6.53 [2 H, (AX)₂, ArH], 6.71 [2 H, (AX)₂, ArH], 7.42–7.55 (3 H, m, ArH) and 7.80–7.86 (4 H, m, ArH); δ_{C} (63 MHz; CDCl_3) 25.2 (CH_3), 54.6 (NCH), 55.8 (OCH_3), 114.7 (ArCH), 114.8 (ArCH), 124.4 (ArCH), 124.5 (ArCH), 125.5 (ArCH), 126.0 (ArCH), 127.7 (ArCH), 127.9 (ArCH), 128.5 (ArCH), 132.8 (ArC), 133.7 (ArC), 141.7 (ArC), 143.1 (ArC) and 152.0 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μm Cellulose-1) 10% ipa in hexane @ 1 mL min⁻¹, t_{R} = 10.1 min (minor), t_{R} = 12.0 min (major); Data was in accordance with literature.

(S)-N-[1-(Thiophen-2-yl)ethyl]-4-methoxyaniline (ja)¹⁶

Obtained using general procedure A as a yellow oil (61% yield); $[\alpha]_{\text{D}}^{25} -8.0$ (*c* 1.0 in CHCl_3 , 79% *ee*, lit.¹⁶ -9.0, *c* 1.0 in CHCl_3 , 89% *ee*); δ_{H} (250 MHz; CDCl_3) 1.63 (3 H, d, *J* 6.6, CH_3), 3.75 (3 H, s, OCH_3), 4.76 (1 H, q, *J* 6.6, NCH), 6.62 [2 H, (AX)₂, ArH], 6.75 [2 H, (AX)₂, ArH], 6.94–6.98 (2 H, m, ArH) and 7.18 (1 H, dd, *J* 4.7 and 1.6, ArH); δ_{C} (63 MHz; CDCl_3) 24.8 (CH_3), 50.6 (NCH), 55.8 (OCH_3), 114.9 (ArCH), 115.2 (ArCH), 123.0 (ArCH), 123.6 (ArCH), 126.7 (ArCH), 141.2 (ArC), 150.6 (ArC) and 152.5 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μm Cellulose-1) 2% ipa

in hexane @ 1 mL min⁻¹, t_{R} = 15.1 min (minor), t_{R} = 17.3 min (major); Data was in accordance with literature.

(S)-N-[1-(Furan-2-yl)ethyl]-4-methoxyaniline (ka)¹⁷

Obtained using general procedure A as a yellow oil (72% yield); $[\alpha]_{\text{D}}^{25} -46$ (*c* 1.0 in CHCl_3 , 44% *ee*, lit.¹⁶ -48, *c* 1.0 in CHCl_3 , 62% *ee*); δ_{H} (250 MHz; CDCl_3) 1.57 (3 H, d, *J* 6.6, CH_3), 3.63 (1 H, br s, NH), 3.76 (3 H, s, OCH_3), 4.58 (1 H, q, *J* 6.6, NCH), 6.18 (1 H, app. d, *J* 3.2, ArH), 6.32 (1 H, dd, *J* 3.2 and 1.8, ArH), 6.63 [2 H, (AX)₂, ArH], 6.79 [2 H, (AX)₂, ArH] and 7.36 (1 H, app. s, ArH); δ_{C} (63 MHz; CDCl_3) 21.0 (CH_3), 48.4 (NCH), 55.7 (OCH_3), 105.1 (ArCH), 110.1 (ArCH), 114.8 (ArCH), 115.2 (ArCH), 141.2 (ArC), 141.4 (ArCH), 152.5 (ArC) and 157.6 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Chiralcel OJ) 10% ipa in hexane @ 1 mL min⁻¹, t_{R} = 45.1 min (major), t_{R} = 56.4 min (minor); Data was in accordance with literature.

