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Memory of Chirality (MOC) Concept in Imino-Aldol Reaction: Enantioselective Synthesis of α,β-Diamino Esters and Aziridines

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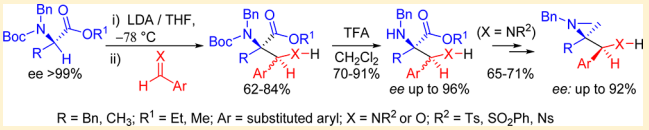
Supporting Information

ABSTRACT: A simple strategy for the synthesis of chiral α,β-diamino- and α-amino,β-hydroxy ester derivatives in high yields with moderate to high *ee* has been developed via asymmetric imino-aldol and aldol reactions, respectively, starting from protected aminoesters employing memory of chirality concept for chiral induction. This strategy has been extended for the enantioselective synthesis of aziridines (*ee* up to 92%). The absolute configuration of the imino-aldol adducts has been determined. The stereochemical outcome of the products has been explained by a suitable mechanism and supported by computational studies.



INTRODUCTION

The asymmetric aldol and imino aldol reactions of enolates with aldehydes (or equivalents) and imines, respectively, are synthetically very important for the construction of β-amino esters,[1] α,β-diamino ester derivatives,[2] nonproteogenic β-amino acids,[3] different polyfunctionalized chiral building blocks,[4] and β-lactam antibiotics,[3,5] etc. The enantioselective synthesis of many of these bioactive compounds were achieved by the addition of chiral enolates with imines where a chiral auxiliary or an untouched stereogenic center of the ester enolate controls the stereoselectivity.[3,6] Other approaches for asymmetric imino-aldol reactions either involve achiral enolates and chiral imines along with achiral Lewis acids[7] or chiral enolate complexes generated from achiral enolates with chiral Lewis acids.[8,9] However, there is no report other than ours for asymmetric imino-aldol reaction without using any external chiral source, for example, chiral auxiliary or a catalyst. To induce asymmetry in imino-aldol reaction without the aid of an external chiral source, we anticipated that a conformationally chiral enolate could be added to an imine following Memory of Chirality (MOC) concept. The phenomenon of MOC was first demonstrated in the field of enolate chemistry by Fuji and Kawabata where enantioselective alkylation of chiral ketones, amides and amino acid esters were achieved through enolate carbanions with a high degree of selectivity.[10−15] A number of synthetically and biologically important compounds including substituted α-amino acids,[11] quaternary amino acids,[3b,c] cyclic amino acids,[12,13] *N*-heterocycles,[14,15] etc. were synthesized utilizing this concept. Recently, we have explored MOC in an asymmetric imino-aldol reaction to obtain α,β-diamino esters with consecutive quaternary and tertiary stereogenic centers in high yields and streoselectivities.[16]

Optically active α,β-diamino acids are found in a variety of antibiotics and natural products.[2a,17] A number of synthetic routes are available in the literature[2,18] for the synthesis of α,β-diamino acids and their derivatives including direct catalytic asymmetric Mannich reaction,[18a−c] opening of aziridine rings,[18d−f] imino-aldol reaction,[2] catalytic asymmetric aza-Henry reaction,[18g] etc. In this article, we report our detailed study for the synthesis of chiral α,β-diamino ester derivatives via the imino-aldol protocol following MOC concept. This methodology was further explored for aldol reaction.

RESULTS AND DISCUSSION

To begin our study, the enolate was generated from *N*-benzyl-*N*-*tert*-butoxycarbonylphenylalanine ethyl ester **1a**[16] by the treatment of KHMDS at −78 °C and was reacted with *N*-benzylidene-4-methylbenzenesulfonamide at the same temperature to afford the corresponding α,β-diamino ester derivative **4a** following the imino-aldol protocol (Scheme 1).[16] The imino-aldol adduct **4a** was isolated as an inseparable mixture of diastereomers. However, **3** did not cyclize to produce the corresponding β-lactam **5** since the negative charge developed on nitrogen was highly delocalized over the sulfonyl group. The ^{1}H NMR spectrum of the imino-aldol adduct **4a** showed broad signals at room temperature possibly because of its existence as a mixture of rotamers. However, the formation of the product **4a** was confirmed by ^{13}C NMR, DEPT NMR and mass spectral analysis.

To restrict the interconversion of possible rotamers of the imino-aldol adduct **4a** at room temperature, extensive low temperature NMR study was carried out at −25, −40 and −55 °C (in $CDCl_3$) with an idea that one of the rotamers might be frozen at lower temperature (see Supporting Information). Resolution of the ^{1}H NMR spectrum was improved to some extent upon lowering the temperature, although it was not completely resolved even at −55 °C (in $CDCl_3$). ^{1}H NMR spectrum of **4a** recorded at higher temperature (60 °C in DMSO-d_6) showed similar broad spectrum as discussed earlier. To simplify the ^{1}H NMR spectrum, *N*-Boc group of **4a** was removed using 1:2 trifluoroacetic acid and dichloromethane to give **6a** as a mixture of diastereomers in 88% yield with *dr* 75:25 (based on ^{1}H NMR study of the crude reaction mixture) (Scheme 2). The diastereomers were separated

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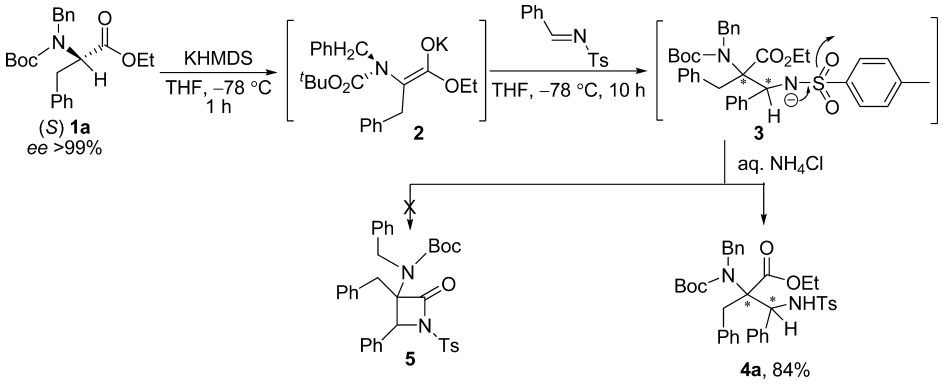
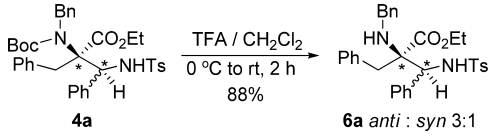
Scheme 1. Addition of *N*-Benzyl-*N*-*tert*-butoxycarbonylphenylalanine Ethyl Ester Enolate to 2-Phenyl-*N*-tosyl Aldimines



Scheme 2. Boc Deprotection of α,β-Diamino Ester Derivatives 4a

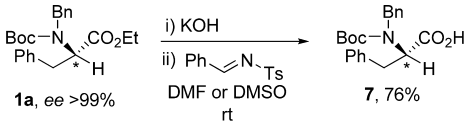


by flash column chromatography. Compound **6a** was characterized by spectroscopic and analytical data.

The reaction of **1a** with *N*-tosylphenylaldimine was studied in different solvents using KHMDS as the base (Table 1, entries 1−4). In all cases, compound **4a** was obtained in moderate yield but with low enantioselectivity (up to 28% for the major diastereomer, based on chiral HPLC analysis of **6a**). The reaction was studied with other bases such as LDA, LiHMDS, NaHMDS and LTMP etc. as shown in Table 1 (entries 5−8). When NaHMDS or LiHMDS was used, the reaction did not proceed (Table 1, entry 5) at all. The best result was obtained using LDA as the base and THF as the solvent where **4a** was obtained with *dr* 83:17 (*ee* 92% for the major diastereomer) (Table 1, entry 6). When toluene was used as the solvent, only a trace amount of **4a** was formed (Table 1, entry 7). However, using LTMP, **4a** was obtained with high yield (80%) and selectivity (based on *ee* 80% for the major diastereomer of **6a**) (Table 1, entry 8). In all the cases, stereoselectivity was determined only after removal of the Boc group from **4a**.

Recently Kawabata et al.[13a] have reported enantioselective cyclization of α-amino acid derivatives at ambient temperature using powdered KOH in DMSO or DMF. Encouraged by this report, we carried out the imino-aldol reaction using KOH in DMSO or DMF at ambient temperature. The addition reaction (imino-aldol) did not proceed under this condition; instead, the corresponding acid **7** was produced by the hydrolysis of the ester group of **1a** (Scheme 3).

Scheme 3. Addition of 1a to 2-Phenyl-*N*-tosyl Aldimines at Ambient Temperature



On the basis of the above results, further studies were carried out using LDA as the base. Although the reaction proceeded smoothly with 1.2 equivalent of enolate, for obtaining better yield and selectivity the use of 2.2 equivalents of enolate was found to be the best. This optimized condition was used in all the subsequent reactions. The reaction was nearly completed within 2 h; however, for further improvement in yield and *ee*, the reaction was continued for 10 h. To extend the scope of this reaction, a variety of *N*-activated imines with electron donating as well as electron withdrawing aryl substitutents were reacted with amino acid ester **1a** to afford the substituted nonracemic α,β-diamino ester derivatives **4b−j** (based on optical rotation) as a mixture of diastereomers in 62−81% yields (Scheme 4). Although ^{1}H NMR signals of imino-aldol adducts **4b−j** were found to be wavy as discussed earlier (low temperature ^{1}H NMR spectra are provided in the Supporting Information), the formation of all the compounds **4b−j** were fully confirmed by ^{13}C NMR, DEPT NMR and HRMS data. The stereoisomers of the imino-aldol products **4b−j** could not be separated at this stage.

To confirm the diastereoselectivity as well as the enantioselectivity, the imino-aldol adducts **4b−j** were subjected

Table 1. Effect of Bases and Solvents on Imino-aldol Reaction

entry	base	solvent	time (h)	yield **4a**[a] (%)	yield **6a**[a] (%)	*ee*[b,c] (%)	*dr*[d] (%)
1	KHMDS	THF	6.0	55	89	4	75:25
2	KHMDS	THF/Toluene 4:1	2.0	71	94	16	58:42
3	KHMDS	THF/Toluene 1:4	2.5	70	92	26	64:36
4	KHMDS	Toluene	2.5	56	87	28	74:26
5	LiHMDS/NaHMDS	THF	14.0	Trace			
6	LDA	THF	10.0	84	88	92	83:17
7	LDA	Toluene	10.0	Trace			
8	LTMP	THF	2.0	80	80	80	64:36

[a]Combined yield of both the diastereomers after purification. [b]HPLC separation was done using Chiral AD-H column (95:5 Hexane/Isopropanol as mobile phase and 1.0 mL/min flow rate). [c]*ee* was determined from HPLC analysis of **6a**. [d]*dr* based on crude ^{1}H NMR analysis of **6a**.

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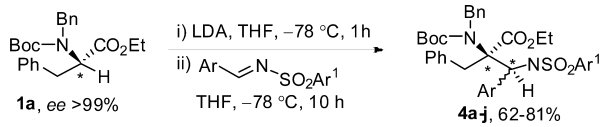
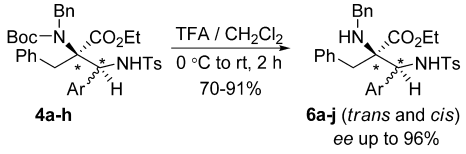
Scheme 4. Synthesis of α,β-Diamino Acid Derivatives 4a−j



a: Ar = Ph, Ar^1 = 4-MeC_6H_4; **b**: Ar = Ph, Ar^1 = Ph; **c**: Ar = Ph, Ar^1 = 4-$NO_2C_6H_4$; **d**: Ar = 3-BrC_6H_4, Ar^1 = 4-MeC_6H_4; **e**: Ar = 2-ClC_6H_4, Ar^1 = 4-MeC_6H_4; **f**: Ar = 4-$NO_2C_6H_4$, Ar^1 = 4-MeC_6H_4; **g**: Ar = 4-$OMeC_6H_4$, Ar^1 = 4-MeC_6H_4; **h**: Ar = 2-furyl, Ar^1 = 4-MeC_6H_4; **i**: Ar = 4-ClC_6H_4, Ar^1 = 4-MeC_6H_4; **j**: Ar = 3-$NO_2C_6H_4$; Ar^1 = 4-MeC_6H_4

Ar, N, SO_2Ar_1	4a-j	Yield
a: Ar = Ph, Ar_1 = 4-MeC_6H_4	**4a**	84
b: Ar = Ph, Ar_1 = Ph	**4b**	62
c: Ar = Ph, Ar_1 = 4-$NO_2C_6H_4$	**4c**	80
d: Ar = 3-BrC_6H_4, Ar_1 = 4-MeC_6H_4	**4d**	68
e: Ar = 2-ClC_6H_4, Ar_1 = 4-MeC_6H_4	**4e**	74
f: Ar = 4-$NO_2C_6H_4$, Ar_1 = 4-MeC_6H_4	**4f**	75
g: Ar = 4-$OMeC_6H_4$, Ar1 = 4-MeC_6H_4	**4g**	65
h: Ar = 2-furyl, Ar_1 = 4-MeC_6H_4	**4h**	74
i: Ar = 4-ClC_6H_4, Ar_1 = 4-MeC_6H_4	**4i**	72
j: Ar = 3-$NO_2C_6H_4$; Ar_1 = 4-MeC_6H_4	**4j**	81

Scheme 5. Boc Deprotection of Compounds 4a−j



a: Ar = Ph, Ar^1 = 4-MeC_6H_4; **b**: Ar = Ph, Ar^1 = Ph; **c**: Ar = Ph, Ar^1 = 4-$NO_2C_6H_4$; **d**: Ar = 3-BrC_6H_4, Ar^1 = 4-MeC_6H_4; **e**: Ar = 2-ClC_6H_4, Ar^1 = 4-MeC_6H_4; **f**: Ar = 4-$NO_2C_6H_4$, Ar^1 = 4-MeC_6H_4; **g**: Ar = 4-MeC_6H_4, Ar^1 = 4-MeC_6H_4; **h**: Ar = 2-furyl, Ar^1 = 4-MeC_6H_4; **i**: Ar = 4-ClC_6H_4, Ar^1 = 4-MeC_6H_4; **j**: Ar = 3-$NO_2C_6H_4$; Ar^1 = 4-MeC_6H_4

to BOC-group deprotection following the aforementioned condition to afford **6b−j** as a mixture of diastereomers with 70−91% yields (Scheme 5, Table 2). Diastereoselectivity was determined by ^{1}H NMR spectrum of the crude reaction mixture and the maximum *dr* (83:17) was achieved in the cases of compounds **6a** and **6c** (Table 2, entries 1, 4). At this stage, the major diastereomers of the α,β-diamino ester derivatives **6a−j** could be separated by flash column chromatography on silica gel (Table 2). The minor diastereomers of **6b**, **6d** and **6h** could not be obtained in pure forms; their *ees* were determined by chiral HPLC analysis comparing the peaks of the mixture with that of the pure major diastereomer. All of the compounds (**6a−j**) were fully characterized by spectral and analytical data.

The substrate scope of the reaction was studied by replacing the benzyl group of **1a** with a less sterically demanding methyl group. When the ester enolate generated from the alanine derivative **1b** was reacted with 2-phenyl-*N*-tosylaldimine, the corresponding addition product **4k** was obtained with 72% yield. Its Boc group was removed to produce the compound **6k** as a mixture of diastereomers in 79% yield (Scheme 6). In this case, lower stereocontrol was observed (major/minor = 55:45 and *ee* 33% for the major diastereomer) probably due to the rapid racemization of the chiral enolate during the course of the reaction. This result is consistent with the work reported by Kawabata et al. where such type of chirality loss was overruled by rapid cyclization in the case of intramolecular reaction, however, in the case of intermolecular reaction lower *ee* (∼33%) of the product was observed.[12a]

To provide evidence in support of the MOC concept in imino-aldol reaction, ester enolate generated from (*S*)-methyl 2-[bis(*tert*-butoxycarbonyl) amino]-3-phenylpropanoate (**1c**) was treated with 2-phenyl-*N*-tosylaldimine to produce the corresponding addition product **4l**.[16] In this case, the enolate having no axial chirality along C−N axis was expected not to induce any chirality into the product (Scheme 7). Although the corresponding addition product **4l** could not be separated in chiral HPLC column (Chiralcel OD-H or AD-H), the Boc deprotected derivative **6l** was well separated in chiracel AD-H column and obtained as a racemate.[20] This interesting result unambiguously supports that the MOC is operating in our imino-aldol reaction with substrates **1a−b**.

