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Asymmetric Ring Opening of *meso*-Epoxides with Aromatic Amines Using (*R*)-(+)-BINOL-Sc(OTf)$_3$-NMM Complex as an Efficient Catalyst

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This work reports the asymmetric ring-opening reaction of *meso*-epoxides with aromatic amines by using the highly efficient in situ generated (*R*)-(+)-BINOL-Sc(OTf)$_3$-*N*-methylmorpholine complex. The asymmetric ring opening of *cis*-stilbene oxide with various substituted aromatic amines gave enantioenriched β-amino alcohols in good yields and with excellent enantioselectivities when the reaction was conducted at 0 °C for 12 h. The reaction proceeded under mild conditions using simple and inexpensive starting materials such as (*R*)-(+)-1,1′-bi-2-naphthol [(*R*)-(+)-BINOL], *meso*-stilbene oxide, aniline derivatives, and 4 Å molecular sieves. This new and versatile catalytic system has competitive advantages such as short reaction times, no additives, and no expensive chiral ligands that require a multistep synthesis under harsh reaction conditions.

Introduction

Enantiomerically pure β-amino alcohols have been found in many biologically active natural products, new therapeutic agents, unnatural amino acids, β-blockers, insecticidal agents, antimalarial agents, and oxazolines.[1] After derivatization, β-amino alcohols have shown strong chelating abilities and steric directing effects. Hence, they are widely used as chiral ligands and auxiliaries for numerous enantioselective organic transformations[2] (see Figure 1). Moreover, β-amino alcohols also play a crucial role in living organisms, and, therefore, the synthesis of enantiomerically pure β-amino alcohols has gained considerable interest.[3] Several strategies for their preparation have been developed such as: (a) a Sharpless osmium-catalyzed aminohydroxylation of olefins,[4] (b) an addition of α-hydroxy ketones to imines,[5] and (c) an aminolytic kinetic resolution of racemic terminal epoxides[6a] and *trans*-aromatic epoxides with anilines.[6b,6c] Among these approaches, the enantioselective ring-opening reaction of epoxides with amines is an important and atom-economical route to synthesize optically enriched β-amino alcohols.

A number of valuable products could be synthesized through a catalytic asymmetric reaction of a *meso*-epoxide with various nucleophiles such as azides,[7] cyanides,[8] alcohols,[9] water,[10] thiols,[11] selenols,[12] indoles,[13,11d] and carboxylic acids.[14] Several reports have appeared for the synthesis of β-amino alcohols through the asymmetric ring opening (ARO) of *meso*-epoxides with anilines.[15] However, despite their potential utility, the above protocols suffer from one or more drawbacks such as low enantioselectivity, a long reaction time, the use of additives, and the use of expensive and toxic chiral ligands that require multiple steps to synthesize. In addition, the synthesis of chiral ligands requires harsh synthetic conditions, which limit their applications. In 1994, Kobayashi et al. reported the use of (*R*)-(+)-1,1′-bi-2-naphthol [(*R*)-(+)-BINOL], Sc(OTf)$_3$ or Yb(OTf)$_3$, and tertiary amines as an efficient catalyst for an asymmetric Diels–Alder reaction.[16] Subsequently, Hou et al. developed the same catalytic protocol for an ARO reaction using (*R*)-(+)-BINOL, Yb(OTf)$_3$, and tertiary amines as the catalyst, which provided up to 80%*ee* for an aliphatic epoxide and only 18%*ee* for an aromatic epoxide.[15a] The major drawbacks of this protocol were the need to carry out the reaction at –78 °C, the low enantioselectivities for

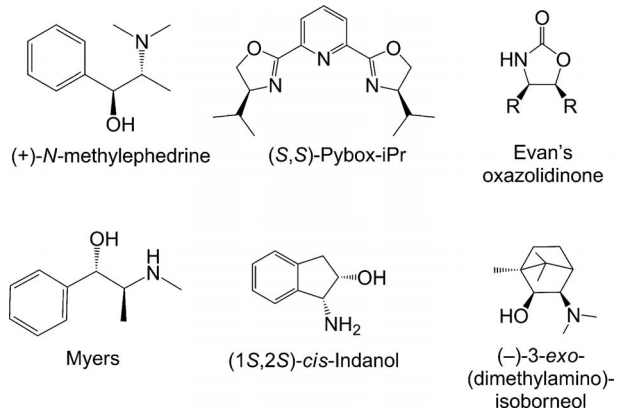

Figure 1. Examples of chiral ligands and auxiliaries that contain β-amino alcohols.