(S)-N-(1-Phenylpropyl)-4-methoxyaniline (la)⁹

Obtained using general procedure A as a yellow oil (15% yield); $[\alpha]_{\text{D}}^{25} -22$ (*c* 1.0 in CHCl_3 , 85% *ee*, lit.⁹ -26.9, *c* 1.0, CHCl_3 , 84% *ee*); δ_{H} (250 MHz; CDCl_3) 0.96 (3 H, t, *J* 7.2, CH_3), 1.74–1.90 (2 H, m, CH_2), 3.71 (3 H, s, OCH_3), 3.85 (1 H, br s, NH), 4.17 (1 H, t, *J* 6.6, NCH), 6.58 [2 H, (AX)₂, ArH], 6.72 [2 H, (AX)₂, ArH] and 7.20–7.37 (5 H, m, ArH); δ_{C} (63 MHz; CDCl_3) 11.0 (CH_2CH_3), 31.8 (CH_2CH_3), 55.8 (OCH_3), 60.7 (NCH), 114.6 (ArCH), 114.9 (ArCH), 126.7 (ArCH), 127.0 (ArCH), 128.6 (ArCH), 142.0 (ArC), 144.3 (ArC) and 152.0 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Chiralcel OD-H) 5% ipa in hexane @ 1 mL min⁻¹, t_{R} = 7.0 min (minor), t_{R} = 7.7 min (major); Data was in accordance with literature.

(S)-N-[2-(4'-Phenylbutyl)]-4-methoxyaniline (ma)¹⁸

Obtained using general procedure A as a light yellow oil (82% yield); $[\alpha]_{\text{D}}^{25} +0.7$ (*c* 5.1 in CHCl_3 , 14% *ee*, lit.¹⁸ -4.0, *c* 2.06 in CHCl_3 , 91% *ee*, *R* isomer); δ_{H} (250 MHz; CDCl_3) 1.25 (3 H, d, *J* 6.3, CH_3), 1.72–2.00 (2 H, m, CH_2), 2.78 (2 H, t, *J* 7.8, CH_2), 3.17 (1 H, br s, NH), 3.46 (1 H, m, NCH), 3.80 (3 H, s, OCH_3), 6.57 [2 H, (AX)₂, ArH], 6.83 [2 H, (AX)₂, ArH] and 7.22–7.37 (5 H, m, ArH); δ_{C} (63 MHz; CDCl_3) 20.9 (CH_3), 32.6 (CH_2), 38.9 (CH_2), 49.0 (NCH), 55.9 (OCH_3), 114.8 (ArCH), 115.0 (ArCH), 125.9 (ArCH), 128.4 (ArCH), 128.5 (ArCH), 141.9 (ArC), 142.2 (ArC) and 151.9 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Chiralcel OD-H) 5% ipa in hexane @ 1 mL min⁻¹, t_{R} = 10.7 min (minor), t_{R} = 11.8 min (major); Data was in accordance with literature.

(S)-N-[2-(3',4'-Dimethoxyphenyl)propyl]-4-methoxyaniline (na)¹⁹

Obtained using general procedure A as a light yellow oil (81% yield); $[\alpha]_{\text{D}}^{25} +4.5$ (*c* 1.0 in CHCl_3 , 15% *ee*, lit.¹⁹ -3.5, *c* 0.3 in CHCl_3 , 66% *ee*, *R* isomer); δ_{H} (250 MHz; CDCl_3) 1.15 (3 H, d, *J* 6.3, CH_3), 2.70 (1 H, dd, *J* 13.5 and 6.9, 1 \times CH_2), 2.84 (1 H, dd, *J* 13.5 and 4.7, 1 \times CH_2), 3.27 (1 H, br s, NH), 3.62–3.72 (1 H, m, NCH), 3.72 (3 H, s, OCH_3), 3.86 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3) and 6.60–6.84 (7 H, m, ArH); δ_{C} (63 MHz; CDCl_3) 20.3 (CH_3), 41.7 (CH_2), 50.3 (NCH), 55.9 (2 \times OCH_3), 111.3 (ArCH), 113.0 (ArCH), 115.0 (ArCH), 121.6 (ArCH), 131.2 (ArC), 141.6

(ArC), 147.6 (ArC), 148.8 (ArC) and 152.1 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux Cellulose-2) 5% ipa in hexane @ 1 mL min⁻¹, t_R = 29.4 min (minor), t_R = 34.9 min (major); Data was in accordance with literature.

