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New Aniline-Containing Amino Alcohols from *trans*-(*R*,*R*)-2-(2-Nitrophenyl)-3-phenyloxirane as Useful Intermediates for the Synthesis of Chiral Ligands, Bases, and Benzoxazine Nucleus

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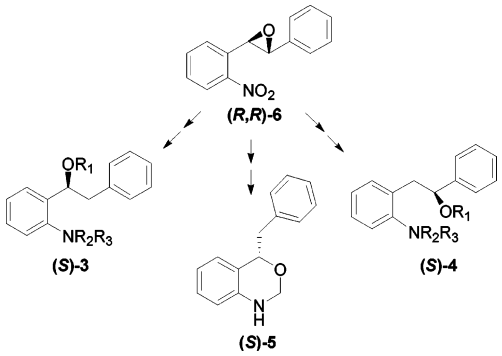

New enantiopure aniline-containing amino alcohols are directly derived from *trans*-(*R*,*R*)-2-(2-nitrophenyl)-3-phenyloxirane, by alternative regioselective double reductions. Subsequent selective alkylation procedures and derivatizations provide a rapid and high-yielding access to different chiral ligands, bases, and benzoxazines, without loss of optical purity.

Amino alcohol subunits are versatile structures, and they are present in many natural[1] and synthetic[2] compounds. They are widely used in numerous catalytic asymmetric reactions[3] (hydrogenation, epoxidation, nucleophilic addition) and as chiral bases in asymmetric desymmetrization of prochiral substrates.[4] Until now, chiral amino alcohols employed as ligands in such processes are still mostly based on a few naturally occurring skeletons, and among these various aminoalcohols, examples of ligands bearing an aniline group are rare.[5] Among the various products directly obtained from *o*-aminobenzyl alcohols of type **1**, 1,4-dihydro-2*H*-benzo[*d*][1,3]oxazines **3** (Figure 1) are of

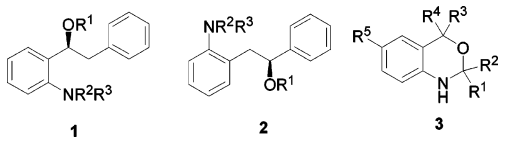

FIGURE 1. Aniline-containing amino alcohols and 1,4-dihydro-2*H*-benzo[*d*][1,3]oxazines.

interest for their biological activities,[6] which are not yet widely studied. Recently, novel 6-arylbenzoxazines were prepared and examined as progesterone receptor (PR) modulators, showing high agonist and/or antagonist activity.[7] They are also used in chiral form as stereoinductors in diastereoselective alkylation reactions.[8]

Although the structural simplicity of these functionalized anilines **1** and **2**, only one literature citation was found for compound **2** (with $R^1 = R^2 = R^3 = H$), which was prepared from *o*-methylaniline and used as an intermediate in the synthesis of indoles.[9]

During our studies on regio- and stereoselective ring opening of 2,3-diaryloxiranes, it was found that such epoxides were suitable starting material for the synthesis of functionalized 1,2-diarylethanols, and this approach has been used to prepare new pyridyl and furyl alcohols,[10] 1,2-diaryl bromohydrins,[11] and acetonides[12] in enantiopure form. We present here a direct synthesis of the desired new aniline-type amino alcohols **1** and **2** from enantiopure (*R*,*R*)-2-(2-nitrophenyl)-3-phenyl oxirane **4** and their elaboration into new ligands and benzoxazines.

(*R*,*R*)-Epoxide **4** was prepared in good yield and >98% ee (determined by HPLC) from the pure (R,R,R,S_S)-(−)-sulfonium salt **5**,[13] commercial 2-nitrobenzaldehyde, and a phosphazene base [EtP2 = Et−N=P(NMe$_2$)$_2$(N=P(NMe$_2$)$_3$] to generate the sulfur ylide (Scheme 1). Numerous methods of reduction of either nitrophenyl group or 2,3-disubstituted oxirane are known. Although stoichiometric metal hydrides or dissolving metals are frequently employed for the reductive ring-opening of epoxides,[14] the need for a practical and environmentally benign version of this reaction has generated interest in heterogeneous catalytic systems. In particular, much interest has been directed

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[‡] Università degli studi della Basilicata.