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aromatic epoxides, and the limited substrate scope. It should be noted that the application of (*R*)-(+)-BINOL and $Sc(OTf)_3$ with tertiary amines has been well explored for various enantioselective organic transformations.[17,2c]

Therefore, this present work involves the search for an efficient catalytic system for an epoxide ring-opening reaction that proceeds enantioselectively. These efforts are a continuation of our previous work on the synthesis of racemic β-amino alcohols through the ring opening of epoxides with anilines.[18] Herein, we report the asymmetric ring-opening reaction of a *meso*-epoxide with aniline and substituted anilines. This reaction, which is catalyzed by (*R*)-(+)-BINOL-$Sc(OTf)_3$-*N*-methylmorpholine and is carried out at 0 °C for 12 h, afforded optically enriched β-amino alcohols in high yields (up to 89%) and with excellent enantiomeric excess values (up to 94% *ee*).

Results and Discussion

The chiral scandium complex was prepared according to a reported procedure.[19] To a stirred solution of (*R*)-(+)-BINOL (0.12 equiv.) in CH_2Cl_2 (2.0 mL) under nitrogen was added $Sc(OTf)_3$ (0.10 equiv.), and the resulting mixture was cooled to 0 °C. *N*-methylmorpholine (NMM, 0.24 equiv.) was subsequently added to the reaction mixture, which was then stirred at 0 °C for 30 min. The unique structure of the catalyst is shown in Figure 2.

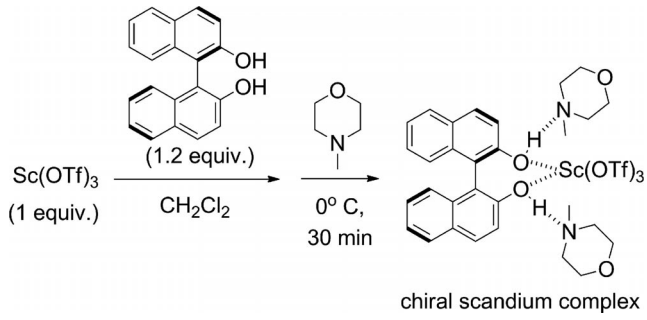


Figure 2. Preparation of chiral scandium complex from (*R*)-(+)-BINOL.

The existence of hydrogen bonds between the phenolic hydrogens of (*R*)-(+)-BINOL and the nitrogens of the tertiary amines is the most characteristic detail of this catalyst. In this chiral catalyst, the axial chirality of (*R*)-(+)-BINOL is transferred through the hydrogen bonds to the amine moiety, and, therefore, the amine plays an important role in the enantioselectivity of the desired product. The chiral scandium complex was studied by fluorescence spectroscopy, and the fluorescence behavior of (*R*)-(+)-BINOL is shown in Figure 3. (*R*)-(+)-BINOL shows maximum fluorescence intensity at 372 nm (λ_{ex} = 342 nm).

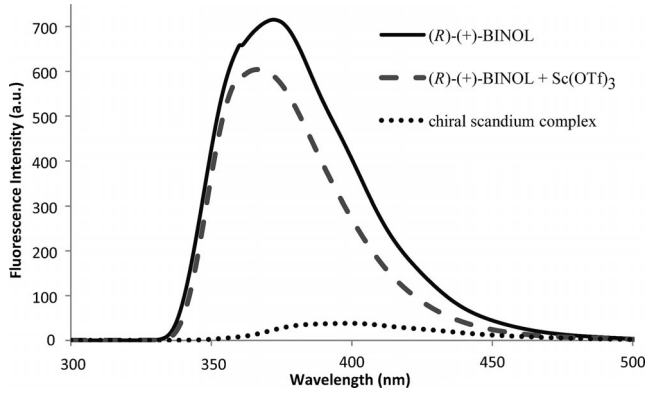


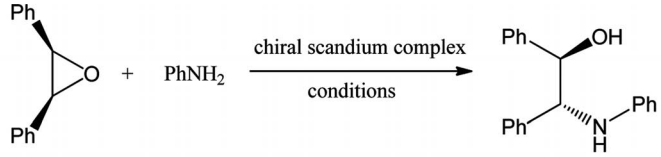
Figure 3. Comparison of the fluorescence spectrum of (*R*)-(+)-BINOL and chiral scandium complex in CH_2Cl_2.

