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Synthesis of new chiral amino ether derivatives: synthetic application of *meso* aziridinium ions prepared from β-amino alcohols

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Abstract—Methods of synthesis of new chiral amino ether derivatives through the opening of aziridinium ions, prepared in situ using *trans*-(±)-2-(1-*N*,*N*-dialkylamino)cyclohexyl mesylate with (*R*)-(+)-1,1′-bi-2-naphthol, are described. The (*R*,*R*,*R*)-diastereomer was obtained as the major product and isolated as an enantiopure salt, and characterized by single crystal X-ray analysis. The C_2-chiral (*R*,*R*,*R*,*R*,*R*)-diamino ether was obtained as the major product by opening of the aziridinium ion, prepared using *trans*-(±)-2-(1-pyrrolidino)cyclohexyl mesylate and (*R*)-(+)-1,1′-bi-2-naphthol in the presence of aq NaOH. This was also characterized by single crystal X-ray analysis.

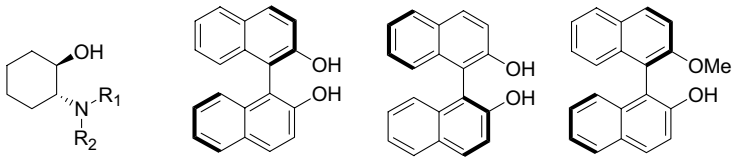
1. Introduction

Chiral amino alcohols are an important class of compounds used widely in asymmetric synthesis[1] for the preparation of chiral catalysts or chiral auxiliaries and in medicinal chemistry as therapeutic agents.[2] Over the past few years, many chiral diamine and amino alcohol ligands have been prepared for application in asymmetric synthesis and for use as intermediates in the synthesis of some analgesics, through reaction of aziridinium ions,[3–8] prepared in situ using chiral amino alcohols. We report herein the results of the reaction of (*R*)-(+)-1,1′-bi-2-naphthol **2** and its derivatives **3** with aziridinium ion intermediate prepared in situ using the racemic amino alcohol **1**.

2. Results and discussion

We have observed that the reaction of aziridinium ion intermediate **4a**, prepared in situ using *trans*-(±)-2-(1-*N*,*N*-dialkylamino) cyclohexanol **1a**, MsCl and Et_3N in THF, with (*R*)-(+)-1,1′-bi-2-naphthol gives the salt (−)-(*R*,*R*,*R*)-**5a**, along with a diastereomeric mixture of the salts of (*R*,*R*,*R*)-**5a** and (*R*,*S*,*S*)-**5b** (Scheme 1).

The HCl salt of (−)-(*R*,*R*,*R*)-**5a** was crystallized from methanol to obtain crystals suitable for single crystal X-ray analysis.[9] The X-ray structure revealed that the configuration at C1 and C2 of the pyrrolidinylcyclohexyl moiety in (−)-(*R*,*R*,*R*)-**5a** is *R*,*R*. The ORTEP diagram of the salt (−)-(*R*,*R*,*R*)-**5a** is shown



(±)-1 (+)-(*R*)-2 (-)-(*S*)-2 (-)-(*R*)-3

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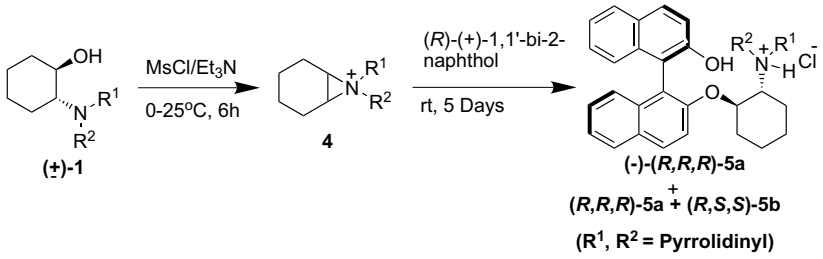


Scheme 1.

in Figure 1. The HCl, salt upon treatment with aq NH_3, gave the free amino ether (−)-(*R*,*R*,*R*)-**8a**.

