Iron(III) trifluoroacetate [$Fe(O_2CCF_3)_3$] catalyzed epoxide opening with amines

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Abstract

Non-hygroscopic, non-toxic, and readily available iron(III) trifluoroacetate [$Fe(O_2CCF_3)_3$] was found to be a highly regioselective catalyst for the ring opening of a wide variety of epoxides with diverse amines under solvent-free conditions. The stereospecific ring opening of (*R*)-styrene oxide (**4**) with *p*-anisidine (**2b**) in the presence of 1 mol% of $Fe(O_2CCF_3)_3$ gave 2-(*p*-methoxyphenyl-amino)-2-phenylethanol (**5b**) in enantiopure form (>99 % *ee*) within 60 minutes.

Keywords: Epoxide, epoxide opening, amino alcohol, iron, solvent-free, green chemistry

Introduction

The 1,2-amino alcohol functionality is found in many naturally occurring molecules (such as alkaloids) and bioactive synthetic molecules exhibiting diverse biological activities[1] (such as *β*-blocking activity,[2a-c] cytotoxicity[2d] etc.). The *β*-amino alcohols have been also extensively used as chiral auxiliars and chiral ligands in asymmetric synthesis.[3] The most frequently used method for the generation of 1,2-amino functionality is the ring opening of epoxides with amines. Per the usual method for the preparation of 1,2-amino alcohols, an epoxide and the excess of the amine are heated together in a protic solvent.[4] However, this method has several limitations, such as moderate chemo- and regio-selectivity, low yields, no toleration of certain functional groups, etc. Therefore, a number of catalytic methods for the ring opening of epoxides with stoichiometric amount of amines have been developed in the literature. Certain metal salts were employed as Lewis acids for this purpose.[5] Several novel concepts have also been described by means of heterogenous catalytic systems,[6a-h] organic molecules (hexafluoro-2-propanol [HFIP][6i] and tributylphosphine [Bu_3P][6j]), water,[6k] and ionic liquids (ILs).[6l] The majority of the existing methods for the aminolytic opening of epoxides suffer from some drawbacks, such as the need for expensive or toxic catalysts, high catalyst loading, long reaction times, low yields, narrow substrate scope, chemo- and regio-selectivity etc. On the other hand, the use of non-toxic,

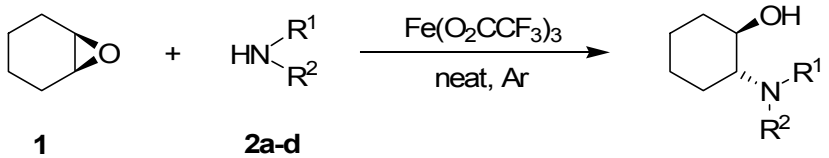
inexpensive, recyclable, and readily available catalysts is indispensable for the sustainable chemical industry.

In respecting the above mentioned considerations, we decided to develop a green method[7] for the synthesis of 1,2-amino alcohols through the epoxide opening with amines. Iron is the most abundant transition metal on earth and its inexpensive salts are non-toxic. Herein, we report the aminolytic epoxide opening catalyzed by iron(III) trifluoroacetate [$Fe(O_2CCF_3)_3$] as a non-toxic, non-hygroscopic, and environmentally friendly catalyst.[8] In contrast to other iron(III) salts (e.g. $FeCl_3$), iron(III) trifluoroacetate is remarkably non-hygroscopic and bench-stable for long periods (e.g. longer than 6 months during our studies).

