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Asymmetric Synthesis of 1-(2-Pyrrolyl)alkylamines by the Addition of Organometallic Reagents to Chiral 2-Pyrroleimines

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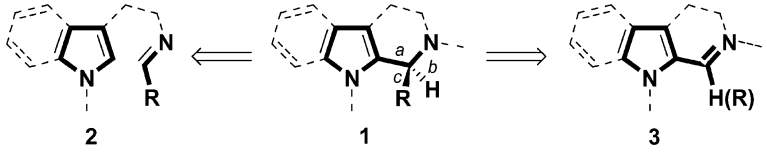
The addition of organometallic (lithium, magnesium, zinc) reagents to 2-pyrroleimines derived from (*S*)-valinol and (*S*)-phenylglycinol gave *N*-substituted-1-(2-pyrrolyl)alkylamines with high yields and diastereoselectivities. The (*S*,*S*)-diastereomers were useful intermediates for the preparation of enantiopure 1-[1-(2-pyrrolyl)alkyl]aziridines by routine cyclization of the β-amino alcohol moiety and for the preparation of (*S*)-*N*-benzoyl 1-[1-(2-pyrrolyl)alkyl]amines and their *N*-substituted derivatives by oxidative cleavage of the chiral auxiliary.

Introduction

The chiral 1-(2-pyrrolyl)alkylamino moiety highlighted in structure **1** (Scheme 1) bears a stereocenter at the benzylic carbon (one configuration is shown) and is a common structural motif in non-cinchona indole alkaloids[1] and terpene indole alkaloids,[2] both of which display potent biological and physiological properties. Mytosene aziridines are also important compounds containing this skeleton fragment.[3]

Given their enormous importance, synthetic methods have been developed for these compounds, but efficient asymmetric procedures for the construction of the heterobenzylic stereocenter are still lacking. In principle, this goal can be accomplished during the formation of any of the four bonds involved. Three of these possibilities concern the formation of bonds *a*, *b*, and *c* as described in Scheme 1. For example, the *a* bond in compounds of type **1** can be formed by the inter- or intramolecular attack of the nucleophilic pyrrole C-2 carbon at the electrophilic carbon of an azomethine compound, which is generally activated by a Lewis acid and an electron-withdrawing *N*-substituent, or an iminium ion, possibly formed in situ (three-component Mannich reaction).[4] For example, the BF_3-mediated addition of pyrrole to (*S*)-*N*-trifluoromethylidene-1-phenylethylamine occurred with good yield but only moderate diastereoselectivity (*dr* 78:22), whereas indole reacted (at C-3) with complete stereocontrol.[4d] In contrast, an allylic 3-methylene-2,3-dihydro-2-indolylindium species generated by a Pd–In bimetallic cascade process from 2-iodo-*N*-allenylaniline added to enantiopure *N*-[(*R*)-*tert*-butylsulfinyl] glyoxylate imine with complete stereocontrol.[4f]

The 1,2-(indolyl)alkylamino moiety has been commonly prepared by the intramolecular version of this approach, namely, the Pictet–Spengler reaction, which has been a key step in the synthesis of a large number of alkaloids.[1s,1t,5,6] In this reaction, an imine or iminium ion functionality, which is formed in situ by *N*-functionalization of tryptamine and its substituted derivatives by reaction with an aldehyde, undergoes intramolecular attack by the indole C-2 carbon. Although the reaction often gives mixtures of diastereomers, a number of highly stereoselective reactions have been reported that rely on the asymmetric induction of the stereocenter(s) present in the tryptamine aliphatic chain, the aldehyde, or the amine substituent (chiral auxiliary). To the best of our knowledge, the Pictet–Spengler reaction has rarely been applied to a pyrrole derivative.[1u]



Scheme 1.

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Alternatively, the stereocenter in structure **1** can be constructed by formation of bond *b* from azomethine compounds of type **3**.[5t,7] For example, quinolizidine alkaloids have often been prepared by a sequence of steps where a tetracyclic quaternary 2-indolyliminium ion (R-substituted *N*-charged cyclic structure **3**) was formed by the Bischler–Napieralski reaction between indole and lactam rings, then subjected to catalytic hydrogenation or hydride reduction. More recently, novel polycyclic indolyldiamines have been prepared by completely diastereoselective hydride reductions of chiral, optically pure 2-indolylketimines.[7f]

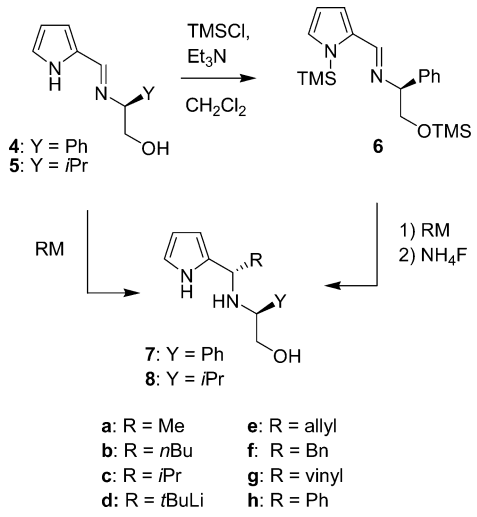
The construction of bond *c* involves the addition of a carbon nucleophile or an organometallic reagent to 2-pyrrolealdimine **3**. However, 2-pyrrole- and 2-indoleimines are less electrophilic than other aromatic imines owing to the electron-donating effect of the pyrrole/indole ring. For example, 9-benzyl-3,4-dihydro-β-carboline was unreactive towards a laterally metalated pyridine, although a successful reaction was observed when the imine was preliminarily activated by the addition of trimethylsilyl trifluoromethanesulfonate.[1d] Similarly, the Lewis acid promoted addition of a ketene silyl acetal to a β-carboline hydrochloride derived from L-tryptophan[1r] and the addition of allyltrimethylsilane to iminium ions derived from D-tryptophan[8] have been described. Benzylic and allylic organometallic reagents reacted smoothly with analogous imines bearing *N*-aryl or *N*-benzenesulfonyl substituents.[9] Recently, the chiral auxiliary approach was exploited for the asymmetric synthesis of 2-(1-aminoalkyl)indoles by the addition of laterally metalated 3-cyano-4-methylpyridine to a 1,3-disubstituted 2-indoleimine derived from an optically pure sulfinamide and a *de* of 82% was obtained under the optimized conditions.[10] Recently, a ring-substituted 2-pyrroleimine prepared from (*R*)-phenylglycinol underwent highly diastereoselective addition of isopropylmagnesium chloride (4–5 equiv.), whereas the addition of allylzinc bromide to an analogous imine prepared from (*R*)-phenyl glycineamide was unsatisfactory.[11] In the addition of an optically pure allylsilane to an acylhydrazone derived from 2-pyrrolealdehyde, the yield and *ee* values were found to be dependent on the pyrrole *N*-substitution: a lower yield (49%) but a higher *ee* value (92%) was obtained with the *N*-Boc pyrrole imine with respect to the unprotected imine (*ee* 48%).[12] Interestingly, tricyclic pyrrole–pyrazine–oxazole structures were prepared from 2-formylpyrroles derived from (*S*)-α-amino esters and (+)- or (–)-norephedrine. However, the potential of such compounds as precursors of chiral iminium ions, suitable substrates for the addition of Grignard reagents, eventually leading to 2-(1-aminoalkyl)pyrroles, has not yet been considered.[13]

Another widely exploited method for the asymmetric synthesis of polycyclic indole alkaloids by construction of the C–R bond *c* in structure **1** is the Diels–Alder cycloaddition of β-carbolines and 2-indoleimine with 1,4-dienes.[14,15] Notably, a chiral 2-pyrroleimine failed to react with 1,3-butadiene.[16] For the sake of completeness, the C–N bond can also be formed by nucleophilic substitution of oxygen-substituted compounds. For example, dihydropyrrolizine esters gave the corresponding amines by reaction with ammonia and alkylamines, but loss of the stereochemical integrity of the stereocenter was observed, which points to an S_N1 mechanism for these reactions.[17]

Following this extensive literature search, we observed that the asymmetric synthesis of 1-(2-pyrrolyl)alkylamines was scarcely explored relative to the analogous indole derivatives. So, we were prompted to study the auxiliary-induced diastereoselective addition of organometallic reagents to 2-pyrroleimines to fill the gap in our long-term investigation on the asymmetric synthesis of benzylic and heterobenzylic amines from chiral imines.[18] It should also be noted that optimization of this route would open an avenue to optically pure compounds with the pyrrolidine, pyrrolizidine and indolizidine skeletons,[19] including alkaloids and pharmacologically interesting molecules, by taking advantage of the possible hydrogenation of the pyrrole nucleus[20] and the nucleophilicity of the pyrrole/pyrrolidine nitrogen atom.