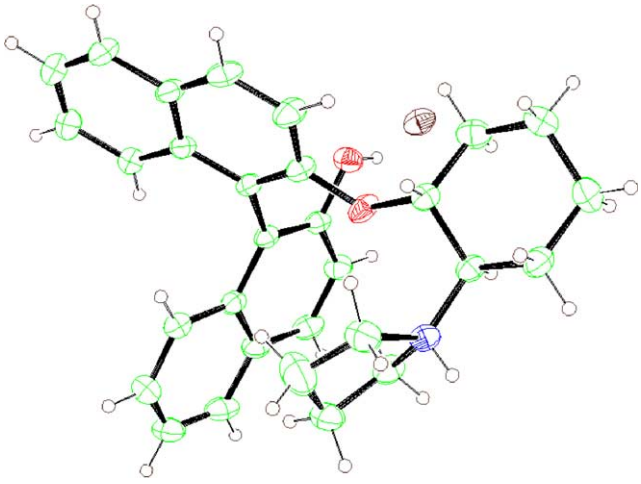
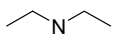


Figure 1. ORTEP diagram of compound **5a**.

The reaction was examined under various conditions in order to optimize the results. It was found that using an excess of *trans*-(±)-2-(1-pyrrolidinyl)-cyclohexanol **1a** (6 mmol) with (*R*)-(+)-1,1′-bi-2-naphthol (2 mmol) in 20 mL of THF, the salt (−)-(*R*,*R*,*R*)-**5a** was obtained in 35% yield after 48 h along with the corresponding diastereomeric mixture of the salts of (*R*,*R*,*R*)-**5a** and (*R*,*S*,*S*)-**5b** in 50% yield. The reaction of the *trans*-(±)-2-(1-pyrrolidinyl)-cyclohexanol **1a** (2 mmol) with (*R*)-(+)-1,1′-bi-2-naphthol (1 mmol) in 10 mL of THF, under refluxing conditions for 24 h gave a diastereomeric mixture of (*R*,*R*,*R*)-**5a** and (*R*,*S*,*S*)-**5b** in 70% yield. The reaction of *trans*-(±)-2-(1-pyrrolidinyl) cyclohexanol **1a** (10 mmol) with (*R*)-(+)-1,1′-bi-2-naphthol (5 mmol) in 25 mL of THF, gave the HCl salt (−)-(*R*,*R*,*R*)-**5a** in 20% yield with its diastereomeric mixture (*R*,*R*,*R*)-**5a** and (*R*,*S*,*S*)-**5b** obtained in 55% yield after 5 days. Using 100 mL of THF, the salt (−)-(*R*,*R*,*R*)-**5a** was obtained in 60% yield and its diastereomeric HCl salt mixture (*R*,*R*,*R*)-**5a** and (*R*,*S*,*S*)-**5b** obtained in 30% yield (Table 1, entry no 1).

This transformation (Scheme 1) was also examined using amino alcohols **1b** and **1c** with the results summarized in Table 1. The reaction of *trans*-(±)-2-(1-*N*,*N*-diethylamino)cyclohexanol **1b** (4 mmol) with (*R*)-(+)-1,1′-bi-2-naphthol (2 mmol) in 40 mL of THF, gave the HCl salt (−)-**6a** in 60% yield and the corresponding diastereomeric HCl salt mixture in 30% yield (Table 1, entry no 2). The reaction of *trans*-(±)-2-(piperidinyl)cyclohexanol **1c** (4 mmol) with (*R*)-(+)-1,1′-bi-2-naphthol (2 mmol) in 40 mL of THF, gave the HCl salt

Table 1. Opening of *meso* aziridinium ions **1a** using (*R*)-(+)-bi-2-naphthol

Entry no	NR^1R^2 **1a–c**	Yield[a,b] (%) (enantiopure HCl salt) **5a–7a**	Yield (%)[a] (diastereomeric HCl salt)[c] **5a** and **5b–7a** and **7b**
1[d]	 **1a**	60 **5a**	30 **5a** and **5b**
2[e]	 **1b**	60 **6a**	30 **6a** and **6b**
3[e]	 **1c**	40 **7a**	35 **7a** and **7b**

[a] Yields are of the isolated product. The yields were calculated based on the (*R*)-(+)-1,1′-bi-2-naphthol used.
[b] The products were identified using IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis for the corresponding free amino ethers.
[c] The diastereomeric ratios were found to be approximately 1:1 from the ^{13}C NMR data of the diastereomeric mixtures of free amino ethers after separation of the enantiomerically pure HCl salt **5a–7a**.
[d] The reaction was carried out using amino alcohol (10 mmol), Et_3N (30 mmol), MsCl (12 mmol) and (*R*)-(+)-bi-2-naphthol (5 mmol) in 100 mL of THF, at 25 °C for 5 days.
[e] The reactions were carried out using amino alcohol (4 mmol), Et_3N (12 mmol), MsCl (4.8 mmol) and (*R*)-(+)-bi-2-naphthol (2 mmol) in 40 mL of THF, at 25 °C for 5 days.