Results and Discussion

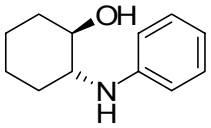
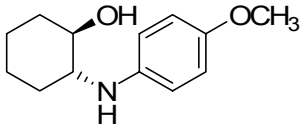
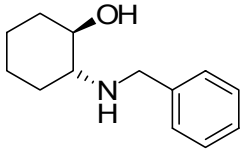
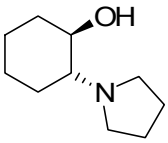
In all of the reactions, an equimolar amount of an epoxide and amine were mixed in a Schlenk tube, in which a suitable amount of iron(III) trifluoroacetate was added under argon. First, cylohexene oxide (**1**) was subjected to the opening with various aromatic and aliphatic amines (**2a-d**) in the presence of $Fe(O_2CCF_3)_3$ (Table 1). The reaction between cyclohexene oxide (**1**) and aniline (**2a**) was rather fast in the presence of 1 mol% of $Fe(O_2CCF_3)_3$ and the corresponding *β*-amino alcohol, *trans*-2-(phenylamino)cyclohexanol (*rac*-**3a**), was obtained nearly in a quantitative yield (97% *y*) within 15 minutes (TLC; Table 1, entry 1). A somewhat milder reaction between cyclohexene oxide (**1**) and *p*-anisidine (**2b**) took place employing 1 mol% of $Fe(O_2CCF_3)_3$ and trans-2-(4-methoxyphenylamino)cyclohexanol (*rac*-**3b**) was isolated in quantitative yield (99% *y*) after 1 h at room temperature (entry 2). In the case of the reactions between cyclohexene oxide (**1**) and the aromatic amines **2a** and **2b**, an exothermic reaction occurred upon addition of $Fe(O_2CCF_3)_3$. However, there was no need for the extra safety precautions when reactions were conducted in 5 mmol scale experiments. On the other hand, the ring opening reactions of cyclohexene oxide (**1**) with the aliphatic amines **2c** and **2d** were sluggish and had to be heated at 60 ^oC for 3 h in the presence of 5 mol% of $Fe(O_2CCF_3)_3$ (entry 3 and 4). *Trans*-2-(benzylamino)cyclohexanol (*rac*-**3c**) was obtained in 87% yield from cyclohexene oxide (**1**) and benzyl amine (**2c**) (entry 3). Again, the reaction between cyclohexene oxide (**1**) and pyrrolidine (**2d**) was performed at 60 ^oC for 3 h in the presence of 5 mol% of $Fe(O_2CCF_3)_3$ and *trans*-2-(pyrrolidino)cyclohexanol (*rac*-**3d**) was isolated in a good yield (90% *y*, entry 4). In all of the cases (entry 1-4), *trans*-2-amino alcohols formed as the sole products (NMR).

Table 1. $Fe(O_2CCF_3)_3$ catalyzed ring opening of cyclohexene oxide (**1**) with aromatic and aliphatic amines under solvent-free conditions[a]



1 **2a-d** (±)-**3a-d**

a: R^1=H, R^2=C_6H_5; **b**: R^1=H, R^2=4-MeO-C_6H_4;
c: R^1=H, R^2=C_6H_5-CH_2; **d**: R^1=R^2=$(CH_2)_4$

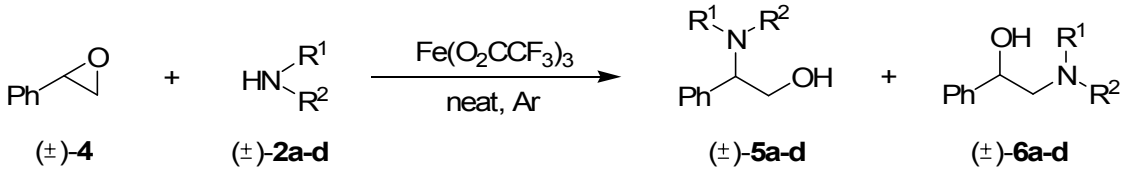
Entry	Amine	$Fe(O_2CCF_3)_3$ (mol%)	*T* (°C)	Time (min)	Product	Yield (%)[b]
1	**2a**	1.0	rt	15	 (±)-**3a**	97
2	**2b**	1.0	rt	60	 (±)-**3b**	99
3	**2c**	5.0	60	180	 (±)-**3c**	87
4	**2d**	5.0	60	180	 (±)-**3d**	90

[a] Reactions were carried out by employing equimolar amounts of epoxide **1** and amines **2a-d** on a 2.5 or 5.0 mmol scale. [b]Yield of isolated product after column chromatography.