After successful demonstration of the memory of chirality in imino-aldol reaction we intended to explore the concept in aldol reaction. Although in recent years memory of chirality concept has become a conceptually new strategy in the field of asymmetric synthesis, surprisingly, MOC based aldol reaction

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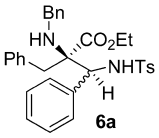
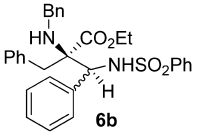
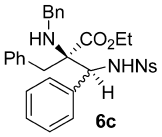
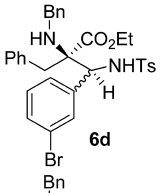
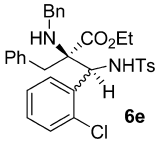
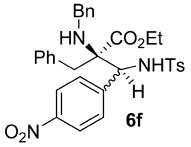
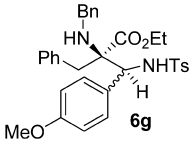
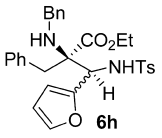
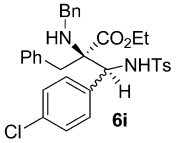
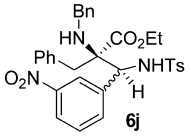
Table 2. Imino-aldol Adducts 6 Generated after Boc Removal from 4a−h

Entry	Product (**6**)[a]	Yield **6** (%)[b]	*dr* (%)[c] **6** (*anti*: *syn*)	*ee* (%) **6a-h** major (*anti*) diastereomer	*ee* (%) **6a-h** minor (*syn*) diastereomer
1	 **6a**	88	83:17	92	80
2	 **6b**	70	71:29	80	80
3	 **6c**	84	83:17[d]	88	-
4	 **6d**	87	71:29	84	62
5	 **6e**	80	79:21[d]	56	-
6	 **6f**	86	73:27	75	43
7	 **6g**	91	75:25	96	70
8	 **6h**	87	67:33	80	88
9	 **6i**	88	75:25	57	67
10	 **6j**	85	62:38	60	33

[a]Corresponding imino-aldol adducts (a mixture of major and minor isomers of **6**) obtained after 10 h. [b]Combined yield of both the diastereomers after purification. [c]*dr* based on crude ^{1}H NMR analysis. [d]Minor diastereomer could not be separated in available chiral HPLC columns.

remained unexplored. Stoodley and co-workers demonstrated the memory of chirality effect in intramolecular aldol cyclization of 1-(3-oxabutyryl) derivatives of L-4-oxaproline and proline isopropyl esters via the involvement of an axially chiral enolate intermediate.[19a,b] Very recently Kawabata and co-workers demonstrated the application of MOC concept in asymmetric

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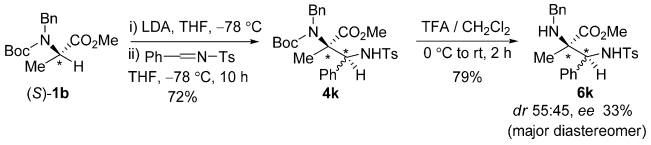
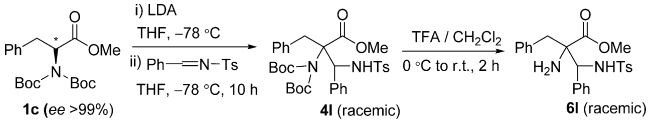
Scheme 6. Addition of *N*-Benzyl-*N*-*tert*-butoxycarbonylalanine Methyl Ester Enolate 1b to 2-Phenyl-*N*-tosylaldimines



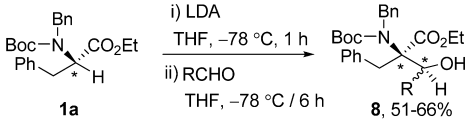
Scheme 7. Synthesis of Compound 6I



aldol reaction followed by cylization to form cyclic 2-oxooxazolidine derivatives in high ee starting from amino acid ester enolate and aldehyde using KHMDS as the base.[19c]

To begin our study in aldol reaction, the ester enolate was generated from *N*-benzyl-*N*-*tert*-butoxycarbonylphenylalanine ethyl ester **1a** using LDA as the base at −78 °C and was reacted with an electron withdrawing aldehyde (4-nitrobenzaldehyde) at the same temperature to afford the corresponding α-amino, β-hydroxy ester derivative **8a** as a mixture of diastereomers (*dr* 3:2.4) in 65% yield (Scheme 8). The formation of the aldol

Scheme 8. Synthesis of α-Amino,β-hydroxy Ester Derivatives 8a−d



R = **a**: 4-$NO_2C_6H_4$, **b**: 3-$NO_2C_6H_4$, **c**: 4-$OMeC_6H_4$,**d**: 3,4-$(OMe)_2C_6H_3$

product was confirmed by ^{1}H NMR, ^{13}C NMR, DEPT NMR and HRMS analysis. The diastereoselectivity of **8a** was confirmed by ^{1}H NMR of the crude reaction mixture after removal of the unreacted starting material by flash column chromatography. Although the major diastereomer could be isolated in pure form in small amount, the minor isomer could not be obtained in pure form. The ee of the minor diastereomer was found to be 68%, however, the major isomer was produced with low ee (16%). The generalization of the methodology was made by studying the aldol reaction of the ester enolate of **1a** with a variety of aldehydes to afford the corresponding α-amino,β-hydroxy ester derivatives **8a−d** in 51−66% yields (Scheme 8, Table 3).

In the case of another electron withdrawing aromatic aldehyde (3-nitrobenzaldehyde), the corresponding addition product **8b** was obtained in 66% yield as a mixture of diastereomers (Table 3, entries 2). Both of the isomers of **8b** could be isolated in pure forms by column chromatography. The ee of the major and the minor isomers were found to be 30 and 76%, respectively. On increasing the reaction temperature to −70 °C, the diastereomeric ratio of **8b** changed to ∼3:2. The major and the minor diastereomers of **8b** were obtained with reduced ee (14 and 67%, respectively). Using electron rich aromatic aldehydes (e.g., 4-methoxybenzaldehyde and 3,4-dimethoxybenzaldehyde), the corresponding addition products (**8c** and **8d**, respectively) were obtained with reduced yields (51−52%) (Table 3, entries 3−4) probably due to the reduced electrophilicity of the carbonyl carbon. All of the compounds were characterized by spectroscopic and analytical data. These results are summarized in Table 3.[19d]

The major and the minor diastereomers of the products **8a−d** were produced with *syn* and *anti* relative stereochemistry, respectively, as determined by the NOE experiments of both the diastereomers of **8b**.[20]

The N-Boc group of **8a** (as a mixture of diastereomers) was deprotected using TFA/DCM (1:2) to give the corresponding NH-free aldol product **9** (Scheme 9). Both the isomers of compound **9** were separated by column chromatography. The major isomer was obtained with very poor ee (9%), although the minor isomer was obtained with good ee (67%) based on chiral HPLC analysis. In the same fashion, other α-amino,β-hydroxy ester derivatives **8c−d** were subjected to Boc group removal step as discussed earlier but even after the Boc group deprotection the diastereomers could not be separated in column chromatography and the enantiomers remained inseparable in available chiral HPLC columns.

The formation of the nonracemic aldol products **8** suggests that memory of chirality concept is operating in the aldol reaction. Unfortunately, in most of the cases, the pure diastereomer could not be isolated by column chromatography and the *ee* also could not be determined. At this stage, the stereocontrol in aldol reaction was further investigated using KHMDS as a base.

When ester enolate generated from **1a** was generated by using KHMDS at −78 °C and reacted with benzaldehyde at the same temperature (Scheme 10), ethyl 3,4-dibenzyl-2-oxo-5-phenyloxazolidine-4-carboxylate (**10a**) was obtained in 55% yield. The intermediate aldolate anion, instead of giving the corresponding aldol product, underwent intramolecular cyclization with the carbamate group to produce **10a** as a single diastereomer with low *ee* (16%).[19d] Very recently similar aldol reaction followed by cylization has been reported by Kawabata et al.[19c] with excellent enantioselectivities (ee up to 94%).

This finding was generalized with a variety of aromatic aldehydes having electron donating (e.g., 3,4-dimethoxybenzaldehyde) and electron withdrawing (2-chlorobenzaldehyde, 3-nitrobenzaldehyde) substituents (Scheme 10). In the case of electron withdrawing aldehydes, compound **10** was obtained in higher yield (up to 59%) as compared to the electron donating ones. However, all of the compounds **10b−d** were obtained as single diastereomers but with very poor ees (4−16%).[19d] Formation of **10** with poor ees from our substrate **1a** using KHMDS as the base is consistent with our earlier observation in imino-aldol reaction. It is interesting to note that using LDA as the base, the substrate **1a** undergoes intermolecular aldol reaction to produce the free aldol products **8**, whereas ethyl 3,4-dibenzyl-5-aryloxooxazolidine-4-carboxylates **10** were obtained via aldol followed by intramolecular cylization with N-Boc group when KHMDS was used as the base.

Different reactivity patterns of the enolates generated from **1a** using LDA or KHMDS as the base could be explained by considering the chelating ability of the counterion Li^+ or K^+ as shown in Scheme 11. In the case of LDA, the counterion Li^+ is strongly coordinating and hence the intermediate aldolate anion remained in chelated form as shown in **12a−b**, whereas K^+, being a less coordinating metal ion, makes the alkoxy anion **15** more available for further attack to carbamate to form the cyclized product **10**. Possible retroaldol reaction from the aldolate anion **15** would regenerate the K-enolate **14**. Probably because of faster racemization of K-enolate **14** being in

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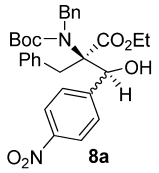
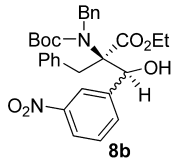
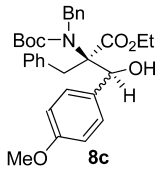
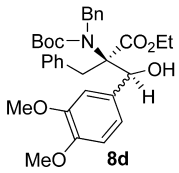
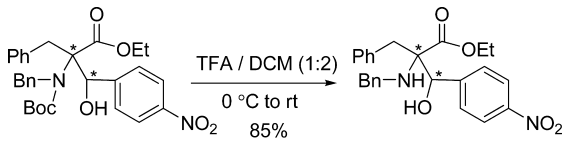
Table 3. Synthesis of α-Amino,β-hydroxy Ester Derivatives 8a−d

Entry	Product (**8a-d**)	Yield (%)	Dr (*syn:anti*)[a]
1.	 **8a**	65	3:2.4[b,c]
2.	 **8b**	66	3:1[b,d]
3.	 **8c**	52	3:1
4.	 **8d**	51	4:1

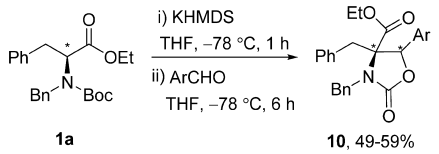
[a]dr based on ^{1}H NMR of the crude reaction mixture after removal of the unreacted ester **1a**. [b]ee (%) for the minor and the major diastereomers of **8** based on chiral HPLC analysis. [c]ee (%) for **8a:** 68 (minor isomer), 16 (major isomer). [d]ee (%) for **8b:** 76 (minor isomer), 30 (major isomer).

Scheme 9. Boc Deprotection of α-Amino,β-hydroxy Ester Derivative 8a



8a **9**

Scheme 10. Synthesis of Ethyl 3,4-Dibenzyl-5-aryloxooxazolidine-4-carboxylates 10a−e



1a **10**, 49-59% single diastereomer

10a: Ar = Ph, Yield: 55%; **10b**: Ar = 3-$NO_2C_6H_4$, Yield: 59%; **10c**: Ar = 2-ClC_6H_4, Yield: 57%; **10d**: Ar = 4-$OMeC_6H_4$, Yield: 49%; **10e**: Ar = 3,4-$OMeC_6H_3$, Yield: 49%.

nonchelated form compared to chelated Li-enolate **11a−b**, the aldolate anion intermediate **15** gets racemized easily and further cyclizes to produce **10** with poor ees.

After successful demonstration of the memory of chirality concept in imino-aldol reaction, we attempted to determine the absolute configuration of α,β-diamino ester derivatives. For this purpose the pure major and minor diastereomers of **6a** were separately crystallized out using 9:1 $CHCl_3$ in hexane. On the basis of X-ray crystallographic analysis, the major diastereomer of **6a** was assigned to be *anti* having relative configuration (2*S*,3*R*) and that of the minor diastereomer of **6a** was found to be *syn* with relative configuration (2*S*,3*S*).[20] Unfortunately, in both the cases the crystals were obtained as a racemate (based on centrosymmetric point group and HPLC analysis) and the mother liquor contained the pure enantiomer. Unfortunately, the pure enantiomer of **6a** (obtained from the mother liquor) in combination of various solvents could not be crystallized and hence we were unable to determine its absolute configuration. However, using our imino-aldol protocol α,β-diamino ester derivatives (e.g., **6a**) could be obtained in enantiomerically pure forms.

Other α,β-diamino ester derivatives **6b**, **6e**, **6g** and **6j** after crystallization from their diastereomeric mixtures resulted the crystals of pure major diastereomers as racemates with *anti* relative stereochemistry (see Supporting Information). In general, the major diastereomer of α,β-diamino ester derivatives were obtained with *anti* geometry following our imino-aldol protocol. Recently, *anti*/*syn* selectivity of α,β-diamino ester derivatives has been nicely explained independently by Davis[21] and de Kimpe et al.[18c]

Next, different derivatization processes were attempted with enantiopure **6a** (major diastereomer). Initially, the ester moiety of **6a** was reduced with lithium borohydride in tetrahydrofuran at room temperature[22] to give the corresponding alcohol **16a** without loss of enantioselectivity (Scheme 12).[23] In this case, the enantiomerically pure alcohol **16a** could not be crystallized from different combination of solvents.

In another attempt, when compound **4a** was subjected to acid group hydrolysis using LiOH in THF or THF/MeOH or THF/MeOH/H_2O or dioxane/H_2O, the racemic amino acid **7** was formed via the C−C bond breaking followed by hydrolysis of the ester group (Scheme 13).