When $Sc(OTf)_3$ was added to the solution of (*R*)-(+)-BINOL, the fluorescence intensity of (*R*)-(+)-BINOL was somewhat quenched with a decrease in the wavelength and maximum emission (λ = 368 nm). Again, the addition of NMM to the solution of (*R*)-(+)-BINOL and $Sc(OTf)_3$ resulted in a dramatic decrease in the fluorescence intensity without any shift to the wavelength (λ = 368 nm), which is probably a result of a ligand to metal energy or electron transfer process[20] and indicates the formation of a complex. The extreme quenching of the fluorescence behavior in the presence of the prepared chiral scandium complex was probably a result of the formation of excited hydrogen-bonded complexes and excited-state proton transfer complexes as shown in Figure 2. The specularity of the titration profiles clearly indicates that the formation of a complex with the phenolic moiety affects the quenching of the fluorescence and decreases the delocalization of (*R*)-(+)-BINOL with a red shift ($\lambda_{ex} \approx$ 400 nm) as shown in Figure 3.

Using this new chiral scandium catalyst, we optimized the reaction conditions for the asymmetric ring-opening reaction of a *meso*-epoxide with aniline and substituted anilines. Our preliminary experiments showed that 10 mol-% of the chiral scandium complex can effectively catalyze the aminolysis of *meso*-epoxides with aniline in high yields and with up to 94% *ee*. To further optimize the reaction conditions, we chose *cis*-stilbene oxide and aniline for the model reaction along with (*R*)-(+)-BINOL-$Sc(OTf)_3$ and *N*,*N*-diisopropylethylamine (DIPEA) as the in situ generated catalyst. The influence of various reaction parameters such as solvent, the amine, molecular sieves, temperature, and time (see Table 1) were examined.

The influence of the solvent on the asymmetric ring-opening reaction was investigated (see Table 1, Entries 1–5). Solvents such as tetrahydrofuran (THF), dichloroethane, toluene, diethyl ether, and dichloromethane were screened. The activity along with the enantioselectivity was significantly higher in polar solvents such as dichloromethane (54% *ee*), and, therefore, it was used for further studies. The chiral scandium complex with the tertiary amines plays an important role in the enantioselectivity of the desired com-

Table 1. Effect of reaction parameters on the asymmetric ring-opening reaction of *meso*-stilbene oxide with aniline.[a]



Entry	Solvent	Amines	MS[b]	Temp. [°C]	Time [h]	% Yield[c]	% *ee*[d]
Effect of solvent							
1	THF	DIPEA	4 Å	r.t.	24	47	racemic
2	$(CH_2Cl)_2$	DIPEA	4 Å	r.t.	24	62	21
3	Et_2O	DIPEA	4 Å	r.t.	24	40	51
4	toluene	DIPEA	4 Å	r.t.	24	56	38
5	CH_2Cl_2	DIPEA	4 Å	r.t.	24	85	54
Effect of tertiary amines							
6	CH_2Cl_2		4 Å	r.t.	24	86	59
7	CH_2Cl_2		4 Å	r.t.	24	83	43
8	CH_2Cl_2		4 Å	r.t.	24	89	60
9	CH_2Cl_2		4 Å	r.t.	24	87	62
10	CH_2Cl_2		4 Å	r.t.	24	85	37
11	CH_2Cl_2		4 Å	r.t.	24	86	56
12	CH_2Cl_2		4 Å	r.t.	24	89	59
13	CH_2Cl_2	NMM	4 Å	r.t.	24	89	80
14	CH_2Cl_2	–	4 Å	r.t.	24	–	–
Effect of molecular sieves							
15	CH_2Cl_2	NMM	3 Å	r.t.	24	81	76
16	CH_2Cl_2	NMM	4 Å	r.t.	24	89	80
17	CH_2Cl_2	NMM	5 Å	r.t.	24	78	71
18	CH_2Cl_2	NMM	–	r.t.	24	72	67
Effect of temperature							
19	CH_2Cl_2	NMM	4 Å	r.t.	24	89	80
20	CH_2Cl_2	NMM	4 Å	0	24	89	94
21	CH_2Cl_2	NMM	4 Å	–15	24	86	79
Effect of time							
22	CH_2Cl_2	NMM	4 Å	0	4	38	94
23	CH_2Cl_2	NMM	4 Å	0	8	72	94
24	CH_2Cl_2	NMM	4 Å	0	12	89	94
25	CH_2Cl_2	NMM	4 Å	0	18	89	94