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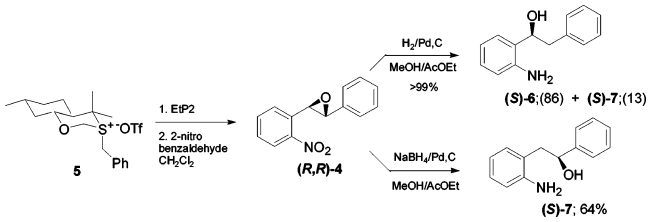
SCHEME 1

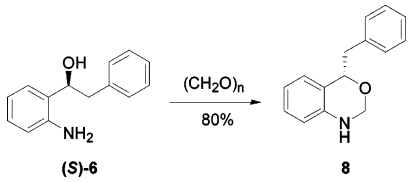


to the use of catalysts based on Ni, Pd, and Pt in order to improve the chemo- and regioselectivity of such reactions, even with enantiopure epoxides.[15] Different hydrogen sources, such as $HCOONH_4$,[16] or catalysts such as Pd/C−ethylendiamine complexes,[17] have been used to improve selectivity and to prevent further hydrogenolysis of the alcoholic C−O bond. Nevertheless, solvolysis with methanol remains a problem, particularly with benzylic epoxides. Recently, Pd nanoparticles, microencapsulated in polyurea, have been described to be very efficient in the reductive ring opening of different benzylic and alkyl epoxides.[18] Many reagents are known to perform mild reductions of the nitroaryl group, but no examples are described for such reactions in the presence of an oxiranyl ring.[19] Thus, we first tried $LiAlH_4$, which had been successfully employed with heteroaromatic epoxides,[10] but the reaction led to a mixture of several opening products in low chemical yield. The use of a milder system, as $FeCl_3 \cdot 6H_2O/H_2NNMe_2$,[20] also led to degradation products, while both hydrogenation with catalytic Ni_2B[21] and reduction with samarium and catalytic I_2[22] were inefficient. On the other hand, the use of procedures which could, in principle, transform both the nitro group and the oxiranyl ring were more successful. Catalytic hydrogenation over Pd/C of epoxide **4** led, quantitatively, to a 86/13 mixture of the two regioisomeric amino alcohols **6** and **7**. After chromatographic purification, amino alcohol **6** was obtained in excellent isolated yield (80%). Alternatively, treatment of epoxide **4** with $NaBH_4$ and a catalytic amount of Pd/C provided amino alcohol **7**, as the only isolable product, ingood yield.

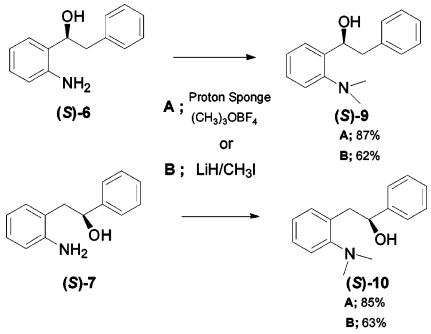
The amino alcohol (*S*)-**6** was first used as a suitable precursor of chiral benzoxazines. Thus, it was transformed into the corresponding benzoxazine **8** in good yield, by ring formation with paraformaldehyde,[23] without loss of sterechemical integrity at the benzylic carbon (Scheme 2).

The direct synthesis of ligands (*S*)-**9** and (*S*)-**10** (Scheme 3) required a chemoselective bis-methylation of the nitrogen, the hydroxyl group being untouched. Toward obtaining *N*,*N*-dialkylanilines, classical alkaline methylation methods with NaH or Ag_2O and CH_3I under various reaction conditions (THF, Et_2O, DMF, acetonitrile as solvents and at different temperatures) were not selective, leading to mixtures of *N*- and

SCHEME 2



SCHEME 3



O-methylated products. On the other hand, using the LiH/CH_3I system, *N*,*N*-dimethyl derivatives (*S*)-**9** and (*S*)-**10** were obtained in acceptable isolated yield (62−63%). Better results were obtained using [1,8-bis(dimethylamino)naphtalene] (Proton Sponge) as a base and trimethyloxonium tetrafluoroborate [$(CH_3)_3OBF_4$, Meerwein salt] as methylating agent, and the target products were obtained in excellent yield (85−87%), together with a small amount (<10%) of trimethylated compound.

This remarkably high *N*-selective methylation in strong alkali medium makes both of the procedures useful tools in the derivatization of different anilino alcohols. The 99% ee for both compounds (*S*)-**9** and (*S*)-**10** was determined by using chiral HPLC, confirming the ee of the starting compounds (*S*)-**6** and (*S*)-**7**.