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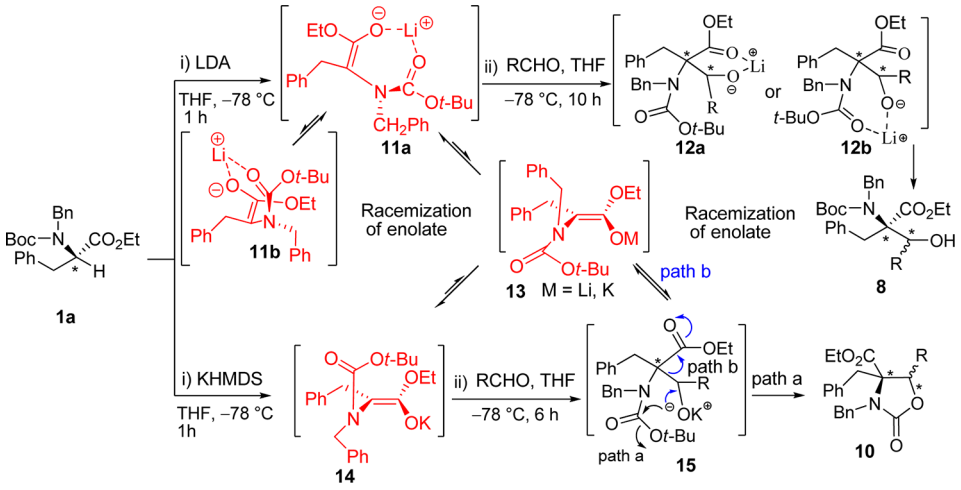
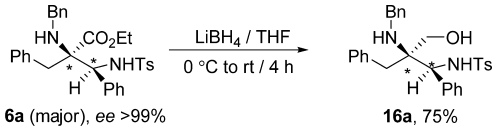
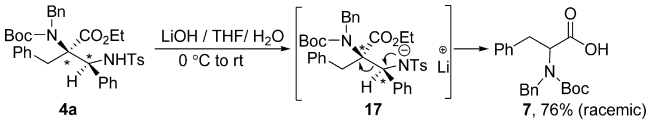
Scheme 11. Comparison between LDA and KHMDS Mediated Aldol Reactions



Scheme 12. Reduction of α,β-Diamino Ester Derivative 6a (Major Diastereomer)



Scheme 13. Attempted Hydrolysis of Imino-aldol Adduct 4a



Furthermore, when enantiopure alcohol **16a** was treated with various alcohol protecting groups in basic medium (TBDMSCl or TBDPSCl in imidazole or *p*-nitrobenzylchloride in the presence of triethylamine in dichloromethane), the reaction did not proceed. Next, the diphenyl acetate ester of enantiopure **16a** was prepared using diphenylacetic acid and DCC in dichloromethane[24] to give the corresponding coupling product, which could not be crystallized.[25]

As discussed earlier, the absolute configuration of α,β-diamino ester derivatives could not be assigned on the basis of X-ray crystallographic data of **6** or its derivatives; hence, other indirect methods were employed to determine the absolute stereochemistry of both stereogenic centers.[20] First, the recovered starting material **1a** after imino-aldol reaction (Table 1, entry 6) at −78 °C showed retention in configuration with partial racemization (based on chiral HPLC analysis). Second, the enolate generated from **1a** using LDA at −78 °C was quenched with water at the same temperature where the regenerated starting material was obtained with retention in configuration along with partial racemization (based on chiral HPLC analysis, Figure 1). These experiments revealed that the stereogenic center of the starting ester (*S*)-**1a** remained unchanged during the course of the reaction. Third, the enolate of **1a** was formed using LDA as the base at −78 °C and was quenched with water at 0 °C, which showed complete racemization of the starting amino acid ester (based on chiral HPLC analysis, Figure 2). This result evidenced that the enolization was completed at −78 °C.

On the basis of these observations, plausible intermediates **18** and **19** were proposed where intermediate **18** was a

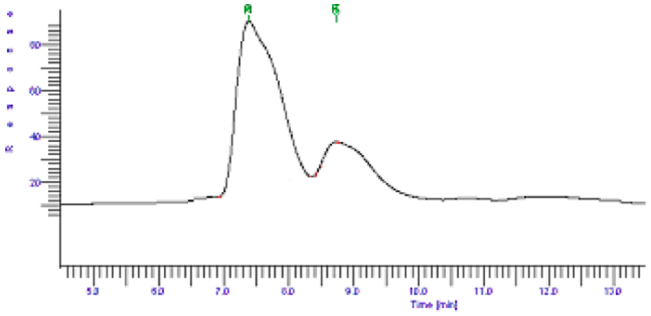


Figure 1. HPLC chromatogram of **1a** (enolate was quenched at −78 °C).

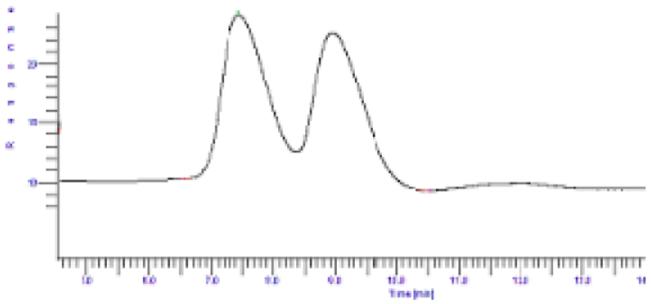


Figure 2. HPLC chromatogram of **1a** (enolate was quenched at 0 °C).

configurationally stable carbanion stabilized by *N*-Boc group and intermediate **19** was a chiral enolate in which the chiral nitrogen was strongly coordinated with the lithium ion. Formation of *anti* isomer as the major diastereomer in imino-aldol reaction with retention of configuration was rationalized by the abstraction of proton from the bottom face of the *N*-benzyl-*N*-*tert*-butoxycarbonylphenylalanine ethyl ester **1a** to give intermediate **18** or **19**. The anionic species thus generated had a chance to react with the imines from the same face (in the intermediate **18**) to produce the major diastereomer of the imino-aldol adduct **4** with retention in configuration (Figure 3). Removal of the Boc group from **4** produced **6** where the stereogenic centers remained unaltered. However, the absolute configuration at the quaternary stereogenic center (C2) becomes *R* as priority order at this center being changed in **4** or **6** compared to **1a** (H of **1a** was replaced by PhCHNHTs).

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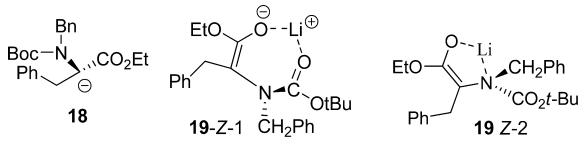


Figure 3. Proposed intermediates for imino-aldol reaction.

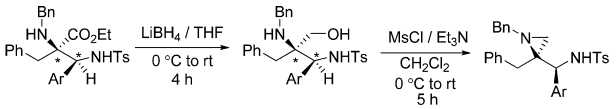
The stereochemistry of both the stereogenic centers in **4** or **6** was compared with the crystal structures of **6** and the absolute stereochemistry was assigned.

From the above discussion it is evident that absolute configuration of quaternary stereogenic center in the imino aldol product **4** is *R*. The X-ray crystallographic analysis revealed that the relative configuration of the major diastereomer of **6a** was (2*R*,3*S*) and hence the absolute configuration of its tertiary stereocenter is *S*. Thus, the absolute configuration of the major diastereomer of the addition product **4** is (2*R*,3*S*).

The stereochemical assignment of the product **6** was further supported by computational studies[20] taking **6a** as an example. For this purpose all the possible structures of the enolate **19** (obtained from the starting material **1a**) with different geometry of the double bond (*E* and *Z*) and the orientation of the protecting groups (Boc and benzyl) attached with nitrogen were modeled and optimized using Gaussian 03 program. The *Z*-enolate was found to be more stable in comparison with *E*-enolate. In the presence of the counter-cation (Li^+) in THF solvent, the possible geometries of the enolate **19** *Z* with different orientation of the protecting groups attached with nitrogen were also modeled and optimized, and we found that enolate **19** *Z*-1 is more stable in comparison to the enolate **19** *Z*-2 by 8.08 kcal mol^{-1}.[20]

Next, the imino aldol strategy has been utilized for the enantioselective synthesis of substituted aziridines. The ester group of **6a** was reduced to the corresponding alcohol **16a** as mentioned earlier. **16a** on cyclization in the presence of mesyl chloride and triethyl amine produced the substituted aziridine **20a** in good yield with high enantioselectivity (*ee* 92%) (Scheme 14). This strategy was successful in the case of **6d** as well and the reaction went smoothly to afford the corresponding aziridine **20b** in 71% yield with 80% *ee* (Scheme 14). **20a**–**b** were characterized by ^{1}H NMR, ^{13}C NMR, IR and mass spectral analysis. Following our methodology, aziridines **20a**–**b** could be synthesized in almost enantiopure form with contiguous quaternary and tertiary stereogenic centers.

Scheme 14. Synthesis of Nonracemic Aziridines 20



6a: Ar = Ph, (ee 92%)
6d: Ar = 3-BrC_6H_4, (ee 80%)

16a, yield 75%, *ee* 92%
16b, yield 73%, *ee* 80%

20a, yield 65%, *ee* 92%
20b, yield 71%, *ee* 80%

CONCLUSION

The memory of chirality concept has been successfully demonstrated in imino-aldol and aldol reactions. Using KHMDS as the base imino-aldol reaction produced α,β-amino ester derivatives with poor *ee* whereas in aldol reaction 2-oxazolidinone derivatives were obtained as a single diastereomer with low *ee*. Interestingly, when LDA was used as a base, the imino-aldol adduct was obtained in good to excellent yield with moderate to high *ee* (up to 96%). Enantiopure α,β-diamino ester derivatives could be obtained using our imino-aldol protocol. Similar results were observed in the case of aldol reaction where α-amino,β-hydroxyl ester derivatives were formed in moderate yield with up to76% *ee* using LDA as the base. Thus, utilizing MOC concept higher stereocontrol was achieved from our substrate when LDA was used as the base. The absolute configuration of the major isomer of the imino-aldol product was assigned to be (2*R*,3*S*). This methodology was further extended for the asymmetric synthesis of substituted aziridines.

EXPERIMENTAL SECTION

General Procedures. Unless otherwise noted, all reactions were carried out in oven-dried glassware under nitrogen atmosphere using anhydrous solvents. Wherever appropriate, all reagents were purified prior to use following Vogel's or Perrin and Armarego guidelines.[26] ^{1}H NMR spectra were recorded on 400 or 500 MHz in $CDCl_3$ as the solvent and TMS as an internal standard. ^{13}C NMR spectra were recorded on 100 or 125 MHz. Melting points were measured using hot stage apparatus and were uncorrected. Infrared spectra were recorded in dichloromethane for liquid compounds and KBr for solid compounds. HRMS were obtained using (ESI) mass spectrometer (TOF). Optical rotations were measured using a 2.0 mL cell with a 1.0 dm path length and are reported as $[\alpha]_D^{25}$ (*c* in g per 100 mL solvent) at 25 °C. Enantiomeric excess (*ee*) was determined using chiralcel OD-H, AD-H or cellulose-2 analytical column (detection at 254 nm). Analytical thin layer chromatography (TLC) was carried out using silica gel 60 F_{254} precoated plates, (0.25 mm thickness). Visualization was performed using UV lamp or I_2 stain. Silica gel 230–400 mesh size was used for flash column chromatography using the combination of ethyl acetate and petroleum ether as eluent. Relative stereochemistry of the major diastereomer was assigned on the basis of X-ray crystallography.

All the *N*-sulfonylaldimines were prepared in the laboratory from the corresponding sulfonamide and aldehyde in the presence of Lewis acid catalyst following a reported procedure.[27]

General Procedure for the Synthesis of N-Benzylated Amino Acid Ester.[28] To a solution of amino acid ester hydrochloride (20.0 mmol) in MeOH (30 mL) were added triethylamine (20.0 mmol) and benzaldehyde (30.0 mmol). The reaction mixture was stirred at room temperature for 1.5 h, cooled to 0 °C and $NaBH_4$ (40.0 mmol) was added in portions. After stirring at room temperature for additional 2 h, the solvent was evaporated to dryness and the residue was extracted with ethyl acetate (3 × 50.0 mL) and washed with H_2O and brine. The organic layer was dried over Na_2SO_4 and the solvent was evaporated. The residue was purified by flash column chromatography on silica gel (230–400 mesh) using 4% ethyl acetate in petroleum ether as the eluent.

General procedure described above was followed to obtain (*S*)-Ethyl 2-(*N*-benzylamino)-3-phenylpropanoate as a colorless liquid in 92% (5.2 g) yield; IR ν_{max} (CH_2Cl_2, cm^{-1}): 3332, 3062, 3028, 2980, 2929, 2851, 1731, 1603, 1494, 1454, 1372, 1337, 1185, 1130, 1027; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.09 (t, *J* = 7.1 Hz, 3H), 2.92 (d, *J* = 6.6 Hz, 2H), 3.46–3.49 (m, 1H), 3.61 (d, *J* = 13.2 Hz, 1H), 3.76 (d, *J* = 13.2 Hz, 1H), 4.02 (q, *J* = 7.1 Hz, 2H), 7.17–7.30 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.9, 39.4, 53.1, 60.1, 61.7, 126.2, 126.6, 127.8, 128.0, 129.0, 137,1, 139.4, 174.0.

General procedure described above was followed to obtain (*S*)-Methyl 2-(*N*-benzylamino)-3-propanoate as a colorless liquid in 87% (3.36 g) yield; IR ν_{max} (CH_2Cl_2, cm^{-1}): 3324, 3086, 3063, 3028, 2977, 2950, 2850, 1736, 1603, 1494, 1453, 1374, 1334, 1200, 1152, 1065, 1044, 1026; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.30 (d, *J* = 7.1 Hz, 3H), 3.37 (q, *J* = 7.1 Hz, 1H), 3.64 (d, *J* = 12.9 Hz, 1H), 3.71 (s, 3H), 3.77 (d, *J* = 12.9 Hz, 1H), 4.70 (s, 1H), 7.21–7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.0, 52.0, 55.9, 65.3, 127.1, 128.2, 128.4, 139.7, 176.2.

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*General Procedure for the Synthesis of (**1a–b**).*[29] To a solution of *N*-benzylated amino acid ester (7.06 mmol) in dry dichloromethane (15.0 mL) were added di-*tert*-butylpyrocarbonate (8.75 mmol) and triethylamine (7.9 mmol) and the mixture was stirred at room temperature for 24 h. The reaction mixture was quenched with 0.5 M aqueous HCl and the aqueous layer was extracted with CH_2Cl_2 (3 × 20.0 mL). The combined organic extract was washed with brine and dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography over silica gel (230−400 mesh) using 4% ethyl acetate in petroleum ether as eluent to provide **1a−b**.

*(S)-Ethyl 2-[(N-Benzyl)-(N-t-butoxycarbonyl)amino]-3-phenylpropanoate (**1a**).* General procedure described above was followed to obtain **1a** as a colorless liquid in 75% (2.03 g) yield as a mixture of two conformers major M and minor m in a ∼5:3 ratio; $[\alpha]_D^{25}$ = −91.0 (*c* 1.30, $CHCl_3$); IR ν_{max} (CH_2Cl_2, cm^{-1}): 3087, 3063, 3029, 2977, 2932, 1740, 1698, 1494, 1453, 1425, 1392, 1366, 1250, 1164, 1079, 1048, 1030, 982; For mixture of rotamers: ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.17 (bs, 3H, M+m), 1.40 (s, 9H, m), 1.50 (s, 9H, M), 3.06−3.11(m, 1H, M), 3.17−3.22(m, 1H, m), 3.30 (d, *J* = 5.50 Hz, 1H, M), 3.32 (d, *J* = 5.50 Hz, 1H, m), 3.51 (d, *J* = 15.3 Hz, 1H, M), 3.78 (d, *J* = 15.6 Hz, 1H, m), 3.88−3.90 (m, 1H, m), 3.98−4.08 (m, 2H, M+m), 4.21−4.27 (m, 1H, M), 4.40 (d, *J* = 15.58 Hz, 1H, m); 4.62 (d, *J* = 15.3 Hz, 1H, M), 7.02−7.14 (m, 10H, m), 7.21−7.28 (m, 10H, M); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 14.1 (m+M), 28.4 (m), 28.5 (M), 35.7 (m), 36.6 (M), 51.9 (m+M), 61.2 (m), 61.3 (M), 80.5 (m), 80.9 (M), 126.5 (m), 126.7 (M), 127.1 (m), 127.4 (M), 127.8 (m), 128.2 (m), 128.3 (M), 128.5 (m), 128.7 (M), 128.9 (m), 129.4 (M), 137.3 (M), 138.1 (m), 138.3 (M+m), 155.2 (M+m), 171.0 (M), 171.1 (m); HRMS (ESI) *m*/*z*: Calcd. for $C_{23}H_{29}NNaO_4$ (M^+ + Na): 406.1994, Found: 406.1994.

*(S)-Methyl 2-[(N-Benzyl)-(N-t-butoxycarbonyl)amino]propanoate (**1b**).* General procedure described above was followed to obtain **1b** as a viscous liquid in 60% (1.24 g) yield. $[\alpha]_D^{25}$ = −36.21 (*c* 1.86, $CHCl_3$); IR ν_{max} (CH_2Cl_2, cm^{-1}): 3064, 3029, 2977, 1747, 1697, 1605, 1496, 1453, 1424, 1366, 1314, 1252, 1219, 1166, 1101, 1068, 1017; For mixture of rotamers: ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.28 (bs, 9H), 1.39 (bs, 3H), 3.59 (s, 3H), 3.85 (bs, 1/2H), 4.26 (bs, 1/2H), 4.47 (bs, 2H), 7.17−7.24 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.5, 15.9, 28.4, 49.6, 50.9, 52.1, 54.6, 55.4, 80.6, 80.7, 126.9, 127.3, 128.0, 128.4, 128.5, 138.2, 139.2, 155.4, 155.7, 172.7, 172.9.

