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Synthesis of chiral non-racemic 1,2-diamines from *O*-acetyl mandelic acid: application in enantioselective deprotonation of epoxides and diethylzinc addition to aldehydes

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Abstract—A variety of 1,2-diamines were synthesized from readily available *O*-acetyl mandelic acid. These diamines were used in the synthesis of key intermediates for the preparation of (−)-utenone A and carbovir involving enantioselective deprotonation of epoxides. The addition of Et_2Zn catalysed by some of these diamines was also studied and although ees were not high, some interesting observations were made in the outcome of the stereochemistry of the product.

1. Introduction

Vicinal diamines are very important in organic synthesis, especially in medicinal chemistry[1] and asymmetric synthesis.[2] Diamines have extensively been used as chiral ligands in a variety of asymmetric transformations such as Mukiyama aldol reactions,[3] Michael additions,[4] Sharpless dihydroxylation,[5] chiral Lewis acid-based reactions,[6] acylation of alcohols,[7] protonation of enolates,[8] conjugate addition[9] and desymmetrization of *meso* ketones[10] and epoxides.[11] Due to the usefulness of such chiral non-racemic 1,2-diamines, numerous studies have been aimed at the design of efficient diastereo- and enantioselective synthetic routes for their acquisition.[12] Conceptually, the simplest procedure for the generation of the 1,2-diamino unit is the amminolysis of the corresponding vicinal dihalides. However, this method, which was applied at the beginning of this century for the preparation of ethylenediamine, mainly yielded elimination products in more complex systems.[13] Although enantiopure 1,2-disubstituted diamines have been frequently obtained through resolution,[14] other methods were increasingly employed in their synthesis. For example, the efficiency and scope of sharpless asymmetric dihydroxylation, and amino-hydroxylation allowed access to various enantiomerically pure diols and amino alcohols. The diol derivatives when activated as mesylates, cyclic sulfites, and sulfates showed a good electrophilic behaviour towards various nitrogen nucleophiles and have been used for the synthesis of optically active C_2 symmetric vicinal diamines.[15,16]

In the past several years we have been involved in the enantioselective deprotonation of epoxides using chiral lithium amide bases derived from diamines **1** (Fig. 1) which were rationally designed in our laboratory by taking cyclohexene oxide as a model substrate.[17] Using these diamines, we were able to synthesize a prostaglandin intermediate **2** in as high as 97% ee.[17a] Following on from our work, O'Brien and coworkers carried out a study on the enantioselective deprotonation of epoxides using diamine **1a** and synthesized some important chiral intermediates.[18] Similar chiral diamines have been used by others for a variety of enantioselective reactions.[19,20] The most frequently used synthetic route to these diamines starts with phenylglycine and involves *N*-protection, amide formation and reduction. There is, however, a racemization

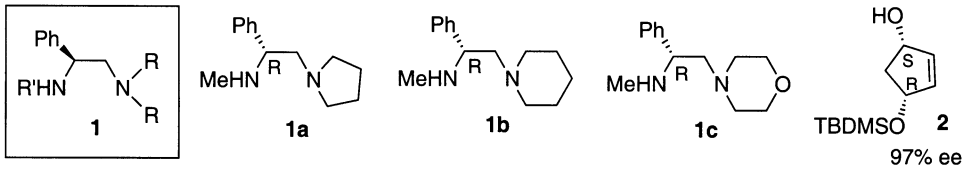

Figure 1.

Keywords: chiral 1,2-diamines; *O*-acetyl mandelic acid; enantioselective deprotonation; epoxides; diethylzinc addition; aldehydes.
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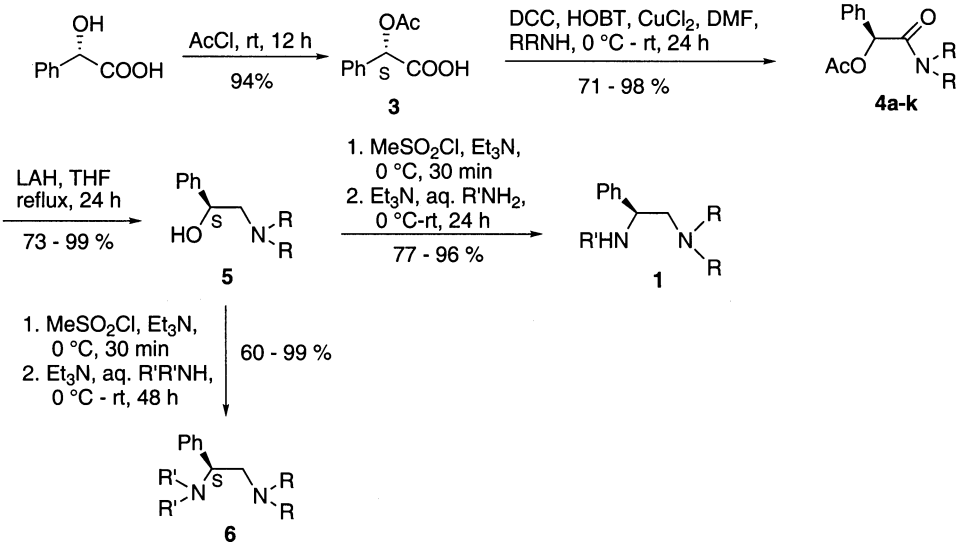


Scheme 1.

problem at the coupling step to an amide which has already been studied in detail and the problem has been minimized to a great extent by using 1-hydroxybenzotriazole (HOBT) in conjunction with DCC and $CuCl_2$.[17a] However, there still remained a need for a flexible and practical synthesis of diamines of type **1**.

Rossiter et al. described the synthesis of diamine **1b** relying on the opening of an aziridinium ion generated from 1,2-amino alcohol.[9] Later on, O'Brien et al. reported a one-pot method for the synthesis of diamines of type **1** from (*R*)-styrene oxide.[18a] In this method, (*R*)-styrene oxide was subjected to ring opening with pyrrolidine under Rossiter's condition to give a mixture of regio-isomeric amino alcohols in a 70:30 ratio. Since both the amino alcohols were going to provide the same aziridinium

Table 1. Chiral non-racemic β-acyloxy amides

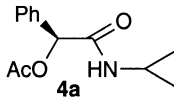
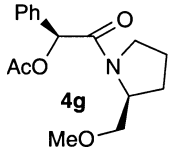
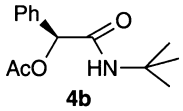
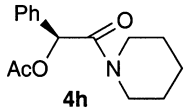
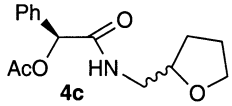
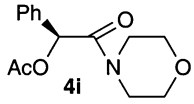
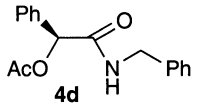
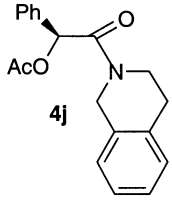
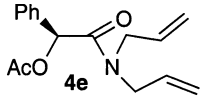
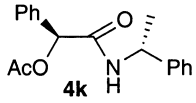
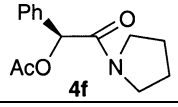
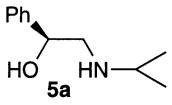
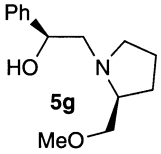
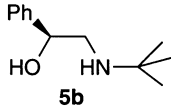
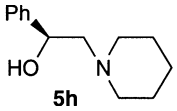
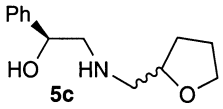
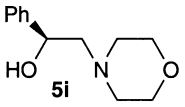
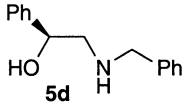
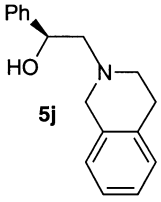
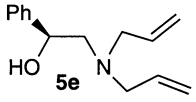
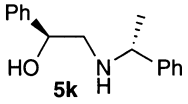
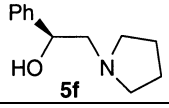
Entry	Chiral non-racemic amides	Isolated yield (%)	Entry	Chiral non-racemic amides	Isolated yield (%)
1	 **4a**	74	7	 **4g**	70
2	 **4b**	86	8	 **4h**	98
3	 **4c**	89	9	 **4i**	90
4	 **4d**	87	10	 **4j**	89
5	 **4e**	71	11	 **4k**	94
6	 **4f**	92			

Table 2. Chiral non-racemic β-amino alcohols

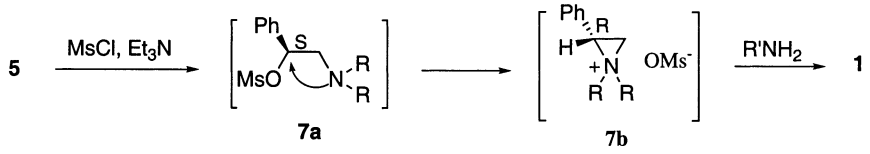
Entry	Chiral β-amino alcohols	Isolated yield (%)	Entry	Chiral β-amino alcohols	Isolated yield (%)
1	 **5a**	77	7	 **5g**	89
2	 **5b**	96	8	 **5h**	98
3	 **5c**	73	9	 **5i**	91
4	 **5d**	86	10	 **5j**	98
5	 **5e**	79	11	 **5k**	88
6	 **5f**	95			

ion, separation of the major regioisomer was not required. Therefore, the ring-opened crude product was directly subjected to mesylation followed by reaction with aqueous methylamine to obtain the chiral non-racemic diamine **1a** in good yield. However, the one-pot method was only successful when reactive amines such as pyrrolidine and piperidine were used in the first step. Besides this, the synthesis of (*S*)-diamines necessitates the use of expensive (*S*)-styrene oxide. So in a further improvement, they showed that phenylglycinol, which is commercially available in both enantiomeric forms, can be used as a precursor to synthesize different *N*,*N*-disubstituted diamines.[18b] The approach is simple, but the cost factor of phenylglycinol makes it less practical. In this paper, we describe full details of a more flexible method for the synthesis of vicinal diamines of type **1** from a cheap and readily available material.[21] The application of these diamines in the asymmetric synthesis of intermediates for natural product synthesis where the key step would be enantioselective deprotonation of epoxides and the use of some of the vicinal diamines in enantioselective addition of Et_2Zn to aldehydes are also described.