To find out as to how active and regioselective our catalytic system was, we employed racemic styrene oxide (*rac*-**4**) as the next epoxide. The ring openings of styrene oxide (*rac*-**4**) with aniline (**2a**) and *p*-anisidine (**2b**) proceeded rather fast and completed within 15 and 60 minutes, respectively (Table 2, entries 1 and 2). The regioisomeric 2-arylamino-2-phenyl-1-ethanols *rac*-**5a** and *rac*-**5b** were obtained in excellent yields (93% *y*) and regioselectivities (**5a**/**6a** = 97:03; **5b**/**6b** = 98:02) by the nucleophilic attack of the aromatic amines **2a** and **2b** at

the benzylic carbon atom of styrene oxide (*rac*-**4**). As per the aliphatic amines, the reactions had to be performed at 60 °C for 3 h in the presence of 5 mol% of $Fe(O_2CCF_3)_3$ in order to ensure complete conversion of styrene oxide (*rac*-**4**) (Table 2, entries 3 and 4). During the reaction of styrene oxide (*rac*-**4**) with benzyl amine (**2c**), the regioisomeric amino alcohols *rac*-**5c** and *rac*-**6c** were obtained in 73 % total yield (entry 3). The regioisomeric ratio 62:38 (**5c/6c** = 62:38) was in favor of the amino alcohol *rac*-**5c** formed by the nucleophilic attack of the benzyl amine (**2c**) at the benzylic carbon of styrene oxide (*rac*-**4**). However, the reaction of styrene oxide (*rac*-**4**) with pyrrolidine (**2d**) resulted in a change of regioselectivity, that is, pyrrolidine (**2d**) preferentially attacked at the terminal carbon atom of styrene oxide (*rac*-**4**) (entry 4). The mixtures of regioisomeric amino alcohols *rac*-**5d** and *rac*-**6d** in favor of *rac*-**6d** (**5d/6d** = 35:65) were obtained in excellent yield (95% *y*). The reversal regioselectivity observed in the ring opening of styrene oxide (*rac*-**4**) with pyrrolidine (**2d**) compared to the aromatic amines **2a-b** and benzyl amine (**2c**) could be explained by the complex formation between nitrogen atom of pyrrolidine (**2d**) and $Fe(O_2CCF_3)_3$ since aliphatic secondary amines are stronger bases than aromatic amines and benzyl amine. The resulting sterically hindered complex species from pyrrolidine (**2d**) and $Fe(O_2CCF_3)_3$ could more easily attack to less hindered carbon of styrene oxide (*rac*-**4**).

Table 2. $Fe(O_2CCF_3)_3$ catalyzed ring opening of racemic styrene oxide (*rac*-**4**) with aromatic and aliphatic amines under solvent-free conditions[a]



(±)-**4** (±)-**2a-d** (±)-**5a-d** (±)-**6a-d**

a: R^1=H, R^2=C_6H_5; **b**: R^1=H, R^2=4-MeO-C_6H_4;
c: R^1=H, R^2=C_6H_5-CH_2; **d**: R^1=R^2=$(CH_2)_4$

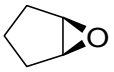
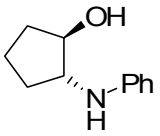
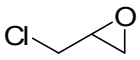
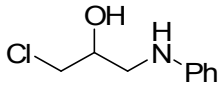
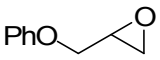
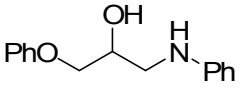
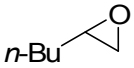
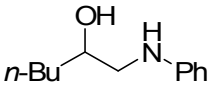
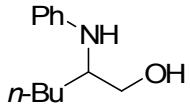
Entry	Amine	$Fe(O_2CCF_3)_3$ (mol%)	*T* (°C)	Time (min)	Yield (%)[b]	Regioisomeric Ratio (**5 : 6**)[c]
1	**2a**	1.0	rt	15	93	93 : 03
2	**2b**	1.0	rt	60	93	98 : 02
3	**2c**	5.0	60	180	73	62 : 38
4	**2d**	5.0	60	180	95	35 : 65

[a]Reactions were carried out by employing equimolar amounts of epoxide **1** and amines **2a-d** on a 2.5 or 5.0 mmol scale. [b]Yield of isolated product after column chromatography. [c]Determined by NMR.