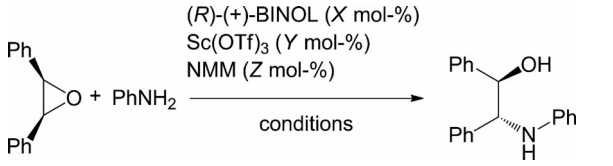
[a] Reagents and conditions: (*R*)-(+)-BINOL (12 mol-%), $Sc(OTf)_3$ (10 mol-%), NMM (24 mol-%), MS (4 Å, 125 mg), *meso*-stilbene oxide (0.5 mmol), aniline (0.6 mmol), dichloromethane (DCM, 2 mL). [b] MS: molecular sieves. [c] Isolated yield. [d] Determined by chiral HPLC analysis on a Chiralcel OD-H column.

pounds. Therefore, various amines such as diisopropylethylamine (54%*ee*), triethylamine (59%*ee*), 2,2,6,6-tetramethylpiperidine (43%*ee*), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 60%*ee*), 1,4-diazabicyclo[2.2.2]octane (DABCO, 62%*ee*), 1-methylimidazole (37%*ee*), 1,2-dimethylimidazole (56%*ee*), 1,2,2,6,6-pentamethylpiperidine (59%*ee*), and NMM (80%*ee*) were screened (see Table 1, Entries 6–14). The reaction did not proceed in the absence of amine, and further experiments were carried out using NMM as the tertiary amine.

Next, we screened the role of the molecular sieves (see Table 1, Entries 15–18). Better results were obtained when the amine was used with 4 Å molecular sieves (80%*ee*) than with either 3 Å (76%*ee*) or 5 Å molecular sieves (71%*ee*). In the absence of molecular sieves, the yield and enantiomeric excess value of the desired product marginally decreased. Very good catalytic activity was obtained by using 4 Å molecular sieves, and it was therefore used in further studies.

Subsequently, we studied the effect of the catalyst loading on the enantioselectivity of the β-amino alcohols. The catalyst loading was screened in a range from 5–15 mol-% (see Table 2 Entries 1–6). The best results were obtained by using 10 mol-% of the catalyst, which provided the desired product in 89% yield and with 80%*ee*. The reaction was unsuccessful in the absence in any one of the components of the chiral scandium complex, that is, (*R*)-(+)-BINOL, $Sc(OTf)_3$, and NMM. The reaction was also sluggish in the presence of only $Sc(OTf)_3$ and NMM [without (*R*)-(+)-BINOL] and gave a racemic compound.

Table 2. Effect of catalyst loading on the asymmetric ring-opening reaction of *meso*-epoxide with aniline.[a]



Entry	Catalyst loading			% Yield[b]	% *ee*[c]
	X [mol-%]	*Y* [mol-%]	*Z* [mol-%]		
1	18	15	36	91	76
2	12	10	24	89	80
3	6	5	12	68	74
4	–	10	24	23	racemic
5	12	–	24	–	–
6	12	10	–	–	–

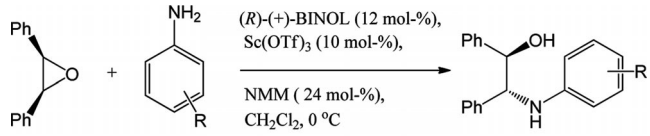
[a] Reagents and conditions: *meso*-stilbene oxide (0.5 mmol), aniline (0.6 mmol), MS (4 Å, 125 mg), DCM (2 mL), r.t., 24 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis on a Chiralcel OD-H column.

Encouraged by these results, we attempted to improve the enantioselectivity of desired products by studying the effect of temperature, and, hence, different reactions were carried out at various temperatures that ranged from room temperature to –15 °C (see Table 1, Entries 19–21). At room temperature, the enantioselectivity of the product was low, whereas decreasing the temperature to 0 °C increased the enantioselectivity up to 94%*ee* along with same yield of the desired product as that obtained at room temperature. A further decrease in the temperature to –15 °C did not have a profound effect on the yield of the product, but the enantioselectivity decreased to 79%*ee*.

Next, we examined the effect of time on the model reaction (see Table 1, Entries 22–25). After 12 h, the maximum yield and enantioselectivity was obtained for the desired product. Hence, the optimized reaction parameters for the asymmetric ring-opening reaction included *cis*-stilbene oxide (0.5 mmol), aniline (0.6 mmol), the chiral scandium catalyst (10 mol-%), MS (4 Å, 125 mg), and dichloromethane (2 mL) at 0 °C for 12 h.