(±)-(E)-N-(4-Phenylbut-3-en-2-yl)-4-methoxyaniline (oa)²⁰

Obtained using general procedure A as a yellow oil (77% yield); 0% ee; δ_H (250 MHz; CDCl₃) 1.41 (3 H, d, *J* 7.6, CH₃), 3.45 (1 H, br s, NH), 3.76 (3 H, s, OCH₃), 4.04–4.14 (1 H, m, NCH), 6.24 (1 H, dd, *J* 16.0 and 6.0, CH=CH), 6.55–6.68 (3 H, m, 2 × ArH and CH=CH), 6.76–6.81 (2 H, m, ArH) and 7.20–7.40 (5 H, m, ArH); δ_C (63 MHz; CDCl₃) 22.2 (CH₃), 51.9 (NCH), 55.8 (OCH₃), 115.0 (ArCH), 115.1 (ArCH), 126.5 (ArCH), 127.4 (ArCH), 128.6 (ArCH), 129.4 (CH), 133.7 (CH), 137.2 (ArC), 141.8 (ArC) and 152.2 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Kromasil 3-Cellucoat OD-H) 5% ipa in hexane @ 1 mL min⁻¹, t_R = 10.2 min, t_R = 11.9 min; Data was in accordance with literature.

(S)-N-(1-Phenylethyl)-aniline (ab)⁹

Obtained using general procedure A as a yellow oil (56% yield); [α]_D +13 (*c* 1.0 in MeOH, 82% ee, lit.⁹ [α]_D +13.9, *c* 1.0 in MeOH, 86% ee); δ_H (250 MHz; CDCl₃) 1.55 (3 H, d, *J* 6.6, CH₃), 4.05 (1 H, br s, NH), 4.51 (1 H, q, *J* 6.6, CH), 6.51–6.55 (2 H, m, ArH), 6.63–6.70 (1 H, m, ArH), 7.08–7.14 (2 H, m, ArH) and 7.21–7.42 (5 H, m, ArH); δ_C (CDCl₃; 63 MHz) 25.1 (CH₃), 53.5 (NCH), 113.4 (ArCH), 117.4 (ArCH), 126.0 (ArCH), 127.0 (ArCH), 128.8 (ArCH), 129.2 (ArCH), 145.4 (ArC) and 147.4 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Kromasil 3-Cellucoat OD-H), 5% ipa in hexane @ 1 mL min⁻¹, t_R = 4.8 min (major), 5.7 min (minor); Data was in accordance with literature.

(S)-N-(1-Phenylethyl)-4-methylaniline (ac)²¹

Obtained using general procedure A as a yellow solid (64% yield), mp 75–76 °C (lit.²¹ 70 °C); [α]_D +27 (*c* 1.0 in ethyl acetate, 84% ee, lit.²¹ [α]_D +27.3, *c* 0.7 in ethyl acetate, 91% ee); δ_H (400 MHz; CDCl₃) 1.54 (3 H, d, *J* 6.6, CH₃), 2.22 (3 H, s, ArCH₃), 3.95 (1 H, br s, NH), 4.49 (1 H, q, *J* 6.6, NCH), 6.47 [2 H, (AX)₂, ArH], 6.94 [2 H, (AX)₂, ArH] and 7.24–7.42 (m, 5H, ArH); δ_C (100 MHz; CDCl₃) 20.5 (CH₃), 25.2 (CH₃), 53.8 (NCH), 113.5 (ArCH), 126.0 (ArCH), 126.4 (ArC), 126.9 (ArCH), 128.7 (ArCH), 129.7 (ArCH), 145.1 (ArC) and 145.6 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μm Cellulose-1) 2% ipa in hexane @ 1 mL min⁻¹, t_R = 10.0 min (minor), 11.7 min (major); Data was in accordance with literature—the signal at δ_H 2.22 ppm is missing from reference 21

(S)-N-(1-Phenylethyl)-4-fluoroaniline (ad)²²

Obtained using general procedure A as a yellow oil (65% yield); [α]_D +20 (*c* 1.05 in CHCl₃, 81% ee, lit.²² [α]_D –16.8, *c* 1.0 in CHCl₃, 84% ee *R* isomer); δ_H (400 MHz; CDCl₃) 1.53 (3 H, d, *J* 6.6, CH₃), 3.95 (1 H, br s, NH), 4.44 (1 H, q, *J* 6.6, NCH), 6.43–6.47 (2 H, m, ArH), 6.79–6.84 (2 H, m, ArH), 7.23–7.28