In principle, the synthesis of **1** and **2**, as precursors of strong chiral bases, requires an *O*-alkylation and a *N*-monoalkylation, which are hardly achievable without the use of protecting groups. Therefore, amino alcohols (*S*)-**6** and (*S*)-**7** were transformed to *N*-Boc derivatives (*S*)-**11** and (*S*)-**12** in high yield by using a $Zn(ClO_4)_2 \cdot 6H_2O/Boc_2O$ system[24] (Scheme 4).

The derivatives were submitted without success to different methylation methods in alkali medium (NaH, LiH, Proton Sponge) and with various alkylating agents (CH_3I, $(CH_3)_2SO_4$, $(CH_3)_3OBF_4$). In the case of (*S*)-**11**, oxazolidinone **13** was the main reaction product in all cases, probably because of the high tendency of the substrate to form a six-membered ring via acyl nucleophilic substitution. In the case of (*S*)-**12**, only the $(CH_3)_3OBF_4$/Proton Sponge system was efficient, although it afforded dimethylated product (*S*)-**14** in poor yield.

To avoid competitive ring closure in alkali medium, we tried a recent *O*-*tert*-butyl alkylation procedure with the use of the couple $(Boc)_2O/Mg(ClO_4)_2$.[25] In order to optimize the synthetic route, the study on this last and following reactions was performed on *racemic* compounds.

Treatment of both *racemic* **11** and **12** with carefully dried

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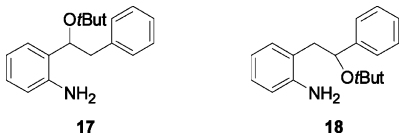
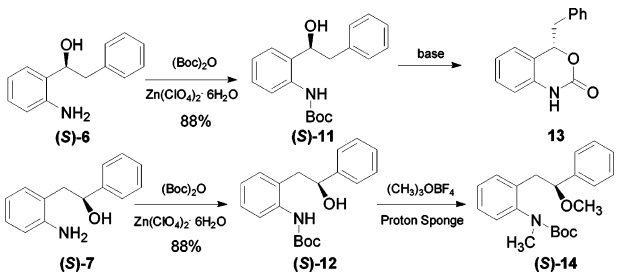
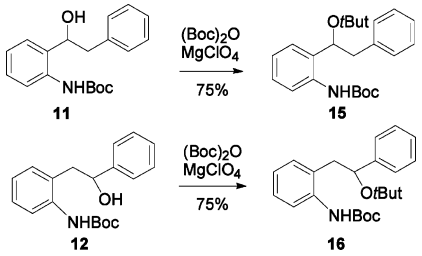


FIGURE 2. Anilino *tert*-butyl ethers **17** and **18**.

SCHEME 4



SCHEME 5



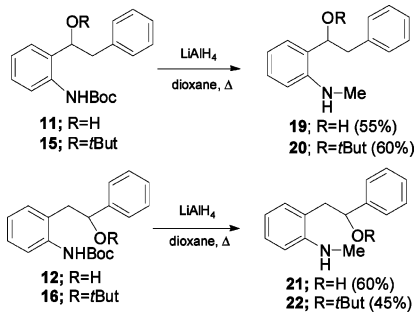
$Mg(ClO_4)_2$ and $(Boc)_2O$, at 40 °C in CH_2Cl_2, afforded the corresponding *O-tert* butyl ethers **15** and **16** in good yield (Scheme 5).

Interesting results, although useless for our synthetic purposes, were obtained when the reaction was performed with *wet* $Mg(ClO_4)_2$.[26] Under these conditions, both **11** and **12** underwent a complete deprotection, together with the expected *tert*-butyl alkylation, affording the corresponding anilinoethers **17** and **18**[27] (Figure 2). Such a transformation, if coupled with the previous *N*-Boc group introduction, represents an efficient two-step methodology for the chemoselective *O*-alkylation of aniline alcohols and competes with those using different NH_2 protecting groups.