Results and Discussion

Optically pure phenylglycinol and valinol are among the most used chiral auxiliaries for the diastereoselective addition of organometallic reagents to imines.[21] In particular, we described that the addition of organolithium reagents to 2-pyridineimines derived from (*S*)-valinol and (*S*)-phenylglycinol occurred effectively and with very high diastereoselectivity following the protection of the OH functionality as its trimethylsilyl ether.[18] Hence, we began our investigation on *N*,*O*-disilylated imine **6**, which was prepared in two steps and in almost quantitative yield from 2-pyrrolealdehyde and (*S*)-phenylglycinol through intermediary unprotected imine **4** (Scheme 2).



Scheme 2.

The addition of organolithium reagents to imine **6** was carried out in diethyl ether at –15 or 0 °C, as no reaction was observed at lower temperatures. By using 2–3 equiv. of the organometallic reagents, good yields of β-hydroxyamines **7** were obtained after protonolysis and de-

silylation of the organometallic adducts with ammonium fluoride in the biphasic system THF/H_2O (Table 1). The (*S*,*S*) configuration of the prevalent diastereomer in products **7** was assumed on the basis of the sense of asymmetric induction previously determined in organometallic reactions of analogous aromatic and heteroaromatic imines.[18] Very high diastereoselectivity (*dr* >95%) was observed in the formation of amines **7a** and **7b** with MeLi and *n*BuLi, respectively, and the main diastereomers (*S*,*S*)-**7a**,**b** were isolated in good yields after column chromatography. Homoallylic amine **7e** was then prepared by using either allylzinc bromide or allylmagnesium chloride in tetrahydrofuran, but a better diastereoselectivity was obtained with the magnesium reagent (*dr* 90:10 vs. >96:4). Instead, no reaction was observed with vinylmagnesium bromide.

Table 1. Preparation of amines **7** by the addition of organometallic reagents to imine **6**.[a]

RM (equiv.)	Solvent	*dr*[b]	(*S*,*S*)-**7**, Yield [%][c]
MeLi (3)	Et_2O	>95:5	**7a**, 87
*n*BuLi (3)	Et_2O	>95:5	**7b**, 82
AllylZnBr (2)	THF	>90:10	**7e**, 81
AllylMgCl (2)	THF	>96:4	**7e**, 83
VinylMgCl (3)	Et_2O	–	no reaction

[a] The organometallic reagent was slowly added to the imine at –15 °C, and the mixture was then stirred for 3 h allowing the temperature to reach 20 °C. [b] Determined by ^{1}H NMR spectroscopic analysis. [c] The crude product was treated with NH_4F (3 equiv.) and a catalytic amount of TBAF in THF/H_2O (1:1), then subjected to column chromatography (SiO_2).

Subsequently, taking into account a recent report,[11] we wished to check the reactivity of unprotected imines **4** and **5** derived from (*S*)-phenylglycinol and (*S*)-valinol, respectively. This choice required the use of an excess amount of the organometallic reagent, as the first two equivalents were quenched by the acidic OH and NH functionalities. Moreover, it was expected that the negatively charged pyrrole substituent would decrease the reactivity of the imine functionality. As a matter of fact, the addition of MeLi (4 equiv.) to imine **4** in THF occurred smoothly at –15 to 0 °C to give amine **7a** in 96% yield with a *dr* >95 (Table 2). Similarly, the reaction with *n*BuLi under the same conditions gave amine **7b** in high yield and with (almost) complete diastereoselectivity; only one diastereomer was observed by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. Similarly, the addition of *i*PrMgCl proceeded smoothly to give **7c** in 92% yield and with complete diastereoselectivity.

In contrast, the addition of *t*BuLi occurred with quite poor diastereoselectivity, although the two diastereomers of **7d** could be separated by column chromatography. A low conversion of imine **4** was observed by TLC and GC analyses after the addition of allylzinc bromide; however, the use of allylmagnesium chloride allowed homoallylic amine **7e** to be obtained in good yield and with high diastereoselectivity (*dr* >95:5). The higher yield and complete stereocontrol were then obtained by using 4 equiv. of the allyldiethylzincate prepared by the addition of allylmagnesium chloride to diethylzinc.[21] Aiming to reduce the overall excess of organometallic reagents, we subsequently developed a more economic protocol that involved the preliminary addition of diethylzinc (2 equiv.) to imine **4**, followed by the addition of allylmagnesium chloride (2 equiv.); in this way, homoallylic amine **7e** was obtained in almost identical yield and with complete stereocontrol. Good results were also obtained by using benzylmagnesium chloride to afford amine

Table 2. Preparation of amines **7** and **8** by the addition of organometallic reagents to imines **4** and **5** in THF.[a]

Imine	Y	RM (equiv.)	*dr*[b]	(*S*,*S*)-**7**, (*S*,*S*)-**8**, Yield [%][c]
4	Ph	MeLi (4)	>95:5	**7a**, 96
4	Ph	*n*BuLi (4)	>99:1	**7b**, 91
4	Ph	*i*PrMgCl (4)	>95:5	**7c**, 92
4	Ph	*t*BuLi (4)[d]	55:45	(*S*,*S*)-**7d**, 31; (*R*,*S*)-**7d**, 28
4	Ph	allylZnBr (4)	–	**7e**, 10[b,e]
4	Ph	allylMgCl (4)	>95:5	**7e**, 87
4	Ph	allylEt_2ZnMgCl (4)	>99:1	**7e**, 89
4	Ph	1. Et_2Zn (2), 2. allylMgCl (2)	>99:1	**7e**, 86
4	Ph	BnMgCl (4)	>95:5	**7f**, 91
4	Ph	vinylMgBr (4)	–	**7g**, 0
4	Ph	PhMgBr (4)	–	**7h**, 0
4	Ph	PhLi (4)	>95:5	**7h**, 95[f]
5	*i*Pr	MeLi (4)	>99:1	**8a**, 91
5	*i*Pr	*n*BuLi (4)	>99:1	**8b**, 87
5	*i*Pr	1. Et_2Zn (2), 2. allylMgCl (2)	>99:1	**8e**, 89
5	*i*Pr	allylMgCl (4)	>99:1	**8e**, 78
5	*i*Pr	BnMgCl (4)	>99:1	**8f**, 90
5	*i*Pr	1. MeLi (2), 2. vinylLi (2)	>99:1	**8g**, 92[f]
5	*i*Pr	PhLi (4)	>95:5	**8h**, 91[f]

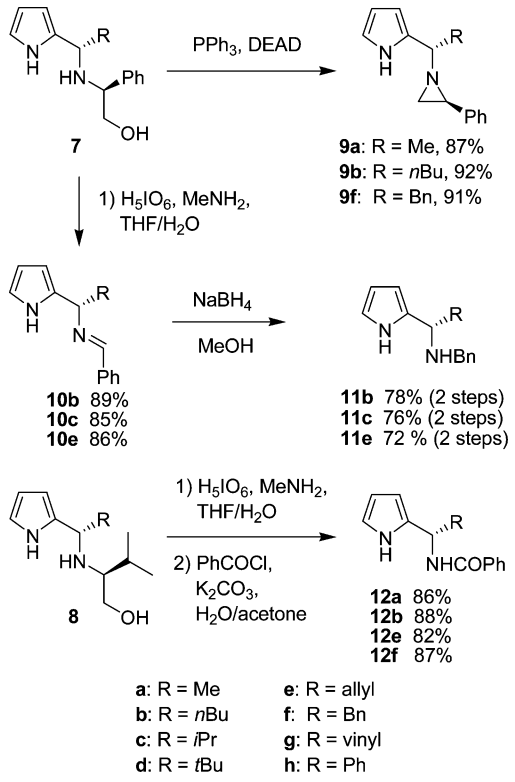
[a] The organometallic reagent (4 equiv.) was slowly added to the imine at –15 °C, and the mixture was stirred for 3 h allowing the temperature to reach 20 °C. [b] Determined by ^{1}H NMR spectroscopic analysis. [c] Yield of the pure (*S*,*S*)-diastereomer that was isolated by column chromatography (SiO_2). [d] The reaction was performed in Et_2O. [e] The product was not isolated. [f] The product decomposed during chromatography on SiO_2.