(1 H, m, ArH) and 7.32–7.38 (4 H, m, ArH); δ_C (100 MHz; CDCl₃) 25.1 (CH₃), 54.1 (NCH), 114.1 (d, ³*J*_{C-F} 6.9, ArCH), 115.5 (d, ²*J*_{C-F} 22.2, ArCH), 125.9 (ArCH), 127.0 (ArCH), 128.8 (ArCH), 143.7 (ArC), 145.1 (ArC) and 155.5 (¹*J*_{C-F} 234.6, ArC); δ_F (235 MHz; CDCl₃) –128.4; Enantiomeric excess was determined by chiral phase HPLC (Kromasil 3-Cellucoat OD-H) 2% ipa in hexane @ 1 mL min⁻¹, t_R = 5.5 min (minor), 6.1 min (major); Data was in accordance with literature.

(S)-N-(1-Phenylethyl)-3-aminopyridine (ae)²³

Obtained using general procedure A as a white solid, except 2 mL of CH₂Cl₂ was used (58% yield), mp 88–90 °C (not reported in literature); [α]_D 0 (*c* 1 in CHCl₃, 10% ee, no literature data reported); δ_H (400 MHz; CDCl₃) 1.55 (3 H, d, *J* 6.6, CH₃), 4.33 (1 H, br s, NH), 4.49 (1 H, q, *J* 6.6, NCH), 6.72 (1 H, ddd, *J* 8.3, 2.7 and 1.2, ArH), 6.97 (1 H, dd, *J* 8.3 and 4.7, ArH), 7.23–7.38 (5 H, m, ArH), 7.91 (1 H, d, *J* 4.2, ArH) and 8.02 (1 H, d, *J* 2.2, ArH); δ_C (100 MHz; CDCl₃) 24.9 (CH₃), 53.3 (NCH), 119.0 (ArCH), 123.6 (ArCH), 125.8 (ArCH), 127.2 (ArCH), 128.8 (ArCH), 136.6 (ArCH), 138.5 (ArCH), 143.3 (ArC) and 144.3 (ArC); Enantiomeric excess was determined by chiral phase HPLC (Phenomenex Lux 3 μm Cellulose-1), 15% ipa in hexane @ 1 mL min⁻¹, t_R = 12.2 min (major), 23.7 min (minor); Data was in accordance with literature.

(S)-N-Benzyl-1-phenylethylamine (af)²⁴

Obtained using general procedure B as a colorless oil (63% yield); [α]_D –44.3 (*c* 0.7 in EtOH, 80% ee, Lit.²⁴ –41.1, *c* 0.6 in EtOH, 91% ee) δ_H (250 MHz; CDCl₃) 1.39 (3 H, d, *J* 6.6, CH₃), 1.59 (1 H, br s, NH), 3.60 (1 H, d, *J* 13.1, 1 × CH₂), 3.68 (1 H, d, *J* 13.1, 1 × CH₂), 3.84 (1 H, q, *J* 6.6, NCH) and 7.23–7.41 (10 H, m, ArH); δ_C (63 MHz; CDCl₃) 24.5 (CH₃), 51.7 (NCH₂), 57.6 (NCH), 126.8 (ArCH), 126.9 (ArCH), 127.0 (ArCH), 128.2 (ArCH), 128.4 (ArCH), 128.5 (ArCH), 140.7 (ArC) and 145.7 (ArC); Enantiomeric excess was determined by comparison of the integrals in the ¹H NMR spectrum in CDCl₃ of the diastereomeric salts formed by addition of excess L-mandelic acid; Data was in accordance with literature.

(S)-N-(2-Phenylethyl)-1-phenylethylamine (ag)²⁵

Obtained using general procedure B as a light yellow oil, except 2 mL of CH₂Cl₂ was used (65% yield); [α]_D –47.8 (*c* 1.1 in CHCl₃, 86% ee, Lit.²⁵ +54.2, *c* 2.84 in CHCl₃, 97% ee *R*-isomer); δ_H (250 MHz; CDCl₃) 1.34 (3 H, d, *J* 6.6, CH₃), 2.70–2.84 (4 H, m, CH₂CH₂), 3.81 (1 H, q, *J* 6.6, NCH) and 7.16–7.36 (10 H, m, ArH); δ_C (63 MHz; CDCl₃) 24.3 (CH₃), 36.5 (CH₂Ph), 48.9 (NCH₂), 58.2 (NCH), 126.1 (ArCH), 126.6 (ArCH), 126.9 (ArCH), 128.4 (ArCH), 128.7 (ArCH), 140.1 (ArC) and 145.7 (ArC); Enantiomeric excess was determined by comparison of the integrals in the ¹H NMR spectrum in CDCl₃ of the diastereomeric salts formed by addition of excess L-mandelic acid; Data was in general accordance with literature—the signal at δ_C 145.7 ppm is missing in the reported ¹³C NMR data in reference 25