*General Procedure for the Imino-aldol Reaction of N-Benzyl-N-t-butoxycarbonylamino Acid Esters (**1a–b**) with Various Imines.* To a solution of diisopropylamine (0.12 mL, 0.848 mmol) in 2.0 mL dry THF was added *n*-BuLi (1.6 M in hexane, 0.53 mL, 0.848 mmol) at 0 °C and stirred for 20 min. It was cooled to −78 °C and a solution of *N*-benzyl-*N*-*tert*-butoxycarbonyl amino acid esters **1a−b** (0.848 mmol) in 1.0 mL dry THF was added to it and allowed to stir for 1 h. *N*-sulfonylimine (0.385 mmol) dissolved in 1.0 mL dry THF was slowly added into the reaction mixture and stirring was continued at the same temperature for 10 h. After completion of the reaction (monitored with TLC), it was quenched with saturated aqueous ammonium chloride solution and extracted with 5.0 mL of ethyl acetate in two portions. The combined organic extract was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel using ethyl acetate in petroleum ether as the eluent to afford the pure products **4a−k**.

*Imino-aldol Reaction of N-Benzyl-N-tert-butoxycarbonyl Amino Acid Esters (**1a–b**) with Various Imines.* The reaction is highly dependent on temperature, solvent, bases and most importantly on time and the corresponding de/ee of the products may change with slight change in any of these conditions.

Characterization Data. *Ethyl 2-Benzyl-2-[(N-benzyl)-(N-t-butoxycarbonyl)amino]-3-(4-methylphenylsulfon-amido)-3-phenylpropanoate (**4a**).*[16] General procedure described above was followed to afford **4a** as a white solid in 84% (0.21 g) yield; Eluent: EtOAc/petroleum ether 10/90; R_f 0.45 (ethyl acetate/petroleum ether: 20/80); $[\alpha]_D^{25}$ = +10.76 (*c* 0.415, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}): 3334, 2978, 2927, 1738, 1696, 1389, 1160, 1090; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ 13.4, 21.0, 21.3, 27.9, 29.6, 37.1, 40.6, 49.5, 61.2, 61.4, 61.9, 71.0, 80.9, 81.1, 81.5, 125.5, 125.8, 126.2, 127.0, 127.2, 127.80, 127.86, 128.0, 128.1, 128.5,128.7, 128.8, 129.4, 129.9, 130.8, 131.2, 134.6, 135.7, 136.8, 138.1, 139.6, 139.9, 141.9, 142.3, 156.1, 157.1, 169.5; HRMS (ESI) *m*/*z* Calcd. for $C_{37}H_{43}N_2O_6S$ (M^+ + H): 643.2842, Found: 643.2834.

*Ethyl 2-Benzyl-2-[(N-benzyl)-(N-t-butoxycarbonyl)amino]-3-phenyl-3-phenylsulf- onamidopropanoate (**4b**).* General procedure described above was followed to afford **4b** as a white solid in 62% (0.15 g) yield; Eluent: EtOAc/petroleum ether 10/90; R_f 0.32 (ethyl acetate/petroleum ether: 15/85); Optical rotation: $[\alpha]_D^{25}$ = +3.70 (*c* 0.415, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}) 3380, 2976, 2926, 1739, 1697, 1451, 1388, 1330, 1253, 1160, 1090, 1021; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ (ppm) 13.4, 27.9, 37.2, 40.5, 49.5, 61.2, 61.4, 61.9, 71.2, 80.9, 81.5, 125.5, 125.7, 126.2, 126.8, 127.3, 127.9, 128.0, 129.4, 129.8, 130.7, 131.1, 131.4, 131.6, 134.5, 135.6, 136.6, 139.5, 139.8, 141.2, 156.0, 157.2, 169.4; HRMS (ESI) *m*/*z*: Calcd. for $C_{36}H_{41}N_2O_6S$ (M^+ + H): 629.2685, Found: 629.2687.

*Ethyl 2-Benzyl-2-[(N-benzyl)-(N-t-butoxycarbonyl)amino]-3-(4-nitrophenylsulfonamido)-3-phenylpropanoate (**4c**).* General procedure described above was followed to afford **4c** as a light yellow solid in 80% (0.21 g) yield; Eluent: EtOAc/petroleum ether 10/90; R_f 0.37 (ethyl acetate/petroleum ether: 15/85); $[\alpha]_D^{25}$ = +40.0 (*c* 0.30, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}): 3302, 2978, 2930, 1743, 1671, 1529, 1454, 1391, 1349, 1165, 1089; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ 13.6, 27.9, 40. 1, 49.2, 61.4, 61.5, 70.7, 82.1, 123.3, 125.5, 126.0, 126.4, 127.6, 127.9, 128.1, 128.2, 129.7, 130.6, 130.9, 134.0, 136.5, 139.2, 146.8, 149.1, 157.8, 169.0; HRMS (ESI) *m*/*z* Calcd. for $C_{36}H_{39}N_3NaO_8S$ (M^+ + Na): 696.2356, Found: 696.2350.

*Ethyl 2-benzyl-2-[(N-benzyl)-(N-t-butoxycarbonyl)amino]-3-(3-bromophenyl)-3-(4-methylphenylsulfonamido)propanoate (**4d**).* General procedure described above was followed to afford **4d** as a white solid in 68% (0.21 g) yield; Eluent: EtOAc/petroleum ether 10/90; R_f 0.33 (ethyl acetate/petroleum ether: 15/85); Optical rotation: $[\alpha]_D^{25}$ +4.05 (*C* 0.37, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}) 3353, 3063, 3031, 2978, 2930, 1740, 1701, 1598, 1495, 1453, 1389, 1368, 1342, 1252, 1160, 1091, 1033; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ (ppm) 13.4, 21.3, 27.9, 38.0, 40.9, 49.4, 60.4, 61.3, 61.6, 71.1, 81.2, 81.7, 122.1, 125.5, 125.8, 126.1, 126.3, 126.7, 127.3, 128.0, 128.2, 128.9, 129.0, 129.2, 130.7, 130.9, 131.0, 131.9, 133.1, 134.4, 135.3, 137.9, 138.9, 139.3, 139.6, 142.4, 142.8, 156.8, 169.3; HRMS (ESI) *m*/*z*: Calcd. for $C_{37}H_{42}BrN_2O_6S$ (M^+ + H) 721.1947, Found: 721.1946.

*Ethyl 2-Benzyl-2-[(N-benzyl)-(N-t-butoxycarbonyl)amino]-3-(2-chlorophenyl)-3-(4-methylphenylsulfonamido)propanoate (**4e**).* General procedure described above was followed to afford **4e** as a white solid in 74% (0.19 g) yield; Eluent: EtOAc/petroleum ether 10/90; R_f 0.45 (ethyl acetate/petroleum ether: 20/80); $[\alpha]_D^{25}$ = +3.45 (*c* 0.26, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}): 3351, 3030, 2925, 1739, 1701, 1368, 1304, 1161, 1088; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ 13.5, 21.3, 27.7, 27.9, 38.1, 42.6, 49.4, 57.2, 60.6, 61.5, 71.1, 80.6, 125.6, 126.2, 126.4, 126.8, 126.9, 127.5, 127.7, 127.9, 128.1, 128.2, 128.8, 128.9, 129.4, 131.1, 131.5, 132.4, 133.8, 134.8, 135.0, 135.2, 137.3, 139.8, 142.3, 145.1, 157.1, 169.9; HRMS (ESI) *m*/*z* Calcd. for $C_{37}H_{41}ClN_2NaO_6S$ (M^+ + Na): 699.2272, Found: 699.2278.

*Ethyl 2-Benzyl-2-[(N-benzyl)-(N-t-butoxycarbonyl)amino]-3-(4-methylphenylsulfonamido)-3-(4-nitrophenyl)propanoate (**4f**).* General procedure described above was followed to afford **4g** as a mixture of diastereomers in the form of white solid in 75% (0.20 g) yield; Eluent: EtOAc/petroleum ether 10/90; R_f 0.30 (ethyl acetate/petroleum ether: 15/85); $[\alpha]_D^{25}$ = +20.0 (*c* 0.40, $CHCl_3$), IR ν_{max} (KBr, cm^{-1}): 3431, 2927, 1741, 1697, 1523, 1452, 1388, 1347, 1254, 1160, 1088; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ 13.4, 21.2, 27.8, 38.5, 41.6, 49.0, 60.4, 61.3, 62.6, 70.5, 81.8, 122.6, 125.5, 125.8, 126.6, 126.9, 127.4, 128.0, 128.2, 128.9, 129.1, 130.6, 131.0, 134.2, 137.5, 138.9, 139.3, 143.0, 143.4, 143.9, 144.5, 147.2, 156.2, 169.4; HRMS (ESI) *m*/*z* Calcd. for $C_{37}H_{41}N_3NaO_8S$ (M^+ + Na): 710.2512, Found: 710.2511.

*Ethyl 2-Benzyl-2-[(N-benzyl)-(N-t-butoxycarbonyl)amino]-3-(4-methoxyphenyl)-3-(4-methylphenylsulfonamido)propanoate (**4g**).* General procedure described above was followed to afford **4g** as a white solid in 65% (0.17 g) yield; Eluent: EtOAc/petroleum ether

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10/90; R_f 0.21 (ethyl acetate/petroleum ether: 15/85); $[\alpha]_D^{25}$ = +8.0 (*c* 0.75, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}): 3432, 3032, 2927, 2855, 1738, 1692, 1609, 1510, 1448, 1388, 1329, 1252, 1159, 1087, 1027; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ (ppm) 13.4, 21.3, 21.4, 27.9, 28.3, 40.5, 46.7, 49.4, 55.2, 61.2, 61.4, 71.2, 80.0, 81.1, 81.4, 113.2, 113.9, 125.5, 125.7, 126.2, 126.6, 127.1, 127.2, 127.5, 127.7, 127.9, 128.0, 128.2, 128.3, 128.7, 129.1, 129.4, 129.6, 130.7, 130.9, 131.1, 134.6, 135.9, 138.4, 139.6, 139.9, 141.9, 142.2, 143.3, 157.1, 159.2, 169.6; HRMS (ES^+) *m*/*z* Calcd. for $C_{38}H_{45}N_2O_7S$ (M^+ + H): 673.2947, Found: 673.2947.

*Ethyl 2-[(N-Benzyl)-(N-t-butoxycarbonyl)amino]-3-(2-furanyl)-3-(4-methylphenylsulfonamido)propanoate (**4h**).* General procedure described above was followed to afford **4h** as a white solid in 74% (0.18 g) yield; Eluent: EtOAc/petroleum ether 15/85; R_f 0.30 (ethyl acetate/petroleum ether: 15/85); $[\alpha]_D^{25}$ = +18.0 (*c* 1.0, $CHCl_3$), IR ν_{max} (KBr, cm^{-1}): 3292, 2977, 2925, 1739, 1673, 1601, 1453, 1390, 1304, 1160, 1088, 1017; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ (ppm) 13.4, 13.8, 21.4, 27.8, 27.9, 40.1, 41.6, 47.1, 48.8, 55.7, 61.2, 61.6, 71.0, 81.6, 94.7, 110.6, 110.9, 125.5, 125.7, 126.0, 126.2, 126.6, 126.9, 127.3, 127.9, 128.0, 128.1, 128.3, 128.4, 128.9, 129.0, 130.7, 133.1, 134.2, 137.8, 139.4, 139.8, 141.9, 142.2, 150.5, 151.2, 155.6, 168.3, 169.0; HRMS (ESI) *m*/*z* Calcd. for $C_{35}H_{41}N_2O_7S$ (M^+ + H): 633.2634, Found: 633.2634.

*Ethyl 2-Benzyl-2-[(N-benzyl)-(N-t-butoxycarbonyl)amino]-3-(4-chlorophenyl)-3-(4-methylphenylsulfonamido)propanoate (**4i**).* General procedure described above was followed to afford **4i** as white solid in 72% (0.19 g) yield; Eluent: EtOAc/petroleum ether 10/90; R_f 0.45 (ethyl acetate/petroleum ether: 20/80); $[\alpha]_D^{25}$ = +5.92 (*c* 1.35, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}): 3351, 2977, 2927, 1740, 1701, 1389, 1160, 1089; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ (ppm) 13.4, 21.3, 27.9, 37.7, 41.1, 49.4, 60.4, 61.2, 61.5, 61.9, 81.2, 81.6, 125.6, 125.8, 126.1, 126.4, 126.9, 127.3, 127.9, 128.0, 128.2, 128.8, 128.9, 130.9, 131.1, 131.2, 133.8, 134.5, 135.4, 137.9, 139.3, 139.7, 142.5, 142.8, 156.7, 169.5; HRMS (ESI) *m*/*z* Calcd. for $C_{37}H_{41}ClN_2O_6S$ (M^+ + Na): 699.2271, Found: 699.2229.

*Ethyl 2-Benzyl-2-[(N-benzyl)-(N-t-butoxycarbonyl)amino]-3-(4-methylphenylsulfonamido)-3-(3-nitrophenyl)propanoate (**4j**).* General procedure described above was followed to afford **4j** as a white solid in 81% (0.21 g) yield; Eluent: EtOAc/petroleum ether 10/90; R_f 0.28 (ethyl acetate/petroleum ether: 15/85); $[\alpha]_D^{25}$ = +8.0 (*c* 0.80, $CHCl_3$), IR ν_{max} (KBr, cm^{-1}): 3433, 2926, 1741, 1697, 1532, 1449, 1388, 1349, 1254, 1160, 1090, 1020; ^{13}C NMR for mixture of diastereomers (100 MHz, $CDCl_3$): δ (ppm) 13.4, 21.1, 27.7, 28.1, 38.6, 41.1, 49.1, 60.0, 61.4, 62.0, 70.7, 81.6, 81.9, 122.4, 125.0, 125.5, 126.6, 126.7, 126.9, 127.5, 128.1, 128.3, 128.5, 128.9, 129.0, 129.2, 129.3, 130.9, 134.1, 134.5, 135.7, 136.4, 137.8, 138.3, 138.9, 139.3, 142.6, 142.9, 147.5, 147.7, 156.5, 169.2; HRMS (ES^+) *m*/*z* Calcd. for $C_{37}H_{42}N_3O_8S$ (M^+ + H): 688.2693, Found: 688.2691.

*Methyl 2-[(N-Benzyl)-(N-t-butoxycarbonyl)amino]-2-methyl-3-(4-methylphenylsulfonamido)-3-phenylpropanoate (**4k**).* General procedure described above was followed to afford **4k** as a white solid in 72% (0.15 g) yield; Eluent: EtOAc/petroleum ether 10/90; R_f 0.23 (ethyl acetate/petroleum ether: 15/85); $[\alpha]_D^{25}$ = −10.0 (*c* 0.30, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}): 3396, 2927, 1742, 1695, 1453, 1391, 1254, 1162, 1046; ^{13}C NMR for the major diastereomer (125 MHz, $CDCl_3$): δ 15.5, 15.9, 28.4, 49.6, 51.0, 52.0, 54.6, 55.4, 80.6, 80.7, 126.9, 127.3, 128.0, 128.4, 128.5, 138.2, 139.2, 155.4, 155.7, 172.7, 172.9; HRMS (ESI) *m*/*z* Calcd. for $C_{30}H_{36}N_2NaO_6S$ (M^+ + Na): 575.2192, Found: 575.2192.

General Method for Removal of Boc Group from Iminoaldol Products (6a−k). To a stirring solution of substrate **4a−k** (0.10 mmol) in dry dichloromethane (1.0 mL) was added trifluoroacetic acid (0.5 mL) at 0 °C. The reaction mixture was stirred at room temperature for 2 h. It was neutralized with aq. saturated $NaHCO_3$ solution and the aqueous layer was extracted with CH_2Cl_2 (3 × 5.0 mL). The combined organic extract was washed with brine and dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (230−400 mesh) using ethyl acetate in petroleum ether as the eluent to provide **6a−k**.