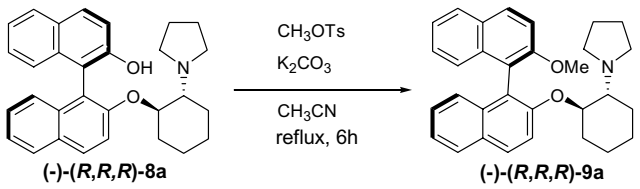
(−)-**7a** in 40% yield and its diastereomeric salt mixture in 35% yield (Table 1, entry no 3). The free amino ethers were obtained by aq NH_3 treatment of the corresponding HCl salts.

It was found that the reaction of monomethoxy-1,1′-bi-2-naphthol (−)-(*R*)-**3** (1 mmol) using excess *trans*-(±)-2-(1-pyrrolidinyl)-cyclohexanol **1a** (6 mmol) gave the diastereomeric free amines mixture (−)-(*R*,*R*,*R*)-**9a** and (+)-(*R*,*S*,*S*)-**9b** in 60% yield; in this case no HCl salt was obtained.

We have also examined the reaction of (*R*)-(−)-monomethoxy-1,1′-bi-2-naphthol (−)-(*R*)-**3** in the presence of aq NaOH, which was expected to increase the nucleophilicity of 1,1′-bi-2-naphthyl moiety. In this run, the reaction at 25 °C gave the diastereomeric mixture (−)-(*R*,*R*,*R*)-**9a** and (+)-(*R*,*S*,*S*)-**9b** in 70% yield whereas under refluxing conditions, the diastereomeric mixture (−)-(*R*,*R*,*R*)-**9a** and (+)-(*R*,*S*,*S*)-**9b** was obtained in 80% yield. Both the isomers could be readily separated by column chromatography on silica gel (Scheme 2).

(−)-(*R*,*R*,*R*)-**9a** was also prepared from free amino ether (−)-(*R*,*R*,*R*)-**8a** obtained by neutralization of the HCl salt (−)-(*R*,*R*,*R*)-**5a** using ammonium hydroxide, methyl tosylate and K_2CO_3 in acetonitrile (Scheme 3). Accordingly, compound (−)-**9a** was assigned the (*R*,*R*,*R*)-configuration and the compound (+)-**9b** was assigned the (*R*,*S*,*S*)-configuration.

We then examined the reaction of the (*R*)-(+)-1,1-bi-2-naphthol with the mesylate of (±)-**1a** in the presence of NaOH. It was found that the reaction at 25 °C gave a diastereomeric mixture of free amino ethers (*R*,*R*,*R*)-**8a** and (*R*,*S*,*S*)-**8b** in 53% yield along with a diastereomeric mixture of (*R*)-(+)-1,1′-bi-2-naphthyl derived diamino

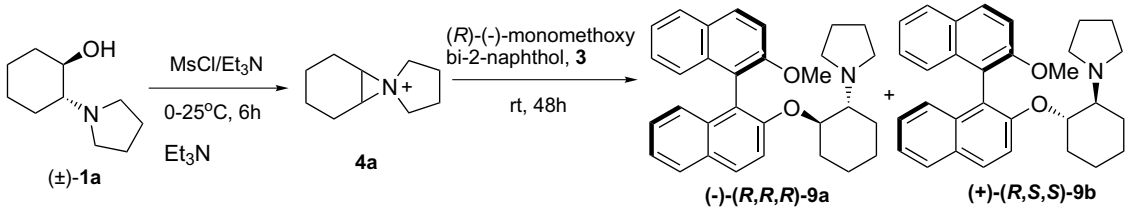


Scheme 3.