2. Results and discussion

We have developed a synthesis of chiral non-racemic diamines from mandelic acid, a starting material which is cheap and commercially available in both enantiomeric forms. The synthetic route for the preparation of vicinal diamines is depicted in Scheme 1. (*S*)-Mandelic acid was treated with neat acetyl chloride at room temperature to give (*S*)-*O*-acetyl mandelic acid **3** as a white crystalline material in near quantitative yield. Treatment of **3** with various amines (primary and secondary) using DCC as condensing reagent and HOBT/$CuCl_2$ as a deracemizing additive, gave the desired amides **4a**–**4k** in good yields (Table 1). The amides were treated with lithium aluminum hydride in tetrahydrofuran (THF) under reflux conditions to provide amino alcohols **5a**–**5k** in very good yields (Table 2). During the reduction, both amide and acetate groups were reduced in one step without racemization and the resulting products were pure enough for further reactions. Thus, the β-amino alcohols obtained from reactions with secondary amines were converted into various diamines using O'Brien's one-pot method.[18a] Treatment of β-amino alcohols **5** with methanesulfonyl chloride in the presence of Et_3N in diethyl ether led to the formation of aziridinium ion **7b**, which was opened with various aliphatic and aromatic amines at room temperature to provide diamines in excellent yields. Initially, aqueous solutions of methylamine and ammonia were used for the opening of aziridinium ion. Later, it was realized that the presence of water (5–10 equiv.) was essential for a successful ring opening reaction. So, in all of the cases studied, some water was added just before addition of the amine. It was assumed that water might be responsible for dissolving the aziridinium ion. It was also necessary to use a large excess of low boiling amines (methylamine, ammonia, and *tert*-butylamine). In the case of high boiling amines, 1.0–5.0 equiv. of amines was enough for completion of the reaction.

The presence of a benzylic position in the aziridinium ion



Scheme 2.

7b increases the regio- and stereoselectivity towards various nucleophiles during the ring opening reaction (Scheme 2). In the case of aziridinium ion opening with primary amines, products **1**, that contain deprotonable proton at one of the amine sites (protic β-diamines) were obtained (Table 3). Similarly, secondary amines gave aprotic diamines **6** (Table 4). Even less nucleophilic amines such as aniline, β-naphthylamines, and other aromatic amines gave diamines in good yield (Table 3, entries 7, 8, 11, 12 and 16). Even hindered amines opened the aziridinium ion in an efficient manner (Table 3, entries 7 and 13). The ring opening was smooth for acyclic and cyclic amines (Table 4).

The postulation of an aziridinium ion intermediate is based on literature precedent of similar reactions.[22] The existence of aziridinium ions has also been postulated in substitution reactions of amino tosylates and in the Mitsunobu reactions of amino alcohols.[23] In order to prove the regio- and stereospecificity in the opening of aziridinium ion **7b**, it was allowed to react with (*R*)-α-methylbenzylamine to provide the diamine **1j**. The absence of the (*R*,*R*) diastereomeric peak in the ^{1}H NMR spectrum indicated that the ring opening reaction was stereospecific (Table 3, entry 10). Comparison of the specific rotation value of the diamine (*S*)-**1a** {$[\alpha]_D^{25}=+97.5$ (c=2.7, $CHCl_3$)} with the literature value[17a] {$[\alpha]_D^{25}=-91.6$ (c=1.8, $CHCl_3$) for (*R*)-**1a**} indicated that there was no racemization during the synthesis of the diamines, and this was also confirmed by chiral HPLC analysis. The net retention of configuration observed in these substitution reactions suggested the neighbouring

Table 3. Chiral non-racemic protic β-diamines

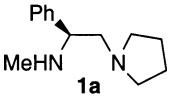
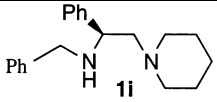
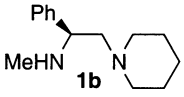
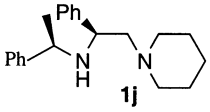
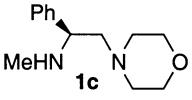
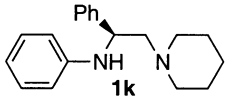
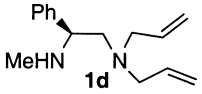
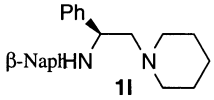
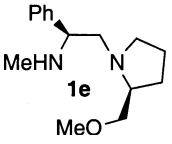
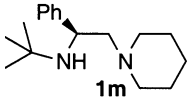
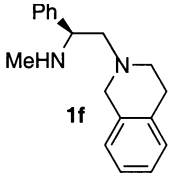
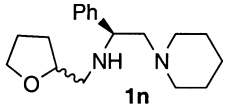
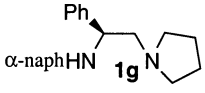
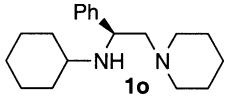
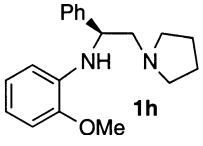
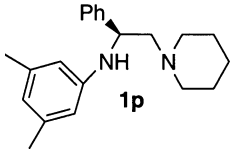
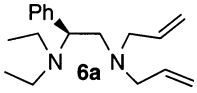
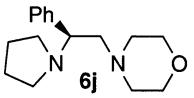
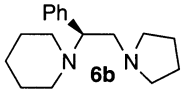
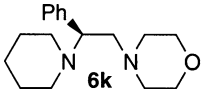
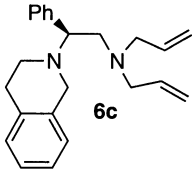
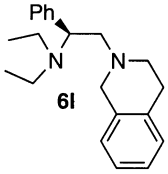
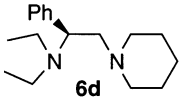
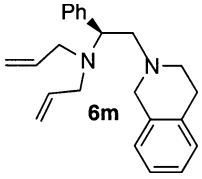
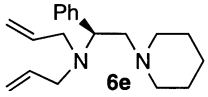
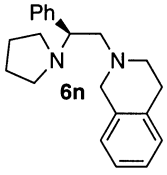
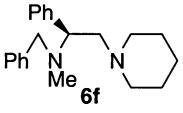
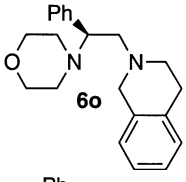
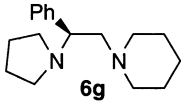
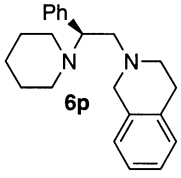
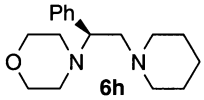
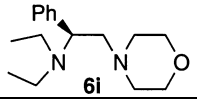
Entry	Chiral non-racemic diamines	Yield (%)	Entry	Chiral non-racemic diamines	Yield (%)
1	 **1a**	80	9	 **1i**	80
2	 **1b**	96	10	 **1j**	87
3	 **1c**	88	11	 **1k**	88
4	 **1d**	90	12	 **1l**	95
5	 **1e**	80	13	 **1m**	96
6	 **1f**	85	14	 **1n**	92
7	 **1g**	80	15	 **1o**	88
8	 **1h**	77	16	 **1p**	87

Table 4. Chiral non-racemic aprotic β-diamines

Entry	Chiral non-racemic diamines	Yield (%)	Entry	Chiral non-racemic diamines	Yield (%)
1	 **6a**	96	10	 **6j**	94
2	 **6b**	62	11	 **6k**	99
3	 **6c**	71	12	 **6l**	87
4	 **6d**	73	13	 **6m**	75
5	 **6e**	60	14	 **6n**	75
6	 **6f**	78	15	 **6o**	75
7	 **6g**	80	16	 **6p**	74
8	 **6h**	80			
9	 **6i**	99			

group participation by the tertiary amine functionality in the amino alcohol **5** (Scheme 2) followed by nucleophilic attack of the external amine at the benzylic position. This was in contrast to episelenium and episulfonium ions, which partially racemize during Ritter type substitution reactions.[24] Thus, we have developed a convenient approach to amino alcohols and diamines of type **1** and **6** starting from mandelic acid.