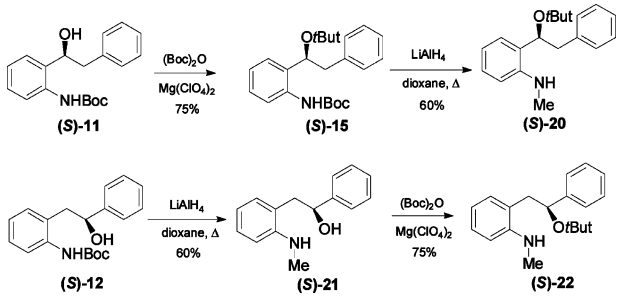
We then decided to transform the carbamate into methyl group by reduction with $LiAlH_4$, previously described only for the synthesis of tertiary methylamines from the corresponding *tert*-butyl carbamates.[28] Since there are no examples of such reactions on anilines, we tested the *racemic N*-Boc-aniline and *tert*-butyl ethers **11**, **12**, **15**, and **16** (Scheme 6). Modest to acceptable yields of the corresponding *N*-methyl derivatives were obtained in all cases. In particular, when the reaction was performed in refluxing 1,4-dioxane, the target *N*-methyl-*tert*-butyl ether **20** was obtained in promising yield from **15**, while for **22** the yield dropped significantly.

Higher overall yields of **22** were obtained by performing the alkylation on **21**, after the reduction of the carbamate, and this route was used for the synthesis of enantiopure derivative (*S*)-

SCHEME 6



SCHEME 7



22. On the other hand, the regioisomer (*S*)-**20** was prepared from (*S*)-**11**, in good yield, via alkylation and subsequent reduction (Scheme 7).

In conclusion, we have described the first examples of efficient, alternative, and regioselective reductions of substituted nonsymmetrical 2,3-diaryloxiranes. The opposite high regioselectivity, obtained on enantiopure (*R*,*R*)-2-(2-nitrophenyl)-3-phenyloxirane, represents a useful tool for divergent syntheses of various 1,2-anilinoarylethanols. We have also described new procedures for selective *N*- and *O*-alkylations, which allowed us to prepare new potential ligands and chiral bases.

Experimental Section

(1*S*)-1-(2-Aminophenyl)-2-phenylethanol (*S*)-6. A mixture of (*R*,*R*)-**4** (1 mmol) and Pd/C 10% (60 mg) in 20 mL of CH_3OH/AcOEt 9/1 was allowed to stir at room temperature under H_2 (1 atm). After 1 h, the catalyst was filtered off and the mixture was evaporated under vacuum. Chromatographic purification on silica gel (petroleum ether/Et_2O = 3/2) of the crude product yielded 86% of (*S*)-**6** and 13% of (*S*)-**7** as white crystals. (*S*)-**6** was recrystallized from Et_2O. Mp: 139 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.15 (A part of ABX system, $^2J_{AB}$ = 13.5 Hz, $^3J_{AX}$ = 5.0 Hz, 1H), 3.27 (B part of an ABX system, $^2J_{AB}$ = 13.5 Hz, $^3J_{BX}$ = 9.1 Hz, 1H), 3.30 (brs, 1H), 4.92 (X part of ABX system, $^3J_{AX}$ = 5.0 Hz, $^3J_{BX}$ = 9.1 Hz, 1H), 6.70 (dd, ^3J = 7.8 Hz, ^4J = 1.0 Hz, 1H), 6.74 (ddd, ^3J = ^3J = 7.8 Hz, ^4J = 1.0 Hz, 1H), 7.07 (dd, ^3J = 7.8 Hz, ^4J = 1.0 Hz, 1H), 7.13 (ddd, ^3J = ^3J = 7.8 Hz, ^4J = 1.0 Hz, 1H), 7.27 (m, 3H), 7.35 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.8, 75.3, 75.4, 116.9, 118.2, 126.6, 127.5, 128.5, 128.6, 129.5, 138.2, 145.0. MS (*m*/*z*): 213 [M^+] (7), 195 (35), 194 (33), 122 (100). $[\alpha]^{25}_D$: +33 (*c* 1.3, $CHCl_3$). Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.9; H, 7.2; N, 6.5.

(1*S*)-2-(2-Aminophenyl)-1-phenylethanol (*S*)-7. A mixture of $NaBH_4$ (6 mmol, 24 equiv) in H_2O (10 mL) was poured into a suspension of Pd/C 10% (100 mg) in CH_3OH (5 mL), under argon, and the mixture was cooled to 0 °C. A solution of epoxide (*R*,*R*)-**4** (1 mmol) in 10 mL of CH_3OH/AcOEt 9/1 was added dropwise. After 1 h, the catalyst was filtered off, and the reaction mixture was poured into an ice−water mixture and extracted with EtOAc. The organic phase was washed with brine, dried on anhydrous Na_2-

(26) In a typical procedure, a $MgClO_4/H_2O$ 1:10 molar ratio was used.