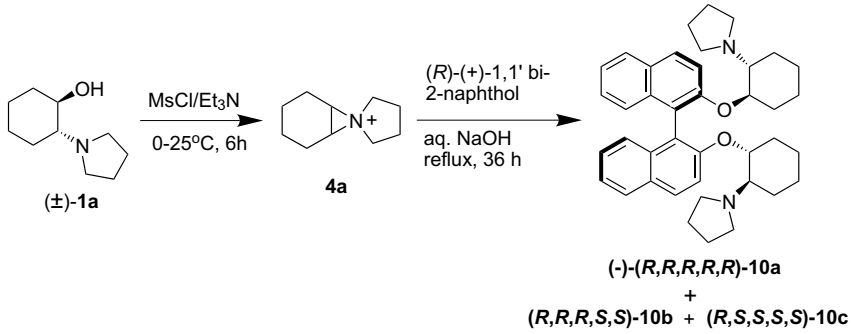
ether **10** in 17% yield. Whereas under refluxing conditions, the diastereomeric mixture of free amino ethers (*R*,*R*,*R*)-**8a** and (*R*,*S*,*S*)-**8b** was obtained in 20% yield and the diastereomeric mixture of diamino ether **10** was obtained in 60% yield. The C_2 symmetric compound (−)-(*R*,*R*,*R*,*R*,*R*)-**10a** was readily isolated in 34% yield from the diastereomeric mixture by column chromatography on silica gel (Scheme 4).

In order to assign the stereochemical configuration of the diamino ether (−)-(*R*,*R*,*R*,*R*,*R*)-**10a**, the reaction of aziridinium ion intermediate **4a** with the free amino ether (−)-(*R*,*R*,*R*)-**8a** was performed. The resulting diastereomeric mixture was separated. The C_2 symmetric isomer obtained in the transformation shown in Scheme 4 had $[\alpha]_D^{25} = -116$, same as that observed for (−)-(*R*,*R*,*R*,*R*,*R*)-**10a** obtained in the transformation shown in Scheme 5. Accordingly, the C_2 symmetric compound (−)-**10a** was assigned the configuration as (*R*,*R*,*R*,*R*,*R*) (Schemes 4 and 5).

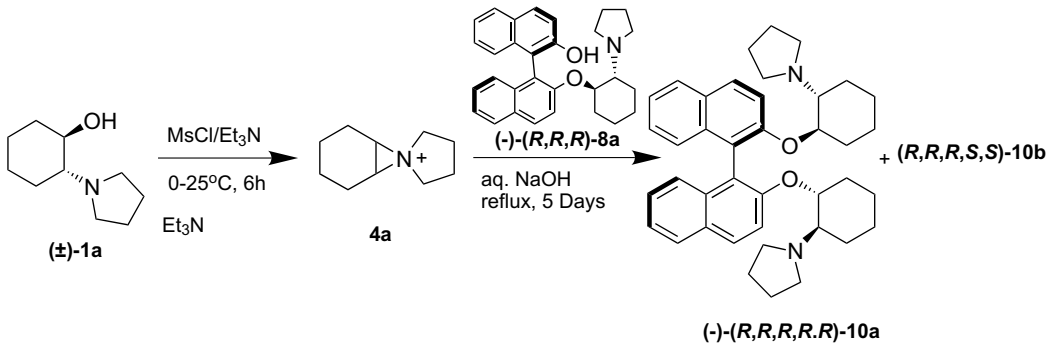
A sample of the C_2 symmetric compound (−)-(*R*,*R*,*R*,*R*,*R*)-**10a** crystallized from dichloromethane/hexane mixture was not suitable for single crystal X-ray analysis. When the sample was further crystallized from a chloroform/methanol mixture and again recrystallized from acetone, crystals suitable for X-ray analysis



Scheme 2.



Scheme 4.



Scheme 5.