The enantioselective deprotonation of symmetrical epoxides to give optically active allylic alcohols using non-enzymatic methods, where enantiotopic proton selection takes place by means of a chiral non-racemic lithium amide (CNLA) base, is a very challenging area in asymmetric synthesis.[25] Recently, we discovered[17] that the CNLA base derived from diamine **1a** was an excellent chiral base for enantioselective deprotonation of epoxides. In order to extend its scope further, we report here the application of both the enantiomers of the chiral diamine **1** in the synthesis of important cyclopentanoid intermediates (Fig. 2). Enantioselective deprotonation of epoxide **8**[26] with a base derived from diamine (*R*)-**1a** under Asami's conditions[26b] was carried out to give **9** in 83% yield and 94% ee. Allylic alcohol **9** is an intermediate[26b] in the synthesis of utenone A **10**[27] which is an antileukemic and considered to be a biosynthetic precursor of other marine natural products.[28] Similarly, we have extended the application of our chiral base chemistry in the synthesis of (−)-carbovir **11**, an

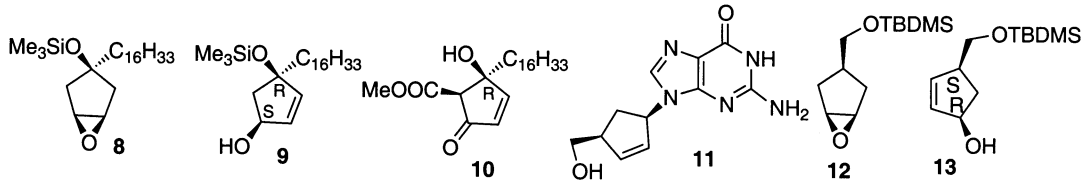
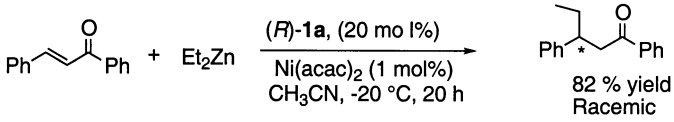


Figure 2.



Scheme 3.

anti-HIV agent. Enantioselective deprotonation of epoxide **12**[29] with (*S*)-**1a** in THF gave an intermediate **13** in 20% yield and 80% ee.[30] The change of solvent to benzene lowered the yield to 14% and the enantioselectivity to 40%. The synthetic utility of **13** has already been shown in the literature by converting it into the anti-HIV agent **11**[30c] Since the *trans*-isomer of the epoxide **12** is also known to be converted into (−)-carbovir,[30a] we studied the enantioselective deprotonation of the *trans*-epoxide with (*R*)-**1a** and observed a poor enantioselectivity (27% ee). This is not surprising in view of our previous experience in this area.[17]

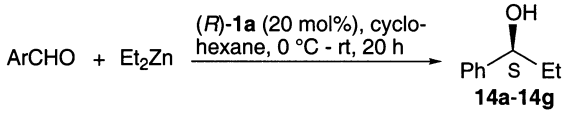
The catalytic enantioselective addition of diethylzinc to aldehydes is an important method for preparing chiral secondary alcohols.[31] Most of the successful results have been obtained by using β-amino alcohols as chiral ligands.[32] Although diamines were also reported to show catalytic activity, there are only a few examples.[33] Asami,[34] and recently Brunel et al.[35] have used proline-based diamines in this type of reaction and reported a maximum of 80% ee for the diethylzinc addition to benzaldehyde.

We were interested to examine the effectiveness of diamines **1** in the addition of diethylzinc to enones and aldehydes. At the outset, a conjugate addition to chalcone using 1.8 equiv. of diethylzinc in the presence of $Ni(acac)_2$ and diamine (*R*)-**1a** (20 mol%) was carried out. The product was obtained in good yield, but there was no asymmetric induction in the reaction (Scheme 3). Changing the substituents on this chiral diamine failed to give any asymmetric induction.

We then changed our attention to study the addition of diethylzinc to aldehydes catalysed by chiral non-racemic diamines of the type **1**. For the initial studies, the reaction of benzaldehyde was examined in different solvents using diamine (*R*)-**1a**, and it was found that cyclohexane was a better solvent than hexane and toluene. Under these conditions, (*S*)-1-phenyl-1-propanol was obtained in 47% ee. The reaction with other aldehydes is summarized in Table 5. In all cases, ligand (*R*)-**1a** gave alcohols of (*S*)-configuration.[36] It was observed that aromatic aldehydes with electron withdrawing groups gave slightly higher enantioselectivity (Table 5; entries 5 and 6).

The effect of other chiral diamines was then examined under the same reaction conditions using *p*-chlorobenzaldehyde as a model substrate, and the results are summarized in Table 6. Although the enantioselectivity remained modest, the stereochemical outcome of the reaction was quite unprecedented. The absolute stereochemistry of the products depended upon the steric size substituent on the nitrogen attached to the chiral centre. In diamines with a N–Me group, the absolute stereochemistry of the newly formed hydroxyl group was opposite to that of the ligand

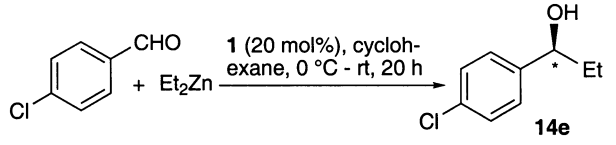
Table 5. Enantioselective addition of Et_2Zn to aldehydes catalysed by (*R*)-**1a**



Entry	Substrate	Yield (%)	ee (%)[a]
1	Benzaldehyde	84	47
2	2,4,6-Trimethylbenzaldehyde	67	46
3	4-Methoxybenzaldehyde	92	37
4	4-Methylbenzaldehyde	76	38
5	4-Chlorobenzaldehyde	88	53
6	4-Fluorobenzaldehyde	77	54
7	Ferrocenealdehyde	65	71

[a] Ee (%) was determined by analysis of 400 MHz ^{1}H NMR spectrum of Mosher esters.

Table 6. Enantioselective addition of Et_2Zn to 4-chlorobenzaldehyde catalysed by (*R*)- or (*S*)-**1**



Entry	Diamine	Yield (%)	ee (%)[a]
1	(*R*)-**1a**	88	53 (*S*)
2	(*R*)-**1b**	92	66 (*S*)
3	(*R*)-**1c**	81	65 (*S*)
4	(*S*)-**1d**	82	6 (*R*)
5	(*S*)-**1e**	94	50 (*R*)
6	(*S*)-**1f**	83	44 (*R*)
7	(*S*)-**1h**	74	2 (*S*)
8	(*S*)-**1j**	87	68 (*S*)
9	(*S*)-**1m**	95	58 (*S*)
10	(*S*)-**1o**	80	4 (*S*)

[a] Ee (%) was determined by analysis of 400 MHz ^{1}H NMR spectrum of Mosher esters.

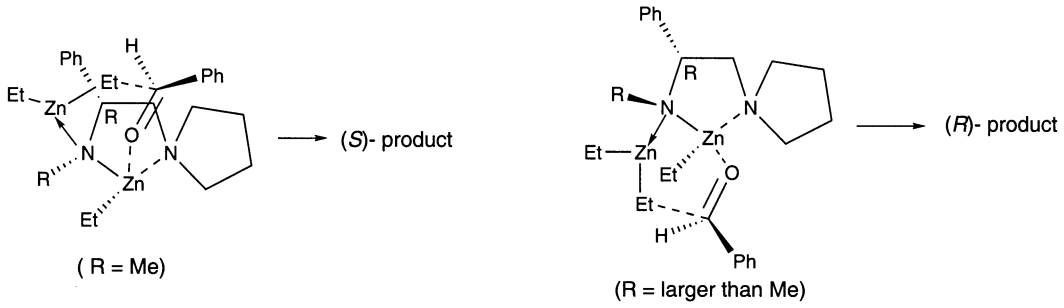


Figure 3.

stereochemistry (Table 6, entries 1–6). However, for substituents sterically larger than a N–Me group, the reverse was true (Table 6, entries 7–10).

The sense of asymmetric induction in the diethylzinc addition reaction can be explained by favourable transition state models as depicted in Fig. 3. If R is Me group, it orients itself *cis* to the phenyl group at the chiral centre. Then, Et_2Zn coordinates to the N atom *trans* to the phenyl group. The aldehyde then approaches the metal in the most appropriate manner (*si* face attack). Thus the product with opposite stereochemistry, as compared to the ligand configuration, is obtained. In the case of ligands when R is larger than a Me group, the R-group prefers to orientate itself in a *trans* fashion with respect to the phenyl group at the chiral centre. In this kind of situation, the *re* face of the aldehyde will be preferred for the addition reaction, thus giving the product with the same stereochemistry as the chiral ligand.

3. Conclusion

In conclusion, we have presented a versatile and practical method for the synthesis of (*S*)-chiral diamines from (*S*)-*O*-acetyl mandelic acid. A variety of amino alcohols and diamines were synthesized in high yields. We have shown application of some of the diamines in the synthesis of key intermediates for natural products and drug compounds. We have also studied Et_2Zn addition reactions catalysed by some of the diamines. Although ees were not high, some interesting observations were made in the outcome of the stereochemistry of the product.

4. Experimental

4.1. General

^1H NMR spectra were recorded on 60, 300, and 400 MHz Jeol spectrometers. Chemical shifts are expressed in part per million downfield from TMS as an internal standard, and coupling constants are reported in hertz. Routine monitoring of reactions was performed using silica gel-G obtained from Acme. All the column chromatographic separations were done by using silica gel (Acme's, 60–120 mesh). Petroleum ether used was of boiling range 60–80°C. Reactions which needed anhydrous conditions were run under an atmosphere of dry nitrogen or argon using flame-dried glassware. The organic extracts were dried over anhydrous sodium sulfate. Evaporation of solvents was performed at reduced pressure. THF and diethyl ether were distilled from sodium benzophenone ketyl under nitrogen. Benzene and dichloromethane were distilled from CaH_2. *N*,*N*-Dimethylformamide (DMF) was distilled from CaH_2 at reduced pressure. Pyridine was distilled from CaH_2 at atmospheric pressure.

4.1.1. (*S*)-*O*-Acetyl mandelic acid (3). (*S*)-Mandelic acid (25 g, 165 mmol) was added to acetyl chloride (59 mL, 825 mmol) portionwise (five times) at rt and stirred overnight. The volatile materials were removed in vacuo. Crystallization of the crude material from benzene gave the pure product as a white crystalline powder (30 g, 94%); mp 96–98°C (lit.[37] mp 95–97.5°C).