(27) When the reaction was performed on amino alcohols **6** and **7**, an approximately equimolar mixture of the different products **11**, **12**, **17**, **18**, and *N*-Boc *tert*-butyl ethers was formed.

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SO_4, and evaporated under vacuum. Chromatographic purification on silica gel (*n*-hexane/Et_2O = 3/2) of the crude product yielded 64% of (*S*)-**7** as a white crystal. Mp: 95 °C (recrystallized from Et_2O). ^1H NMR (500 MHz, $CDCl_3$): δ = 2.90 (A part of ABX system, $^2J_{AB}$ = 14.0 Hz, $^3J_{AX}$ = 3.5 Hz, 1H), 3.03 (B part of ABX system, $^2J_{AB}$ = 14.0 Hz, $^3J_{BX}$ = 9.0 Hz, 1H), 5.00 (X part of ABX system, $^3J_{AX}$ = 3.5 Hz, $^3J_{BX}$ = 9.0 Hz, 1H), 6.74 (d, ^3J = 7.8 Hz, 1H), 6.78 (dd, ^3J = ^3J = 7.8 Hz, 1H), 7.02 (d, ^3J = 7.8 Hz, 1H), 7.10 (dd, ^3J = ^3J = 7.8 Hz, 1H), 7.30 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.8, 75.8, 116.7, 119.7, 124.3, 125.9, 127.9, 128.5, 131.5, 144.4, 145.5. MS (*m*/*z*): 213 [M^+] (11), 193 (16), 107 (100), 106 (71), 79 (22), 77 (26). $[\alpha]^{25}_D$: −2.5 (*c* 1.6 $CHCl_3$). Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.7; H, 7.1; N, 6.4.

(4*S*)-4-Benzyl-1,4-dihydro-2*H*-benzo[*d*][1,3]oxazine 8. To a mixture of paraformaldehyde (20 mg, 2 equiv) in benzene (20 mL) was added a solution of 60 mg (0.3 mmol) of (*S*)-**6** in 5 mL of benzene, and the reaction mixture was kept at reflux for 1 h. Once cooled to room temperature, the solvent was removed, and the crude was dissolved in diethyl ether, washed with H_2O, dried with anhydrous Na_2SO_4, and evaporated under vacuum. Compound **8** was obtained in 95% yield as an oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.06 (A part of ABX system, $^2J_{AB}$ = 14.2 Hz, $^3J_{AX}$ = 8.1 Hz, 1H), 3.28 (B part of ABX system, $^2J_{AB}$ = 14.2 Hz, $^3J_{BX}$ = 3.4 Hz, 1H), 4.24 (s, 1H), 4.57 (A part of AB system, $^2J_{AB}$ = 10.3 Hz, 1H), 4.84 (B part of AB system, $^2J_{AB}$ = 10.3 Hz, 1H), 5.22 (X part of ABX system, $^3J_{AX}$ = 8.1 Hz, $^3J_{BX}$ = 3.4 Hz, 1H), 7.03 (m, 2H), 7.25 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 42.2, 72.8, 76.2, 118.9, 120.6, 125.7, 126.4, 127.5, 128.3, 129.4, 129.6, 138.4. MS (*m*/*z*): 225 [M^+] (7), 194 (2), 134 (100), 116 (9), 106 (7), 91 (14), 77 (14). $[\alpha]^{25}_D$: −27 (*c* 0.5 $CHCl_3$). Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.8; H, 6.7; N, 6.3.

(1*S*)-1-(2-*N*,*N*-Dimethylaminophenyl)-2-phenylethanol (*S*)-9 was obtained in 87% (method A) and 62% yield (method B) from (*S*)-**6** after chromatographic purification on silica gel (petroleum ether/Et_2O = 3/2). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.61 (s, 6H), 3.11 (AB part of ABX system, $^2J_{AB}$ = 14.4 Hz, $^3J_{AX}$ = 7.5 Hz, $^3J_{BX}$ = 5.5 Hz, 2H), 5.18 (X part of ABX system, $^3J_{AX}$ = 7.5 Hz, $^3J_{BX}$ = 5.5 Hz, 1H), 7.10−7.31 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.2, 75.1, 122.1, 125.2, 126.0, 127.9, 128.1, 130.0, 138.2, 138.9, 152.0. MS (*m*/*z*): 241 [M^+] (9), 223 (69), 150 (100), 132 (24), 120 (27), 106 (27), 91 (28) (99% ee; HPLC Chiralcel OD, *n*-hexane/2-propanol 90/10, 0.5 mL/min). $[\alpha]^{25}_D$: −2.0 (*c* 1.2, $CHCl_3$). Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N; 5.80. Found: C, 79.5; H, 7.9; N 5.8.