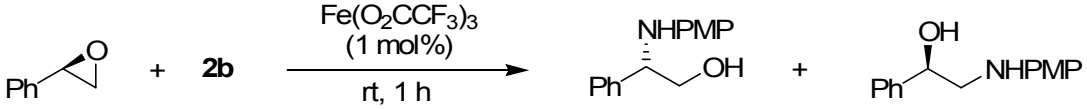
To extend the generality and selectivity of $Fe(O_2CCF_3)_3$ catalyzed aminolytic epoxide opening further, we allowed various epoxides to react with aniline (**2a**) in the presence of 1 mol% of $Fe(O_2CCF_3)_3$ (Table 3). The treatment of cyclopentene oxide (**7**) with an equimolar amount of aniline (**2a**) at room temperature for 3 h in the presence of 1 mol% of $Fe(O_2CCF_3)_3$ gave *trans*-2-(phenylamino)cyclopentanol (*rac*-**8**) in good yield (79% *y*; Table 3, entry 1). The reaction of epichlorohydrin (*rac*-**9**) with aniline (**2a**) at room temperature for 1 h in the presence of 1 mol% of $Fe(O_2CCF_3)_3$ afforded the amino alcohol *rac*-**10** as the sole regioisomer formed by the nucleophilic attack of aniline (**2a**) at the less hindered carbon atom of the epoxide ring (82% *y*; entry 2). The reaction of phenoxymethyl oxirane (*rac*-**11**) with aniline (**2a**) in turn furnished the corresponding amino alcohol *rac*-**12** as only one regioisomeric product in good yield (78% *y*; entry 3). While the reaction of epichlorohydrin (*rac*-**9**) and phenoxymethyl oxirane (*rac*-**11**) gave the corresponding amino alcohols *rac*-**10** and *rac*-**12** in good yields under *full-regioselectivity*, in the reaction between 1-hexene oxide (*rac*-**13**) and aniline (**2a**) a moderate yield (58% *y*) and somewhat diminished regioselectivity (*rac*-**14**/*rac*-**15** = 84:16; entry 4) were observed. It was also observed that the reaction between *rac*-**13** and **2a** was rather exothermic and **2a** was not fully consumed at the end of the reaction (TLC). Additionally, another (side) product was observed on the TLC plate which was then isolated by column chromatography. The isolated side product (one spot on the TLC plate) was a mixture of two dimerization products formed from the reaction of two equivalents of 1-hexene oxide (*rac*-**13**) and one equivalent of aniline (**2a**) (GCMS, NMR). We isolated the mixture of the side products in a 25% yield. According to the NMR and GC spectra of the side products, the dimerization of 1-hexene oxide (*rac*-**13**) with aniline (**2a**) catalyzed by $Fe(O_2CCF_3)_3$ proceeded via the ring opening of the second 1-hexene oxide molecule (*rac*-**13**) by the nucleophilic attack of the oxygen atom of the amino alcohols *rac*-**14** and *rac*-**15**, and not the nitrogen atom.

In order to elucidate the stereospecificity of the $Fe(O_2CCF_3)_3$ catalyzed aminolytic epoxide opening, the reaction of enantiomerically pure (*R*)-styrene oxide (**4**, >99% *ee*) with *p*-anisidine (**2b**) was performed (Scheme 1). We are pleased to report that the corresponding amino alcohol **5b** was obtained in enantiopure form in high yield and under high regioselectivity from enantiopure (*R*)-styrene oxide (**4**) and *p*-anisidine (**2b**) in the presence of 1 mol% of $Fe(O_2CCF_3)_3$ (93% *y*, **5b**/**6b** = 98:02, >99% *ee* for **5b**). To the best of our knowledge, this is the first report on the synthesis of **5b** in enantiopure form.[9] Since enantiomerically pure epoxides are currently available by the hydrolytic kinetic resolution (HKR) of epoxides, this method could be rather useful for the synthesis of enantiopure 1,2-amino alcohols from enantiopure epoxides and amines.[10]

Table 3. $Fe(O_2CCF_3)_3$ catalyzed ring openings of various epoxides with aniline (**2a**)

Entry	Epoxide	$Fe(O_2CCF_3)_3$ (mol%)	*T* (°C)	Time (min)	Product	Yield (%)[a]
1		1.0	rt	180		79
	7				(±)-**8**	
2		1.0	rt	60		82
	(±)-**9**				(±)-**10**	
3		1.0	rt	15		78
	(±)-**11**				(±)-**12**	
4		1.0	rt	60	  84 : 16	58
	(±)-**13**				(±)-**14** (±)-**15**	

[a]Isolated yield after column chromatography.



Scheme 1. Stereospecific ring opening of (*R*)-styrene oxide (**4**) with *p*-anisidine (**2b**) catalyzed by $Fe(O_2CCF_3)_3$. PMP: *p*-methoxyphenyl.