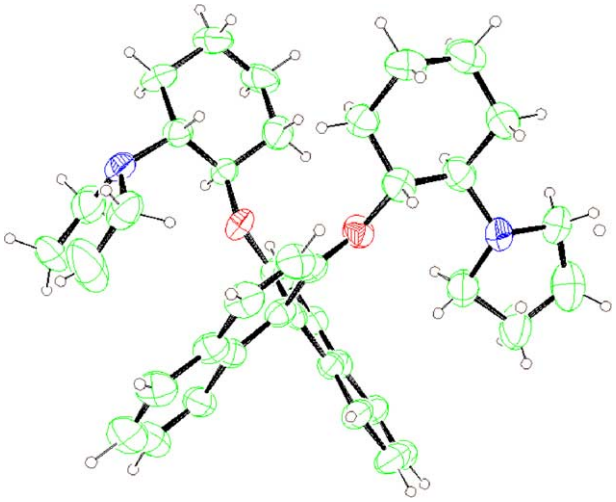


Figure 2. ORTEP diagram of compound **10a**.

were obtained.[10] The X-ray structure clearly confirmed an (*R*,*R*,*R*,*R*)-configuration. The ORTEP diagram of the (−)-(*R*,*R*,*R*,*R*)-**10a** is shown in Figure 2.

3. Conclusion

In conclusion, a series of chiral amino ether derivatives were obtained through the opening of an aziridinium ion using chiral 1,1′-bi-2-naphthol. The methods described here should be useful in the preparation of such chiral ligands of increasing complexity for further synthetic exploitations.

4. Experimental

4.1. Preparation of compounds 5a–7a and 8a–c: general procedure

To a solution of *trans*-(±)-2-(1-pyrrolidinyl)cyclohexanol **1a** (1.69 g, 10 mmol) in dry THF (100 mL) was added Et_3N (3.93 mL, 30 mmol) and MsCl (0.95 mL, 12 mmol) at 0 °C with stirring and the contents allowed to stir at room temperature for 6 h. Et_3N (2.62 mL, 20 mmol) was added. After stirring for 2 h, (*R*)-(+)-1,1′-bi-2-naphthol (1.43 g, 5 mmol) was added in THF (15 mL) and allowed to stir at 25 °C for 5 days. Water (10 mL) was added and the mixture was extracted with ether (2 × 50 mL), washed with brine, dried over anhydrous $MgSO_4$ and concentrated in vacuo to yield a gummy residue. Ether (15 mL) was added and a white solid precipitated. After evaporation of ether, a diastereomeric mixture of (*R*,*R*,*R*)-**5a** and (*R*,*S*,*S*)-**5b** was isolated. The precipitated fraction was washed with ether (10 mL), DCM (5 mL) and THF (5 mL) to obtain the salt (−)-(*R*,*R*,*R*)-**5a**. A solution of aq NH_3 (25 mL) and ether (30 mL) were added to the salt at 0 °C and stirred for 15 min. After obtaining a clear solution, the organic layer was separated and the aqueous layer extracted with ether (2 × 25 mL). The combined organic extract was washed with H_2O, brine and dried over $MgSO_4$. After evaporation, the compound (−)-(*R*,*R*,*R*)-**8a** was obtained.

4.1.1. Spectral data: (−)-(*R*,*R*,*R*)-5a. 1.42 g, 60% yield and (5 mmol) of (*R*)-(+)-1,1′-bi-2-naphthol was used. Mp >300 °C; $[\alpha]_D^{25} = -92$ (*c* 0.22, CH_3OH); IR (KBr): 3123, 3050, 2939, 2636, 1622, 1589, 1506, 1433, 1342, 1265, 1238, 1084, 810, 773, 748, 694 cm^{-1}. Stereochemical configuration was assigned by X-ray crystal structure analysis.

4.1.2. (−)-(*R*,*R*,*R*)-8a. 1.25 g, 57% yield and (5 mmol) of (*R*)-(+)-1,1′-bi-2-naphthol was used. Mp 71–72 °C; $[\alpha]_D^{25} = -170$ (*c* 0.09, $CHCl_3$); IR (KBr): 3450, 3057, 2932, 2856, 1620, 1591, 1506, 1460, 1263, 1238, 812, 748 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.9–1.7 (m, 12H), 1.8–2.0 (m, 1H), 2.1–2.4 (m, 5H), 4.3–4.5 (m, 1H), 6.9–7.6 (m, 8H), 7.8–8.1 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 22.2, 22.5, 23.1, 27.7, 28.4, 51.2, 63.3, 78.4, 115.7, 116.8, 117.5, 123.0, 124.2, 125.2, 126.1, 127.0, 127.9, 128.0, 129.1, 129.5, 130.5, 134.2, 134.5, 151.4, 154.1; MS (EI): *m*/*z* 437 (m^+). Anal. Calcd for $C_{30}H_{31}NO_2$: C, 82.35; H, 7.14; N, 3.20. Found: C, 82.44; H, 7.18; N, 3.17.