(S)-N-(3-Phenylpropyl)-1-phenylethylamine (ah)²⁶

Obtained using general procedure B as a brown oil (76% yield); $[\alpha]_D -40$ (c 1.1 in CHCl_3 , 84% *ee*, $[\alpha]_D$ not reported in literature); δ_H (250 MHz; CDCl_3) 1.30 (1 H, br s, *NH*), 1.37 (3 H, d, J 6.6, CH_3), 1.75–1.87 (2 H, m, CH_2), 2.45–2.74 (4 H, m, NCH_2 and PhCH_2), 3.77 (1 H, q, J 6.6, *NCH*) and 7.16–7.39 (10 H, m, *ArH*); δ_C (63 MHz; CDCl_3) 24.4 (CH_3), 32.0 (CH_2), 33.8 (CH_2), 47.4 (NCH_2), 58.4 (*NCH*), 125.8 (*ArCH*), 126.6 (*ArCH*), 126.9 (*ArCH*), 128.36 (*ArCH*), 128.44 (*ArCH*), 128.5 (*ArCH*), 142.3 (*ArC*) and 146.0 (*ArC*); Enantiomeric excess was determined by comparison of the integrals in the ^1H NMR spectrum in CDCl_3 of the diastereomeric salts formed by addition of excess L-mandelic acid; ^{13}C NMR data in accordance with literature, while two methylene signals have been omitted in the literature ^1H NMR data.

(S)-N-(Furan-2-ylmethyl)-1-phenylethylamine (ai)²⁶

Obtained using general procedure B as a colorless oil (65% yield); $[\alpha]_D -78$ (c 0.4 in CHCl_3 , 86% *ee*, $[\alpha]_D$ not reported in literature); δ_H (250 MHz; CDCl_3) 1.38 (3 H, d, J 6.6, CH_3), 1.66 (1 H, br s, *NH*), 3.59 (1 H, d, J 14.4, $1 \times \text{CH}_2$), 3.69 (1 H, d, J 14.4, $1 \times \text{CH}_2$), 3.80 (1 H, q, J 6.6, *NCH*), 6.12 (1 H, dd, J 0.4 and 3.1, *ArH*), 6.32 (1 H, dd, J 1.8 and 3.1, *ArH*), 7.23–7.40 (6 H, m, *ArH*); ^{13}C NMR (63 MHz; CDCl_3) δ_C 24.3 (CH_3), 44.0 (NCH_2), 57.1 (*NCH*), 106.8 (*ArCH*), 110.1 (*ArCH*), 126.8 (*ArCH*), 127.0 (*ArCH*), 128.5 (*ArCH*), 141.7 (*ArCH*), 145.1 (*ArC*) and 154.1 (*ArC*); Enantiomeric excess was determined by comparison of the integrals in the ^1H NMR spectrum in CDCl_3 of the diastereomeric salts formed by addition of excess L-mandelic acid; Data was in accordance with literature.

(S)-N-(Thiophen-2-ylmethyl)-1-phenylethylamine (aj)