In summary, we have shown that a very low amount of $Fe(O_2CCF_3)_3$ (down to 1 mol%) can catalyze the ring opening reactions of a wide variety of epoxides with aromatic and aliphatic amines to give corresponding 1,2-amino alcohols under solvent-free conditions. High yields, high regioselectivities, and short reaction times were the general features of this catalytic system. Furthermore, stereospecific ring opening of (*R*)-styrene oxide (**4**) with *p*-anisidine (**2b**) could be conducted without loss of enantiopurity. The non-toxicity, ready availability of $Fe(O_2CCF_3)_3$ along with the great abundance of iron in nature could make this catalytic system rather attractive for the large scale applications in the chemical industry.

Experimental Section

General Procedures. All of the reactions were carried out in oven-dried Schlenk tubes under a positive pressure of argon. Epoxides were purchased from Aldrich or Fluka, and were used as received. Iron(III) trifluoroacetate [$Fe(O_2CCF_3)_3$] was prepared according to the usual procedure described in the literature.[8a] Thin layer chromatography (TLC) was conducted on aluminum sheets that were pre-coated with silica gel *SIL G/UV*$_{254}$ from MN GmbH & Co., in which the spots were visualized in UV-light (λ = 254 nm) and/or by staining with 5% of a phosphomolybdic acid solution in ethanol. Chromatographic separations were performed using silica gel (MN-silicagel 60, 230-400 mesh). The melting points were measured in open glass capillary using a Gallenkamp melting point apparatus and were uncorrected. NMR spectra were recorded on Bruker DPX400 NMR spectrometer. Chemical shifts δ are reported in parts per million (ppm) relative to the residual protons in the NMR solvent ($CHCl_3$: δ 7.24) and carbon resonance of the solvent ($CDCl_3$: δ 77.0). Mass spectra were recorded on a gas chromatography with mass sensitive detector from ThermoQuest Finnigan Multi Mass (EI, 70 eV) using Standard Method (column: Phenomenex Zebron ZB-5 capillary column, 60 m, 0.25 ID; inlet: 250 ^oC (split modus); det: 230 ^oC; He, 15 kpa (constant pressure modus); oven: 50 ^oC (2 min), 20 ^oC/min, 150 ^oC (10 min), 20 ^oC/min, 270 ^oC (17 min)). The specific rotation was measured on Dr. Kernchen Sucromat Digital Automatic Saccharimeter using 10 mL cell with a 1 dm path length and the sample concentration is given in g/100 mL unit.

All the products are known in the literature and were characterized by NMR and GC-MS. NMR spectra were found to be consistent with those reported in the literature (*rac*-**3a**[5a], *rac*-**3b**[5a], *rac*-**3c**[5a], *rac*-**3d**[5a], *rac*-**5a**[5a], *rac*-**5b**[5a], *rac*-**5c**[5u], *rac*-**6c**[5g], *rac*-**5d**[11], *rac*-**6d**[11], *rac*-**8**[5a], *rac*-**10**[5a], *rac*-**12**[5a], *rac*-**14**[12]). Selected spectral data were given below. Although heat evolution took place in the ring opening of epoxides with aromatic amines there was no safety problem in all reactions.

***trans*-2-(4-Methoxyphenylamino)cyclohexanol (*rac*-3b) (representative procedure).** To the mixture of cyclohexene oxide (**1**, 491 mg, 5.0 mmol) and *p*-anisidine (**2b**, 616 mg, 5.0 mmol) were added 20 mg of $Fe(O_2CCF_3)_3$ (50 μmol, 1 mol%) in one portion and the mixture was stirred at room temperature under argon. After completion of the reaction, as indicated Table 1 (1 h,

TLC), the amino alcohol *rac*-**3b** was isolated as a light brown solid by column chromatography (1.094 g, 99%). Mp 72 °C (lit.[5ab] 59 °C). R_f = 0.40 (silica gel; *n*-hexane/EtOAc, 7:3). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.96-1.05 (m; 1H), 1.25-1.39 (m; 3H), 1.68-1.72 (m; 2H), 2.07-2.12 (m; 2H), 2.99 (ddd, *J* = 4.0, 8.6, 12.0 Hz; 1H), 3.04 (br s; 2H), 3.31 (ddd, *J* = 4.0, 8.0, 12.0 Hz; 1H), 3.74 (s; 3H), 6.68 (d, *J* = 8.8 Hz; 2H), 6.78 (d, *J* = 8.8 Hz; 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 24.2 (t), 25.0 (t), 31.5 (t), 33.1 (t), 55.7 (q), 61.5 (d), 74.3 (d), 114.8 (d), 116.3 (d), 141.6 (s), 152.8 (s). GC-MS: τ_R = 29.50 min (*rac*-**3b**); m/z (%) = 221 ([M]$^+$, 100), 178 ([M-43]$^+$, 12), 162 (([M-59]$^+$, 83), 148 (27), 136 (54), 123 (19), 108 (35). Anal. Calcd. For $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.37; H, 8.52; N, 6.62.