7f in high yield and with *dr* >95:5. No reaction was observed with vinylmagnesium bromide or phenylmagnesium bromide; however, phenyllithium proved to be more reactive and gave desired amine **7h**. Unfortunately, crude amine **7h** decomposed upon attempted purification by column chromatography perhaps owing to the acidity of the methine proton linked to the carbon stereocenter.

We then moved to evaluate the degree of asymmetric induction offered by (*S*)-valinol-derived 2-pyrroleimine **5** in the same organometallic reactions carried out on imine **4**. We were delighted to observe that even better results were obtained, as complete stereocontrol was achieved in the preparation of amines **8a**,**b**,**e**–**h** (Table 2). These results are in line with the previously observed evidence that better stereocontrol was provided by valinol as the chiral auxiliary for imines with respect to phenylglycinol.[18] The reaction with *tert*-butyllithium was not carried out, as we had no chance to improve significantly the diastereoselectivity previously obtained with imine **4**. β-Amino alcohols **8g**,**h** were obtained by using vinyllithium and phenyllithium, respectively. Vinyllithium was prepared by the reaction of tri(*n*-butyl)vinyltin and *n*BuLi; however, we found it more convenient to initially add two equivalents of MeLi to imine **5**, as the first two equivalents of the organometallic reagent are consumed by the acidic NH and OH groups, followed by the addition of another two equivalents of vinyllithium. As previously observed with amine **7h**, novel amines **8g**,**h** underwent decomposition during attempted chromatographic purification. Nevertheless, it is likely that crude amines **7h** and **8g**,**h**, which were obtained with satisfactory purity, could be used as such in subsequent steps involving transformation of the alkene functionality.

At this point we assessed the possibility of using β-amino alcohol **7** for the construction of new optically active, pyrrole-containing molecules, such as aziridines by intramolecular cyclization and secondary amines through oxidative cleavage of the chiral auxiliary (Scheme 3). For the first goal we followed the same protocol previously applied for the synthesis of analogous 1-(2-pyridyl)alkylaziridines.[18b,18c] As a matter of fact, pyrrole–aziridines **9a**,**b**,**f** were successfully obtained in high yields by treatment of β-hydroxyamines **7a**,**b**,**f** with triphenylphosphane and diethylazodicarboxylate (DEAD) in THF at room temperature.

The hydrogenolysis of **7a** with ammonium formate and Pd/C in ethanol at reflux gave disappointing results, as a complex mixture of products was obtained. Instead, the oxidation reaction with the use of periodic acid and methylamine in THF/H_2O was successful; however, starting from β-amino alcohols **7b**,**c**,**e**, benzaldimines **10b**,**c**,**e** were isolated, and they were stable towards hydrolysis under the reaction conditions. In particular, imine **10c** was isolated as a solid and could be purified simply by washing with pentane. Crude imines **10b**,**c**,**e** were readily reduced to corresponding benzylamines **11b**,**c**,**e** by sodium borohydride in methanol (Scheme 3). It is noteworthy that this procedure is more convenient than the usual stepwise removal of the chiral auxiliary followed by *N*-benzylation. The primary amines were formed by carrying out the oxidative procedure on the valinol derivatives **8**; in this case, the crude compounds were preferably treated with benzoyl chloride and potassium carbonate in acetone/H_2O mixture to easily obtain the corresponding pure *N*-benzoyl derivatives **12a**,**b**,**e**,**f** in good yields.



Scheme 3.

Conclusions

We developed a convenient asymmetric route to 1-[2-(pyrrolyl)]alkylamines by exploiting the highly diastereoselective addition of organometallic reagents to chiral 2-pyrroleimines derived from (*S*)-phenylglycinol and (*S*)-valinol. Although a larger excess of organometallic reagents was needed, better diastereoselectivities were obtained by working with the imines with unprotected N–H and O–H functionalities. Complete or excellent stereocontrol was achieved, especially with the (*S*)-valinol-derived imine. Removal of the chiral auxiliaries was achieved by an oxidative procedure to give the corresponding imines or primary amines, from which the *N*-benzyl and *N*-benzoylamines could be easily prepared. Pyrrole–aziridines were also prepared by cyclization of the (*S*)-phenylglycinol derived secondary amines. Future efforts in our laboratory will be devoted to converting unsaturated amines **7h** and **8g,h** into bicyclic compounds by linking the pyrrole-NH and alkene functionalities.

Experimental Section

General: Melting points are uncorrected. Optical rotations were measured with a digital polarimeter in a 1-dm cell and $[\alpha]_D$ values

are given in 10^{-1} deg cm^3 g^{-1}. ^{1}H NMR spectra were recorded with Varian Inova and Gemini instruments for samples in $CDCl_3$, which was stored over Mg: ^{1}H NMR chemical shifts are reported relative to $CHCl_3$ (δ_H = 7.27 ppm), and assignments are given as follows: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, br. s = broad singlet, dd = doublet of doublets, and dt = doublet of triplets. Infrared spectra were recorded with a Nicolet FT-380 spectrometer. MS spectra were taken at an ionizing voltage of 70 eV with a Hewlett–Packard 5975 spectrometer with GLC injection. Molecular weight was determined with an Agilent Technologies MS 1100 instrument. Chromatographic separations were performed on columns of SiO_2 (Merck, 230–400 mesh) at medium pressure. All the organic, inorganic, and organometallic reagents and reactants and anhydrous solvents were purchased from Aldrich.

Preparation of Imines 4 and 5: To a solution of (*S*)-phenylglycinol (0.823 g, 6 mmol) or (*S*)-valinol (0.618 g, 6 mmol) in anhydrous CH_2Cl_2 (30 mL) was added anhydrous $MgSO_4$ (5 g) and 2-pyrrolecarboxaldehyde (0.571 g, 6 mmol), and the mixture was stirred overnight. The solid was filtered off through a pad of Celite, and the organic phase was concentrated under reduced pressure. The residue was crystallized from pentane/CH_2Cl_2 (5:1) to give the imine, which was used in the following step without purification.

(*S*)-*N*-(2-Pyrrolmethylidene)phenylglycinol (4): Yield: 1.262 g (98%). White solid. M.p. 109–109.6 °C. $[\alpha]_D^{20}$ = +24.3 (*c* = 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.03 (dd, *J* = 3.6 Hz, *J*^{2} = 12.2 Hz, 1 H), 4.20 (dd, *J* = 9.9 Hz, *J* = 12.2 Hz, 1 H), 4.46 (dd, *J* = 3.6 Hz, *J* = 9.9 Hz, 1 H), 6.20 (m, 2 H), 6.99 (m, 1 H), 7.38 (m, 5 H), 7.75 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 67.9, 76.6, 109.6, 117.7, 122.9, 126.9, 127.4, 128.6, 128.9, 140.7, 154.6 ppm. IR (KBr): $\tilde{\nu}$ = 3331, 3113, 3061, 2921, 2854, 1640, 1425, 1366, 1313, 1073, 1061, 1043, 813, 737, 701 cm^{-1}. GC–MS: *m*/*z* (%) = 183 (100), 156 (12), 214 (7), 80 (7). $C_{13}H_{14}N_2O$ (214.11): calcd. C 72.87, H 6.59, N 13.07; found C 72.57, H 6.62, N 13.10.

(*S*)-*N*-(2-Pyrrolmethylidene)valinol (5): Yield: 1.051 g (97%). White solid. M.p. 122.4–123 °C. $[\alpha]_D^{20}$ = +121.5 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.9 Hz, 3 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 1.81 (sept, *J* = 6.9 Hz, 1 H), 2.92 (dd, *J* = 3.5 Hz, *J* = 8.8 Hz, 1 H), 3.83 (dd, *J* = 3.5 Hz, *J* = 11.8 Hz, 1 H), 3.96 (dd, *J* = 8.8 Hz, *J* = 11.8 Hz, 1 H), 6.16 (dd, *J* = 2.6 Hz, *J* = 3.6 Hz, 1 H), 6.26 (m, 1 H), 6.89 (m, 1 H), 7.66 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.0, 19.6, 30.7, 64.5, 78.3, 109.3, 116.7, 122.3, 129.0, 153.7 ppm. IR (KBr): $\tilde{\nu}$ = 3239, 3114, 3085, 2966, 2924, 2868, 2843, 1633, 1473, 1419, 1373, 1359, 1317, 1217, 1131, 1075, 1053, 1035, 934, 824, 761, 735 cm^{-1}. GC–MS: *m*/*z* (%) = 149 (100), 80 (47), 137 (38), 68 (26), 106 (24), 180 (23). $C_{10}H_{16}N_2O$ (180.13): calcd. C 66.63, H 8.95, N 15.54; found C 66.31, H 8.98, N 15.51.