*Ethyl 2-Benzyl-2-(N-benzylamino)-3-(4-methylphenylsulfonamido)-3-phenylpropanoate **6a**.*[16] General procedure described above was followed to afford **6a** (major) and **6a** (minor) as a white solid in 88% (0.048 g) overall yield (combined yield of both the diastereomers). It was obtained as a mixture of diastereomers with *dr* 83:17 (based on ^1H NMR analysis of crude reaction mixture) where the diastereomers were separated through flash column chromatography (eluent: EtOAc/petroleum ether 10/90).

*For the Major Diastereomer **6a**.* R_f 0.45 (ethyl acetate/petroleum ether: 20/80); mp: 158−160 °C; Optical rotation: $[\alpha]_D^{25}$ = +10.25 (*c* 0.335, $CHCl_3$) for a 92% *ee* sample; Optical purity was determined by chiral HPLC analysis (Chiralcel AD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 72.6 min (major), T_R 2: 97.3 min (minor); IR ν_{max} (KBr, cm^{-1}): 3344, 3281, 2925, 2854, 2354, 1732, 1600, 1454, 1263, 1161, 1091, 1019; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.03 (t, *J* = 7.2 Hz, 3H), 2.20 (s, 3H), 3.04 (d, *J* = 14.8 Hz, 1H), 3.33 (d, *J* = 14.8 Hz, 1H), 3.51 (d, *J* = 12.4 Hz, 1H), 3.66 (d, *J* = 12.4 Hz, 1H), 3.95 (q, *J* = 7.2 Hz, 2H), 4.83 (d, *J* = 6.6 Hz, 1H), 6.2 (brs, 1H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.97−7.06 (m, 4H), 7.08−7.23 (m, 11H), 7.31 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.7, 21.2, 38.7, 46.9, 61.6, 61.7, 68.8, 126.8, 127.0, 127.6, 127.7, 128.26, 128.28, 128.3, 128.4, 128.9, 129.8, 130.4, 135.9, 136.3, 137.9, 139.5, 142.5, 173.1; HRMS (ES^+) *m*/*z*: Calcd. for $C_{32}H_{34}N_2O_4S$ (M^+ + H): 543.2329, Found: 543.2337.

*For the Minor Diastereomer **6a**.* R_f 0.44 (ethyl acetate/petroleum ether: 20/80); mp: 118−120 °C; Optical rotation $[\alpha]_D^{25}$ −10.77 (*c* 0.65, $CHCl_3$) for a 80% *ee* sample; Optical purity was determined by chiral HPLC analysis (Chiralcel AD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 35.1 min (major), T_R 2: 43.2 min (minor); IR ν_{max} (KBr, cm^{-1}): 3347, 3296, 2959, 2924, 2853, 1730, 1661, 1600, 1454, 1264, 1161, 1090, 1019; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.08 (t, *J* = 7.1 Hz, 3H), 2.25 (s, 3H), 3.02 (d, *J* = 15.2 Hz, 1H), 3.34 (d, *J* = 15.2 Hz, 1H), 3.74 (d, *J* = 11.8 Hz, 1H), 3.81 (d, *J* = 11.8 Hz, 1H), 3.98 (q, *J* = 7.1 Hz, 2H), 4.73 (d, *J* = 7.7 Hz, 1H), 6.10 (d, *J* = 7.7 Hz, 1H), 6.85−6.88 (m, 2H), 6.98−7.09 (m, 4H), 7.22−7.33 (m, 11H), 7.70 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.9, 21.5, 38.7, 48.9, 61.7, 62.4, 71.1, 127.0, 127.5, 128.19, 128.2, 128.3, 128.7, 128.8, 128.9, 129.2, 130.3, 130.4, 135.0, 135.3, 136.8, 137.2, 143.0, 171.1; HRMS (ES^+) *m*/*z*: Calcd. for $C_{32}H_{34}N_2O_4S$ (M^+ + H): 543.2329, Found: 543.2328.

*Ethyl 2-Benzyl-2-(N-benzylamino)-3-phenyl-3-(phenylsulfonamido)propanoate **6b**.* General procedure described above was followed to afford **6b** (major) and **6b** (minor) as a white solid in 70% (0.037 g) overall yield (combined yield of both the diastereomers). The compound was isolated as a mixture of diastereomers with *dr* 71:29 (based on ^1H NMR analysis of crude reaction mixture) where the major and minor diastereomers could not be separated through flash column chromatography (eluent: EtOAc/petroleum ether 10/90), R_f 0.30 (ethyl acetate/petroleum ether: 15/85); Optical rotation: $[\alpha]_D^{25}$ +7.29 (*c* 0.415, $CHCl_3$).

*For the Major Diastereomer **6b**.* *ee* 80%; Optical purity was determined by chiral HPLC analysis of the mixture (Chiralcel OD-H column) using 99/1 hexane/isopropanol, flow rate = 0.8 mL/min, T_R 1: 38.1 min (major), T_R 2: 53.4 min (minor). Major diastereomer was obtained in pure form after recrystallization and it was injected in HPLC to identify the pair of peaks for each diastereomers; IR ν_{max} (CH_2Cl_2, cm^{-1}): 3303, 3062, 3029, 2925, 2853, 1731, 1602, 1495, 1451, 1325, 1209, 1163, 1090, 1064, 1029, 912; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.03 (t, *J* = 7.1 Hz, 3H), 3.07 (brs, 1H), 3.34 (d, *J* = 14.9 Hz, 1H), 3.51 (d, *J* = 12.5 Hz, 1H), 3.68 (d, *J* = 12.5 Hz, 1H), 3.96 (q, *J* = 7.0 Hz, 2H), 4.86 (brs, 1H), 6.30 (brs, 1H), 6.90−7.32 (m, 18H), 7.44 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.8, 38.8, 47.0, 61.7, 61.9, 68.9, 126.8, 126.9, 127.2, 127.8, 127.9, 128.2, 128.3, 128.4, 128.7, 129.8, 130.4, 131.9, 135.7, 135.8, 135.9, 140.8, 172.9; HRMS (ES^+) *m*/*z*: Calcd. for $C_{31}H_{32}N_2O_4S$ (M^+ + H): 529.2161, Found: 529.2161.

*For the Minor Diastereomer **6b**.* *ee* 80%; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column) using 99/1 hexane/isopropanol, flow rate = 0.8 mL/min, T_R 1: 47.7 min (major), T_R 2: 67.5 min (minor).

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Ethyl 2-Benzyl-2-(N-benzylamino)-3-(4-nitrophenylsulfonamido)-3-phenylpropanoate ***6c***. General procedure described above was followed to afford **6c** (major) and **6c** (minor) as a pale yellow solid in 84% (0.48 g) overall yield (combined yield of both the diastereomers). It was obtained as a mixture of diastereomers with *dr* 83:17 (based on ^{1}H NMR analysis of crude reaction mixture) where the major diastereomer **6c** was separated through flash column chromatography (eluent: EtOAc/petroleum ether 10/90).

For the Major Diastereomer ***6c***. R_f 0.37 (ethyl acetate/petroleum ether: 15/85); mp: 112−114 °C; Optical rotation: $[\alpha]_D^{25}$ = +20.00 (*c* 0.25, $CHCl_3$) for a 88% *ee* sample; Optical purity was determined by chiral HPLC analysis (Chiralcel AD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 14.2 min (minor); T_R 2: 17.0 min (major); IR ν_{max} (KBr, cm^{-1}): 3430, 3334, 2926, 1729, 1604, 1529, 1456, 1408, 1347, 1252, 1205, 1164, 1092, 1022; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.05 (t, *J* = 7.0 Hz, 3H), 3.08 (d, *J* = 14.5 Hz, 1H), 3.35 (d, *J* = 14.5 Hz, 1H), 3.51 (d, *J* = 12.5 Hz, 1H), 3.71 (d, *J* = 12.5 Hz, 1H), 3.97−4.05 (m, 2H), 4.88 (s, 1H), 6.49 (brs, 1H), 6.95 (m, 4H), 7.03−7.08 (m, 3H), 7.13−7.23 (m, 8H), 7.52 (d, *J* = 9.0 Hz, 2H), 7.88 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.8, 38.7, 47.0, 61.6, 62.1, 68.8, 123.4, 127.0, 127.2, 127.6, 127.9, 128.0, 128.2, 128.3, 128.4, 129.7, 130.5, 135.4, 139.2, 146.0, 146.4, 149.2, 173.2; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{31}H_{31}N_3O_6S$ (M$^+$ + H): 574.2011, Found: 574.2014.

For the Minor Diastereomer ***6c***. Minor diastereomer could not be isolated in pure form. Optical purity of this isomer could not be determined as it was inseparable in chiral HPLC columns (Chiralcel AD-H, OD-H).

Ethyl 2-Benzyl-2-(N-benzylamino)-3-(3-bromophenyl)-3-(4-methylphenylsulfonamido)propanoate ***6d*** *(Table 2, entry 4)*. General procedure described above was followed to afford **6d** (major) and **6d** (minor) as a white solid in 87% (0.054 g) overall yield (combined yield of both the diastereomers). It was obtained as a mixture of diastereomers with *dr* 71:29 (based on ^{1}H NMR analysis of crude reaction mixture) where the major diastereomer was separated through flash column chromatography (eluent: EtOAc/petroleum ether 10/90), R_f 0.30 (ethyl acetate/petroleum ether: 15/85).

For the Major Diastereomer ***6d***. Optical rotation: $[\alpha]_D^{25}$ = +3.03 (*c* 0.66, $CHCl_3$) for a 84% *ee* sample; Optical purity was determined by chiral HPLC analysis (Chiralcel AD-H column) using 90/10 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 20.3 min. (major), T_R 2: 28.5 min. (minor); IR ν_{max} (CH_2Cl_2, cm^{-1}): 3291, 3062, 3029, 2925, 2854, 1732, 1597, 1494, 1452, 1336, 1209, 1161, 1093, 1030; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.05 (t, *J* = 7.1 Hz, 3H), 2.24 (s, 3H), 3.04 (d, *J* = 14.9 Hz, 1H), 3.29 (d, *J* = 14.9 Hz, 1H), 3.51 (d, *J* = 12.4 Hz, 1H), 3.69 (d, *J* = 12.4 Hz, 1H), 3.98 (q, *J* = 7.1 Hz, 2H), 4.77 (d, *J* = 7.1 Hz), 6.22 (brs, 1H), 6.83−7.05 (m, 4H), 7.09−7.32 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.8, 21.4, 38.6, 46.9, 60.9, 62.0, 68.7, 122.1, 126.7, 127.0, 127.3, 127.5, 127.8, 128.4, 128.5, 129.3, 129.9, 130.3, 130.7, 131.5, 135.5, 137.5, 138.4, 139.2, 143.0, 172.8. HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{32}H_{33}BrN_2O_4S$ (M$^+$ + H): 621.1426, Found 621.1429.

For the Minor Diastereomer ***6d***. It could not be isolated in pure form; *ee* 62%; Optical purity was determined by chiral HPLC analysis (Chiracel OD-H column) using 97/3 hexane/isopropanol, flow rate = 0.8 mL/min, T_R 1: 21.8 min (major), T_R 2: 26.5 min (minor).

Ethyl 2-Benzyl-2-(N-benzylamino)-3-(2-chlorophenyl)-3-(4-methylphenylsulfonamido)propanoate ***6e***. General procedure described above was followed to afford **6e** (major) and **6e** (minor) as a white solid in 80% (0.046 g) overall yield (combined yield of both the diastereomers). It was obtained as a mixture of diastereomers with *dr* 79:21 (based on ^{1}H NMR of the crude reaction mixture) where the diastereomers were separated through flash column chromatography (eluent: EtOAc/petroleum ether 10/90).

For the Major Diastereomer ***6e***. mp: 160−162 °C; R_f 0.50 (ethyl acetate/petroleum ether: 20/80); $[\alpha]_D^{25}$ = +12.45 (*c* 1.36, $CHCl_3$) for a 56% *ee* sample; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column), 97/3 hexane/isopropanol, flow rate = 0.8 mL/min, T_R 1: 19.19 min (minor), T_R 2: 23.93 min (major); IR ν_{max} (KBr, cm^{-1}): 3344, 3282, 3029, 2962, 2885, 1729, 1305, 1261, 1160, 1093, 1021; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.05 (t, *J* = 7.1 Hz, 3H), 2.19 (s, 3H), 2.96 (d, *J* = 14.4 Hz, 1H), 3.44 (d, *J* = 14.6 Hz, 1H), 3.52−3.59 (m, 2H), 3.91−4.06 (m, 2H), 5.39 (d, *J* = 6.8 Hz, 1H), 6.32 (brs, 1H), 6.85−6.94 (m, 3H), 6.99−7.24 (m, 13H), 7.39 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.7, 21.3, 38.2, 47.5, 56.9, 62.3, 69.4, 126.5, 127.1, 127.3, 127.8, 128.5, 128.8, 129.1, 129.2, 129.6, 130.4, 134.6, 134.8, 135.3, 137.2, 142.8, 172.4; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{32}H_{34}ClN_2O_4S$ (M$^+$ + H): 577.1928, Found: 577.1929.

For the Minor Diastereomer ***6e***. R_f 0.48 (ethyl acetate/petroleum ether: 20/80); Optical purity could not be determined as it was inseparable in chiral HPLC columns (Chiralcel AD-H, OD-H); mp: 169−170 °C; IR ν_{max} (KBr, cm^{-1}): 3348, 3279, 2980, 2924, 1736, 1597, 1495, 1444, 1371, 1219, 1162, 1064, 1033; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.93 (t, *J* = 7.1 Hz, 3H), 2.18 (s, 3H), 2.97 (d, *J* = 14.9 Hz, 1H), 3.31 (d, *J* = 14.9 Hz, 1H), 3.67 (d, *J* = 11.9 Hz, 1H), 3.77 (d, *J* = 11.9 Hz, 1H), 3.92−3.97 (m, 2H), 5.36 (s, 1H), 6.00 (brs, 1H), 6.87 (d, *J* = 8.1 Hz, 2H), 6.97−7.05 (m, 2H), 7.09−7.27 (m, 12H), 7.37 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.6, 21.4, 36.6, 46.0, 56.6, 61.7, 69.7, 126.1, 126.7, 127.0, 127.3, 128.1, 128.3, 128.5, 128.8, 129.1, 129.3, 130.1, 134.2, 134.3, 136.0, 136.5, 139.0, 142.9, 171.7; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{32}H_{34}ClN_2O_4S$ (M$^+$ + H): 577.1928, Found: 577.1922.

Ethyl 2-Benzyl-2-(N-benzylamino)-3-(4-methylphenylsulfonamido)-3-(4-nitrophenyl)propanoate ***6f***. General procedure described above was followed to afford **6f** (major) and **6f** (minor) as a white solid in 86% (0.051 g) overall yield (combined yield of both the diastereomers). The compound was isolated (eluent: EtOAc/petroleum ether 10/90) as a mixture of diastereomers with *dr* 73:27 (based on ^{1}H NMR analysis of crude reaction mixture); R_f 0.30 (ethyl acetate/petroleum ether: 15/85); Optical rotation: $[\alpha]_D^{25}$ = +17.80 (*c* 1.3, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}): 3343, 3290, 3030, 2925, 1733, 1601, 1522, 1495, 1453, 1346, 1162.