***trans*-2-(Benzylamino)cyclohexanol (*rac*-3c).** The amino alcohol *rac*-**3c** was obtained as a light brown solid in 87% yield after column chromatography. Mp 69-70 °C (lit.[5g] 73-74 °C). R_f = 0.57 (silica gel; EtOAc/MeOH/Et_3N, 10:0.5:0.5). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.87-0.96 (m; 1H), 1.15-1.17 (m; 3H), 1.63-1.65 (m; 2H), 1.92-1.94 (m; 1H), 2.05-2.09 (m; 1H), 2.19-2.24 (m, 1H), 3.10-3.12 (m; 1H), 3.60 (d, *J* = 12.8 Hz; 1H), 3.86 (d, *J* = 12.8 Hz; 1H); 7.14-7.25 (m; 5H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 24.3 (t), 25.1 (t), 30.5 (t), 33.3 (t), 50.8 (t), 63.1 (d), 73.8 (d), 126.9 (d), 128.0 (d), 128.4 (d), 140.5 (s). GC-MS: τ_R = 27.01 min (*rac*-**3c**); m/z (%) = 205 ([M]$^+$, 34), 146 ([M-59]$^+$, 94), 132 (25), 120 (34), 114 (42), 91 (100), 65 (24). Anal. Calcd. For $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82. Found: C, 76.32; H, 9.22; N, 7.22.

***trans*-2-(Pyrrolidino)cyclohexanol (*rac*-3d).** The amino alcohol *rac*-**3d** was obtained as a light brown oil in 90% yield after column chromatography. R_f = 0.47 (silica gel; EtOAc/MeOH/Et_3N, 10:0.5:0.5). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.17-1.21 (m; 4H), 1.68-1.73 (m; 7H), 2.06-2.07 (m; 1H), 2.39-2.44 (m; 1H), 2.49-2.55 (m; 2H), 2.61-2.67 (m, 2H), 3.27-3.31 (m; 1H), 3.95 (br s; 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 21.1 (t), 23.6 (t), 24.2 (t), 25.3 (t), 32.3 (t), 47.1 (t), 64.9 (d), 70.7 (d). GC-MS: τ_R = 21.12 min (*rac*-**3d**); m/z (%) = 169 ([M]$^+$, 27), 126 ([M-43]$^+$, 13), 110 ([M-59]$^+$, 100), 97 (47), 84 (59), 69 (28), 42 (15), 41 (31).

2-(4-Methoxyphenylamino)-2-phenylethanol (*rac*-5b). The mixture of the regioisomeric amino alcohols *rac*-**5b** and *rac*-**6b** was isolated as a light brown viscose oil in 93% yield after column chromatography. The regioisomeric ratio was found to be *rac*-**5b**/*rac*-**6b** = 98:02 by means of NMR (Table 2, entry 2). R_f = 0.48 (silica gel; *n*-hexane/EtOAc, 7:3). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.72 (s; 3H), 3.73 (dd, *J* = coupling constants could not be determined because this signal appeared under the CH_3 signal at δ 3.72 ppm; 1H), 3.94 (dd, *J* = 4.0, 11.2 Hz; 1H), 4.45 (dd, *J* = 4.0, 7.6 Hz; 1H), 6.57 (d, *J* = 8.8 Hz; 2H), 6.73 (d, *J* = 8.8 Hz; 2H), 7.28-7.38 (m; 5H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 55.7 (q), 60.9 (d), 67.3 (t), 114.8 (d), 115.3 (d), 126.7 (d), 127.5 (d), 128.8 (d), 140.4 (s), 141.4 (s), 152.4 (s). GC-MS: τ_R = 32.03 min (*rac*-**5b**); m/z (%) = 243 ([M]$^+$, 25), 212 ([M-31]$^+$, 100), 134 (15), 108 (13), 91 (8), 77 (15).