(*S*)-*N*-[(1-Trimethylsilylpyrrol-2-yl)methylidene]phenylglycinol Trimethylsilyl Ether (6): Crude imine **4** (1.26 g, 5.9 mmol) was dissolved in CH_2Cl_2 (20 mL), and triethylamine (1.23 g, 12 mmol) and chlorotrimethylsilane (1.30 g, 12 mmol) were added to the solution cooled to 0 °C. After 3 h, the solvent was removed under reduced pressure. A solution of cyclohexane/diethyl ether (1:1, 50 mL) was added, and the solid precipitate was filtered off through a pad of Celite. The organic solvent was evaporated under reduced pressure to leave imine **6**, which was used in the following step without purification. Yield: 2.074 g (98%). White solid. M.p. 94.2–94.9 °C (pentane/Et_2O, 5:1). $[\alpha]_D^{20}$ = –48.1 (*c* = 0.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 9 H), 0.58 (s, 9 H), 3.93 (d, *J* = 6.7 Hz, 2 H), 4.37 (t, *J* = 6.7 Hz, 1 H), 6.36 (dd, *J* = 2.6 Hz, *J* = 3.3 Hz, 1 H), 6.78 (dd, *J* = 1.5 Hz, *J* = 3.3 Hz, 1 H), 7.05 (m, 1 H), 7.37 (m, 2 H), 7.51 (m, 3 H), 8.26 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –0.5, 1.6, 67.6, 77.3, 100.4, 120.5, 127.1, 127.8, 128.2, 129.5, 141.4, 153.0 ppm. IR (KBr): $\tilde{\nu}$ = 3105, 3062, 2962, 2908, 2857, 1640, 1451, 1425, 1247, 1122, 1084, 1051, 916, 902, 842, 739, 700 cm^{-1}. GC–MS: *m*/*z* (%) = 255 (100), 73 (34), 183 (22), 150 (19), 343 (15), 358 (12). $C_{19}H_{30}N_2OSi_2$ (358.19): calcd. C 63.63, H 8.43, N 7.81; found C 63.48, H 8.45, N 7.79.

Preparation of β-Amino Alcohols 7 and 8. Typical Procedure: Methyllithium (1.6 M in diethyl ether, 2.4 mL, 3.8 mmol) was added to a magnetically stirred solution of imine **4** (0.203 g, 0.95 mmol) in THF (15 mL) cooled to –15 °C. After 30 min, the reaction mixture was slowly warmed to room temperature and stirring was continued for 24 h. The mixture was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (10 mL) at 0 °C, and the organic material was then extracted with diethyl ether (3 × 10 mL). The collected ethereal layer was dried with Na_2SO_4 and concentrated to leave the crude product. The diastereomeric ratio was determined by ^{1}H NMR spectroscopic analysis. Flash column chromatography (SiO_2; cyclohexane/ethyl acetate, 1:1) gave product **7a**. This compound and all β-amino alcohols **7** and **8** prepared, decomposed on attempted GC–MS and HPLC–MS analyses.

(*S*)-*N*-[(*S*)-1-(2-Pyrrolyl)ethyl]phenylglycinol (7a): Yield: 0.210 g (96%). White solid. M.p. 86.9–87.4 °C (Et_2O). $[\alpha]_D^{20}$ = +34.5 (*c* = 0.8, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39 (d, *J* = 6.7 Hz, 3 H), 2.66 (br. s, 2 H), 3.57 (dd, *J* = 8.1 Hz, *J* = 10.8 Hz, 1 H), 3.74 (dd, *J* = 4.3 Hz, *J* = 10.8 Hz, 1 H), 3.80 (q, *J* = 6.7 Hz, 1 H), 3.96 (dd, *J* = 4.3 Hz, *J* = 8.1 Hz, 1 H), 5.97 (m, 1 H), 6.13 (m, 1 H), 6.97 (m, 1 H), 7.34 (m, 5 H), 8.68 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.0, 47.7, 61.1, 66.8, 104.4, 107.9, 116.7, 127.3, 127.7, 128.7, 135.6, 140.4 ppm. IR (nujol): $\tilde{\nu}$ = 3295, 2090, 2955, 2928, 2854, 1540, 1459, 1261, 1090, 735 cm^{-1}. $C_{14}H_{18}N_2O$ (230.14): calcd. C 73.01, H 7.88, N 12.16; found C 72.82, H 7.91, N 12.15.

(*S*)-*N*-[(*S*)-1-(2-Pyrrolyl)pentyl]phenylglycinol (7b): Yield: 0.235 g (91%). Yellow oil. $[\alpha]_D^{20}$ = +48.6 (*c* = 0.7, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.3 Hz, 3 H), 1.24 (m, 4 H), 1.74 (m, 2 H), 2.51 (br. s, 2 H), 3.59 (dd, *J* = 7.5 Hz, *J* = 10.8 Hz, 1 H), 3.72 (dd, *J* = 4.3 Hz, *J* = 8.0 Hz, 1 H), 3.77 (dd, *J* = 4.5 Hz, *J* = 10.8 Hz, 1 H), 3.91 (dd, *J* = 4.4 Hz, *J* = 7.5 Hz, 1 H), 5.97 (m, 1 H), 6.13 (q, *J* = 2.8 Hz, 1 H), 6.69 (m, 1 H), 7.23–7.43 (m, 5 H), 8.54 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 22.7, 25.6, 27.9, 53.3, 61.2, 66.1, 105.4, 107.8, 116.7, 127.1, 127.5, 128.6, 134.0, 140.9 ppm. IR (neat): $\tilde{\nu}$ = 3424, 3023, 2856, 2863, 1495, 1391, 1264, 1093, 1021 cm^{-1}. $C_{17}H_{24}N_2O$ (272.19): calcd. C 74.96, H 8.88, N 10.28; found C 74.85, H 8.89, N 10.26.

(*S*)-*N*-[(*S*)-2-Methyl-1-(2-pyrrolyl)propyl]phenylglycinol (7c): Yield: 0.243 g (92%). Yellowish oil. $[\alpha]_D^{20}$ = +32.4 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (d, *J* = 6.7 Hz, 3 H), 0.97 (d, *J* = 6.7 Hz, 3 H), 2.02 (dsept, *J* = 5.7 Hz, *J* = 6.7 Hz, 1 H), 2.50 (br. s, 2 H), 3.61 (dd, *J* = 5.8 Hz, *J* = 10.2 Hz, 1 H), 3.67 (d, *J* = 5.7 Hz, 1 H), 3.78 (dd, *J* = 4.5 Hz, *J* = 5.7 Hz, 1 H), 3.84 (dd, *J* = 4.5 Hz, *J* = 10.2 Hz, 1 H), 5.98 (m, 1 H), 6.15 (q, *J* = 2.8 Hz, 1 H), 6.65 (m, 1 H), 7.25–7.39 (m, 5 H), 8.39 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.0, 19.7, 32.2, 59.5, 61.2, 63.4, 106.3, 107.6, 114.2, 127.1, 127.2, 127.3, 128.5, 132.2, 141.2 ppm. IR (neat): $\tilde{\nu}$ = 3422, 3024, 2853, 2865, 1492, 1261, 1099, 1021, 742 cm^{-1}. $C_{16}H_{22}N_2O$ (258.17): calcd. C 74.38, H 8.58, N 10.84; found C 74.15, H 8.60, N 10.83.

(*S*)-*N*-[(*S*)-2,2-Dimethyl-1-(2-pyrrolyl)propyl]phenylglycinol [(*S*,*S*)-7d]: Yield: 0.081 g (31%). Yellowish oil. $[\alpha]_D^{20}$ = +40.7 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (s, 9 H), 2.15 (br. s, 2 H), 3.51 (s, 1 H), 3.59 (dd, *J* = 5.9 Hz, *J* = 8.1 Hz, 1 H), 3.63

(dd, J = 8.1 Hz, J = 12.2 Hz, 1 H), 3.83 (dd, J = 5.9 Hz, J = 12.2 Hz, 1 H), 5.92 (m, 1 H), 6.08 (q, J = 2.7 Hz, 1 H), 6.55 (m, 1 H), 7–21–7.32 (m, 5 H), 8.07 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.1, 35.4, 61.5, 64.2, 64.3, 107.0, 107.6, 115.8, 127.1, 127.3, 128.4, 132.0, 142.1 ppm. IR (neat): $\tilde{\nu}$ = 3425, 2953, 2868, 2867, 1478, 1391, 1362, 1260, 1095 cm^{-1}. $C_{17}H_{24}N_2O$ (272.19): calcd. C 74.96, H 8.88, N 10.28; found C 74.98, H 8.91, N 10.26.