4.1.3. (−)-(*R*,*R*,*R*)-6a. 0.57 g, 60% yield and (2 mmol) of (*R*)-(+)-1,1′-bi-2-naphthol was used. Mp >300 °C; $[\alpha]_D^{25} = -30$ (*c* 0.14, CH_3OH); IR (KBr): 3117, 2939, 2644, 1622, 1589, 1506, 1433, 1342, 1265, 1238, 1084, 810, 773, 748, 694 cm^{-1}.

4.1.4. (−)-(*R*,*R*,*R*)-8b. 0.48 g, 55% yield and (2 mmol) of (*R*)-(+)-1,1′-bi-2-naphthol was used. Mp 85–86 °C; $[\alpha]_D^{25} = -75$ (*c* 0.20, $CHCl_3$); IR (KBr): 3497, 3057,

2935, 2858, 1620, 1591, 1504, 1462, 1263, 1238, 808, 746 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.55 (t, $J = 10$ Hz, 6H), 1.1–1.4 (m, 5H), 1.5–1.7 (m, 3H), 1.9–2.2 (m, 5H), 2.4–2.5 (m, 1H), 4.2–4.4 (m, 1H), 7.0–7.5 (m, 8H), 7.8–8.1 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.0, 24.1, 25.2, 29.9, 31.4, 44.4, 62.1, 78.2, 115.7, 116.1, 117.1, 117.4, 123.0, 124.0, 125.1, 125.3, 126.1, 127.0, 127.8, 128.0, 129.4, 129.5, 130.4, 134.2, 134.6, 151.3, 154.0. MS (EI): *m/z* 439 (m^+). Anal. Calcd for $C_{30}H_{33}NO_2$: C, 81.97; H, 7.57; N, 3.19. Found: C, 82.18; H, 7.51; N, 3.26.

4.1.5. (−)-(*R*,*R*,*R*)-7a. 0.39 g, 40% yield and (2 mmol) of (*R*)-(+)-1,1′-bi-2-naphthol was used. Mp >300 °C; $[\alpha]_D^{25} = -91$ (*c* 0.12, CH_3OH); IR (KBr): 3082, 2934, 1620, 1589, 1506, 1433, 1267, 1234, 1084, 810, 773, 748, 694 cm^{-1}.

4.1.6. (−)-(*R*,*R*,*R*)-8c. 0.34 g, 38% yield and (2 mmol) of (*R*)-(+)-1,1′-bi-2-naphthol was used. Mp 79–80 °C; $[\alpha]_D^{25} = -136$ (*c* 0.32, $CHCl_3$); IR (KBr): 3506, 3055, 2930, 2854, 1620, 1591, 1504, 1462, 1263, 1238, 810, 746 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.0–1.4 (m, 11H), 1.5–1.7 (m, 3H), 1.9–2.1 (m, 3H), 2.1–2.2 (m, 3H), 4.1–4.3 (m, 1H), 7.1–7.5 (m, 8H), 7.8–8.0 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.1, 24.6, 25.0, 26.7, 28.3, 31.3, 50.5, 67.3, 77.7, 115.8, 116.9, 117.3, 117.6, 123.0, 124.0, 125.2, 125.4, 126.2, 126.9, 127.9, 128.0, 129.2, 129.5, 130.2, 134.3, 134.6, 151.5, 154.0. MS (EI): *m/z* 451 (m^+). Anal. Calcd for $C_{31}H_{33}NO_2$: C, 82.45; H, 7.37; N, 3.10. Found: C, 82.62; H, 7.35; N, 3.09.