2-(Benzylamino)-2-phenylethanol (*rac*-5c) and 2-(benzyl-amino)-1-phenylethanol (*rac*-6c). The regioisomeric amino alcohols *rac*-**5c** and *rac*-**6c** could be separated by column chromatography from each other. The total yield of the reaction was 73%, and the ratio of the isolated regioisomers (*rac*-**5c**/*rac*-**6c**) was found to be 62:38 by proportion of the isolated regioisomers. ***rac*-5c:** Light yellow oil. R_f = 0.69 (silica gel; EtOAc/MeOH/Et_3N, 10:0.5:0.5).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.58-3.66 (m; 2H), 3.73 (dd, J = 4.4, 10.8 Hz; 1H), 3.80 (d, J = 13.2 Hz; 1H), 3.87 (dd, J = 4.4, 8.8 Hz; 1H), 7.31-7.43 (m; 10H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 51.1 (t), 63.8 (d), 66.7 (t), 126.9 (d), 127.3 (d), 127.4 (d), 128.1 (d), 128.3 (d), 128.5 (d), 140.0 (s), 140.1 (s). GC-MS: τ_R = 28.55 min (*rac*-**5c**); m/z (%) = 196 ([M-31]$^+$, 92), 91 (100), 65 (19). ***rac*-6c:** Mp 87-88 ^{o}C. R_f = 0.40 (silica gel; EtOAc/MeOH/Et_3N, 10:0.5:0.5). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.65 (dd, J = 9.0, 12.2 Hz; 1H), 2.79 (dd, J = 3.8, 12.2 Hz; 1H), 3.70 (d, J = 6.0 Hz; 2H), 4.62 (dd, J = 3.6, 9.2 Hz; 1H), 7.14-7.24 (m; 10H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 53.5 (t), 56.5 (t), 71.8 (d), 125.8 (d), 127.0 (d), 127.4 (d), 128.0 (d), 128.3 (d), 128.4 (d), 139.9 (s), 142.6 (s). GC-MS: τ_R = 29.16 min (*rac*-**6c**) m/z (%) = 120 ([M-107]$^+$, 97), 91 (100), 77 (15), 65 (15).

2-Pyrrolidino-2-phenylethanol (*rac*-5d) and 1-phenyl-2-pyrrolidinoethanol (*rac*-6d). The mixture of the regioisomeric amino alcohols *rac*-**5d** and *rac*-**6d** was obtained as a light brown oil in 95% total yield. The regioisomeric ratio 35:65 (*rac*-**5d**/*rac*-**6d**) was determined by means of NMR. R_f = 0.45 (silica gel; EtOAc/MeOH/Et_3N, 10:0.5:0.5). ***rac*-5d:** ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.62-1.65 (m; 4H), 2.64-2.65 (m; 4H), 3.34 (t, J = 5.8 Hz; 1H), 3.71 (dd, J = 5.8, 10.6 Hz; 1H), 3.77 (dd, J = 5.8, 10.6 Hz; 1H), 7.14-7.30 (m; 5H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 23.1 (t), 51.2 (t), 64.4 (t), 70.0 (d), 127.2 (d), 127.4 (d), 128.5 (d), 139.4 (s). GC-MS: τ_R = 23.99 min (the mixture of *rac*-**5d** and *rac*-**6d** gave only one signal on GC chromatogram); m/z (%) = 160 ([M-31]$^+$, 100), 91 (59), 84 (95), 77 (21), 55 (27), 42 (43). ***rac*-6d:** ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.69-1.72 (m; 4H), 2.40 (dd, J = 3.2, 12.2 Hz; 1H), 2.41-2.45 (m; 4H), 2.66 (dd, J = 6.8, 12.0 Hz; 1H), 4.61 (dd, J = 3.2, 10.8 Hz; 1H), 7.14-7.30 (m; 5H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 23.6 (t), 53.8 (t), 64.1 (t), 70.7 (d), 125.7 (d), 128.1 (d), 128.3 (d), 142.5 (s).