4.2. General procedure for coupling of (*S*)-*O*-acetyl mandelic acid with various amines

To a mixture of (*S*)-*O*-acetyl mandelic acid (5 g, 25 mmol), anhydrous $CuCl_2$ (4 g, 30 mmol), and HOBT (4.1 g, 30 mmol) in dry DMF (100 mL) was added dropwise a solution of DCC (6.2 g, 30 mmol) in DMF (15 mL) at 0°C, and the mixture was stirred for 30 min. Amine (50 mmol) was added and the stirring was continued for 24 h (0°C, rt). The reaction mixture was diluted with EtOAc (100 mL) and washed with cold 0.1N HCl, saturated $NaHCO_3$, and brine. The organic layer was dried over anhydrous sodium sulfate, and the solvent was evaporated in vacuo. The crude material was purified by column chromatography on silica gel using petroleum ether–EtOAc as eluent to give the pure amides **4** (Table 1).

4.2.1. *S*(+)-*N*-Isopropyl-*O*-acetyl mandelamide (4a). Yield 74% as a white solid; mp 94–98°C; R_f 0.60 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}=+94.7$ (c=1.0, $CHCl_3$); IR (KBr) 1620, 1730 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.07 (d, J=6 Hz, 6H), 2.09 (s, 3H), 3.98–4.05 (m, 1H), 5.94–6.07 (m, 2H), 7.20–7.45 (m, Ph, 5H). Anal. calcd for $C_{13}H_{17}NO_3$: C, 66.38; H, 7.23; N, 5.95; found: C, 66.42; H, 7.18; N, 5.98.

4.2.2. *S*(+)-*N*-*tert*-Butyl-*O*-acetyl mandelamide (4b). Yield 86% as a white solid; mp 74–79°C; R_f 0.65 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}=+69.7$ (c=6.25, $CHCl_3$); IR (KBr) 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.48 (s, 9H), 2.10 (s, 3H), 5.85–5.92 (m, 2H), 7.41–7.48 (m, Ph, 5H). Anal. calcd for $C_{14}H_{19}NO_3$: C, 67.46; H, 7.63; N, 5.62; found: C, 67.24; H, 7.83; N, 5.68.

4.2.3. *S*(+)-*N*-[*O*-(Acetyl)mandelyl]THF-2-yl-methylamine (4c). Yield 89% (mixture of diastereomers) as a viscous liquid; R_f 0.70 (50% EtOAc in petroleum ether); IR (neat) 3010, 1730, 1625, 1220, 830 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.82 (m, 4H), 2.12 (s, 3H), 2.78 (m, 1H), 3.30 (m, 1H), 3.72 (m, 3H), 6.05 (s, 1H), 7.40 (s, 5H, Ph). Anal. calcd for $C_{15}H_{19}NO_4$: C, 64.98; H, 6.85; N, 5.05; found: C, 65.12; H, 6.89; N, 5.18.

4.2.4. *S*(+)-*N*-Benzyl-*O*-acetyl mandelamide (4d). Yield 86% as a white solid; R_f 0.90 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+120.3 (c=4.7, $CHCl_3$); IR (KBr) 2960, 1730, 1620, 850, 720 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 2.20 (s, 3H), 4.20 (d, J=6 Hz, 2H), 5.96 (s, 1H), 7.1–7.58 (m, 10H, Ph). Anal. calcd for $C_{17}H_{17}NO_3$: C, 72.08; H, 6.01; N, 4.95; found: C, 71.83; H, 6.10; N, 4.98.

4.2.5. *S*(+)-*N*,*N*-Diallyl-*O*-acetyl mandelamide (4e). Yield 71% as a white solid; mp 68–70°C; R_f 0.80 (25% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+157 (c=1.0, $CHCl_3$); IR (KBr) 3010, 1720, 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.15 (s, 3H), 3.70–3.90 (m, 3H), 4.17 (dd, J=15, 6 Hz, 1H), 5.0–5.21 (m, 4H), 5.50–5.61 (m, 1H), 5.61–5.80 (m, 1H), 6.18 (s, 1H), 7.39–7.50 (m, Ph, 5H); MS (CI, m/z): 274 (M^+). Anal. calcd for $C_{16}H_{19}NO_3$: C, 70.32; H, 6.95; N, 5.12; found: C, 70.46; H, 6.73; N, 5.34.

4.2.6. (*S*)-1-[*O*-(Acetyl)mandelyl]pyrrolidine (4f). Yield 92% as white solid; mp 116–118°C; R_f 0.40 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+146.9 (c=4.2, $CHCl_3$); IR (KBr) 1710, 1620 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.65–2.0 (m, 4H), 2.15 (s, 3H), 3.0–3.15 (m, 1H), 3.36–3.44 (m, 1H), 3.53–3.66 (m, 2H), 6.02 (s, 1H), 7.36–7.59 (m, Ph, 5H); MS (CI, m/z): 248 (M^++1), 188 (base peak). Anal. calcd for $C_{14}H_{17}NO_3$: C, 68.01; H, 6.88; N, 5.66; found: C, 68.26; H, 6.88; N, 5.64.

4.2.7. (*S*)-1-[*O*-(Acetyl)mandelyl]-2-[(*S*)-methoxymethyl]-pyrrolidine (4g). Yield 70% as a white solid; mp 96–100°C; R_f 0.60 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+70.76 (c=1.0, $CHCl_3$); IR (KBr) 1720, 1060 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.70–1.95 (m, 2H), 2.15 (s, 3H), 3.10–3.62 (m, 4H), 3.20 (s, 3H), 4.30 (m, 3H), 6.0 (s, 1H), 7.30–7.60 (m, Ph, 5H); MS (CI, m/z): 292 (M^++1). Anal. calcd for $C_{16}H_{21}NO_4$: C, 65.97; H, 7.21; N, 4.81; found: C, 65.67; H, 7.46; N, 4.79.

4.2.8. (*S*)-1-[*O*-(Acetyl)mandelyl]piperidine (4h). Yield 98% as a white solid; mp 107–108°C; R_f 0.60 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+119 (c=3.0, $CHCl_3$); IR (KBr) 1710, 1620, 1220 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.38–1.80 (m, 6H), 2.15 (s, 3H), 3.20–3.75 (m, 4H), 6.20 (s, 1H), 7.30–7.50 (m, Ph, 5H); MS (CI, m/z): 262 (M^++1). Anal. calcd for $C_{15}H_{19}NO_3$: C, 68.96; H, 7.27; N, 5.36; found: C, 68.92; H, 7.34; N, 5.30.

4.2.9. (*S*)-1-[*O*-(Acetyl)mandelyl]morpholine (4i). Yield 90% as a white solid; mp 92–93°C; R_f 0.50 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+118.4 (c=4.6, $CHCl_3$); IR (KBr) 1725, 1620 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.16 (s, 3H), 3.15–3.78 (m, 8H), 6.20 (s, 1H), 7.40 (s, Ph, 5H); MS (CI, m/z): 264 (M^++1), 176 (base peak); Anal. calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.46; N, 5.32; found: C, 63.80; H, 6.24; N, 5.38.

4.2.10. (*S*)-1-[*O*-(Acetyl)mandelyl]tetrahydroisoquinoline (4j). Yield 89% as a white solid; mp 104–106°C; R_f 0.50 (25% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+190.8 (c=1.0, $CHCl_3$); IR (KBr) 3030, 1720, 1630, 1200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.18 (s, 3H), 2.30–2.90 (m, 2H), 3.50–3.90 (m, 2H), 4.60–4.90 (m, 2H), 6.34 (s, 1H), 7.04–7.47 (m, 9H); MS (CI, m/z): 310 (M^++1), 250, 222 (base peaks). Anal. calcd for $C_{19}H_{19}NO_3$: C, 73.78; H, 6.14; N, 4.53; found: C, 73.63; H, 6.26; N, 4.68.

4.2.11. (*S*)(+)-*N*-[(*R*)-α-Methylbenzyl]-*O*-acetyl mandelamide (4k). Yield 94% as a white solid; mp 126–128°C; R_f 0.70 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+282 (c=1.0, $CHCl_3$); IR (KBr) 3320, 1730, 1650, 1220 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.49 (d, J=6.9 Hz, 3H), 2.16 (s, 3H), 5.18 (quintet, J=7 Hz, 1H), 6.08 (s, 1H), 6.32–6.34 (bd, J=7 Hz, 1H, *–NH*), 7.29–7.36 (m, 10H); MS (CI, m/z): 298 (M^++1) (base peak), 238. Anal. calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.39; N, 4.71; found: C, 72.64; H, 6.26; N, 4.68.

4.3. General procedure for LAH reduction of (*S*)-*O*-acetyl mandelamides

To a suspension of LAH (20 mmol) in THF (50 mL), was added amide 4 (5 mmol) in THF (10 mL) at rt and it was refluxed for 12 h. Excess LAH was destroyed by addition of EtOAc (0.5 mL). After cooling to 0°C, water was added (0.5 mL), followed by the 4N NaOH (0.5 mL). After 5 min, 1.5 mL water was added and the mixture was stirred for 15 min. Resulting white precipitate was filtered through celite, filtrate was dried over anhydrous sodium sulfate, and solvent was removed in vacuo. The resulting crude material was pure enough for further reaction. In a few cases it was necessary to purify. For analytical purpose, most of the samples were purified over silica gel column chromatography using petroleum ether–EtOAc as eluent to afford the pure amino alcohols **5** (Table 2).