For the Major Diastereomer ***6f***. mp: 84−86 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.0 (t, *J* = 7.3 Hz, 3H), 2.21 (s, 3H), 3.03 (d, *J* = 14.3 Hz, 1H), 3.22 (d, *J* = 14.3 Hz, 1H), 3.50 (d, *J* = 12.8 Hz, 1H), 3.65 (d, *J* = 12.8 Hz, 1H), 3.89−3.96 (m, 2H), 4.90 (d, *J* = 6.5 Hz, 1H), 6.40 (brs, 1H), 6.92 (d, *J* = 8.0 Hz, 2H), 7.06−7.29 (m, 12H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.85 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.8, 21.3, 38.7, 46.7, 60.4, 62.1, 68.6, 122.7, 126.8, 127.2, 127.5, 128.5, 128.6, 129.2, 129.7, 129.8, 130.1, 134.9, 137.2, 138.7, 143.5, 144.2, 147.2, 172.4; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{32}H_{33}N_3O_6S$ (M$^+$ + H): 588.2168, Found: 588.2168; $[\alpha]_D^{25}$ = +54.0 (*c* 0.2, CH_2Cl_2) for a 75% ee sample. Optical purity was determined by chiral HPLC analysis (Lux 5u Cellulose-2 column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 106.4 min (major), T_R 2: 122.6 min (minor)

For the Minor Diastereomer ***6f***. *ee* 43%, Optical purity was determined by chiral HPLC analysis (Lux 5u Cellulose-2 column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 120.6 min. (major), T_R 2: 153.2 min. (minor)

Ethyl 2-Benzyl-2-(N-benzylamino)-3-(4-methoxyphenyl)-3-(4-methylphenylsulfonamido)propanoate ***6g*** *(Table 2, entry 7)*. General procedure described above was followed to afford **6g** (major) and **6g** (minor) as a white solid in 91% (0.052 g) yield. The compound was isolated (eluant: EtOAc/petroleum ether 8/92) as a mixture of diastereomers with *dr* 75:25 (based on ^{1}H NMR analysis); R_f 0.18 (ethyl acetate/petroleum ether: 15/85); Optical rotation: $[\alpha]_D^{25}$ = +11.70 (*c* 0.85, $CHCl_3$); IR ν_{max} (CH_2Cl_2, cm^{-1}): 3328, 3292, 3062, 3029, 2955, 2925, 2853, 1732, 1610, 1513, 1495, 1454, 1326, 1250, 1160, 1093, 1032, 916.

For the Major Diastereomer ***6g***. mp: 115−117 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.05 (t, *J* = 6.8 Hz, 3H), 2.2 (s, 3H), 3.06 (brs, 1H), 3.30 (d, *J* = 14.6 Hz, 1H), 3.52 (d, *J* = 12.7 Hz, 1H), 3.64−3.70 (m, 4H), 3.98 (q, *J* = 6.8 Hz, 2H), 4.78 (brs, 1H), 6.14 (brs, 1H), 6.52 (d, *J* = 8.6 Hz, 2H), 6.90−7.23 (m, 14H), 7.32 (d, *J* = 8.04 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.8, 21.3, 38.7, 46.9, 55.2, 61.1, 61.8, 68.8, 113.2, 126.8, 126.9, 127.1, 127.7, 128.3, 128.4, 128.9, 129.6, 129.8, 130.4, 135.9, 137.9, 139.6, 142.5, 159.2, 173.2; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{33}H_{36}N_2O_5S$ (M$^+$ + H): 573.2423, Found: 573.2421; $[\alpha]_D^{25}$ = +13.94 (*c* 0.416, CH_2Cl_2) for a 96% ee sample, Optical purity was determined by chiral HPLC analysis

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(Lux 5u Cellulose-2 column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 75.9 min (major), T_R 2: 64.3 min (minor).

For the Minor Diastereomer ***6g***. *ee* 70%; Optical purity was determined by chiral HPLC analysis (Lux 5u Cellulose-2 column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 120.9 min (major), T_R 2: 90.5 min (minor).

Ethyl 2-Benzyl-2-(N-benzylamino)-3-(2-furanyl)-3-(4-methylphenylsulfonamido)propanoate ***6h*** *(Table 2, entry 8).* General procedure described above was followed to afford **6h** (0.046 g) as a white solid in 87% overall yield (combined yield of both the diastereomers). The compound was isolated as a mixture of diastereomers with *dr* 67:33 (based on ^{1}H NMR analysis of the crude reaction mixture) where a little amount of pure major diastereomer was isolated through flash column chromatography (eluent: EtOAc/petroleum ether 10/90) which was injected in chiral HPLC condition (see below) to identify pair of peaks for each diastereomer; R_f 0.30 (ethyl acetate/petroleum ether: 15/85).

For the Major Diastereomer ***6h***. mp: 110−112 °C; Optical rotation: $[\alpha]_D^{25}$ = +9.23 (*c* 1.3, $CHCl_3$) for a 80% *ee* sample; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column) using 97/3 hexane/isopropanol, flow rate = 0.8 mL/min, T_R 1: 19.5 min (minor), T_R 2: 25.5 min (major); IR ν_{max} (KBr, cm^{-1}): 3359, 3294, 3030, 2923, 1735, 1600, 1495, 1453, 1336, 1162, 1091, 1016; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.05 (t, *J* = 7.2 Hz, 3H), 2.27 (s, 3H), 3.12 (d, *J* = 15.2 Hz, 1H), 3.34 (d, *J* = 15.2 Hz, 1H), 3.50 (d, *J* = 12.2 Hz, 1H), 3.70 (d, *J* = 12.2 Hz, 1H), 3.91−3.98 (m, 2H), 4.93 (d, *J* = 7.3 Hz, 1H), 5.97 (d, *J* = 3.3 Hz, 1H), 6.02−6.04 (m, 1H), 6.08 (brs, 1H), 7.04 (d, *J* = 8.1 Hz, 2H), 7.10−7.23 (m, 11H), 7.45 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm): 13.9, 21.5, 38.4, 46.4, 55.9, 62.0, 68.8, 109.5, 110.4, 126.9, 127.0, 128.2, 128.45, 128.53, 128.7, 129.3, 129.9, 130.7, 135.8, 137.8, 141.9, 142.8, 149.9, 172.9; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{30}H_{32}N_2O_5S$ (M^+ + H): 533.2110, Found: 533.2110.

For the Minor Diastereomer ***6h***. It could not be isolated in pure form; *ee* 88%; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column) using 97/3 hexane/isopropanol, flow rate = 0.8 mL/min, T_R 1: 16.2 min (minor), T_R 2: 22.2 min (major).

Ethyl 2-Benzyl-2-(N-benzylamino)-3-(4-chlorophenyl)-3-(4-methylphenylsulfonamido)propanoate ***6i*** *(Scheme 4).* General procedure described above was followed to afford **6i** (major) and **6i** (minor) as a white solid in 88% (0.051 g) yield. It was obtained as a mixture of diastereomers with *dr* 75:25 (based on ^{1}H NMR); R_f 0.45 (ethyl acetate/petroleum ether: 20/80); $[\alpha]_D^{25}$ = +9.33 (*c* 0.965, $CHCl_3$); IR ν_{max} (KBr, cm^{-1}): 3344, 3279, 3029, 2925, 2853, 1735, 1333, 1161, 1092, 1075 cm^{-1}.

For the Major Diastereomer ***6i***. mp: 131−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.03 (t, *J* = 7.1 Hz, 3H), 2.26 (s, 3H), 3.02 (d, *J* = 14.7 Hz, 1H), 3.26 (d, *J* = 14.7 Hz, 1H), 3.50 (d, *J* = 12.5 Hz, 1H), 3.66 (d, *J* = 12.4 Hz, 1H), 3.94 (q, *J* = 7.1 Hz, 2H), 4.77 (d, *J* = 7.8 Hz, 1H), 6.18 (brs, 1H), 6.86−6.95 (m, 6H), 7.08−7.26 (m, 10H), 7.30 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.8, 21.3, 38.7, 46.9, 60.9, 61.9, 68.7, 126.9, 127.0, 127.2, 127.6, 127.9, 128.4, 128.5, 129.1, 129.9, 130.0, 130.3, 133.7, 134.9, 135.5, 137.7, 143.0, 172.8; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{32}H_{34}ClN_2O_4S$ (M^+ + H): 577.1928, Found: 577.1923; $[\alpha]_D^{25}$ = +12.01 (*c* 0.33, CH_2Cl_2) for a 57% ee sample, Optical purity was determined by chiral HPLC analysis (Lux 5u Cellulose-2 column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 41.2 min (major), T_R 2: 57.7 min (minor).

For the Minor Diastereomer ***6i***. *ee* 67%; Optical purity was determined by chiral HPLC analysis (Lux 5u Cellulose-2 column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 59.9 min (major), T_R 2: 48.6 min (minor).

Ethyl 2-Benzyl-2-(N-benzylamino)-3-(4-methylphenylsulfonamido)-3-(3-nitrophenyl)propanoate ***6j*** *(Scheme 4).* General procedure described above was followed to afford **6j** (major) and **6j** (minor) as a white solid in 85% (0.05 g) overall yield (combined yield of both the diastereomers). The compound was isolated (eluent: EtOAc/petroleum ether 6/94) as a mixture of diastereomers with *dr* 62:38 (based on ^{1}H NMR analysis of crude reaction mixture); R_f 0.21 (ethyl acetate/petroleum ether: 15/85); Optical rotation: $[\alpha]_D^{25}$ = +24.0 (*c* 0.50, $CHCl_3$); IR ν_{max} (CH_2Cl_2, cm^{-1}): 3343, 3294, 3063, 3030, 2924, 2853, 1732, 1599, 1530, 1494, 1451, 1412, 1348, 1267, 1210, 1161, 1091, 1029.

For the Major Diastereomer ***6j***. mp 64−66 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.04 (t, *J* = 7.1 Hz, 3H), 2.20 (s, 3H), 3.06 (d, *J* = 14.4 Hz, 1H), 3.24 (d, *J* = 14.4 Hz, 1H), 3.55 (d, *J* = 12.4 Hz, 1H), 3.69 (d, *J* = 12.4 Hz, 1H), 3.97 (q, *J* = 7.1 Hz, 2H), 4.90 (d, *J* = 6.8 Hz, 1H), 6.36 (brs, 1H), 6.89 (d, *J* = 8.1 Hz, 2H), 7.09−7.33 (m, 12H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.77 (s, 1H), 7.88−7.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.8, 21.2, 38.7, 46.9, 60.3, 62.1, 68.6, 122.5, 122.7, 123.6, 126.8, 127.2, 127.4, 127.7, 128.6, 128.8, 129.2, 129.9, 130.1, 134.9, 135.2, 137.4, 138.6, 143.3, 147.7, 172.4; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{32}H_{33}N_3O_6S$ (M^+ + H): 588.2168, Found: 588.2166; $[\alpha]_D^{25}$ = +25.15 (*c* 0.33, CH_2Cl_2) for a 60% ee sample, Optical purity was determined by chiral HPLC analysis (Lux 5u Cellulose2 column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 113.8 min (major), T_R 2: 78.2 min (minor).

For the Minor Diastereomer ***6j***. *ee* 33%, Optical purity was determined by chiral HPLC analysis (Lux 5u Cellulose2 column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 63.0 min (major), T_R 2: 95.7 min (minor).

Methyl 2-[(N-Benzylamino]-2-methyl-3-(4-methylphenylsulfonamido)-3-phenylpropanoate ***6k*** *(Scheme 6).* General procedure described above was followed to afford **6k** (major) and **6k** (minor) as a white solid in 71% (0.32 g) overall yield (combined yield of both the diastereomers). The compound was isolated as a mixture of diastereomers with *dr* 55:45 (based on ^{1}H NMR analysis of the crude reaction mixture) where the major diastereomer was separated through flash column chromatography (eluent: EtOAc/petroleum ether 10/90); R_f 0.17 (ethyl acetate/petroleum ether: 15/85).

For the Major Diastereomer ***6k***. mp: 134−136 °C; Optical purity (*ee* 33%) was determined by chiral HPLC analysis (Chiralcel OD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 14.9 min (major), T_R 2: 18.4 min (minor); IR ν_{max} (KBr, cm^{-1}): 3340, 3279, 2923, 1707, 1496, 1378, 1309, 1257, 1168; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.28 (s, 3H), 2.28 (s, 3H), 3.51−3.59 (s, 2H), 3.62 (s, 3H), 4.53 (s, 1H), 6.09 (bs, 1H), 6.98 (d, *J* = 8.2 Hz, 2H), 7.09−7.12 (m, 5H), 7.25−7.33 (m, 5H), 7.43 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 17.8, 21.5, 48.2, 52.4, 63.1, 65.9, 127.3, 127.9, 128.2, 128.6, 129.2, 136.1, 136.7, 139.6, 143.1, 174.6; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{25}H_{28}N_2O_4S$ (M^+ + H): 453.1848, Found: 453.1848.

For the Minor Diastereomer ***6k***. IR ν_{max} (KBr, cm^{-1}): 3431, 3287, 2998, 1727, 1597, 1478, 1413, 1326, 1288, 1160, 1091, 1066, 982; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.25 (s, 3H), 2.25 (s, 3H), 3.57 (s, 3H), 3.62−3.68 (m, 2H), 4.66 (d, *J* = 9.2 Hz, 1H), 6.0 (d, *J* = 9.45 Hz, 1H), 6.84 (d, *J* = 7.35 Hz, 2H), 6.93 (d *J* = 7.95 Hz, 2H), 7.012−7.04 (m, 2H), 7.06−7.08 (m, 1H), 7.28−7.33 (m, 4H), 7.39 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 20.3, 21.4, 48.2, 52.1, 66.3, 126.8, 127.2, 127.8, 128.3, 128.6, 129.1, 136.4, 140.0, 174.4; HRMS (ES$^+$) *m*/*z*: Calcd. for $C_{25}H_{28}N_2O_4S$ (M^+ + H): 453.1848, Found: 453.1847. Optical purity of this isomer could not be determined as it was inseparable in chiral HPLC columns (Chiralcel AD-H, OD-H, AS-H).

*Methyl 2-Amino-2-benzyl-3-(4-methylphenylsulfonamido)-3-phenylpropanoate (****6l****).* Compound **6l** was obtained by Boc deprotection of the corresponding addition product **4l** in 89% (38.9 mg) yield as a white solid; IR ν_{max} (KBr, cm^{-1}): 3378, 3170, 2953, 1748, 1597, 1443, 1329, 1158, 1090, 1059; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.14 (d, *J* = 13.4 Hz, 1H), 2.21 (s, 3H), 3.20 (d, *J* = 13.4 Hz, 1H), 3.59 (s, 3H), 4.77 (d, *J* = 9.1 Hz, 1H), 6.19 (d, *J* = 9.5 Hz, 1H), 6.86−7.21 (m, 12H), 7.34 (d, *J* = 7.6 Hz, 2H); HRMS (ESI) *m*/*z* Calcd. for $C_{24}H_{26}N_2O_4S$ (M^+ + H): 439.1692, Found: 439.1692.

*2-(Benzyl(tert-butoxycarbonyl)amino)-3-phenylpropanoic acid (****7****).* To a suspension of KOH (0.047 g, 0.848 mmol) in 2.0 mL dry THF was added a solution of *N*-benzyl-*N*-*tert*-butoxycarbonyl amino acid ester **1a** (0.848 mmol) in 1.0 mL dry THF and allowed to stir for 1 h. 2-Phenyl-*N*-tosylimine (0.385 mmol) dissolved in 1.0 mL dry THF was slowly added into the reaction mixture and the stirring was continued at the same temperature for 2 h. After completion of the

reaction (monitored with TLC), it was quenched with saturated aqueous ammonium chloride solution and extracted with 2 × 5.0 mL of ethyl acetate. The combined organic extract was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on a silica gel using ethyl acetate in petroleum ether as the eluent to afford **7** as a colorless liquid in 66% (0.2 g) yield as a 1:1 mixture of rotamers (R and r); IR ν_{max} (CH_2Cl_2, cm^{-1}): 2977, 2928, 2853, 1744, 1699, 1454, 1367, 1250, 1161; For mixture of rotamers: ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.43 (s, 9H, R), 1.51 (s, 9H, r), 3.08−3.12 (m, 1H, r), 3.27−3.28 (m, 3H, 2R+r), 3.48 (d, J = 15.0 Hz, 1H, R), 3.71 (d, J = 16.0 Hz, 1H, r), 3.88−3.89 (m, 1H, R), 4.13−4.15 (m, 1H, r), 4.37 (d, J = 16.0 Hz, 1H, r), 4.61 (d, J = 15.0 Hz, 1H, R), 7.04−7.09 (m, 7H, r), 7.21−7.28 (m, 13H, 10R+3r); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 28.4, 28.5, 35.4, 36.5, 52.1, 52.9, 61.0, 62.6, 81.54, 81.55, 126.8, 127.3, 127.5, 127.8, 128.4, 128.7, 128.8, 129.4, 136.9, 137.4, 137.7, 138.0, 155.2, 156.1, 175.6, 176.9; HRMS (ES^+) m/z: Calcd. for $C_{21}H_{25}NaNO_4$ (M^+ + Na): 378.1681, Found: 378.1654.