***trans*-2-(Phenylamino)cyclopentanol (*rac*-8).** The amino alcohol *rac*-**8** was obtained as a colourless crystalline solid in 79% yield after column chromatography. Mp 63-65 ^{o}C (lit.[5ab] 54-55 ^{o}C). R_f = 0.34 (silica gel; *n*-hexane/EtOAc, 7:3). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.39-1.47 (m; 1H), 1.64-1.71 (m; 1H), 1.75-1.86 (m; 2H), 1.96-2.05 (m; 1H), 2.25-2.34 (m, 1H), 3.63 (dd, J = 6.4, 10.8 Hz; 1H), 4.06 (dd, J = 4.8, 8.4 Hz; 1H), 6.72 (d, J = 8.0 Hz; 2H), 6.78 (t, J = 7.2 Hz; 1H), 7.24 (t, J = 8.0 Hz; 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 20.8 (t), 30.9 (t), 32.6 (t), 61.9 (d), 77.9 (d), 113.3 (d), 117.4 (d), 129.1 (d), 147.6 (s). GC-MS: τ_R = 25.36 min (*rac*-**8**); m/z (%) = 177 ([M]$^+$, 72), 132 ([M-45]$^+$, 100), 118 ([M-59]$^+$, 58), 106 (90), 93 (54), 77 (53), 65 (18), 51 (27). Anal. Calcd. For $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.23; H, 8.44; N, 8.25.

1-Phenylamino-2-hexanol (*rac*-14) and 2-phenylamino-1-hexanol (*rac*-15). The mixture of the regioisomeric alcohols *rac*-**14** and *rac*-**15** was obtained as a colourless powders in 58% yield after column chromatography. The regioisomeric ratio (*rac*-**14**/*rac*-**15** = 84:16) was determined by means of NMR. R_f = 0.48 (silica gel; DCM/EtOAc, 10:0.5). ***rac*-14:** ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, J = 7.2 Hz; 3H), 1.25-1.45 (m; 6H), 2.90 (dd, J = 8.8, 12.6 Hz; 1H), 3.16 (dd, J = 8.8, 12.8 Hz; 1H), 3.63-3.74 (m; 1H), 6.56 (d, J = 8.0 Hz; 2H), 6.64 (t, J = 7.2 Hz; 1H), 7.09 (t, J = 8.0 Hz; 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.0 (q), 22.7 (t), 27.7 (t), 34.8 (t), 50.3 (t), 70.3 (d), 113.3 (d), 117.8 (d), 129.2 (d), 148.3 (s). GC-MS: τ_R = 25.34 min (*rac*-**14**); m/z (%) = 193 ([M]$^+$, 44), 106 ([M-87]$^+$, 100), 77 (57), 51 (18). ***rac*-15:** ^{1}H-NMR (400 MHz,

$CDCl_3$): δ = 0.85 (t, J = 7.2 Hz; 3H), 1.25-1.45 (m; 6H), 3.36-3.44 (m; 2H), 3.64 (dd, J = 3.6, 10.4 Hz; 1H), 6.56 (d, J = 8.0 Hz; 2H), 6.64 (t, J = 7.2 Hz; 1H), 7.09 (t, J = 8.0 Hz; 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.0 (q), 22.7 (t), 28.3 (t), 31.9 (t), 55.3 (t), 64.4 (d), 113.6 (d), 117.7 (d), 129.3 (d), 147.8 (s). GC-MS: τ_R = 24.53 min (*rac*-**15**); m/z (%) = 193 ($[M]^+$, 18), 162 ($[M-31]^+$, 100), 118 (37), 106 (70), 93 (20), 77 (18).

Enantiopure 2-(4-methoxyphenylamino)-2-phenylethanol (5b, Scheme 1). The reaction of commercially available enantiopure (*R*)-styrene oxide (**4**, >99% *ee*; 240 mg, 2.0 mmol) with *p*-anisidine (**2b**) in the presence of 1 mol% of $Fe(O_2CCF_3)_3$ at room temperature for 1 h afforded the enantiopure amino alcohol **5b** (>99% *ee*) as a light brown oil in 93% yield and high regioselectivity (**5b**/**6b** = 98:02). HPLC: Chiralpak AD-H; *n*-hexane/^{i}PrOH (90:10); 0.8 ml/min, 34 bar; Detection: 254 nm (UV-VIS); τ_R = 8.3 min (**6b**), τ_R = 10.5 min (*ent*-**6b**), τ_R = 12.1 min (**5b**), τ_R = 15.6 min (*ent*-**5b**). $[\alpha]_D^{25}$ = +29.5^o (c = 0.20, $CHCl_3$).

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