4.3.1. (*S*)-2-(*iso*propylamino)-1-phenylethanol (5a). Yield 77% as a white solid; mp 68–72°C; R_f 0.20 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+52.5 (c=4.0, $CHCl_3$); IR (KBr) 3450, 3340, 860 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.96 (d, J=9 Hz, 6H), 2.49–2.65 (m, 2H), 3.40–3.53 (m, 1H), 4.01 (bs, 1H, *OH*), 4.58–4.65 (m, 1H), 7.33 (m, 5H, Ph). Anal. calcd for $C_{11}H_{17}NO$: C, 73.74; H, 9.49; N, 7.82; found: C, 73.34; H, 9.41; N, 7.72.

4.3.2. (*S*)-2-(*tert*-Butylamino)-1-phenylethanol) (5b). Yield 96% as a white solid; mp 69–71°C; R_f 0.20 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+45.1 (c=1.75, $CHCl_3$); IR (KBr) 3500, 3010, 2930, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.08 (s, 9H), 2.20–2.74 (m, 2H), 3.49–3.66 (bs, 1H, *OH*), 4.58–4.66 (m, 1H), 7.28 (m, 5H, Ph). Anal. calcd for $C_{12}H_{19}NO$: C, 74.61; H, 9.84; N, 7.25; found: C, 74.48; H, 9.78; N, 7.30.

4.3.3. (*S*)-1-Phenyl-2-[(tetrahydrofuran-2-ylmethyl)-amino]-ethanol (5c). Yield 73% as a viscous liquid; R_f 0.30 (50% EtOAc in petroleum ether); IR (neat) 3450,

1220, 830, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.09–1.89 (m, 4H), 2.54–2.73 (m, 3H), 3.56–3.87 (m, 5H), 4.67 (m, 1H), 7.35 (m, 5H, Ph). Anal. calcd for $C_{13}H_{19}NO_2$: C, 70.58; H, 8.59; N, 6.33; found: C, 70.72; H, 8.62; N, 6.29.

4.3.4. (*S*)-2-(Benzylamino)-1-phenylethanol (5d). Yield 86% as a white solid; R_f 0.5 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}=+59.7$ (c=1.0, $CHCl_3$); IR (KBr) 3470, 3020, 2950, 760 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 3.65 (m, 4H), 4.72 (m, 1H), 7.34 (m, 10H, Ph).). Anal. calcd for $C_{15}H_{17}NO$: C, 79.79; H, 7.49; N, 6.17; found: C, 79.90; H, 7.56; N, 6.18.

4.3.5. (*S*)-2-(*N*,*N*-Diallylamino)-1-phenylethanol (5e). Yield 79% as a viscous liquid; R_f 0.80 (25% EtOAc in petroleum ether); $[\alpha]_D^{25}=+58.6$ (c=4.12, $CHCl_3$); IR (neat) 3420, 3020, 1420 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.40–2.60 (m, 3H), 3.10–3.40 (m, 3H), 4.60–4.75 (m, 1H), 5.15–5.20 (m, 4H), 5.80–6.0 (m, 2H), 7.35 (m, 5H, Ph); MS (*m*/*z*): 219 (M^++2), 218 (M^++1), 202 (base peak), 200. Anal. calcd for $C_{14}H_{19}NO$: C, 77.41; H, 8.75; N, 6.45; found: C, 77.52; H, 8.64; N, 6.89.

4.3.6. (*S*)-2-(Pyrrolidin-1-yl)-1-phenylethanol (5f). Yield 95% as a white solid; mp 68–69°C; R_f 0.20 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}=+51.5$ (c=1.3, $CHCl_3$) {lit.[31b] $[\alpha]_D^{27}$ +43.8° (c=0.96, MeOH)}; IR (KBr) 3500, 1100 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.70–1.85 (m, 4H), 2.45–2.55 (m, 3H), 2.73–2.78 (m, 3H), 4.70 (dd, J=9, 3 Hz, 1H), 7.34 (m, 5H, Ph); MS (*m*/*z*): 192 (M^++1), 174. Anal. calcd for $C_{12}H_{17}NO$: C, 75.39; H, 8.90; N, 7.32; found: C, 75.42; H, 8.76; N, 7.62.

4.3.7. (*S*)-2-[(*S*)-2′-Methoxymethylpyrrolidin-1-yl)]-1-phenylethanol (5g). Yield 89% as a viscous liquid; R_f 0.60 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}=+94.2$ (c=6.8, $CHCl_3$); IR (neat) 3450, 1120 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.50–1.85 (m, 4H), 2.20–3.10 (m, 6H), 3.40 (s, 3H), 3.45 (m, 1H), 4.0 (bs, 1H, *OH*), 4.75 (m, 1H), 7.33 (m, 5H, Ph); MS (*m*/*z*): 236 (M^++1), 218. Anal. calcd for $C_{14}H_{21}NO_2$: C, 71.48; H, 8.93; N, 5.95; found: C, 71.93; H, 8.74; N, 6.02.

4.3.8. (*S*)-2-(Piperdin-1-yl)-1-phenylethanol (5h).[31b] Yield 99% as a white solid; mp 84–85°C; R_f 0.60 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}=+81.4$ (c=1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.40–1.75 (m, 6H), 2.35–2.50 (m, 4H), 2.60–2.80 (m, 2H), 4.71 (dd, J=12, 4 Hz, 1H), 7.34 (m, 5H, Ph).

4.3.9. (*S*)-2-(Morpholin-1-yl)-1-phenylethanol (5i). Yield 91% as a white solid; mp 96–98°C; R_f 0.50 (50% EtOAc in petroleum ether); 96% ee (chiracel OD column 0.46×25 cm^2, solvent: hexane/isopropanol ratio 90:10; flow rate 0.5 mL/min; UV 254 nm; R_T: 15.6 min for *S*-enantiomer and 14.65 min for *R*-enantiomer); $[\alpha]_D^{25}=+61.8$ (c=2.7, $CHCl_3$); IR (KBr) 3450, 3030, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.40–2.61 (m, 6H), 2.75 (bs, 1H, *OH*), 3.70–3.80 (m, 4H), 4.75 (dd, J=9, 3.5 Hz, 1H), 7.33 (m, 5H, Ph); MS (*m*/*z*) 208 (M^++1), 190 (base peak). Anal. calcd for $C_{12}H_{17}NO_2$: C, 69.56; H, 8.21; N, 6.76; found: C, 69.82; H, 8.24; N, 6.84.

4.3.10. (*S*)-2-(Tetrahydroisoquinolin-1-yl)-1-phenylethanol (5j). Yield 98% as a white solid; mp 75–77°C; R_f 0.80 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}=+64.0$ (c=1.0, $CHCl_3$); IR (KBr) 3350, 3020, 830 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.60–2.80 (m, 4H), 2.90–3.10 (m, 2H), 3.68 (d, J=14 Hz, 1H), 3.94 (d, J=14 Hz, 1H), 4.86 (dd, J=9.0, 3.0 Hz, 1H), 7.35 (m, 9H, aromatics); MS (*m*/*z*): 254 (M^++1) (base peak), 236. Anal. calcd for $C_{17}H_{19}NO$: C, 80.63; H, 7.50; N, 5.53; found: C, 80.61; H, 7.46; N, 5.62.

4.3.11. (*S*)-2-[(*R*)-α-Methylbenzylamino)]-1-phenylethanol (5k). Yield 88% as white solid; mp 124–130°C; R_f 0.80 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}=+134.0$ (c=1.45, $CHCl_3$) {lit.[38] $[\alpha]_D^{25}=-111.0$ (c=1, $CHCl_3$) for *R*,*S* isomer}.

4.4. General procedure for synthesis of diamine 1[18]

To a stirred solution of amino alcohol **5** (5 mmol) in dry ether (20 mL) was added Et_3N (2 mL, 15 mmol) at rt. It was cooled to 0°C, and methanesulfonyl chloride (0.465 mL, 6 mmol) was added dropwise. The resulting reaction mixture became difficult to stir. After 30 min, more Et_3N (1.4 mL, 10 mmol) and the corresponding amine (1–50 equiv. was used; see Section 2), and water (10 equiv.) were added and the resulting biphasic reaction mixture was stirred at 0°C to rt for 20 h. The organic and aqueous layers were separated, and the aqueous layer was extracted with diethyl ether (three times). The combined ether extracts were washed with saturated $NaHCO_3$ and brine. The organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo. Methyl amine substituted diamines (Table 3; entries 1–6) were purified by Kugelrohr distillation. Other diamines (Table 3; entries 7–16) were purified by column chromatography over silica gel using EtOAc–petroleum ether as eluent to afford the pure diamines **1**.

Aprotic diamines **6** were prepared as per the general procedure mentioned above, except that the reactions with the amines were carried out for 48 h at rt. All the aprotic diamines were purified by column chromatography over silica gel using EtOAc–petroleum ether as eluent (Table 4).

4.4.1. (*S*)-*N*-Methyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine (1a). Yield 80% as a yellow viscous liquid; bp 118°C (1 mm); R_f 0.70 (10% MeOH in DCM); $[\alpha]_D^{25}=+82.5$ (c=5.5, $CHCl_3$) {lit.[17] $[\alpha]_D^{25}=-64.0$ (c=1.4, EtOH) for *R* enantiomer}.

4.4.2. (*S*)-*N*-Methyl-1-phenyl-2-(piperidin-1-yl)ethanamine (1b). Yield 96% as a colourless oil; R_f 0.80 (10% MeOH in DCM); $[\alpha]_D^{25}=+97.5$ (c=2.7, $CHCl_3$) {lit.[17] $[\alpha]_D^{25}=-91.6$ (c=1.8, $CHCl_3$) for *R* enantiomer}.

4.4.3. (*S*)-*N*-Methyl-1-phenyl-2-(morpholin-1-yl)ethanamine (1c). Yield 88% as a colourless liquid; R_f 0.75 (10% MeOH in DCM); $[\alpha]_D^{25}=+93.1$ (c=2.9, $CHCl_3$) {lit.[17] $[\alpha]_D^{25}=-92.0$ (c=1.2, $CHCl_3$) for *R* enantiomer}.