4.2. Preparation of (−)-(*R*,*R*,*R*)-9a and (+)-(*R*,*S*,*S*)-9b

To a solution of *trans*-(±)-2-(1-pyrrolidinyl)cyclohexanol **1a** (0.34 g, 2 mmol) in dry THF (20 mL) was added Et_3N (0.84 mL, 6 mmol) and MsCl (0.188 mL, 2.4 mmol) at 0 °C and the contents allowed to stir at 25 °C for 6 h. Et_3N (0.56 mL, 4 mmol) was added. After stirring for 2 h, (−)-(*R*)-3-monomethoxy-bi-2-naphthol (0.6 g, 2 mmol) was added in THF (10 mL) followed by NaOH (0.16 g, 4 mmol) in H_2O (2 mL) and allowed to reflux for 48 h. A solution of aq NH_3 was added (30% solution, 5 mL). The mixture was extracted with ether (2 × 25 mL), washed with brine and dried over anhydrous $MgSO_4$ and concentrated to obtained diastereomeric mixture of (−)-(*R*,*R*,*R*)-**9a** and (+)-(*R*,*S*,*S*)-**9b** (0.72 g, 80% yield). The mixture of (−)-(*R*,*R*,*R*)-**9a** and (+)-(*R*,*S*,*S*)-**9b** was purified on silica gel column using chloroform/methanol (98:2) as eluent to isolate the isomer (−)-(*R*,*R*,*R*)-**9a** (0.38 g, 42% yield) and (+)-(*R*,*S*,*S*)-**9b** (0.25 g, 28% yield). For (−)-(*R*,*R*,*R*)-**9a** mp 114–115 °C; $[\alpha]_D^{25} = -87$ (*c* 0.23, $CHCl_3$); IR (KBr) 3055, 2928, 2862, 2793, 1622, 1593, 1508, 1460, 1354, 1263, 1091, 1020, 808, 775, 740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.75–1.85 (m, 11H), 2.05–2.24 (m, 1H), 2.25–2.45 (m, 1H), 2.5–3.0 (m, 4H), 3.78 (s, 3H), 4.5–4.7 (m, 1H), 6.9–7.5 (m, 8H), 7.87 (t, $J = 8$ Hz, 2H), 7.95 (d, $J = 10$ Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 22.6, 22.9, 24.1, 28.3, 30.4, 52.6, 56.4, 66.5, 75.9, 113.8, 115.4, 119.2, 121.5, 123.5, 124.1, 125.1, 125.3, 126.3, 126.6, 128.0, 129.0, 129.6, 134.2, 135.3, 150.8, 154.8; MS (EI): *m/z* 451 (m^+). Anal. Calcd for $C_{31}H_{33}NO_2$: C, 82.45; H, 7.36; N, 3.10. Found: C, 82.51; H, 7.32; N, 3.14. For (+)-(*R*,*S*,*S*)-**9b** mp 129–130 °C; $[\alpha]_D^{25} = +106$ (*c* 0.18, $CHCl_3$); IR (KBr) 3052, 2926, 2864, 2793, 1622, 1593, 1507, 1460, 1356, 1265, 1090, 1020, 808, 775, 742 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.7–1.9 (m, 13H), 2.0–2.3 (m, 2H), 2.6–3.2 (m, 2H), 3.75 (s, 3H), 4.3–4.5 (m, 1H), 7.0–7.5 (m, 8H), 7.7–8.1 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 19.2, 22.4, 23.1, 27.8, 29.2, 51.2, 56.3, 64.5, 71.8, 113.3, 117.3, 119.6, 121.6, 123.5, 123.8, 125.3, 125.4, 126.2, 127.8, 128.9, 129.2, 129.4, 130.9, 134.0, 134.3, 152.0, 155.0.