(*S*)-*N*-[(*R*)-2,2-Dimethyl-1-(2-pyrrolyl)propyl]phenylglycinol [(*S*,*R*)-7d]: Yield: 0.072 g (28%). Yellowish oil. $[\alpha]_D^{20}$ = +109.6 (c = 1.9, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39 (s, 9 H), 2.33 (br. s, 2 H), 3.26 (s, 1 H), 3.55 (dd, J = 4.6 Hz, J = 8.1 Hz, 1 H), 3.61 (dd, J = 8.1 Hz, J = 10.0 Hz, 1 H), 3.68 (dd, J = 4.6 Hz, J = 10.0 Hz, 1 H), 5.97 (m, 1 H), 6.19 (m, 1 H), 6.77 (m, 1 H), 7.22 (2 H), 7.31–7.40 (m, 3 H), 8.44 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.0, 34.8, 61.7, 63.1, 66.7, 107.6, 108.3, 116.5, 127.4, 127.7, 128.6, 130.4, 140.1 ppm. IR (neat): $\tilde{\nu}$ = 3425, 3029, 2853, 2868, 1492, 1392, 1363, 1260, 1096, 1028 cm^{-1}. $C_{17}H_{24}N_2O$ (272.19): calcd. C 74.96, H 8.88, N 10.28; found C 74.82, H 8.89, N 10.26.

(*S*)-*N*-[(*S*)-1-(2-Pyrrolyl)-3-buten-1-yl]phenylglycinol (7e): Yield: 0.217 g (89%). Yellow oil. $[\alpha]_D^{20}$ = +16.5 (c = 0.4, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.40 (br. s, 2 H), 2.79 (m, 2 H), 3.84 (dd, J = 7.6 Hz, J = 10.8 Hz, 1 H), 4.01 (dd, J = 4.5 Hz, J = 10.8 Hz, 1 H), 4.09 (t, J = 5.9 Hz, 1 H), 4.19 (dd, J = 4.5 Hz, J = 7.6 Hz, 1 H), 5.36 (dd, J = 10.8 Hz, J = 17.2 Hz, 2 H), 6.01 (m, 1 H), 6.23 (m, 1 H), 6.38 (d, J = 2.7 Hz, 1 H), 6.91 (dd, J = 1.5 Hz, J = 2.7 Hz, 1 H), 7.52–7.61 (m, 5 H), 8.73 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.9, 52.5, 61.3, 66.4, 105.3, 108.0, 116.7, 117.9, 127.3, 127.7, 128.7, 133.6, 134.7, 140.3 ppm. IR (neat): $\tilde{\nu}$ = 3364, 3102, 3076, 2958, 2930, 2873, 1466, 1437, 1093, 1044, 2026, 914, 796, 717 cm^{-1}. $C_{16}H_{20}N_2O$ (256.16): calcd. C 74.97, H 7.86, N 10.93; found C 75.02, H 7.87, N 10.89.

(*S*)-*N*-[(*S*)-2-Phenyl-1-(2-pyrrolyl)ethyl]phenylglycinol (7f): Yield: 0.265 g (91%). White solid. M.p. 115.2–116.2 °C (pentane/Et_2O, 1:1). $[\alpha]_D^{20}$ = +82.5 (c = 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.94 (br. s, 2 H), 3.08 (d, J = 6.6 Hz, 2 H), 3.55 (dd, J = 7.4 Hz, J = 10.8 Hz, 1 H), 3.71 (dd, J = 4.3 Hz, J = 10.8 Hz, 1 H), 3.86 (dd, J = 4.3 Hz, J = 7.4 Hz, 1 H), 3.08 (t, J = 6.6 Hz, 1 H), 5.98 (m, 1 H), 6.12 (q, J = 6.7 Hz, 1 H), 6.63 (m, 1 H), 7.09 (m, 2 H), 7.24–7.38 (m, 8 H), 8.19 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.3, 54.9, 61.6, 66.1, 105.3, 108.0, 116.6, 126.4, 127.2, 127.6, 128.2, 128.6, 129.3, 133.7, 138.5, 140.8 ppm. IR (nujol): $\tilde{\nu}$ = 3353, 3028, 2926, 2856, 1539, 1453, 1261, 1094, 1027, 749 cm^{-1}. $C_{20}H_{22}N_2O$ (306.17): calcd. C 78.40, H 7.24, N 9.14; found C 78.50, H 7.27, N 9.11.

(*S*)-*N*-[(*S*)-1-Phenyl-1-(2-pyrrolyl)methyl]phenylglycinol (7h): The crude compound (0.263 g, 95%) was not purified owing to decomposition during column chromatography. Relevant absorptions for structural identification were drawn from ^{1}H NMR spectroscopic analysis. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.22 (br. s, 2 H), 3.62–6.70 (m, 3 H), 4.73 (s, 1 H), 5.84 (m, 1 H), 6.13 (q, J = 3.1 Hz, 1 H), 6.71 (m, 1 H), 7.26–7.49 (m, 10 H), 8.54 (br. s, 1 H) ppm. The compound was not eluted by GC–MS analysis.

(*S*)-*N*-[(*S*)-1-(2-Pyrrolyl)ethyl]valinol (8a): Yield: 0.179 g (91%, from 1 mmol of **5**). Yellow oil. $[\alpha]_D^{20}$ = –7.7 (c = 0.9, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, J = 6.8 Hz, 3 H), 0.95 (d, J = 6.8 Hz, 3 H), 1.39 (d, J = 6.5 Hz, 3 H), 1.77 (sept, J = 6.8 Hz, 1 H), 2.2 (br. s, 2 H), 2.45 (dd, J = 4.1 Hz, J = 6.2 Hz, 1 H), 3.64 (dd, J = 6.2 Hz, J = 10.8 Hz, 1 H), 3.39 (dd, J = 4.1 Hz, J = 10.8 Hz, 1 H), 4.01 (q, J = 6.5 Hz, 1 H), 6.02 (m, 1 H), 6.15 (m, 1 H), 6.72 (m, 1 H), 8.55 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.4, 19.3, 22.3, 29.2, 48.9, 60.0, 61.1, 104.4, 107.8, 116.7, 135.7 ppm. IR (neat): $\tilde{\nu}$ = 3394, 2961, 2927, 2874, 1465, 1373, 1262, 1104, 1029, 793, 747, 720 cm^{-1}. MS (EI): m/z = 197 [M + H]$^+$, 94 [M – valinol]$^+$. $C_{11}H_{20}N_2O$ (196.16): calcd. C 67.31, H 10.27, N 14.27; found C 67.02, H 10.30, N 14.23.

(*S*)-*N*-[(*S*)-1-(2-Pyrrolyl)pentyl]valinol (8b): Yield: 0.207 g, 0.173 g (87%, from 1 mmol of **5**). Yellow oil. $[\alpha]_D^{20}$ = –4.6 (c = 0.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, J = 5.2 Hz, 3 H), 0.89 (d, J = 6.7 Hz, 3 H), 0.92 (d, J = 6.7 Hz, 3 H), 1.25 (m, 4 H), 1.62 (m, 2 H), 1.74 (m, 1 H), 1.98 (br. s, 2 H), 2.36 (ddd, J = 4.3 Hz, J = 5.3 Hz, J = 8.0 Hz, 1 H), 3.41 (dd, J = 5.6 Hz, J = 10.8 Hz, 1 H), 3.64 (dd, J = 4.1 Hz, J = 10.8 Hz, 1 H), 3.77 (dd, J = 5.9 Hz, J = 8.0 Hz, 1 H), 5.99 (m, 1 H), 6.13 (q, J = 2.9 Hz, 1 H), 6.72 (m, 1 H), 8.42 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 18.5, 19.2, 22.5, 26.4, 29.2, 36.3, 54.2, 60.3, 61.1, 105.5, 107.4, 116.6, 134.0 ppm. IR (neat): $\tilde{\nu}$ = 3362, 3301, 3101, 2957, 2929, 2860, 1567, 1464, 1026, 925, 792, 717 cm^{-1}. MS (EI): m/z = 136.1 [M – nBu]$^+$. $C_{14}H_{26}N_2O$ (238.20): calcd. C 70.54, H 10.99, N 11.75; found C 70.59, H 10.97, N 11.71.