4.4.4. (*S*)-*N*-Methyl-1-phenyl-2-(*N*,*N*-diallylamino)ethanamine (1d). Yield 90% as a viscous liquid; R_f 0.70 (5% MeOH in DCM); $[\alpha]_D^{25}=+83.1$ (c=4.9, $CHCl_3$); IR (neat) 3330, 3020, 2960, 1680, 750 cm^{-1}; ^1H NMR

($CDCl_3$, 400 MHz) δ 2.28 (s, 3H), 2.32–2.70 (m, 3H), 2.90–3.10 (m, 2H), 3.20–3.40 (m, 2H), 3.53–3.62 (m, 1H), 5.10–5.22 (m, 4H), 5.79–5.92 (m, 2H), 7.20–7.40 (m, 5H, Ph); MS (CI, *m/z*) 232 (M^++2), 231 (M^++1), 200. Anal. calcd for $C_{15}H_{22}N_2$: C, 78.26; H, 9.56; N, 12.17; found: C, 78.34; H, 9.42; N, 12.24.

4.4.5. (*S*)-*N*-Methyl-1-phenyl-2-[(*S*)-2′-(methoxymethylpyrrolidin-1-yl)ethanamine (1e). Yield 82% as a viscous liquid; R_f 0.80 (10% MeOH in DCM); $[\alpha]_D^{25}$=+16.0 (*c*=1.75, $CHCl_3$); IR (neat) 3420, 1150, 860 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.40–1.92 (m, 4H), 2.30–3.20 (m, 7H), 3.30 (s, 3H), 3.95 (s, 1H, *–NH*), 4.72 (m, 1H), 7.26 (m, 5H, Ph); MS (CI, *m/z*): 250 (M^++2), 249 (M^++1), 218 (base peak). Anal. calcd for $C_{15}H_{24}N_2O$: C, 72.58; H, 9.67; N, 11.29; found: C, 72.64; H, 9.82; N, 11.46.

4.4.6. (*S*)-*N*-Methyl-1-phenyl-2-(tetrahydroisoquinolin-1-yl)ethanamine (1f). Yield 85% as a viscous liquid; R_f 0.9 (5% MeOH in DCM); $[\alpha]_D^{25}$=+41.3 (*c*=7.2, $CHCl_3$); IR (neat) 3350, 3020 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.30 (s, 3H), 2.50–3.20 (m, 7H), 3.57 (d, *J*=16 Hz, 1H), 3.76 (dd, *J*=10, 3 Hz, 1H), 3.87 (d, *J*=16 Hz, 1H), 7.12–7.41 (m, 9H, aromatics); MS (CI, *m/z*): 268 (M^++2), 267 (M^++1), 265, 236. Anal. calcd for $C_{18}H_{22}N_2$: C, 81.20; H, 8.27; N, 10.52; found: C, 81.34; H, 8.29; N, 10.56.

4.4.7. (*S*)-*N*-α-Naphthyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine (1g). Yield 80% as a yellow viscous oil; R_f 0.40 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=−115 (*c*=4.0, $CHCl_3$); IR (neat) 3450, 3320, 3200, 3020, 2800, 820 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.78–1.83 (m, 4H), 2.63–2.80 (m, 5H), 3.14 (t, *J*=9 Hz, 1H), 4.48 (d, *J*=11 Hz, 1H), 6.20 (bs, 1H, *–NH*), 6.27 (d, *J*=6 Hz, 1H), 7.10–8.20 (m, 11H). Anal. calcd for $C_{22}H_{24}N_2$: C, 83.54; H, 7.59; N, 8.86; found: C, 83.92; H, 7.64.

4.4.8. (*S*)-*N*-*ortho*-Anisyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine (1h). Yield 77% as a viscous liquid; R_f 0.45 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=−28.7 (*c*=3.5, $CHCl_3$); IR (neat) 3450, 3400, 3050, 2950, 2800, 1600, 830 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.80 (m, 4H), 2.40–2.61 (m, 5H), 2.90 (t, *J*=12 Hz, 1H), 3.92 (s, 3H), 4.26 (dd, *J*=12, 4 Hz, 1H), 5.61 (bs, 1H, *–NH*), 6.23 (m, 1H), 6.62 (m, 2H), 6.78 (m, 1H), 7.22 (m, 1H), 7.31 (t, *J*=6.5 Hz, 2H), 7.42 (d, *J*=6 Hz, 2H). Anal. calcd for $C_{19}H_{24}N_2O$: C, 77.03; H, 8.11; N, 9.46; found: C, 77.32; H, 8.14; N, 9.40.

4.4.9. (*S*)-*N*-Benzyl-1-phenyl-2-(piperidin-1-yl)ethanamine (1i). Yield 80% as white crystals; mp 62–63°C; R_f 0.60 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+114 (*c*=6.3, $CHCl_3$) {lit.[18] $[\alpha]_D^{25}$=−108.6 (*c*=2, $CHCl_3$) for *R* enantiomer}.

4.4.10. (1*S*)-*N*-[(1*R*)-Phenylethyl]-1-phenyl-2-(piperidin-1yl)ethanamine (1j). Yield 87% as a colourless viscous liquid; R_f 0.75 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+134.9 (*c*=7.5, $CHCl_3$) {lit.[18h] $[\alpha]_D^{25}$=−41.6 (*c*=1, $CHCl_3$) for *RR* isomer}.

4.4.11. (*S*)-*N*-Phenyl-1-phenyl-2-(piperidin-1-yl)ethanamine (1k). Yield 88% as a white crystalline solid; mp 63–64°C; R_f 0.70 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+7.2 (*c*=6.5, $CHCl_3$); IR (KBr) 3350, 3030, 2920, 2800, 1600, 820 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.40–1.62 (m, 6H), 2.20–2.40 (bs, 2H), 2.42–2.60 (m, 4H), 4.29 (dd, *J*=7.5, 2.5 Hz, 1H), 5.34 (bs, 1H, *–NH*), 6.55 (d, *J*=7.6 Hz, 2H), 6.68 (t, *J*=7 Hz, 1H), 7.10 (t, *J*=7 Hz, 2H), 7.25–7.28 (m, 1H), 7.35 (t, *J*=8 Hz, 2H), 7.44 (d, *J*=7.5 Hz, 2H); MS (CI, *m/z*): 282 (M^++2), 281 (M^++1), 279, 250. Anal. calcd for $C_{19}H_{24}N_2$: C, 81.42; H, 8.57; N, 10.00; found: C, 81.72; H, 8.63; N, 10.12.

4.4.12. (*S*)-*N*-β-Naphthyl-1-phenyl-2-(piperidin-1-yl)ethanamine (1l). Yield 95% as a white solid; mp 90–92°C; R_f 0.70 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+31.2 (*c*=7.6, $CHCl_3$); IR (KBr) 3300, 3020, 2910, 2800, 1620, 830, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.48 (m, 2H), 1.62 (m, 4H), 2.34 (bs, 2H), 2.6 (m, 4H), 4.41 (dd, *J*=7, 2.5 Hz, 1H), 5.51 (s, 1H, *–NH*), 6.56 (d, *J*=2 Hz, 1H), 7.01 (dd, *J*=9, 2 Hz, 1H), 7.15 (t, *J*=6.0 Hz, 1H), 7.27 (t, *J*=7.5 Hz, 2H), 7.36 (t, *J*=7.5 Hz, 2H), 7.41 (d, *J*=7 Hz, 1H), 7.49 (d, *J*=7.5 Hz, 2H), 7.62 (d, *J*=9 Hz, 1H), 7.66 (d, *J*=9 Hz, 1H). Anal. calcd for $C_{23}H_{26}N_2$: C, 83.64; H, 7.88; N, 8.48; found: C, 83.88; H, 7.92.

4.4.13. (*S*)-*N*-(1,1-Dimethylethyl)-1-phenyl-2-(piperidin-1-yl)ethanamine (1m). Yield 96% as a viscous liquid; R_f 0.90 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+88 (*c*=7.0, $CHCl_3$) {lit.[18h] $[\alpha]_D^{25}$=−77 (*c*=1, $CHCl_3$) for *R* enantiomer}.

4.4.14. (*S*)-*N*-Tetrahydrofuranylmethyl-1-phenyl-2-(piperidin-1-yl)ethanamine (1n). Yield 92% as a viscous liquid; R_f 0.80 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+75.7 (*c*=6.0, $CHCl_3$); IR (neat) 3500, 3310, 3020, 2920, 2800, 1590, 830 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.35–1.42 (m, 3H), 1.40–1.62 (m, 4H), 1.80–2.0 (m, 3H), 2.20–2.42 (m, 4H), 2.40–2.62 (m, 6H), 3.65–4.10 (m, 3H), 7.20–7.38 (m, 5H, Ph). Anal. calcd for $C_{18}H_{28}N_2O$: C, 75.00; H, 9.72; N, 9.72; found: C, 74.72; H, 9.84.

4.4.15. (*S*)-*N*-Cyclohexyl-1-phenyl-2-(piperidin-1yl)ethanamine (1o). Yield 88% as yellow crystals; mp 58–60°C; R_f 0.65 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+93 (*c*=7.0, $CHCl_3$); IR (KBr) 3450, 2950 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.95–1.20 (m, 5H), 1.38–1.80 (m, 11H), 1.95–2.20 (m, 2H), 2.20–2.35 (m, 4H), 2.37 (t, *J*=12 Hz, 1H), 2.60 (bs, 1H), 3.94 (dd, *J*=10, 3 Hz, 1H), 7.20–7.43 (m, 5H, Ph). Anal. calcd for $C_{19}H_{30}N_2$: C, 79.72; H, 10.49; N, 9.79; found: C, 79.52; H, 10.54.