Obtained using general procedure B as a yellow oil (64% yield); $[\alpha]_D -42.5$ (c 0.8 in CHCl_3 , 83% *ee*); ν_{\max} (ATR)/ cm^{-1} 2963, 1492, 1451; δ_H (400 MHz; CDCl_3) 1.40 (3 H, d, J 6.6, CH_3), 1.65 (1 H, br s, *NH*), 3.81–3.89 (2 H, m, CH_2), 3.88 (1 H, q, J 6.6, *NCH*), 6.88–6.89 (1 H, m, *ArH*), 6.96 (1 H, dd, J 3.4 and 5.1, *ArH*), 7.23 (1 H, dd, J 1.2 and 5.1, *ArH*), 7.26–7.31 (1 H, m, *ArH*) and 7.35–7.39 (4 H, m, *ArH*); δ_C (CDCl_3 ; 100 MHz) 24.4 (CH_3), 46.1 (NCH_2), 57.1 (*NCH*), 124.3 (*ArCH*), 124.7 (*ArCH*), 126.6 (*ArCH*), 126.8 (*ArCH*), 127.1 (*ArCH*), 128.5 (*ArCH*), 144.5 (*ArC*) and 145.2 (*ArC*); m/z (EI^+) 217.0923 (4%, M^+ , $\text{C}_{13}\text{H}_{15}\text{NS}$ requires 217.0925), 202 (60), 97 (100); Enantiomeric excess was determined by comparison of the integrals in the ^1H NMR spectrum in CDCl_3 of the diastereomeric salts formed by addition of excess L-mandelic acid.

(S)-N-Benzyl-1-phenylpropylamine (lf)²⁷

Obtained using general procedure B as a colorless oil (66% yield); $[\alpha]_D -37$ (c 1.0 in CHCl_3 , 73% *ee*, Lit.²⁷ +32, c 0.2 in CHCl_3 , 89% *ee* for *R*-isomer); δ_H (400 MHz; CDCl_3) 0.86 (3 H, t, J 7.4, CH_3), 1.65–1.87 (3 H, m, CH_2 and *NH*), 3.57–3.61 (2 H, m, *NCH* and $1 \times \text{NCH}_2$), 3.71 (1 H, d, J 13.2, $1 \times \text{NCH}_2$) and 7.27–7.42 (10 H, m, *ArH*); δ_C (100 MHz; CDCl_3) 10.8 (CH_3), 31.2 (CH_2), 51.6 (NCH_2), 64.2 (*NCH*), 126.8 (*ArCH*), 126.9 (*ArCH*), 127.5 (*ArCH*), 128.2 (*ArCH*), 128.3 (*ArCH*), 140.8 (*ArC*) and 144.1

(*ArC*); Enantiomeric excess was determined by comparison of the integrals in the ^1H NMR spectrum in CDCl_3 of the diastereomeric salts formed by addition of excess L-mandelic acid; Data was in accordance with literature.

(R)-N-Benzyl-2-methyl-1-phenylpropylamine (pf)²⁸

Obtained using general procedure B as a colorless oil (62% yield); $[\alpha]_D +56$ (c 1.05 in CHCl_3 , 76% *ee*, Lit.²⁸ +63.1, c 1.4 in CHCl_3 94% *ee*); δ_H (400 MHz; CDCl_3) 0.77 (3 H, d, J 6.8, CH_3), 1.00 (3 H, d, J 6.6, CH_3), 1.61 (1 H, br s, *NH*), 1.86–1.92 (1 H, m, *CH*), 3.37 (1 H, d, J 9.0, *NCH*), 3.49 (1 H, d, J 13.3, $1 \times \text{NCH}_2$), 3.67 (1 H, d, J 13.3, $1 \times \text{NCH}_2$) and 7.24–7.38 (10 H, m, *ArH*); δ_C (100 MHz; CDCl_3) 19.5 (CH_3), 19.7 (CH_3), 34.5 (*CH*), 51.8 (NCH_2), 68.8 (*NCH*), 126.8 ($2 \times \text{ArCH}$), 128.0 (*ArCH*), 128.2 (*ArCH*), 128.3 (*ArCH*), 141.0 (*ArC*) and 142.9 (*ArC*); Enantiomeric excess was determined by comparison of the integrals in the ^1H NMR spectrum in CDCl_3 of the diastereomeric salts formed by addition of excess L-mandelic acid; Data was in accordance with literature.

(S)-N-(1-Phenylethyl)-4-methoxyaniline 4 (aa)

Obtained using general procedure B but for 4 h instead of 8 h as a brown oil (68% yield, 84% *ee*); Data as previously reported.