(*S*)-*N*-[(*S*)-1-(2-Pyrrolyl)-3-buten-1-yl]valinol (8e): Yield: 0.173 g (78%, from 1 mmol of **5**). Yellow oil. $[\alpha]_D^{20}$ = –12.4 (c = 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (d, J = 6.8 Hz, 3 H), 0.93 (d, J = 6.8 Hz, 3 H), 1.74 (sept, J = 6.8 Hz, 1 H), 1.96 (br. s, 2 H), 2.37 (dd, J = 4.1 Hz, J = 5.3 Hz, 1 H), 2.46 (dd, J = 6.7 Hz, J = 6.9 Hz, 2 H), 3.43 (dd, J = 5.3 Hz, J = 10.8 Hz, 1 H), 3.68 (dd, J = 4.1 Hz, J = 10.8 Hz, 1 H), 3.90 (t, J = 6.7 Hz, 1 H), 5.08–5.17 (m, 2 H), 5.76 (m, 1 H), 6.01 (m, 1 H), 6.14 (q, J = 2.7 Hz, 1 H), 6.72 (m, 1 H), 8.52 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.7, 19.3, 29.2, 41.3, 53.3, 60.4, 61.2, 105.3, 107.8, 116.6, 117.4, 133.9, 135.1 ppm. IR (neat): $\tilde{\nu}$ = 3296, 3090, 3062, 2956, 2928, 2858, 1582, 1454, 1379, 1264, 1093, 1027, 934 cm^{-1}. MS (EI): m/z = 120 [M – valinol]$^+$. $C_{13}H_{22}N_2O$ (222.17): calcd. C 70.23, H 9.97, N 12.60; found C 69.96, H 9.99, N 12.58.

(*S*)-*N*-[(*S*)-2-Phenyl-1-(2-pyrrolyl)ethyl]valinol (8f): Yield: 0.245 g (90%, from 1 mmol of **5**). White solid. M.p. 109.5–110.8 °C (pentane/Et_2O, 1:1). $[\alpha]_D^{20}$ = –9.8 (c = 0.8, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (d, J = 6.8 Hz, 3 H), 0.90 (d, J = 6.8 Hz, 3 H), 1.58 (br. s, 2 H), 1.69 (sept, J = 6.8 Hz, 1 H), 2.29 (dd, J = 4.1 Hz, J = 4.9 Hz, 1 H), 2.91 (dd, J = 7.6 Hz, J = 13.6 Hz, 1 H), 3.00 (dd, J = 6.0 Hz, J = 13.6 Hz, 1 H), 3.34 (dd, J = 4.9 Hz, J = 11.2 Hz, 1 H), 3.53 (dd, J = 4.1 Hz, J = 11.2 Hz, 1 H), 2.29 (dd, J = 6.0 Hz, J = 7.6 Hz, 1 H), 5.59 (m, 1 H), 6.14 (q, J = 2.7 Hz, 1 H), 6.69 (m, 1 H), 7.10–7.16 (m, 2 H), 7.20–7.32 (m, 3 H), 8.33 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.0, 19.5, 29.4, 44.4, 55.4, 60.4, 61.5, 105.3, 108.1, 116.4, 126.5, 128.4, 129.2, 134.1, 138.8 ppm. IR (KBr): $\tilde{\nu}$ = 3295, 3021, 2948, 2818, 1711, 1492, 1457, 1361, 1334, 1095, 1040, 989, 798, 753, 729, 728, 714, 700 cm^{-1}. MS (EI): m/z = 170 [M – valinol]$^+$. $C_{17}H_{24}N_2O$ (272.19): calcd. C 74.96, H 8.88, N 10.28; found C 74.62, H 8.91, N 10.25.

(*S*)-*N*-[(*S*)-1-(2-Pyrrolyl)-2-propen-1-yl]valinol (8): The crude compound (0.191 g, 92%) could not be purified owing to decomposition during column chromatography. The structure was confirmed by ^{1}H NMR spectroscopic analysis. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (d, J = 6.9 Hz, 3 H), 0.97 (d, J = 6.9 Hz, 3 H), 1.87 (m, 1 H), 2.58 (dd, J = 4.1 Hz, J = 7.2 Hz, 1 H), 3.39 (dd, J = 7.2 Hz, J = 10.7 Hz, 1 H), 3.66 (dd, J = 4.1 Hz, J = 10.7 Hz, 1 H), 4.43 (d, J = 7.6 Hz, 1 H), 5.18 (dd, J = 1.4 Hz, J = 10.0 Hz, 1 H), 5.25 (dd, J = 1.4 Hz, J = 17.4 Hz, 1 H), 5.90 (ddd, J = 7.6 Hz, J = 10.0 Hz, J^3 = 17.4 Hz, 1 H), 6.07 (m, 1 H), 6.17 (t, J = 3.1 Hz, 1 H), 6.75 (dd, J = 1.4 Hz, J = 2.7 Hz, 1 H), 8.78 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.9, 19.3, 28.8, 57.3, 60.6, 61.1, 105.3, 108.1, 116.0, 117.1, 132.8, 139.5 ppm. The compound was not eluted by GC–MS analysis.

(*S*)-*N*-[(*S*)-1-Phenyl-1-(2-pyrrolyl)methyl]valinol (8h): The crude compound (0.235 g, 91%) could not be purified owing to decomposition during column chromatography. The structure was confirmed by ^{1}H NMR spectroscopic analysis. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (d, J = 6.9 Hz, 3 H), 0.98 (d, J = 6.9 Hz, 3 H), 1.95 (m, 1 H), 2.07 (br. s, 2 H), 2.45 (dd, J = 4.1 Hz, J = 6.8 Hz, 1 H), 3.40 (dd, J = 6.8 Hz, J = 10.8 Hz, 1 H), 3.58 (dd, J = 4.1 Hz, J = 10.8 Hz, 1 H), 5.05 (s, 1 H), 6.01 (m, 1 H), 6.14 (q, J = 3.1 Hz, 1 H), 6.71 (m, 1 H), 7.29–7.45 (m, 5 H), 8.32 (br. s, 1 H) ppm. The compound was not eluted by GC–MS analysis.

Preparation of Aziridines 9. Typical Procedure: To a solution of β-amino alcohol **7a** (0.299 g, 1.3 mmol) in THF (20 mL) was added PPh_3 (0.511 g, 1.95 mmol) and then DEAD (0.340 g, 1.95 mmol) was added dropwise. After stirring for 4 h, the mixture was concentrated under reduce pressure, and the residue was subjected to flash chromatography (SiO_2; cyclohexane/ethyl acetate, 9:1) to give compound **9a** as yellow oil.

(*S*)-2-Phenyl-1-[(*S*)-1-(2-pyrrolyl)ethyl]aziridine (9a): Yield: 0.240 g (87%). Yellow oil. $[\alpha]_D^{20}$ = +85.4 (c = 0.8, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.54 (d, J = 6.6 Hz, 3 H), 1.89 (d, J = 3.5 Hz, 1 H), 2.10 (d, J = 6.7 Hz, 1 H), 2.55 (dd, J = 3.5 Hz, J = 6.6 Hz, 1 H), 2.93 (q, J = 6.6 Hz, 1 H), 6.02 (m, 1 H), 6.16 (q, J = 2.8 Hz, 1 H), 6.66 (m, 1 H), 7.21–7.35 (m, 5 H), 8.44 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0, 36.8, 41.1, 63.2, 104.4, 107.9, 116.6, 126.3, 127.0, 128.4, 134.4, 139.8 ppm. IR (neat): $\tilde{\nu}$ = 3214, 3103, 2922, 2856, 1460, 1383, 805, 748, 712 cm^{-1}. GC–MS: m/z (%) = 118 (100), 93 (91), 94 (50) (54) 92, 156 (12), 197 (9), 212 (5). $C_{14}H_{16}N_2$ (212.13): calcd. C 79.21, H 7.60, N 13.20; found C 79.02, H 7.63, N 13.18.

(*S*)-2-Phenyl-1-[(*S*)-1-(2-pyrrolyl)pentyl]aziridine (9b): Yield: 0.304 g (92%). White solid. M.p. 78.3–79.6 °C. $[\alpha]_D^{20}$ = +74.8 (c = 0.7, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, J = 6.7 Hz, 3 H), 1.36–1.38 (m, 6 H), 1.92 (d, J = 3.4 Hz, 1 H), 2.14 (d, J = 6.6 Hz, 1 H), 2.55 (dd, J = 3.4 Hz, J = 6.6 Hz, 1 H), 2.76 (dd, J = 5.2 Hz, J = 7.8 Hz, 1 H), 6.01 (m, 1 H), 6.15 (q, J = 2.7 Hz, 1 H), 6.67 (dd, J = 1.7 Hz, J = 2.7 Hz, 1 H), 7.16–7.22 (m, 2 H), 7.24–7.34 (m, 3 H), 8.44 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 22.8, 28.2, 36.4, 37.9, 40.1, 68.3, 105.4, 107.5, 116.6, 126.3, 126.8, 128.3, 133.1, 140.0 ppm. IR (KBr): $\tilde{\nu}$ = 3218, 3100, 3055, 2924, 2852, 1461, 1388, 1135, 1096, 1029, 807, 744, 718, 699 cm^{-1}. GC–MS: m/z (%) = 106 (100), 118 (74), 1636 (62), 80 (51), 91 (34), 197 (16), 254 (10). $C_{17}H_{22}N_2$ (254.18): calcd. C 80.27, H 8.72, N 11.01; found C 80.35, H 8.75, N 11.00.