4.4.16. (*S*)-*N*-(3,5-Dimethylphenyl)-1-phenyl-2-(piperidin-1-yl)ethanamine (1p). Yield 87% as a yellow viscous liquid; R_f 0.95 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+10.1 (*c*=4.5, $CHCl_3$); IR (neat) 3450, 3340, 3010, 2920, 1590 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.40–1.62 (m, 6H), 2.18 (s, 6H), 2.20–260 (m, 6H), 4.26 (dd, *J*=10, 4 Hz, 1H), 5.42 (bs, 1H, *–NH*), 6.17 (s, 2H), 6.34 (s, 1H), 7.24–7.42 (m, 5H). Anal. calcd for $C_{21}H_{28}N_2$: C, 81.82; H, 9.09; N, 9.09; found: C, 81.62; H, 9.14.

4.4.17. (*S*)-*N*,*N*-Diethyl-1-phenyl-2-(diallylamino)ethanamine (6a). Yield 96% as a viscous liquid; R_f 0.80 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+4.4 (*c*=4.3, $CHCl_3$);

IR (neat) 3020, 2960, 730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.03 (t, J=9 Hz, 6H), 2.60–3.23 (m, 10H), 4.01 (t, J=6 Hz, 1H), 5.12 (m, 4H), 5.79 (m, 2H), 7.31 (m, 5H, Ph). Anal. calcd for $C_{18}H_{28}N_2$: C, 79.41; H, 10.29; N, 10.29; found: C, 79.32; H, 10.44.

4.4.18. (*S*)-*N*-[1-phenyl-2-(pyrrolidin-1-yl)ethyl]piperidine (6b). Yield 62% as a viscous liquid; R_f 0.40 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+3.8 (c=2.9, $CHCl_3$); IR (neat) 1210, 770 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25–1.34 (m, 2H), 1.50–1.58 (m, 4H), 1.62–1.70 (m, 4H), 2.36–2.39 (m, 4H), 2.48–2.60 (m, 3H), 2.90–3.07 (m, 3H), 3.69 (t, J=5 Hz, 1H), 7.19–7.38 (m, 5H, Ph); MS (CI, m/z): 259 (M^++1) (base peak), 174. Anal. calcd for $C_{17}H_{26}N_2$: C, 79.06; H, 10.07; N, 10.09; found: C, 78.96; H, 10.32; N, 10.14.

4.4.19. (*S*)-*N*-[1-Phenyl-2-(diallylamino)ethyl]tetrahydroisoquinoline (6c). Yield 71% as a viscous liquid; R_f 0.80 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+11.6 (c=2.5, $CHCl_3$); IR (neat) 3010, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.65–2.89 (m, 6H), 3.05–3.10 (m, 4H), 3.60 (d, J=14 Hz, 1H), 3.71 (t, J=6 Hz, 1H), 3.76 (d, J=14 Hz, 1H), 5.06–5.14 (m, 4H), 5.68–5.79 (m, 2H), 6.92–7.16 (m, 4H), 7.21–7.38 (m, 5H, aromatics); MS (CI, m/z): 333 (M^++1), 200.

4.4.20. (*S*)-*N*,*N*-Diethyl-1-phenyl-2-(piperdin-1-yl)ethanamine (6d). Yield 73% as a viscous liquid; R_f 0.60 (20% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+4.2 (c=2.4, $CHCl_3$); IR (neat) 1360, 780 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.01 (t, J=6 Hz, 6H), 1.32–1.40 (m, 2H), 1.42–1.58 (m, 4H), 2.28–2.49 (m, 6H), 2.58–2.82 (m, 4H), 3.91 (t, J=6.5 Hz, 1H), 7.18–7.36 (m, 5H, aromatics); MS (CI, m/z): 262 (M^++2), 188 (base peak). Anal. calcd for $C_{17}H_{28}N_2$: C, 78.46; H, 10.76; N, 10.38; found: C, 78.42; H, 10.24; N, 10.38.

4.4.21. (*S*)-*N*,*N*-Diallyl-1-phenyl-2-(piperidin-1-yl)ethanamine (6e). Yield 60% as a viscous liquid; R_f 0.80 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+15.7 (c=1.9, $CHCl_3$); IR (neat) 3040, 920 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.38 (m, 2H), 1.52 (m, 4H), 2.41 (m, 4H), 2.71 (m, 1H), 2.80–2.92 (m, 3H), 3.26 (dd, J=15, 6 Hz, 2H), 4.02 (t, J=6 Hz, 1H), 5.08–5.19 (m, 4H), 5.78–5.92 (m, 2H), 7.19–7.36 (m, 5H, Ph); MS (CI, m/z): 286 (M^++2), 188, 119.

4.4.22. (*S*)-*N*-benzyl-*N*-Methyl-1-phenyl-2-(piperidin-1-yl)ethanamine (6f). Yield 78% as a colourless viscous liquid; R_f 0.80 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+19.2 (c=4.0, $CHCl_3$); IR (neat) 1220, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.14 (s, 3H), 2.21–2.48 (m, 4H), 2.68 (q, J=6 Hz, 1H), 3.01 (q, J=6 Hz, 1H), 3.39 (d, J=14 Hz, 1H), 3.63 (d, J=14 Hz, 1H), 3.66 (t, J=6.0 Hz, 6H), 3.85 (t, J=6.5 Hz, 1H), 7.20–7.40 (m, 10H, Ph); MS (CI, m/z): 311 (M^++3) (base peak), 190. Anal. calcd for $C_{21}H_{28}N_2$: C, 81.81; H, 9.09; N, 9.05; found: C, 81.76; H, 9.16; N, 9.24.

4.4.23. (*S*)-*N*-[1-Phenyl-2-(piperidin-1-yl)ethyl]pyrrolidine (6g). Yield 80% as a yellow viscous liquid; R_f 0.40 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+7.9 (c=2.2, $CHCl_3$); IR (neat) 1220, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.22–1.28 (m, 2H), 1.38–1.45 (m, 4H), 1.66–1.77 (m, 4H), 2.32–2.36 (m, 4H), 2.52–2.69 (m, 5H), 2.95–3.01 (m, 1H), 3.43 (t, J=6 Hz, 1H), 7.21–7.38 (m, 5H, Ph); MS (CI, m/z): 259 (M^++1) (base peak), 188, 128. Anal. calcd for $C_{17}H_{26}N_2$: C, 79.06; H, 10.07; N, 10.85; found: C, 79.26; H, 10.24; N, 10.38.

4.4.24. (*S*)-*N*-[1-Phenyl-2-(piperidin-1-yl)ethyl]morpholine (6h). Yield 80% as a colourless viscous oil; R_f 0.60 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+6.0 (c=2.0, $CHCl_3$); IR (neat) 1120, 780 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.28–1.40 (m, 2H), 1.41–1.58 (m, 4H), 2.36–2.46 (m, 6H), 2.48–2.61 (m, 3H), 2.86 (dd, J=14, 6 Hz, 1H), 3.51 (t, J=5 Hz, 1H), 3.65 (t, J=6 Hz, 4H), 7.20–7.39 (m, 5H, Ph). Anal. calcd for $C_{17}H_{26}N_2O$: C, 74.45; H, 9.49; N, 10.22; found: C, 74.52; H, 9.54.

4.4.25. (*S*)-*N*,*N*-Diethyl-1-phenyl-2-(morpholin-4-yl)ethanamine (6i). Yield 99% as a viscous liquid; R_f 0.60 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+1.3 (c=3.0, $CHCl_3$); IR (neat) 1310, 810 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.03 (t, J=9 Hz, 6H), 2.37–2.44 (m, 4H), 2.44–2.51 (m, 2H), 2.63–2.72 (m, 4H), 3.63 (t, J=4.5 Hz, 4H), 3.92 (t, J=6 Hz, 1H), 7.26–7.32 (m, 5H, Ph); MS (CI, m/z): 263 (M^++1), 190. Anal. calcd for $C_{16}H_{26}N_2O$: C, 73.28; H, 9.92; N, 10.68; found: C, 73.29; H, 9.68; N, 10.72.

4.4.26. (*S*)-*N*-[1-Phenyl-2-(morpholin-4-yl)ethyl]pyrrolidine (6j). Yield 94% as a yellow viscous liquid; R_f 0.40 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+10.9 (c=3.2, $CHCl_3$); 98% ee (chiracel OD column 0.46×25 cm^2, solvent: hexane/isopropanol ratio 90:10; flow rate 0.5 mL/min; UV 254 nm; R_T: 7.87 min for *S*-enantiomer and 15.25 min for *R*-enantiomer); IR (neat) 1120, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.70–1.74 (m, 4H), 2.37–2.45 (m, 6H), 2.59–2.66 (m, 3H), 2.88–2.94 (m, 1H), 3.36 (dd, J=7.5, 3 Hz, 1H), 3.56 (t, J=4.5 Hz, 4H), 7.18–7.39 (m, 5H, aromatics). MS (CI, m/z): 261 (M^++1) (base peak), 190. Anal. calcd for $C_{16}H_{24}N_2O$: C, 73.84; H, 9.23; N, 10.76; found: C, 74.26; H, 9.36; N, 10.89.