(1*S*)-2-(2-*N*,*N*-Dimethylaminophenyl)-1-phenylethanol (*S*)-10 was obtained in 85% (method A) and 63% yield (method B) from (*S*)-**7** after chromatographic purification on silica gel (petroleum ether/Et_2O = 2/3). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.80 (s, 6H), 3.09 (A part of ABX system, $^2J_{AB}$ = 14.4 Hz, $^3J_{AX}$ = 2.2 Hz, 1H), 3.24 (B part of ABX system, $^2J_{AB}$ = 14.4 Hz, $^3J_{BX}$ = 8.5 Hz, 1H), 4.97 (X part of ABX system, $^3J_{AX}$ = 2.2 Hz, $^3J_{BX}$ = 8.5 Hz, 1H), 7.08 (m, 3H), 7.25−7.45 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.9, 44.9, 75.8, 76.5, 120.1, 125.3, 125.6, 126.8, 127.9, 128.0, 132.0, 145.5, 151.8. MS (*m*/*z*): 241 [M^+] (9), 223 (9), 207 (22), 134 (100), 118 (22), 91 (15) (99% ee; HPLC Chiralcel OD, *n*-hexane/2-propanol 90/10, 0.5 mL/min). $[\alpha]^{25}_D$: −73.0 (c 1.0, $CHCl_3$). Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N; 5.80. Found: C, 79.7; H, 7.9; N 5.7.

(1*S*)-1-(2-*N*-Boc-aminophenyl)-2-phenylethanol *tert*-Butyl Ether (*S*)-15. Anhydrous $Mg(ClO_4)_2$ (0.10 mmol) and (*S*)-**11** (1 mmol) were dissolved in 15 mL of anhydrous CH_2Cl_2. Then Boc_2O (2.3 mmol) was added, and the mixture was stirred at reflux for 24 h. The crude was poured into ice−water and extracted with CH_2Cl_2. The *tert*-butyl ether (*S*)-**15** was purified by chromatography on silica gel with a mixture of petroleum ether/Et_2O = 4:1 and obtained in 75% yield as colorless oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 9H), 1.57 (s, 9H), 2.86 (A part of ABX system, $^2J_{AB}$ = 13.2 Hz, $^3J_{AX}$ = 5.5 Hz, 1H), 3.04 (B part of ABX system, $^2J_{AB}$ = 13.2 Hz, $^3J_{BX}$ = 8.4 Hz, 1H), 4.61 (X part of ABX system, $^3J_{AX}$ = 5.5 Hz, $^3J_{BX}$ = 8.4 Hz, 1H), 6.90 (m, 2H), 7.20 (m, 6H), 8.07 (d, ^3J = 7.9 Hz, 1H), 9.04 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 27.8, 28.4, 44.0, 75.4, 78.2, 79.5, 120.2, 122.1, 125.8, 126.1, 127.4, 127.9, 129.9, 131.1, 137.6, 138.5, 153.2. $[\alpha]^{25}_D$: −9 (c 1, $CHCl_3$). MS (*m*/*z*): 369 (1) [M], 278 (11), 222 (30), 166 (63), 122 (100). Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.8; H, 8.6; N, 3.6.