With these optimized conditions in hand, we screened the reaction between *cis*-stilbene oxide and different aromatic aniline derivatives as the nucleophile (see Table 3, Entries 1–10). In all of the cases, the desired β-amino alcohol was obtained with high enantioselectivity. Among the various nucleophiles employed, *para*-substituted anilines (i.e., 4-methylaniline, 4-methoxyaniline, 3-fluoro-4-methoxyaniline, and 4-bromoaniline) afforded the desired amino alcohols with *ee* values above 82% with the exception of 4-bromoaniline, which gave 68%*ee* (see Table 3, Entries 3 and 5–7). On the other hand, 2-methylaniline and 2-methoxyaniline gave the desired chiral β-amino alcohols in 76 and 67%*ee*, respectively (see Table 3, Entries 2 and 4). These results imply that the steric interactions from the *ortho*-substituted nucleophile disfavors a high enantioselectivity. The sterically hindered aniline 2,4,6-trimethylaniline maintained a good yield and led to 64%*ee* (see Table 3, Entry 8). The α- and β-naphthylamines smoothly underwent the reaction to provide the desired product in very good yield with enantioselectivities of 74 and 81%*ee*, respectively (see Table 3, Entries 9 and 10). The aliphatic epoxide cyclohexane oxide also furnished a good yield (96%) but a poor enantiomeric excess value (22%*ee*) when it underwent the reaction with aniline.

Table 3. Enantioselective ring-opening reaction of *meso*-stilbene oxide with aromatic amines.[a]



Entry	Aniline	R group	Time [h]	% Yield[b]	% *ee*[c]
1		H	10	91	94
2		2-Me	20	86	76
3		4-Me	16	90	82
4	NH2	2-OMe	22	81	67
5		4-OMe	14	89	88
6	R	3-F-4-OMe	16	92	83
7		4-Br	18	87	68
8	NH2		34	78	64
9	NH2		12	90	74
10	NH2		14	92	81

[a] Reagents and conditions: (*R*)-(+)-BINOL (12 mol-%), $Sc(OTf)_3$ (10 mol-%), NMM (24 mol-%), MS (4 Å, 125 mg), *meso*-stilbene oxide (0.5 mmol), aniline derivative (0.6 mmol), DCM (2 mL), r.t., 24 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis on a Chiralcel OD-H column.

Conclusions

In this work, we have developed a simple and efficient chiral scandium catalyst for the synthesis of β-amino alcohols. The enantioselective ring-opening reaction of *meso*-epoxide with aniline derivatives gave enantiomerically pure β-amino alcohols in high yields and with excellent enantioselectivities (up to 94%*ee*) when conducted at 0 °C for 12 h. This reaction proceeded under mild conditions using simple and inexpensive starting materials such as the (*R*)-(+)-BINOL catalyst, *meso*-stilbene oxide, aniline derivatives, and 4 Å molecular sieves. Obviously, this new and versatile catalytic system has competitive advantages such as short reaction times, no additives, and no expensive chiral ligands that require a multistep synthesis under harsh reaction conditions. This inexpensive and effective chiral catalyst system is particularly attractive with a bright future in industrial-scale applications.

Experimental Section

General Methods: All chemicals were purchased from M/S Sigma Aldrich, S. D. Fine Chemicals, and commercial suppliers. All sol-

vents were distilled before use. The experiments were carried out under nitrogen. The progress of the reaction was monitored by thin layer chromatography using Merck silica gel 60 F254 plates. Products were purified by column chromatography on silica gel (60–120 mesh). The ^1H and ^{13}C NMR spectroscopic data were recorded with a Varian Inova 400 MHz spectrometer in either $CDCl_3$ or [D_6]DMSO. Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane as the internal standard. The coupling constants (J) are reported in Hz, and the splitting patterns of the proton signals are described as s (singlet), d (doublet), t (triplet), and m (multiplet). The IR spectra were recorded with an FTIR (Perkin–Elmer). Optical rotations were measured by using a polarimeter (Rudolph instrument). The enantiomeric excess values (*ee*) of the products were determined by HPLC analysis with an Agilent-HPLC on Daicel Chiralpak-IB and Chiralcel OD-H chiral columns using propan-2-ol/hexane as the eluent. Racemic compounds were prepared by using racemic 1,1-binaphthol.