Attempted Hydrolysis of Compound ***4a.*** To a suspension of LiOH (0.047 g, 0.848 mmol) in 2 mL dry THF (MeOH or THF/MeOH/H_2O or dioxane/H_2O etc.) was added a solution of *N*-benzyl-*N*-*tert*-butoxycarbonyl amino acid esters **4a** (0.848 mmol) in 1.0 mL dry THF at 0 °C. The reaction was monitored by TLC. The reaction was acidified with 2(N) HCl up to pH 2 and was extracted with 3 × 5.0 mL of diethyl ether. The combined organic extract was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified on a silica gel column by flash column chromatography using ethyl acetate in petroleum ether as the eluent to afford **7** as a colorless liquid in 66% (0.2 g) yield. Spectrum was same as above.

General Procedure for the Aldol Reaction of *N*-Benzyl-*N*-*tert*-butoxycarbonyl Phenylalanine Ethyl Ester 1a with a Variety of Aldehydes in the Presence of LDA. To a solution of diisopropylamine (0.10 mL, 0.75 mmol) in 2 mL dry THF was added *n*-BuLi (1.6 M in hexane, 0.50 mL, 0.75 mmol) at 0 °C and stirred for 20 min. It was cooled to −78 °C and a solution of *N*-benzyl-*N*-*tert*-butoxycarbonyl phenylalanine ethyl ester **1a** (0.75 mmol) in 1.0 mL dry THF was added to it and allowed to stir for 1 h. Aldehydes (0.50 mmol) dissolved in 1.0 mL dry THF was slowly added into the reaction mixture and stirring was continued at the same temperature for 10 h. The reaction (monitored with TLC) was quenched with saturated aqueous ammonium chloride solution and extracted with 5.0 mL of ethyl acetate in two portions. The combined organic extract was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on a silica gel column using ethyl acetate in petroleum ether as the eluent to afford the pure products **8a**−**d**.

Ethyl 2-Benzyl-2-(benzyl(tert-butoxycarbonyl)amino)-3-hydroxy-3-(4-nitrophenyl)propanoate ***8a.*** General procedure described above was followed to afford **8a** as a white solid in 65% (0.17 g) overall yield. It was obtained as a mixture of diastereomers with *dr* 3:2.4 (based on ^1H NMR analysis of crude reaction mixture) where little amount of pure major diastereomer was separated by flash column chromatography (eluent: EtOAc/petroleum ether 10/90) and was injected in chiral HPLC to identify pair of peaks. Optical purity was determined by chiral HPLC analysis (Chiralcel AD-H column); 95/5 hexane/isopropanol, flow rate = 1.0 mL/min; for the minor diastereomers *ee* 68% (T_R 1: 17.4 min, T_R 2: 34.4 min) and for the major diastereomer *ee* 16% (T_R 1: 23.1 min, T_R 2: 44.8 min); R_f 0.20 (ethyl acetate/petroleum ether: 15/85). The pure major diastereomer was injected in aforesaid HPLC condition to identify pair of peaks; mp: 105−112 °C; IR ν_{max} (KBr, cm^{-1}): 3481, 2926, 2855, 1743, 1677, 1521, 1388, 1349, 1269, 1159, 1036; For the major diastereomer ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.19 (brs, 3H), 1.23 (brs, 9H), 2.75 (d, J = 13.2 Hz, 1H), 3.48 (d, J = 13.2 Hz, 1H), 3.68 (d, J = 17.7 Hz, 1H), 3.85−3.92 (m, 1H), 4.25−4.12 (m, 1H), 4.36 (d, J = 17.7 Hz, 1H), 5.68 (s, 1H), 7.03−7.19 (m, 6H), 7.21−7.28 (m, 4H), 7.64 (d, J = 8.6 Hz, 2H), 8.18 (d, J = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.9, 28.1, 36.8, 48.0, 61.2, 70.5, 73.7, 81.3, 123.2, 125.8, 126.6, 127.3, 128.0, 128.2, 129.2, 131.1, 135.4, 139.7, 147.5, 147.7, 155.6, 172.2; HRMS (ES^+) m/z: Calcd. for $C_{30}H_{34}N_2O_7$ (M^+ + Na): 557.2263, Found: 557.2263. The minor diastereomer could not be isolated in pure form.

Ethyl 2-Benzyl-2-(benzyl(tert-butoxycarbonyl)amino)-3-hydroxy-3-(3-nitrophenyl)propanoate ***8b.*** General procedure described above was followed to afford **8b** as a pale yellow solid in 66% (0.18 g) overall yield as a mixture of diastereomers (*dr* 3:1). Both the isomers could be obtained in pure forms after purification through flash column chromatography (eluent: EtOAc/petroleum ether 10/90); Optical purity of **8b** (obtained at −78 °C) was determined by chiral HPLC analysis (Cellulose-2 column); 98/2 hexane/isopropanol, flow rate = 1.0 mL/min; for the major diastereomer *ee* 30% (T_R 1: 18.6 min, T_R 2: 22.3 min) and for the minor diastereomer *ee* 76% (T_R 1: 41.1 min, T_R 2: 55.9 min); Optical purity of **8b** (obtained at −70 °C): for the major diastereomer *ee* 14% (T_R 1: 20.74 min, T_R 2: 25.31 min) and for the minor diastereomer *ee* 67% (T_R 1: 45.1 min, T_R 2: 62.5 min); mp: 62−63 °C; R_f 0.20 (ethyl acetate/petroleum ether: 15/85); IR ν_{max} (KBr, cm^{-1}): 3440, 2955, 2925, 2854, 1741, 1697, 1531, 1453, 1391, 1350, 1267, 1158. For the major diastereomer: ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.20 (bs, 9H), 1.27 (bs, 3H), 2.75 (d, J = 12.8 Hz, 1H), 3.44 (d, J = 12.8 Hz, 1H), 3.64 (d, J = 18.6 Hz, 1H), 3.82−3.98 (m, 1H), 4.12−4.18 (m, 1H), 4.39 (d, J = 18.6 Hz, 1H), 5.69 (s, 1H), 7.11−7.23 (m, 10H), 7.49−7.51 (m, 1H), 7.83−7.96 (m, 1H), 8.11−8.16 (m, 1H,), 8.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.7, 27.9, 36.8, 48.9, 61.1, 70.6, 73.5, 81.9, 122.8, 123.3, 125.9, 126.5, 127.1, 127.9, 128.1, 128.8, 131.0, 134.5, 135.4, 139.5, 142.2, 148.2, 155.5, 170.6; HRMS (ES^+) m/z: Calcd. for $C_{30}H_{34}N_2O_7$ (M^+ + Na): 557.2256, Found: 557.2256. For the Minor Diastereomer. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.20 (m, 3H), 1.28 (bs, 9H), 3.0 (d, J = 13.4 Hz, 1H), 3.09 (d, J = 13.4 Hz, 1H), 3.24 (d, J = 18.0 Hz, 1H), 3.96−3.98 (m, 1H), 4.01−4.06 (m, 1H), 4.28 (d, J = 18.0 Hz, 1H), 5.52 (s, 1H), 7.60−7.63 (m, 10H), 7.60−7.63 (m, 1H), 7.91−7.93 (m, 1H), 8.25−8.27 (m, 1H,), 8.44 (s, 1H); HRMS (ES^+) m/z: Calcd. for $C_{30}H_{34}N_2O_7$ (M^+ + Na): 557.2264, Found: 557.2264.

Ethyl 2-Benzyl-2-(benzyl(tert-butoxycarbonyl)amino)-3-hydroxy-3-(4-methoxyphenyl)propanoate ***8c.*** General procedure described above was followed to afford **8c** as a thick liquid in 52% (0.13 g) overall yield. It was obtained as an inseparable mixture of diastereomers with *dr* 3:1 (based on ^1H NMR analysis of crude reaction mixture) after purification through flash column chromatography (eluent: EtOAc/petroleum ether 10/90). R_f 0.26 (ethyl acetate/petroleum ether: 15/85); IR ν_{max} (CH_2Cl_2, cm^{-1}) 3489, 2977, 2928, 1742, 1692, 1513, 1453, 1386, 1366, 1252, 1159; For the major diastereomer: ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.25 (brs, 12H), 2.63 (d, J = 13.2 Hz, 1H), 3.24 (d, J = 18.3 Hz, 1H), 3.42 (d, J = 13.2 Hz, 1H), 3.79 (s, 3H), 3.79−3.83 (m, 1H), 4.06−4.15 (m, 2H), 5.63 (s, 1H), 6.89 (d, J = 8.0 Hz, 2H), 7.05−7.14 (m, 6H), 7.17−7.23 (m, 4H), 7.36 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.9, 28.3, 35.8, 48.7, 55.4, 61.1, 70.0, 73.8, 80.9, 113.6, 125.9, 126.4, 126.9, 127.7, 128.1, 129.3, 131.3, 131.4, 136.2, 140.2, 155.9, 159.5, 172.0; HRMS (ES^+) m/z: Calcd. for $C_{31}H_{37}NO_6$ (M^+ + H): 520.2699, Found: 520.2695.

Ethyl 2-Benzyl-2-(benzyl(tert-butoxycarbonyl)amino)-3-(3,4-dimethoxyphenyl)-3-hydroxypropanoate ***8d.*** General procedure described above was followed to afford **8d** as a thick liquid in 51% (0.14 g) overall yield; It was obtained as an inseparable mixture of diastereomers with *dr* 4:1 (based on ^1H NMR analysis of crude reaction mixture) after purification through flash column chromatography (eluent: EtOAc/petroleum ether 10/90). R_f 0.29 (ethyl acetate/petroleum ether: 30/70); IR ν_{max} (CH_2Cl_2, cm^{-1}) 3456, 2926, 2854, 1741, 1693, 1516, 1453, 1388, 1367, 1262, 1157, 1029. For the major diastereomer: ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.25 (brs, 12H), 2.65 (d, J = 13.4 Hz, 1H), 3.26 (d, J = 18.3 Hz, 1H), 3.45 (d, J = 13.4 Hz, 1H), 3.80−3.94 (m, 1H), 3.88 (brs, 6H), 4.09−4.13 (m, 1H), 4.16 (d, J = 18.3 Hz, 1H), 5.63 (s, 1H), 6.85−6.91 (m, 2H), 6.96 (s, 1H), 7.04−7.13 (m, 6H), 7.18−7.22 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.7, 28.1, 35.7, 48.7, 55.9, 56.0, 60.9, 70.2, 73.8, 80.9, 110.9, 111.5, 120.6, 125.8, 126.3, 126.8, 127.6, 128.0, 131.3, 131.6, 136.1, 140.0, 148.6, 148.8, 155.7, 173.6; HRMS (ES^+) m/z: Calcd. for $C_{32}H_{39}NO_7$ (M^+ + H): 550.2804, Found: 550.2803.

Ethyl 2-Benzyl-2-(benzylamino)-3-hydroxy-3-(4-nitrophenyl)-propanoate ***9.*** To a stirring solution of substrate **8a** (0.10 mmol)

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in dry dichloromethane (1.0 mL) was added trifluoroacetic acid (0.5 mL) at 0 °C. The reaction mixture was stirred at room temperature for 2 h. It was neutralized with aq. saturated $NaHCO_3$ solution and the aqueous layer was extracted with CH_2Cl_2 (3 × 5.0 mL). The combined organic extract was washed with brine and dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (230−400 mesh) using ethyl acetate in petroleum ether (20:80) as eluent to provide **9** as a pale yellow paste in 85% (0.04 g) yield; Optical purity was determined by chiral HPLC analysis (Cellulose-2 column), 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, for the minor diastereomer *ee* 67% (T_R 1: 32.40 min, T_R 2: 37.82 min); for the major diastereomers *ee* 9% (T_R 1: 30.8 min, T_R 2: 41.48 min); R_f 0.25 (ethyl acetate/petroleum ether: 25/75); IR ν_{max} (CH_2Cl_2, cm^{-1}): 3438, 3340, 2960, 2925, 2854, 1728, 1602, 1520, 1346, 1019; For the major diastereomer: ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.11 (t, J = 7.2 Hz, 3H), 2.92 (d, J = 14.2 Hz, 1H), 3.01 (d, J = 14.2 Hz, 1H),3.66 (d, J = 12.8 Hz, 1H), 3.86 (d, J = 12.8 Hz, 1H), 4.09 (q, J = 7.2 Hz, 2H), 5.14 (s, 1H), 7.07−7.28 (m 10H), 7.60 (d, J = 8.3 Hz, 2H), 8.12 (d, J = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.9, 38.3, 47.9, 61.7, 69.2, 74.2, 122.9, 127.8, 128.6, 128.8, 128.9, 129.2, 130.1, 130.3, 135.2, 139.4, 147.2, 147.6, 173.2; HRMS (ES^+) m/z: Calcd. for $C_{25}H_{26}N_2O_5$ (M^+ + H): 435.1920, Found: 435.1923. For the minor diastereomer: ^1H NMR (500 MHz, $CDCl_3$): δ 1.18 (t, J = 7.33, 3H), 2.98 (d, J = 14.05 Hz, 1H), 3.07 (d, J = 14.05 Hz, 1H), 3.72 (d, J = 12.83 Hz, 1H), 3.92 (d, J = 12.83 Hz, 1H), 4.13−4.17 (m, 2H), 4.24 (bs, 1H), 7.14 (d, J = 7.64 Hz, 2H), 7.25−7.34 (m, 8H), 7.67 (d, J = 8.55 Hz, 2H), 8.18 (d, J = 7.94 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.1, 38.3, 61.7, 69.2, 74.2, 76.9, 123.0, 127.3, 127.5, 127.8, 128.6, 128.8, 129.3, 13.3, 135.3, 139.5, 147.2, 147.7.; HRMS (ESI) calcd for $C_{25}H_{27}N_2O_5$ $(M + H)^+$ 435.1914, found 435.1921.

General Procedure for the Aldol Reaction of *N*-Benzyl-*N*-*tert*-butoxycarbonyl Phenylalanine Ethyl Ester 1a with Various Aldehydes using KHMDS. A KHMDS solution in THF (0.5 M in Toluene, 1.5 mL, 0.75 mmol) was diluted with dry THF and cooled to −78 °C. A solution of compound **1a** (0.75 mmol) in dry THF (1.0 mL) was added dropwise to the KHMDS solution. After 1 h, the corresponding aldehyde (0.5 mmol), dissolved in 1.0 mL dry THF was added dropwise into the reaction mixture and stirring was continued for 6 h. The reaction was monitored with TLC. After 6 h, it was quenched with saturated aqueous ammonium chloride solution and extracted with 5 mL of ethyl acetate in two portions. The combined organic extract was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified on a silica gel column by flash column chromatography using ethyl acetate in petroleum ether as the eluent to afford the pure products **10a−e**.

Ethyl 3,4-Dibenzyl-2-oxo-5-phenyloxazolidine-4-carboxylate ***10a***. General procedure described above was followed when **1a** reacted with benzaldehyde to afford **10a** as a thick liquid in 55% (0.11 g) yield as a single diastereomer (based on ^1H NMR analysis of crude reaction mixture). The compound was purified through flash column chromatography (eluent: EtOAc/petroleum ether 20/80). R_f 0.30 (ethyl acetate/petroleum ether: 20/80); 16% *ee*; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column) using 97/3 hexane/isopropanol, flow rate = 0.8 mL/min, T_R 1: 36.7 min (major), T_R 2: 41.4 min (minor); IR ν_{max} (KBr, cm^{-1}): 3064, 3032, 2924, 2853, 1763, 1738, 1496, 1454, 1391, 1356, 1202, 1092, 1049; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 0.75 (t, J = 7.2 Hz, 3H), 3.23−3.29 (m, 1H), 3.41−3.53 (m, 3H), 4.50 (AB quartet, J_{gem} = 15.5 Hz, 2H), 5.36 (s, 1H), 7.12−7.15 (m, 2H), 7.21−7.23 (m, 2H), 7.26−7.36 (m, 9H), 7.40−7.42 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.2, 37.1, 47.6, 61.8, 73.2, 78.9, 125.9, 127.6, 127.8, 128.2, 128.4, 128.7, 128.9, 129.1, 130.6, 133.8, 134.2, 136.2, 158.4, 169.2; HRMS (ES^+) m/z: Calcd. for $C_{26}H_{25}NO_4$ (M^+ + H): 416.1861, Found: 416.1860.