3-(2-Chlorophenyl)-propylamine 5

KOH powder (2 g, 36.1 mmol) and 2-chlorobenzaldehyde (5.07 g, 36.1 mmol) were stirred in acetonitrile (300 mL) at room temperature for 24 h and then poured into a 1 : 1 mixture of ice-water (300 g). The mixture was extracted with dichloromethane (3×150 mL), the combined extracts washed with brine (50 mL) and dried over MgSO_4 . After filtration, the filtrate was concentrated and the residue was purified by chromatography on silica gel (petroleum ether–ethyl acetate = 20 : 1 to 5 : 1) to give 1.57 g 2-chloro-cinnamionitrile as white solid; mp 35–37 °C (not reported in literature), δ_H (250 MHz; CDCl_3) 5.92 (1 H, d, J 16.6, *CH*), 7.28–7.48 (3 H, m, *ArH*), 7.56 (1 H, dd, J 1.9 and 7.5, *ArH*) and 7.51 (1 H, d, J 16.6, *CH*); δ_C (63 MHz; CDCl_3) 99.0 (*CH*), 117.8 (*C*), 127.0 (*CH*), 127.4 (*CH*), 130.3 (*CH*), 131.6 (*C*), 132.1 (*CH*), 134.4 (*C*) and 146.3 (*CH*); ^{13}C NMR not reported in the literature, while reported ^1H NMR data is at much lower resolution.²⁹

A suspension of 2-chloro-cinnamionitrile (1.57 g, 9.6 mmol) and CoCl_2 (2.42 g, 18.6 mmol) in MeOH (60 mL) was cooled to 0 °C under N_2 atmosphere. NaBH_4 (3.5 g, 93 mmol) was added portionwise over 30 min. The resulting mixture was allowed to warm to room temperature and stirred overnight. 6*N* HCl (20 mL) was added, and the reaction carefully basified with 2*N* aqueous NaOH to pH 11. The resulting mixture was extracted with diethyl ether (3×150 mL), the combined organic phases washed with brine (50 mL) and dried over MgSO_4 . After filtration, the solvent was evaporated under reduced pressure to afford the desired amine (1.2 g) as light brown oil; δ_H (250 MHz; CDCl_3) 1.14 (2 H, br s, *NH*), 1.73–1.85 (2 H, m, CH_2), 2.70–2.82 (4 H, m, CH_2CH_2) and 7.11–7.37 (4 H, m, *ArH*); δ_C (63 MHz; CDCl_3) 30.9 (CH_2), 33.9 (CH_2), 41.9 (CH_2), 126.7 (*ArCH*), 127.3 (*ArCH*), 129.5 (*ArCH*), 130.3 (*ArCH*) and 139.7 (*ArCH*); Data was in general accordance with literature, although 1 signal in the ^{13}C NMR was ambiguous due to the low concentration of the sample.³⁰

(R)-3-(2-Chlorophenyl)-N-(1-(3-methoxyphenyl)ethyl)propan-1-amine 6 [(+)-NPS R-568]³¹

Obtained using general procedure B as a light brown oil, except 2 mL of CH₂Cl₂ was used with 1 mol% of (R)-1 as catalyst (67% yield); [α]_D +41.2 (c 0.8 in CHCl₃, 89% ee, Lit.³¹ +41.9, c 1.1 in CHCl₃ assumed to be 100% ee); δ _H (250 MHz; CDCl₃) 1.37 (3 H, d, *J* 6.6, CH₃), 1.74–1.89 (2 H, m, CH₂), 2.47–2.65 (2 H, m, CH₂), 2.68–2.86 (2 H, m, CH₂), 3.77 (1 H, q, *J* 6.6, NCH), 3.84 (3 H, s, OCH₃), 6.80 (1 H, ddd, *J* 1.0, 2.4 and 8.3, ArH), 6.91–6.93 (2 H, m, ArH), 7.09–7.35 (5 H, m, ArH); δ _C (63 MHz; CDCl₃) 24.3 (CH₃), 30.2 (CH₂), 31.3 (CH₂), 47.3 (CH₂), 55.2 (OCH₃), 58.3 (NCH), 112.1 (ArCH), 112.2 (ArCH), 119.0 (ArCH), 126.7 (ArCH), 127.2 (ArCH), 129.4 (2 × ArCH), 130.3 (ArCH), 133.9 (ArC), 139.8 (ArC), 147.7 (ArC) and 159.8 (ArC); Enantiomeric excess was determined by comparison of the integrals in the ¹H NMR spectrum in CDCl₃ of the diastereomeric salts formed by addition of excess L-mandelic acid; Data in general agreement with the literature, although ¹³C NMR data in reference 31 has an additional signal and data has been misassigned.

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