General Procedure for the Asymmetric Ring-Opening Reaction of *meso*-Epoxide with Aniline Derivatives: To a stirred solution of molecular sieves (4 Å, 125 mg) in CH_2Cl_2 (2.0 mL) under nitrogen were added (*R*)-(+)-BINOL (0.12 mmol) and $Sc(OTf)_3$ (0.10 mmol). The resulting mixture was cooled to 0 °C. NMM (0.24 mmol) was added, and the reaction mixture was stirred at 0 °C for 0.5 h. The epoxide (0.5 mmol) and the aniline derivative (0.6 mmol) were then subsequently added to the mixture, which was stirred at 0 °C until the starting materials disappeared (monitored by TLC). The reaction mixture was then filtered through a plug of silica gel, which was washed with CH_2Cl_2 (25 mL). The filtrate was dried with anhydrous $NaSO_4$ and concentrated under reduced pressure (rotary evaporator). The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate) to give the desired β-amino alcohol. All products were characterized by appropriate spectroscopic techniques, and the data were in agreement with reported values.

(1*R*,2*R*)-1,2-Diphenyl-2-(phenylamino)ethanol:[15e] See Table 3, Entry 1. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralcel OD-H column; hexane/*i*PrOH, 90:10; flow rate: 1 mL/min): t_R = 15.7 min (major), t_R = 20.9 min (minor); 94%*ee*. $[a]_D^{25}$ = 40.0 (*c* = 0.10, CH_2Cl_2). IR: $\tilde{\nu}$ = 3399, 3048, 3027, 2920, 2850, 1601, 1503, 1453, 1430, 1317, 1263, 1049, 752, 699 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 7.34–7.10 (m, 10 H), 6.91 (t, J = 10 Hz, 2 H), 6.49 (d, J = 10.8 Hz, 2 H), 6.41 (t, J = 9.6 Hz, 1 H), 5.94 (d, J = 9.6 Hz, 1 H), 5.66 (d, J = 6.8 Hz, 1 H), 4.74 (t, J = 6.4 Hz, 1 H), 4.47 (t, J = 8.8 Hz, 1 H) ppm. D_2O exchange ^1H NMR (400 MHz, [D_6]DMSO): δ = 7.34–7.10 (m, 10 H), 6.91 (t, J = 10 Hz, 2 H), 6.49 (d, J = 10.8 Hz, 2 H), 6.41 (t, J = 9.6 Hz, 1 H), 4.74 (d, J = 6.4 Hz, 1 H), 4.47 (d, J = 8.8 Hz, 1 H) ppm. LC–MS: m/z = 290 $[M + H]^+$.

(1*R*,2*R*)-1,2-Diphenyl-2-(*o*-tolylamino)ethanol:[15k] See Table 3, Entry 2. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralpak IB column; hexane/*i*PrOH, 90:10; flow rate: 0.8 mL/min): t_R = 14.1 min (major), t_R = 21.6 min (minor); 76%*ee*. IR: $\tilde{\nu}$ = 3412, 3058, 3032, 2921, 2851, 1606, 1509, 1452, 1240, 1048, 748, 699 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 7.36–7.13 (m, 10 H), 6.92 (d, J = 9.6 Hz, 1 H), 6.75, (t, J = 10 Hz, 1 H), 6.40 (t, J = 9.6 Hz, 1 H), 6.13 (d, J = 10.8 Hz, 1 H), 5.87 (d, J = 6.8 Hz, 1 H), 5.03 (d, J = 8 Hz, 1 H), 4.80 (t, J = 6.4 Hz, 1 H), 4.48 (t, J = 7.2 Hz, 1 H), 2.1 (s, 3 H) ppm. LC–MS: m/z = 304 $[M + H]^+$.

(1*R*,2*R*)-1,2-Diphenyl-2-(*p*-tolylamino)ethanol:[15k] See Table 3, Entry 3. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralpak IB column; hexane/*i*PrOH, 90:10; flow rate: 0.5 mL/min): t_R = 19.5 min (minor), t_R = 21.1 min (major); 82%*ee*. IR: $\tilde{\nu}$ = 3403, 3042, 3028, 2922, 2851, 1618, 1518, 1453, 1046, 754, 699 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 7.32–7.09 (m, 10 H), 6.72 (d, J = 10.8 Hz, 2 H), 6.4 (d, J = 11.2 Hz, 2 H), 5.71 (d, J = 9.6 Hz, 1 H), 5.63 (d, J = 6.4 Hz, 1 H), 4.72 (t, J = 6.4 Hz, 1 H), 4.43 (t, J = 8.8 Hz, 1 H), 2.04 (s, 3 H) ppm. LC–MS: m/z = 304 $[M + H]^+$.