4.3. Preparation of (−)-(*R*,*R*,*R*,*R*,*R*)-10a

To a solution of *trans*-(±)-2-(1-pyrrolidinyl) cyclohexanol **1a** (0.34 g, 2 mmol) in dry THF (20 mL) was added Et_3N (0.84 mL, 6 mmol) and MsCl (0.188 mL, 2.4 mmol) at 0 °C and the contents allowed to stir at 25 °C for 6 h. Et_3N (0.56 mL, 4 mmol) was then added. After stirring for 2 h, (+)-(*R*)-1,1′-bi-2-naphthol (0.286 g, 1 mmol) was added in THF (10 mL) followed by NaOH (0.16 g, 4 mmol) in H_2O (5 mL) and the reaction mixture refluxed for 36 h. Aqueous ammonia (30% solution, 5 mL) was then added. The solution was extracted with ether (2 × 15 mL), washed with brine and dried over anhydrous $MgSO_4$ and evaporated. The crude product was purified on silica gel column using chloroform/methanol (96:4) as eluent to isolate the diastereomeric mixture of the free amino ether (0.087 g, 20% yield) with diamino ether diastereomeric mixture obtained (0.35 g, 60% yield). The mixture was further purified on a silica gel column using chloroform/methanol (95:5) as eluent to isolate (−)-(*R*,*R*,*R*,*R*,*R*)-**10a** (0.20 g, 34% yield). Mp 243–244 °C; $[\alpha]_D^{25} = -116$ (*c* 0.89, $CHCl_3$); IR (KBr) 3055, 2937, 2862, 1620, 1591, 1508, 1456, 1070, 817, 744 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.0–1.8 (m, 22H), 2.0–2.6 (m, 12H), 4.3–4.55 (m, 2H), 7.0–7.5 (m, 8H), 7.7–8.0 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 22.3, 22.7, 22.9, 27.5, 29.4, 51.8, 65.0, 77.2, 115.8, 120.9, 123.8, 125.4, 126.4, 128.0, 129.4, 134.5, 152.0. Anal. Calcd for $C_{40}H_{48}N_2O_2$: C, 81.59; H, 8.22; N, 4.76. Found: C, 81.55; H, 8.25; N, 4.80. For a mixture of (*R*,*R*,*R*,*R*,*R*)-**10a** and (*R*,*R*,*R*,*S*,*S*)-**10b** ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.9, 22.0, 22.2, 22.4, 22.8, 23.1, 26.9, 27.5, 28.7, 29.1, 51.7, 64.5, 64.6, 64.9, 76.5, 77.1, 116.0, 116.5, 117.9, 120.9, 121.5, 122.0, 123.7, 123.8, 125.4, 125.6, 126.2, 127.9, 129.2, 129.5, 134.2, 134.5, 152.3, 152.5.

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9. Crystal structure data for compound **5a**: The θ range for data collection is 1.85°–27.47°. Empirical formula $C_{30}H_{32}NO_2Cl$, colourless needles ($0.3 \times 0.4 \times 0.5$ mm), crystal system is orthorhombic, space group $P2_12_12_1$, unit cell dimensions: $a = 9.8187(10)$ Å, $b = 11.6355(10)$ Å, $c = 21.9851$ Å. Volume 2511.7(4) Å^3, $Z = 4$, $D_{calcd} = 1.222$ mg/m^3, absorption coefficient is 0.151 mm^{-1}, $F(000) = 981$, index ranges $0 \leqslant h \leqslant 12$, $0 \leqslant k \leqslant 15$, $0 \leqslant l \leqslant 28$, total reflections collected were 3248 out of which 2228 were independent reflections with $R(\text{int}) = 0.000$ and $R(\text{sigma}) = 0.0401$. The structure was solved by direct methods and refined by full-matrix least-squares procedure using the SHELX 86 and SHELX 97 program package, respectively. The refinement was carried out using 2228 observed [$F > 4\sigma(F)$] reflections and converged to a final $R1 = 0.0527$, $wR2 = 0.1094$ and goodness of fit is 1.043 with largest difference peak and hole 0.198 and -0.215 e Å^{-3}, respectively (deposition number: CCDC 245988).
10. Crystal structure data for compound **10a**: The θ range for data collection is 1.91°–27.48°. Empirical formula $C_{40}H_{48}N_2O_2$, pale yellow needles ($0.16 \times 0.08 \times 0.20$ mm), crystal system is monoclinic, space group $P2_1$, unit cell dimensions: $a = 10.95362(2)$ Å, $b = 12.511(3)$ Å, $c = 15.672(3)$ Å. Volume 2094.2(7) Å^3, $Z = 3$, $D_{calcd} = 1.391$ mg/m^3, absorption coefficient is 0.085 mm^{-1}, $F(000) = 942$, index ranges $0 \leqslant h \leqslant 12$, $0 \leqslant k \leqslant 15$, $0 \leqslant l \leqslant 28$, total reflections collected were 5011 out of which 1939 were independent reflections with $R(\text{int}) = 0.000$ and $R(\text{sigma}) = 0.0487$. The structure was solved by direct methods and refined by full-matrix least-squares procedure using the SHELX 86 and SHELX 97 program package, respectively. The refinement was carried out using 1939 observed [$F > 4\sigma(F)$] reflections and converged to a final $R1 = 0.0952$, $wR2 = 0.2472$ and goodness of fit is 1.058 with largest difference peak and hole 0.543 and -0.200 e Å^{-3}, respectively (deposition number: CCDC 245989).