(*S*)-2-Phenyl-1-[(*S*)-2-phenyl-1-(2-pyrrolyl)ethyl]aziridine (9f): Yield: 0.341 g (91%). White solid. M.p. 80.9–81.3 °C (pentane). $[\alpha]_D^{20}$ = +94.4 (c = 0.3, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.72 (d, J = 6.6 Hz, 1 H), 2.05 (d, J = 3.5 Hz, 1 H), 2.48 (dd, J = 3.5 Hz, J = 6.6 Hz, 1 H), 3.80 (t, J = 6.5 Hz, 1 H), 3.14 (dd, J = 6.5 Hz, J = 13.1 Hz, 1 H), 3.22 (dd, J = 6.5 Hz, J = 13.1 Hz, 1 H), 5.89 (m, 1 H), 6.11 (q, J = 2.7 Hz, 1 H), 6.62 (dd, J = 1.6 Hz, J = 2.7 Hz, 1 H), 7.15–7.22 (m, 5 H), 7.26–7.35 (m, 5 H), 8.28 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.9, 38.5, 40.1, 43.9, 69.9, 105.5, 107.6, 126.2, 126.9, 128.1, 128.3, 129.7, 132.4, 138.6, 139.9 ppm. IR (KBr): $\tilde{\nu}$ = 3426, 3175, 3107, 3059, 3026, 2976, 2917, 2832, 1494, 1454, 1396, 1125, 1100, 1030, 1014, 744, 725 699 cm^{-1}. GC–MS: m/z = 168 (100), 169 (94), 197 (66), 118 (60). $C_{20}H_{20}N_2$ (288.16): calcd. C 83.30, H 6.99, N 9.71; found C 83.42, H 7.01, N 9.68.

Preparation of Amines 11b,c,e through Imines 10b,c,e. Typical Procedure: Phenylglycinol derivative **7b** (0.136 g, 0.5 mmol) and $MeNH_2$ (40% in H_2O, 0.6 mL) were dissolved in THF (5 mL). Then, a solution of H_5IO_6 (0.400 g) in H_2O (5 mL) was added dropwise. After stirring for 1 h at room temperature, most of the solvent was evaporated under reduced pressure, and the organic materials were extracted with Et_2O (3 × 20 mL). The collected ethereal layer was dried with Na_2SO_4 and concentrated to leave intermediate imine **10b**. This was dissolved in MeOH and $NaBH_4$ (0.75 mmol, 0.028 g) was added at 0 °C. After 1 h, the mixture was quenched with H_2O (5 mL), and the mixture was then concentrated to remove most of the MeOH. The organic materials were extracted with Et_2O (3 × 20 mL). and the collected ethereal layer was dried with Na_2SO_4 and concentrated to leave a yellow oil that was subjected to flash chromatography (SiO_2; cyclohexane/ethyl acetate, 8:2) to give compound **11b** (0.39 mmol) as a yellow oil.

(*S*)-*N*-[1-(2-Pyrrolyl)butyl]benzaldimine (10b): Yield: 0.117 g (93%), >90% pure. Brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, J = 6.4 Hz, 3 H), 1.32 (m, 4 H), 1.94 (m, 2 H), 4.44 (t, J = 6.6 Hz, 1 H), 6.09 (m, 1 H), 6.18 (q, J = 2.9 Hz, 1 H), 6.74 (m, 1 H), 7.45 (m, 3 H), 7.79 (m, 2 H), 8.32 (s, 1 H), 8.57 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.6, 136.0, 134.0, 130.7, 128.5, 128.2, 116.6, 108.0, 104.3, 68.7, 32.3, 28.5, 22.5, 14.0 ppm. GC–MS: m/z (%) = 106 (100), 80 (60), 136 (56), 183 (56), 93 (16), 240 (7).

(*S*)-*N*-[2-Methyl-1-(2-pyrrolyl)propyl]benzaldimine (10c): Yield: 0.096 g (85%). White solid. M.p. 135.2–135.8 °C (pentane). $[\alpha]_D^{20}$ = –31.2 (c = 0.7, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (d, J = 6.7 Hz, 3 H), 0.96 (d, J = 6.7 Hz, 3 H), 2.12 (dsept, J = 6.6 Hz, J = 6.7 Hz, 1 H), 4.14 (d, J = 6.6 Hz, 1 H), 6.06 (m, 1 H), 6.19 (q, J = 2.9 Hz, 1 H), 6.74 (q, J = 2.6 Hz, 1 H), 7.44 (m, 3 H), 7.79 (m, 2 H), 8.31 (s, 1 H), 8.60 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.6, 136.2, 133.1, 130.6, 128.5, 128.2, 116.3, 107.8, 104.8, 75.2, 35.2, 19.4, 19.2 ppm. IR (neat): $\tilde{\nu}$ = 3457, 3249, 2964, 2868, 2825, 1634, 1447, 1383, 1096, 1012, 725, 696 cm^{-1}. GC–MS: m/z (%) = 183 (100), 104 (51), 121 (36), 80 (32), 156 (6), 226 (3). $C_{15}H_{18}N_2$ (226.15): calcd. C 79.61, H 8.02, N 12.38; found C 79.31, H 8.05, N 12.35.

(*S*)-*N*-[1-(2-Pyrrolyl)-3-buten-1-yl]benzaldimine (10e): Isolated impure as a brown oil (0.096 g, 86%). Relevant absorptions for structural identification of the main compound were drawn from ^{1}H NMR spectroscopic analysis. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.68 (m, 2 H), 4.51 (dd, J = 6.3 Hz, J = 7.6 Hz, 1 H), 5.11 (m, 2 H), 5.80 (m, 1 H), 6.06 (m, 1 H), 6.17 (q, J = 3.2 Hz, 1 H), 6.75 (m, 1 H), 7.42 (m, 3 H), 7.77 (m, 2 H), 8.30 (s, 1 H), 8.61 (br. s, 1 H) ppm.

(*S*)-Benzyl-1-(2-pyrrolyl)pentylamine (11b): Yield: 0.094 g (78%). Yellow oil. $[\alpha]_D^{20}$ = –26.5 (c = 0.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, J = 6.8 Hz, 3 H), 1.32 (m, 4 H), 1.73 (m, 2 H), 2.11 (br. s, 1 H), 3.65 (d, J = 13.4 Hz, 1 H), 3.74 (d, J = 13.4 Hz, 1 H), 3.80 (t, J = 7.0 Hz, 1 H), 6.09 (m, 1 H), 6.20 (q, J = 2.7 Hz, 1 H), 6.79 (m, 1 H), 7.31–7.39 (m, 5 H), 8.69 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 22.6, 28.3, 36.4, 51.4, 55.9, 106.1, 107.7, 116.6, 126.9, 128.1, 128.4, 133.7, 140.4 ppm. IR (neat): $\tilde{\nu}$ = 3432, 3376, 3297, 3062, 3027, 2955, 2928, 2857, 1494, 1453, 1092, 1026, 792, 717 cm^{-1}. $C_{16}H_{22}N_2$ (242.18): calcd. C 79.29, H 9.15, N 11.56; found C 79.06, H 9.16, N 11.53. The compound was not eluted by GC–MS analysis.

(*S*)-Benzyl[2-methyl-1-(2-pyrrolyl)propyl]amine (11c): Yield: 0.087 g (76%). Yellow oil. $[\alpha]_D^{20}$ = –37.6 (c = 0.8, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (d, J = 6.7 Hz, 3 H), 0.95 (d, J = 6.7 Hz, 3 H), 1.87 (sept, J = 6.7 Hz, 1 H), 3.52 (d, J = 5.8 Hz, 1 H), 3.58 (d, J = 13.1 Hz, 1 H), 3.71 (d, J = 13.1 Hz, 1 H), 6.04 (m, 1 H), 6.15 (m, 1 H), 6.76 (m, 1 H), 7.25–7.38 (m, 5 H), 8.58 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8, 19.7, 33.9, 52.0, 62.1, 106.9, 107.7, 116.2, 126.9, 128.1, 128.4, 131.1, 140.6, 150.9 ppm. IR (nujol): $\tilde{\nu}$ = 3430, 3371, 3062, 3024, 2953, 2922,

2853, 1491, 1022, 794 cm^{-1}. $C_{15}H_{20}N_2$ (228.16): calcd. C 78.90, H 8.83, N 12.27; found C 79.10, H 8.85, N 12.26. The compound was not eluted by GC–MS analysis.