(1*R*,2*R*)-2-[(2-Methoxyphenyl)amino]-1,2-diphenylethanol:[15e] See Table 3, Entry 4. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralpak IB column; hexane/*i*PrOH, 80:20; flow rate: 1 mL/min): t_R = 6.7 min (major), t_R = 18.8 min (minor); 67%*ee*. IR: $\tilde{\nu}$ = 3410, 3052, 3029, 2924, 2853, 1601, 1511, 144, 1429, 1364, 1225, 1176, 1125, 1027, 768, 738, 700 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 7.34–7.16 (m, 10 H), 6.75 (t, J = 8.4 Hz, 1 H), 6.47 (m, 2 H), 6.13 (d, J = 10 Hz, 1 H), 5.86 (d, J = 6.4 Hz, 1 H), 5.51 (d, J = 8 Hz, 1 H), 4.75 (t, J = 6 Hz, 1 H), 4.45 (t, J = 7.6 Hz, 1 H), 3.82 (s, 3 H) ppm. LC–MS: m/z = 320 $[M + H]^+$.

(1*R*,2*R*)-2-[(4-Methoxyphenyl)amino]-1,2-diphenylethanol:[15k] See Table 3, Entry 5. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralcel OD-H column; hexane/*i*PrOH, 90:10; flow rate: 1 mL/min): t_R = 33.2 min (minor), t_R = 40.3 min (major); 88%*ee*. IR: $\tilde{\nu}$ = 3434, 3056, 3032, 2924, 2852, 1624, 1522, 1454, 1246, 1040, 756, 699 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 7.31–7.09 (m, 10 H), 6.56 (d, J = 12 Hz, 2 H), 6.44 (d, J = 11.6 Hz, 2 H), 5.63 (d, J = 6.4 Hz, 1 H), 5.56 (d, J = 9.2 Hz, 1 H), 4.70 (t, J = 6.8 Hz, 1 H), 4.39 (t, J = 8.4 Hz, 1 H), 3.54 (s, 3 H) ppm. LC–MS: m/z = 320 $[M + H]^+$.

(1*R*,2*R*)-2-[(3-Fluoro-4-methoxyphenyl)amino]-1,2-diphenylethanol: See Table 3, Entry 6. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralcel OD-H column; hexane/*i*PrOH, 90:10; flow rate: 1 mL/min): t_R = 22.4 min (minor), t_R = 25.1 min (major); 83%*ee*. IR: $\tilde{\nu}$ = 3417, 3028, 2923, 2852, 1631, 1518, 1454, 1227, 1027, 759, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.17 (m, 12 H), 6.71–6.67 (m, 1 H), 6.32–6.29 (m, 1 H), 6.22–6.20 (m, 1 H), 4.82 (d, J = 7 Hz, 1 H), 4.34 (d, J = 6 Hz, 1 H), 3.72 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.54, 142.45, 140.61, 140.05, 128.76, 128.43, 128.14, 127.80, 127.44, 126.72, 116.31, 115.76, 109.52, 109.49, 103.50, 103.28, 78.20, 65.64, 57.55 ppm. LC–MS: m/z = 338 $[M + H]^+$.

(1*R*,2*R*)-2-[(4-Bromophenyl)amino]-1,2-diphenylethanol:[15k] See Table 3, Entry 7. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralcel OD-H column; hexane/*i*PrOH, 90:10; flow rate: 0.8 mL/min): t_R = 23.1 min (minor), t_R = 25.3 min (major); 68%*ee*. IR: $\tilde{\nu}$ = 3435, 3058, 3026, 2924, 2851, 1595, 1348, 1353, 1018, 769, 700 cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 7.35–7.11 (m, 10 H), 7.03 (d, J = 11.2 Hz, 2 H), 6.47 (d, J = 11.6 Hz, 2 H), 6.27 (d, J = 9.6 Hz, 1 H), 5.67 (d, J = 6.4 Hz, 1 H), 4.75 (t, J = 6 Hz, 1 H), 4.46 (t, J = 9.6 Hz, 1 H) ppm. LC–MS: m/z = 368 $[M + H]^+$.