Ethyl 3,4-Dibenzyl-5-(3-nitrophenyl)-2-oxooxazolidine-4-carboxylate ***10b***. General procedure described above was followed when **1a** reacted with 3-nitrobenzaldehyde to afford **10b** as a sticky solid in 59% (0.13 g) yield as a single diastereomer (based on ^1H NMR analysis of crude reaction mixture). The compound was purified through flash column chromatography (eluent: EtOAc/petroleum ether 20/80). R_f 0.24 (ethyl acetate/petroleum ether: 20/80); 10% *ee*; Optical purity was determined by chiral HPLC analysis (Chiralcel AD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 35.5 min (major), T_R 2: 42.5 min (minor); IR ν_{max} (KBr, cm^{-1}): 3065, 3032, 2925, 2853, 1765, 1719, 1533, 1451, 1390, 1353, 1276, 1202, 1095, 1048; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 0.77 (t, J = 7.2 Hz, 3H), 3.23−3.29 (m, 1H), 3.41−3.54 (m, 3H), 4.54 (AB quartet, J_{gem} = 15.1 Hz, 2H), 5.42 (s, 1H), 7.18−7.20 (m, 2H), 7.27−7.35 (m, 6H), 7.42−7.49 (m, 4H), 8.05 (s, 1H), 8.14 (dd, J = 7.9, 2.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.4, 37.1, 47.6, 62.3, 72.8, 77.8, 121.5, 123.9, 128.2, 128.3, 128.7, 129.3, 129.5, 130.8, 132.2, 133.5, 135.8, 136.6, 148.1, 157.8, 169.0; HRMS (ES^+) m/z: Calcd. for $C_{26}H_{24}N_2O_6$ (M^+ + H): 461.1713, Found: 461.1714.

Ethyl 3,4-Dibenzyl-5-(2-chlorophenyl)-2-oxooxazolidine-4-carboxylate ***10c***. General procedure described above was followed when **1a** reacted with 2-chlorobenzaldehyde to afford **10c** as a thick liquid in 57% (0.13 g) yield as a single diastereomer (based on ^1H NMR analysis of crude reaction mixture). The compound was purified through flash column chromatography (eluent: EtOAc/petroleum ether 20/80). R_f 0.30 (ethyl acetate/petroleum ether: 20/80); 4% *ee*; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 18.3 min (minor), T_R 2: 27.4 min (major); IR ν_{max} (KBr, cm^{-1}): 3065, 3032, 2924, 2854, 1764, 1749, 1444, 1395, 1355, 1279, 1208, 1024; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 0.75 (t, J = 7.2 Hz, 3H), 3.24 (dq, J = 7.2, 7.3 Hz, 1H), 3.44 (dq, J = 6.9, 7.3 Hz, 1H, 1H), 3.61 (AB quartet, J_{gem} = 15.5 Hz, 2H), 4.50 (AB quartet, J_{gem} = 15.5 Hz, 2H), 5.36 (s, 1H), 7.12−7.15 (m, 2H), 7.21−7.23 (m, 2H), 7.26−7.36 (m, 8H), 7.40−7.42 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.1, 38.9, 47.6, 61.9, 73.2, 76.6, 126.9, 127.7, 127.9, 128.5, 128.7, 128.8, 128.9, 129.4, 130.2, 130.3, 132.5, 133.8, 133.9, 136.6, 157.9, 168.8; HRMS (ES^+) m/z: Calcd. for $C_{26}H_{24}ClNO_4$ (M^+ + H): 450.1472, Found: 450.1474.

Ethyl 3,4-Dibenzyl-2-oxo-5-(4-methoxyphenyl)-oxazolidine-4-carboxylate ***10d***. General procedure described above was followed when **1a** reacted with 4-methoxybenzaldehyde to afford **10d** as a white solid in 49% (0.11 g) yield as a single diastereomer (based on ^1H NMR analysis of crude reaction mixture). The compound was purified through flash column chromatography (eluent: EtOAc/petroleum ether 20/80). R_f 0.20 (ethyl acetate/petroleum ether: 20/80); 4% *ee*; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 21.9 min (minor), T_R 2: 34.5 min (major); IR ν_{max} (KBr, cm^{-1}): 3062, 3031, 2922, 2852, 1763, 1737, 1612, 1515, 1454, 1391, 1355, 1253, 1177, 1028; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 0.83 (t, J = 7.2 Hz, 3H), 3.33−3.37 (m, 1H), 3.42−3.54 (m, 3H), 3.76 (s, 3H), 4.48 (AB quartet, J_{gem} = 15.5 Hz, 2H), 5.31 (s, 1H), 6.81 (d, J = 7.2 Hz, 2H), 7.12 (d, J = 7.2 Hz, 4H), 7.25−7.33 (m, 6H), 7.40 (d, J = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.5, 37.3, 47.8, 53.4, 61.9, 73.4, 79.1, 113.7, 126.1, 127.5, 127.7, 127.9, 128.6, 129.0, 129.2, 130.8, 134.1, 136.4, 158.6, 160.0, 169.4; HRMS (ES^+) m/z: Calcd. for $C_{27}H_{27}NO_5$ (M^+ + H): 446.1968, Found: 446.1970.

Ethyl 3,4-Dibenzyl-5-(3,4-dimethoxyphenyl)-2-oxooxazolidine-4-carboxylate ***10e***. General procedure described above was followed when **1a** reacted with 3,4-dimethoxybenzaldehyde to afford **10e** as a white solid in 49% (0.12 g) yield as a single diastereomer (based on ^1H NMR analysis of crude reaction mixture). The compound was purified through flash column chromatography (eluent: EtOAc/petroleum ether 20/80). R_f 0.20 (ethyl acetate/petroleum ether: 30/70); 10% *ee*; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 40.2 min (minor), T_R 2: 53.7 min (major); IR ν_{max} (KBr, cm^{-1}): 2923, 2851, 1762, 1748, 1517, 1453, 1390, 1356, 1266, 1242, 1142, 1024; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 0.81 (t, J = 7.2 Hz, 3H), 3.37−3.50 (m, 3H), 3.52−3.57 (m, 1H), 3.79 (s, 3H), 3.84 (s, 3H), 4.46 (AB quartet, J_{gem} = 15.2 Hz, 2H), 5.32 (s, 1H), 6.72−6.78 (m, 3H), 7.12−7.14 (m, 2H), 7.25−7.32 (m, 6H), 7.41 (d, J = 7.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 13.6, 37.8, 47.8, 55.9, 56.0, 61.9, 73.5, 79.3, 109.1, 110.7, 118.8, 126.6, 127.8, 127.9, 128.6,

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129.0, 129.1, 130.7, 134.1, 136.5, 148.9, 149.4, 158.5, 169.4; HRMS (ES^+) m/z: Calcd. for $C_{28}H_{29}NO_6$ (M^+ + H): 476.2073, Found: 476.2076.

General Procedure for Reduction of Ethyl Ester using $LiBH_4$.[23] To a stirring solution of ester **6a**, **6d** (50 mg, 0.10 mmol) in dry THF (1.0 mL) were added $LiBH_4$ (2 M in THF) (3 mmol) and methanol (0.10 mL) at 0 °C. The reaction mixture was stirred at room temperature for 12 h. The reaction was quenched with water. Most of the methanol was evaporated under reduced pressure. The mixture was extracted with ethyl acetate (3 × 5.0 mL), the combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography over silica gel (230−400 mesh) using ethyl acetate in petroleum ether to give **16a**, **16b**.

[2-Benzyl-2-(N-benzylamino)-3-hydroxy-1-phenylpropyl]-4-methylbenzenesulfonamide ***16a***. General procedure described above was followed for the reduction of **6a** (major diastereomer) to provide **16a** as a white solid in 75% (0.04 g) yield. R_f 0.10 (ethyl acetate/petroleum ether: 15/85); mp: 205−207 °C; Optical rotation: $[\alpha]_D^{25}$ = +52.0 (*c* 0.50, $CHCl_3$) for a 92% *ee* sample. Optical purity was determined by chiral HPLC analysis (Chiralcel AD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 51.9 min (major), T_R 2: 88.7 min (minor); IR ν_{max} (KBr, cm^{-1}): 3453, 3328, 3061, 3028, 2924, 2854, 1600, 1494, 1453, 1324, 1158, 1090, 1027; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.21 (s, 3H), 2.40 (d, J = 13.7 Hz, 1H), 2.97 (d, J = 13.7 Hz, 1H), 3.32 (d, J = 12.2 Hz, 1H), 3.41 (d, J = 12.2 Hz, 1H), 3.57 (d, J = 11.6 Hz, 1H), 3.71 (d, J = 11.5 Hz, 1H), 4.5 (s, 1H), 6.22 (brs, 1H), 6.89 (d, J = 8.3 Hz, 2H), 7.00−7.25 (m, 15H), 7.35 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.3, 29.7, 38.7, 46.2, 60.5, 62.4, 126.9, 127.0, 127.1, 127.6, 128.0, 128.6, 128.8, 129.0, 129.08, 129.12, 130.5, 134.9, 136.50, 136.80, 136.83, 142.9; HRMS (ES^+) m/z: Calcd. for $C_{30}H_{33}N_2O_3S$ (M^+ + H): 501.2211, Found: 501.2210.

[(2-Benzyl-2-(N-benzylamino)-1-(3-bromophenyl)-3-hydroxypropyl]-4-methylbenzenesulfonamide ***16b***. General method described above was followed for the reduction of **6d** (major diastereomer) to afford **16b** as a white solid in 73% (0.034 g) yield. R_f 0.13 (ethyl acetate/petroleum ether: 20/80); *ee* 80%; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column), 95/5 hexane/isopropanol, flow rate = 1.0 mL/min, T_R 1: 26.3 min (minor), T_R 2: 31.5 min (major); IR ν_{max} (KBr, cm^{-1}): 3490, 3328, 2923, 2854, 1596, 1451, 1332, 1159, 1092; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 2.30 (s, 3H), 2.54 (d, J = 13.7 Hz, 1H), 2.99 (d, J = 14.0 Hz, 1H), 3.48 (d, J = 12.4 Hz, 1H), 3.56 (d, J = 12.4 Hz, 1H), 3.59 (d, J = 11.4 Hz, 1H), 3.71 (d, J = 11.0 Hz, 1H), 4.58 (s, 1H), 7.00 (d, J = 8.2 Hz, 2H), 7.14−7.31 (m, 14H), 7.41 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 21.4, 39.1, 45.9, 60.1, 61.6, 62.9, 122.1, 126.90, 126.94, 127.2, 127.3, 127.7, 128.5, 128.6, 129.2, 129.4, 130.3, 130.4, 131.8, 136.4, 136.6, 139.2, 139.8, 143.2; HRMS (ES^+) m/z: Calcd. for $C_{30}H_{31}BrN_2O_3S$ (M^+ + H): 579.1317, Found: 579.1317.

General Procedure for the Synthesis of Aziridine. To a solution of alcohol **16a**, **16b** (30 mg, 0.059 mmol) (single diastereomer) in dry CH_2Cl_2 (0.5 mL) were added mesyl chloride (2 mmol) and triethylamine (2.5 mmol). The reaction mixture was stirred at room temperature for 5 h. It was poured into water and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extract was washed with brine and dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography over silica gel (230−400 mesh) using 10% ethyl acetate in petroleum ether as eluent to provide **20a**, **20b**.

[2-Benzyl(N-benzylaziridin-2-yl)-phenylmethyl]-4-methylbenzenesulfonamide ***20a***:[16] General procedure described above was followed to provide **20a** as a white solid in 65% (0.019 g) yield. R_f 0.33 (ethyl acetate/petroleum ether: 15/85); mp: 140−142 °C; Optical rotation: $[\alpha]_D^{25}$ = +31.80 (*c* 0.22, $CHCl_3$) for a 92% *ee* sample; Optical purity was determined by chiral HPLC analysis (Chiralcel AD-H column) using 95/5 hexane/isopropanol, flow rate = 1.0 mL/min. T_R 1: 28.3 min (major), T_R 2: 35.3 min (minor); IR ν_{max} (KBr, cm^{-1}): 3286, 3060, 3029, 2923, 2854, 1600, 1495, 1454, 1426, 1324, 1286, 1163, 1089, 1062, 1044, 1030; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.21 (s, 3H), 2.27 (s, 2H), 2.47 (d, J = 14.9 Hz, 1H), 2.67 (d, J = 14.9 Hz, 1H), 3.46 (d, J = 13.4 Hz, 1H), 3.85 (d, J = 13.4 Hz, 1H), 4.23 (d, J = 7.6 Hz, 1H), 5.52 (d, J = 7.8 Hz, 1H), 6.72 (d, J = 7.8 Hz, 2H), 6.87−7.04 (m, 6H), 7.18−7.34 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.3, 29.7, 34.0, 35.7, 44.1, 56.5, 126.7, 126.8, 127.3, 127.4, 127.9, 128.1, 128.4, 128.5, 128.6, 129.0, 129.2, 137.2, 139.2, 139.3, 142.3, 142.4; HRMS (ES^+) m/z: Calcd. for $C_{30}H_{30}N_2O_2S$ (M^+ + H): 483.2106, Found: 483.2106.

[2-Benzyl-(3-bromophenyl)(N-benzylaziridin-2-yl)methyl]-4-methylbenzenesulfonamide ***20b***. General procedure described above was followed to provide **20b** as a white solid in 71% (0.020 g) yield. R_f 0.26 (ethyl acetate/petroleum ether: 20/80); *ee* 80%; Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column); 97/3 hexane/isopropanol, flow rate = 0.8 mL/min. T_R 1: 24.3 min (minor), T_R 2: 32.1 min (major); IR ν_{max} (KBr, cm^{-1}): 3278, 3061, 3028, 2922, 2852, 1596, 1494, 1452, 1332, 1160, 1093, 1075; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 2.30 (s, 3H), 2.31 (d, J = 14.4 Hz, 1H), 2.37 (bs, 1H), 2.51 (d, J = 14.8 Hz, 1H), 2.77 (d, J = 14.8 Hz, 1H), 3.56 (d, J = 13.4 Hz, 1H), 3.88 (d, J = 13.4 Hz, 1H), 4.22 (d, J = 7.6 Hz, 1H), 5.62 (bs, 1H), 6.76 (bs, 1H), 6.84 (t, J = 7.9 Hz, 1H), 6.97 (d, J = 8.3 Hz, 2H), 7.01 (d, J = 6.9 Hz, 2H), 7.19 (d, J = 8.3 Hz, 1H), 7.24−7.36 (m, 8H), 7.39−7.40 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 21.5, 34.2, 35.9, 43.9, 56.0, 56.7, 122.2, 126.5, 126.7, 127.1, 127.6, 128.4, 128.7, 128.8, 129.18, 128.19, 129.7, 130.5, 131.2, 136.7, 137.7, 139.0, 141.1, 142.8; HRMS (ES^+) m/z: Calcd. for $C_{30}H_{29}BrN_2O_2S$ (M^+ + H): 561.1211, Found: 561.1210.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, characterization, X-ray crystallographic data of some of the compounds, computational results and related data, copies of ^1H NMR, ^{13}C NMR spectra of all new compounds and HPLC chromatograms for *ee* determination. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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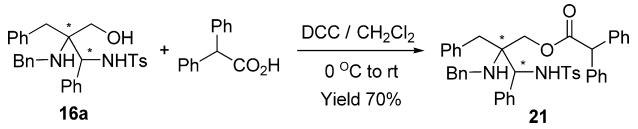

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