(1*S*)-1-(2-*N*-Methylaminophenyl)-2-phenylethanol *tert*-Butyl Ether (*S*)-24. Following the above procedure on compound (*S*)-**19** and after chromatographic purification on silica gel (petroleum ether/Et_2O = 3:2), (*S*)-**24** was obtained in 60% yield as an oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.88 (s, 9H), 2.79 (s, 3H), 2.83 (A prt of ABX system, $^2J_{AB}$ = 13.5 Hz, $^3J_{AX}$ = 5.4 Hz, 1H), 3.05 (B part of ABX system, $^2J_{AB}$ = 13.5 Hz, $^3J_{BX}$ = 8.6 Hz, 1H), 4.49 (X part of ABX system, $^3J_{AX}$ = 5.4 Hz, $^3J_{BX}$ = 8.6 Hz, 1H), 6.49 (dd, ^3J = ^3J = 7.3 Hz, 1H), 6.56 (d, ^3J = 7.3 Hz, 1H), 6.72 (d, ^3J = 7.3 Hz, 1H), 7.15 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.1, 30.2, 42.5, 44.6, 74.7, 111.5, 116.3, 125.9, 127.5, 127.6, 127.9, 128.5, 130.0, 133.5, 139.4. $[\alpha]^{25}_D$: −8.7 (c 1, $CHCl_3$). Anal. Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.4; H, 8.9; N, 5.0.

(1*S*)-2-(2-*N*-Methylaminophenyl)-1-phenylethanol (*S*)-21. To a solution of (*S*)-**12** (1 mmol) in 20 mL of 1,4-dioxane was added $LiAlH_4$ (1 mmol, 4 equiv) in one portion, and the reaction mixture was refluxed for 3 h. The crude was then poured into ice−water and extracted with Et_2O (3 × 20 mL). The organic layers were collected, dried with anhydrous Na_2SO_4, and evaporated under vacuum. After chromatographic purification on silica gel (petroleum ether/Et_2O = 3:2), (*S*)-**21** was obtained in 60% yield as oil. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.82 (s, 3H), 2.90 (A part of ABX system, $^2J_{AB}$ = 14.1 Hz, $^3J_{AX}$ = 4.0 Hz, 1H), 3.00 (B part of ABX system, $^2J_{AB}$ = 14.1 Hz, $^3J_{BX}$ = 8.6 Hz, 1H), 4.95 (X part of ABX system, $^3J_{AX}$ = 4.0 Hz, $^3J_{BX}$ = 8.6 Hz, 1H), 6.74 (m, 2H), 7.03 (d, ^3J = 6.6 Hz, 1H), 7.30 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 30.9, 41.9, 75.4, 110.7, 117.5, 123.6, 125.6, 127.6, 128.0, 128.4, 130.9, 144.2, 148.0. $[\alpha]^{25}_D$: −4.0 (*c* 0.5, $CHCl_3$). MS (*m*/*z*): 227 [M^+] (18), 209 (11), 132 (28), 121 (49), 120 (100), 106 (11), 91 (22), 77 (13). Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.4; H, 7.3; N, 6.3.

(1*S*)-2-(2-*N*-Methylaminophenyl)-1-phenylethanol *tert*-Butyl Ether (*S*)-22. Following the procedure described for compound (*S*)-**15**, (*S*)-**22** was obtained from (*S*)-**21** in 75% yield as a colorless oil after purification by chromatography on silica gel with a mixture of petroleum ether/Et_2O = 4:1. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (s, 9H), 2.82 (s, 3H), 2.84 (A part of ABX system, $^2J_{AB}$ = 14.0 Hz, $^3J_{AX}$ = 3.8 Hz, 1H), 2.95 (B part of ABX system, $^2J_{AB}$ = 14.0 Hz, $^3J_{BX}$ = 8.4 Hz, 1H), 4.90 (X part of ABX system, $^3J_{AX}$ = 3.8 Hz, $^3J_{BX}$ = 8.4 Hz, 1H), 6.73 (m, 2H), 6.94 (d, ^3J = 6.8 Hz, 1H), 7.21 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.7, 31.9, 41.9, 43.6, 75.4, 112.6, 119.3, 124.7, 125.6, 127.7, 128.2, 128.5, 131.2, 143.9, 146.4. MS (*m*/*z*): 283 [M^+] (26), 210 (8)163 (36), 121 (17), 120 (8), 107 (100), 91 (19), 57 (22). $[\alpha]^{25}_D$: −6.0 (c 0.3, $CHCl_3$). Anal. Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.6; H, 8.9; N, 4.8.

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Supporting Information Available: Experimental procedures for compounds (*R*,*R*)-**4**, (*S*)-**9**, (*S*)-**10**, (*S*)-**11**, (*S*)-**12**, **13**, **14**, **16**−**18**, and (*S*)-**19**. ^1H and ^{13}C NMR of compounds **6**−**12**, **15**, and **20**−**22**. This material is available free of charge via the Internet at http://pubs.acs.org.

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