(1*R*,2*R*)-2-(Mesitylamino)-1,2-diphenylethanol: See Table 3, Entry 8. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralpak-IB column; hexane/*i*PrOH, 20:80; flow rate: 1 mL/min): t_R = 6.0 min (minor), t_R = 6.5 min (major); 64%*ee*. IR: $\tilde{\nu}$ = 3439, 3048, 3027, 2922, 2853, 1483, 1440, 1223, 1055, 758, 699 cm^{-1}. ^1H

NMR (400 MHz, $CDCl_3$): δ = 7.25–7.14 (m, 10 H), 7.01–6.99 (m, 2 H), 6.70 (s, 2 H), 5.03 (d, J = 9 Hz, 1 H), 4.10 (d, J = 9 Hz, 1 H), 2.16 (s, 3 H), 2.08 (s, 6 H) ppm. ^{13}C NMR (100 MHz): δ = 140.95, 140.86, 140.57, 131.92, 130.03, 129.77, 128.50, 128.19, 127.95, 127.76, 127.72, 127.15, 76.68, 69.56, 20.66, 19.18 ppm. LC–MS: m/z = 332 $[M + H]^+$.

(1*R*,2*R*)-2-(Naphthalen-1-ylamino)-1,2-diphenylethanol:[15e] See Table 3, Entry 9. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralcel OD-H column; hexane/*i*PrOH, 90:10; flow rate: 1 mL/min): t_R = 20.8 min (major), t_R = 42.8 min (minor); 74%*ee*. IR: $\tilde{\nu}$ = 3410, 3052, 3032, 2921, 2851, 1860, 1528, 1281, 1051, 766, 699 cm^{-1}.

(1*R*,2*R*)-2-(Naphthalen-2-ylamino)-1,2-diphenylethanol:[15p] See Table 3, Entry 10. The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralcel OD-H column; hexane/*i*PrOH, 90:10; flow rate: 1 mL/min): t_R = 28.8 min (major), t_R = 32.2 min (minor); 81%*ee*. IR: $\tilde{\nu}$ = 3401, 3044, 3028, 2923, 2853, 1630, 1602, 1519, 1483, 1396, 1342, 1272, 1226, 1180, 1045, 831, 744, 700 cm^{-1}. ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 7.56–7.45 (m, 2 H), 7.34–7.11 (m, 13 H), 7.02 (t, J = 9.6 Hz, 1 H), 6.48 (s, 1 H), 6.34 (d, J = 10.4 Hz, 1 H), 5.70, (d, J = 6.4 Hz, 1 H), 4.81 (t, J = 6.4 Hz, 1 H), 4.63 (t, J = 9.6 Hz, 1 H) ppm. LC–MS: m/z = 340 $[M + H]^+$.

(1*R*,2*R*)-2-(Phenylamino)cyclohexanol:[15e] The title compound was purified by silica gel chromatography (petroleum ether/ethyl acetate, 80:20). HPLC analysis (Daicel Chiralcel OD-H column; hexane/*i*PrOH, 85:15; flow rate: 1 mL/min): t_R = 8.2 min (major), t_R = 9.4 min (minor); 22%*ee*. GC–MS (70 eV): m/z (%) = 106 (36.4), 118 (23.5), 132 (100), 148 (12.5), 191 (47.5). IR: $\tilde{\nu}$ = 3394, 3052, 3025, 2938, 2923, 1917, 1600, 1514, 1497, 1322, 1259, 1152, 1100, 1056, 864, 799, 690 cm^{-1}.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H and ^{13}C NMR spectra and the HPLC chromatograms of the β-amino alcohol products.

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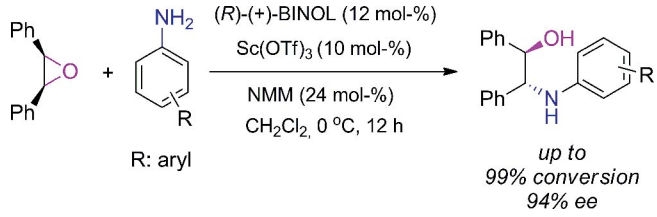
Epoxide Ring Opening



A simple and efficient protocol was developed for the asymmetric ring opening of a *meso*-epoxide with various amines using a chiral scandium complex. The system was optimized with respect to various reaction parameters. Under mild conditions, the reaction afforded a wide variety of enantiomerically pure β-amino alcohols in high yields and with excellent enantioselectivities.

Keywords: Synthetic methods / Asymmetric catalysis / Enantioselectivity / Epoxides / Amines / Amino alcohols