(*S*)-Benzyl-[1-(2-pyrrolyl)-3-buten-1-yl]amine (11e): Yield: 0.081 g (72%). Yellowish oil. $[\alpha]_D^{20}$ = –13.9 (*c* = 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.04 (br. s, 1 H), 2.53 (m, 2 H), 3.66 (d, *J* = 13.2 Hz, 1 H), 3.77 (d, *J* = 13.2 Hz, 1 H), 3.90 (t, *J* = 5.5 Hz, 1 H), 5.16 (m, 2 H), 5.82 (m, 1 H), 6.12 (m, 1 H), 6.22 (dq, *J* = 2.7 Hz, *J* = 5.5 Hz, 1 H), 6.79 (m, 1 H), 7.30–7.41 (m, 5 H), 8.72 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.2, 51.1, 54.7, 105.6, 107.9, 116.6, 117.8, 126.9, 128.0, 128.4, 133.5, 135.1, 140.3 ppm. IR (nujol): $\tilde{\nu}$ = 3430, 3373, 3292, 3065, 2957, 2922, 2853, 1499, 1454, 797 cm^{-1}. $C_{15}H_{18}N_2$ (226.15): calcd. C 79.61, H 8.02, N 12.38; found C 79.91, H 8.05, N 12.36. The compound was not eluted by GC–MS analysis.

Preparation of *α*-Substituted Benzamides 12a,b,e,f. Typical Procedure: Valinol derivative **8b** (0.238 g, 1.1 mmol) and $MeNH_2$ (40% in H_2O, 1.3 mL, 17 mmol) were dissolved in THF (5 mL) and a solution of H_5IO_6 (0.907 g, 4.0 mmol) in H_2O (5 mL) was added dropwise. The mixture was stirred for 2 h at room temperature. The organic materials were extracted with Et_2O (3 × 20 mL), and the collected ethereal layer was then washed with brine, dried with Na_2SO_4, and concentrated to leave the primary amine as a yellow oil. This was dissolved in acetone (5 mL), and then H_2O (5 mL), K_2CO_3 (0.304 g, 2.2 mmol), and benzoyl chloride (191 μL, 1.7 mmol) was added while magnetically stirring. After 12 h, most of the solvent was evaporated under reduced pressure, and the organic materials were extracted with Et_2O (3 × 20 mL). The collected ethereal layer was dried with Na_2SO_4 and concentrated to leave a white solid, which was crystallized from acetone to give pure **12b**.

(*S*)-*N*-[1-(2-Pyrrolyl)ethyl]benzamide (12a): Yield: 0.203 g (86%). White solid. M.p. 167.9–168.5 °C. $[\alpha]_D^{20}$ = –74.1 (*c* = 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.69 (d, *J* = 7.0 Hz, 3 H), 5.34 (qd, *J* = 7.0 Hz, *J* = 7.2 Hz, 1 H), 6.12 (m, 2 H), 6.33 (d, *J* = 7.2 Hz, 1 H), 6.75 (m, 1 H), 7.72–7.78 (m, 5 H), 9.36 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, Cl_3): δ = 18.3, 43.0, 104.1, 107.3, 117.9, 126.9, 128.6, 131.7, 134.0, 134.3, 168.0 ppm. IR (KBr): $\tilde{\nu}$ = 3396, 3312, 2925, 1853, 1625, 1578, 1524, 1331, 1083, 1031, 736, 717, 655 cm^{-1}. GC–MS: *m*/*z* (%) = 105 (100), 77 (74), 93 (55), 214 (46), 121 (24), 199 (18). $C_{13}H_{14}N_2O$ (214.11): calcd. C 72.87, H 6.59, N 13.07; found C 73.03, H 6.58, N 13.05.

(*S*)-*N*-[1-(2-Pyrrolyl)pentyl]benzamide (12b): Yield: 0.247 g (88%). White solid. M.p. 137.5–138.2 °C. $[\alpha]_D^{20}$ = –90.7 (*c* = 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 5.2 Hz, 3 H), 1.47 (m, 4 H), 1.96 (m, 1 H), 2.15 (m, 1 H), 5.17 (dt, *J* = 6.1 Hz, *J* = 8.3 Hz, 1 H), 6.08 (m, 1 H), 6.12 (q, *J* = 2.9 Hz, 1 H), 6.26 (d, *J* = 8.3 Hz, 1 H), 6.73 (m, 1 H), 7.39–7.55 (m, 5 H), 9.18 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 22.4, 28.7, 32.4, 47.5, 104.1, 107.4, 117.6, 126.9, 128.5, 131.6, 133.6, 134.1, 168.1 ppm. IR (KBr): $\tilde{\nu}$ = 3336, 2957, 2927, 2856, 1625, 1533, 1337, 12643, 1091, 1029, 801, 722 cm^{-1}. GC–MS: *m*/*z* (%) = 105 (100), 106 (97), 77 (61), 199 (42), 135 (36), 121 (27), 256 (11). $C_{16}H_{20}N_2O$ (256.16): calcd. C 74.97, H 7.86, N 10.93; found C 74.76, H 7.89, N 10.89.

(*S*)-*N*-[1-(2-Pyrrolyl)-3-buten-1-yl)]benzamide (12e): Yield: 0.217 g (82%). White solid. M.p. 122.3–122.8 °C (Et_2O). $[\alpha]_D^{20}$ = –53.7 (*c* = 2.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.83 (m 2 H), 5.22 (m, 2 H), 5.25 (m, 1 H), 5.95 (m, 1 H), 6.10 (m, 1 H), 6.14 (q, *J* = 2.9 Hz, 1 H), 6.52 (d, *J* = 6.9 Hz, 1 H), 6.74 (m, 1 H), 7.37–7.46 (m, 3 H), 7.47–7.54 (m, 2 H), 9.39 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 36.9, 46.6, 104.5, 107.4, 117.8, 118.4, 126.9, 128.5, 131.6, 132.7, 134.0, 134.4, 168.1 ppm. IR (nujol): $\tilde{\nu}$ = 3320, 3081, 3001, 2922, 2853, 1626, 1577, 1529, 1489, 1292, 720, 691 cm^{-1}. GC–MS: *m*/*z* (%) = 105 (100), 77 (51), 199 (46), 118 (42), 240 (6). $C_{15}H_{16}N_2O$ (240.13): calcd. C 74.97, H 6.71, N 11.66; found C 75.16, H 6.70, N 11.68.

(*S*)-*N*-[2-Phenyl-1-(2-pyrrolyl)ethyl)]benzamide (12f): Yield: 0.278 g (87%). White solid. M.p. 115.5–116.4 °C (cyclohexane/CH_2Cl_2, 9:1). $[\alpha]_D^{20}$ = –61.8 (*c* = 0.8, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.26 (dd, *J* = 9.8 Hz, *J* = 14.2 Hz, 1 H), 3.48 (dd, *J* = 5.7 Hz, *J* = 14.2 Hz, 1 H), 3.96 (ddd, *J* = 4.3 Hz, *J* = 8.3 Hz, *J* = 9.8 Hz, 1 H), 6.10 (q, *J* = 2.7 Hz, 1 H), 6.14 (m, 1 H), 6.27 (d, *J* = 8.3 Hz, 1 H), 6.72 (m, 1 H), 7.17–7.38 (m, 3 H), 7.69–7.50 (m 3 H), 7.51–7.64 (m, 4 H), 9.35 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, Cl_3): δ = 38.8, 48.8, 104.6, 107.5, 118.0, 126.8, 128.5, 128.6, 128.7, 129.0, 130.2, 131.7, 133.7, 168.5 ppm. IR (KBr): $\tilde{\nu}$ = 3056, 2925, 2676, 1690, 1622, 1532, 1423, 1291, 1174, 1042, 1017, 935, 804, 778, 707 cm^{-1}. GC–MS: *m*/*z* (%) = 105 (100), 168 (56), 199 (55), 169 (52), 77 (48), 121 (15). $C_{19}H_{18}N_2O$ (290.14): calcd. C 78.59, H 6.25, N 9.65; found C 78.14, H 6.27, N 9.62.

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