4.4.27. (*S*)-*N*-[1-Phenyl-2-(morpholin-4-yl)ethyl]piperidine (6k). Yield 99% as a viscous liquid; R_f 0.40 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+16.0 (c=6.2, $CHCl_3$); IR (neat) 1210, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.22–1.38 (m, 2H), 1.42–1.58 (m, 4H), 2.38–2.42 (m, 6H), 2.46–2.58 (m, 2H), 2.69–2.76 (m, 1H), 2.92 (dd, J=14, 6 Hz, 1H), 3.57–3.66 (m, 5H), 7.21–7.36 (m, 5H, Ph); MS (CI, m/z) 275 (M^++1) (base peak), 190. Anal. calcd for $C_{17}H_{26}N_2O$: C, 74.45; H, 9.48; N, 10.21; found: C, 75.02; H, 9.76; N, 10.19.

4.4.28. (*S*)-*N*,*N*-Diethyl-1-phenyl-2-(tetrahydroisoquinolin-2-yl)ethanamine (6l). Yield 87% as a viscous liquid; R_f 0.70 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}$=+5.0 (c=1.4, $CHCl_3$); IR (neat) 1215, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.05 (t, J=9 Hz, 6H), 2.38–2.46 (m, 2H), 2.62–2.94 (m, 7H), 3.10–3.16 (m, 1H), 3.64 (d, J=14 Hz, 1H), 3.73 (d, J=14 Hz, 1H), 4.04 (t, J=6.5 Hz, 1H), 6.92–7.41 (m, 9H, aromatics).

4.4.29. (*S*)-*N*,*N*-Diallyl-1-phenyl-2-(tetrahydroisoquinolin-2-yl)ethanamine (6m). Yield 75% as viscous liquid;

R_f 0.70 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}=+15.6$ ($c=2.3$, $CHCl_3$); IR (neat) 3010, 1440, 780 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.64–2.96 (m, 8H), 3.12–3.16 (m, 1H), 3.21–3.34 (m, 1H), 3.70 (d, $J=4.5$ Hz, 2H), 4.16 (t, $J=6$ Hz, 1H), 5.10–5.21 (m, 4H), 5.79–5.94 (m, 2H), 6.95–7.41 (m, 9H, aromatics); MS (CI, *m/z*): 333 ($M^+ +1$), 236, 132. Anal. calcd for $C_{23}H_{28}N_2$: C, 83.12; H, 8.41; N, 8.43; found: C, 83.26; H, 8.48; N, 8.68.

4.4.30. (*S*)-*N*-[1-Phenyl-2-(tetrahydroisoquinolin-2-yl)-ethyl]pyrrolidine (6n). Yield 75% as viscous liquid; R_f 0.80 (50% EtOAc in petroleum ether); $[\alpha]_D^{25}=+24.5$ ($c=3.15$, $CHCl_3$); IR (neat) 1210, 1090, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.71–1.78 (m, 4H), 2.45–2.50 (m, 2H), 2.64–2.69 (m, 4H), 2.71–2.83 (m, 3H), 3.13 (q, $J=5$ Hz, 1H), 3.43 (t, $J=6$ Hz, 1H), 3.56 (d, $J=14$ Hz, 1H), 3.64 (d, $J=14$ Hz, 1H), 6.92–6.98 (m, 1H), 7.01–7.18 (m, 3H), 7.20–7.42 (m, 5H, aromatics); MS (CI, *m/z*): 307 ($M^+ +1$) (base peak), 236. Anal. calcd for $C_{21}H_{26}N_2$: C, 82.35; H, 8.49; N, 9.15; found: C, 82.42; H, 8.44; N, 9.26.

4.4.31. (*S*)-*N*-[1-Phenyl-2-(tetrahydroisoquinolin-2-yl)-ethyl]morpholine (6o). Yield 94% as a yellow viscous liquid; R_f 0.60 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}=+15.7$ ($c=3.5$, $CHCl_3$); IR (neat) 1200, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.41–2.64 (m, 6H), 2.66–2.82 (m, 4H), 3.17 (dd, $J=11$, 4 Hz, 1H), 3.59–3.72 (m, 6H), 6.94–7.39 (m, 9H, aromatics); MS (CI, *m/z*) 323 ($M^+ +1$) (base peak), 236. Anal. calcd for $C_{21}H_{26}N_2O$: C, 78.26; H, 8.07; N, 8.69; found: C, 78.34; H, 8.56; N, 8.72.

4.4.32. (*S*)-*N*-[1-Phenyl-2-(tetrahydroisoquinolin-2-yl)-ethyl]piperidine (6p). Yield 74% as a yellow viscous liquid; R_f 0.70 (10 EtOAc in petroleum ether); $[\alpha]_D^{25}=+14.1$ ($c=3.2$, $CHCl_3$); IR (neat) 1220, 790 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24–1.40 (m, 2H), 1.43–1.61 (m, 4H), 2.18–2.26 (m, 4H), 2.72–2.84 (m, 4H), 2.82–2.86 (m, 1H), 3.12–3.17 (m, 1H), 3.65 (d, $J=14$ Hz, 2H), 3.73 (t, $J=6$ Hz, 1H), 6.96–7.10 (m, 1H), 7.11–7.16 (m, 3H), 7.21–7.38 (m, 5H, aromatics); MS (CI, *m/z*): 321 ($M^+ +1$) (base peak), 236. Anal. calcd for $C_{22}H_{28}N_2$: C, 82.50; H, 8.75; N, 8.73; found: C, 82.72; H, 8.36; N, 8.42.

4.4.33. *cis*-(1*S*,4*R*)-4-Hexadecyl-4-trimethylsiloxy-2-cyclopentene-1-ol (9). *n*-BuLi (E-Merck, 1.74 M in hexane, 1.15 mL, 2.0 mmol) was added to a solution of (*R*)-diamine **1a** (480 mg, 2.2 mmol) in toluene (10 mL) at 0°C. After 15 min stirring, the epoxide **8** (400 mg, 1.0 mmol) was added and the mixture stirred (0°C, rt) for 24 h. The reaction mixture was taken up in diethyl ether (30 mL) followed by washing with aqueous tartaric acid, water, brine. The organic layer was dried, and removal of the solvent under reduced pressure gave the crude product. The crude material was purified on silica gel column using EtOAc–petroleum ether as eluent provide the pure allylic alcohol **9** (328 mg, 83%) as a colourless oil; R_f 0.50 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}=-20.8$ ($c=1.25$, $CHCl_3$) {lit.[26b] $[\alpha]_D^{25}=-18.1$ ($c=1.02$, $CHCl_3$) for 89% ee}.

4.4.34. *cis*-(1*R*,4*S*)-4-*tert*-Butyldimethylsiloxymethyl-2-cyclopenten-1-ol (13). *n*-BuLi (E-Merck 1.74 M in hexane, 1.15 mL, 2.0 mmol) was added to a solution of diamine (*S*)-**1a** (480 mg, 2.2 mmol) in THF (10 mL) at 0°C. After 15 min stirring, the epoxide **12** (230 mg, 1.0 mmol) was added and the mixture was stirred for 48 h. Most of the THF was removed in vacuo at 0°C, and the crude material was taken up in diethyl ether (20 mL). It was washed with aqueous tartaric acid, water, brine, and dried. Solvent was removed under reduced pressure and the crude material was purified on silica gel column to provide the pure allylic alcohol **13** (62 mg, 27%) as a colourless liquid; R_f 0.50 (10% EtOAc in petroleum ether); $[\alpha]_D^{25}=-36.8$ ($c=1.85$, $CHCl_3$) {lit.[30a,c] $[\alpha]_D^{25}=-44.3$ ($c=1.5$, $CHCl_3$) for (1*S*) isomer with 95% ee, $[\alpha]_D^{25}=+33.2$ ($c=0.78$, $CHCl_3$) for (1*R*) isomer with 72% ee}.

4.5. General procedure for the enantioselective addition of diethylzinc to aldehydes catalysed by vicinal diamines

To a flame dried flask, carbonyl compound (1 mmol) and diamine **1a** (40 mg, 0.2 mmol, 20 mol%) were added, dissolved in dry cyclohexane (8 mL) and stirred for 20 min. The reaction mixture was cooled to 0°C. Diethylzinc (2 mL, 2 mmol, and 1 M hexane solution) was added over a period of 5 min. The reaction mixture was stirred for 20 h at 0°C to room temperature. Saturated NH_4Cl (5 mL) and 1N HCl (5 mL) were added to quench the reaction and the mixture was extracted with EtOAc (three times). The combined organic layers were washed with water, brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the resulting oily substrate was purified by silica gel column chromatography using EtOAc–petroleum ether as eluent to give pure alcohols **14**.

4.6. Determination of enantiomeric purity of optically active alcohols[39]

General procedure for making MTPA ester of (*S*)-**14e**. To a solution of (*S*)-**14e** (5 mg), Et_3N (3 equiv.) and a crystal of DMAP in dichloromethane (0.5 mL) was added (*S*)-MTPACl (1.5 equiv., 98% ee) at room temperature. Reaction mixture was allowed to stand until the starting material was fully consumed. If necessary, some more amount of MTPACl and Et_3N were added to make sure that the reaction was complete. Reaction mixture was filtered through a short silica gel column to get the mixture of two diastereomeric MTPA esters; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.93 (t, $J=9$ Hz, 3H), 1.79–2.01 (m, 2H), 3.54 (s, 3H), 5.77 (dd, $J=9$, 3 Hz, 1H) (for *SS* from major (*S*)-1-hydroxy-propyl(4-chloro)benzene), 5.85 (dd, $J=9$, 3 Hz, 1H) (for *RS* from minor (*R*)-1-hydroxy-propyl-(4-chloro)benzene), 7.12–7.40 (m, 9H, aromatics). Based on above 400 MHz NMR data, the enantiomeric excess of (*S*)-1-hydroxy-propyl(4-chloro)benzene was 66.5%. The optical purity of the (*R*)-Mosher acid was 98%. So, corrected value of the optical purity was 68% using diamine **1j**.

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