SYNTHESIS OF OPTICALLY PURE 1-(2-PYRIDINYL)ETHYLAMINE AND 4-(2-PYRIDINYL)-1,3-OXAZOLIN-2-ONE*

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Abstract - Several (*R*)-1-(2-pyridinyl)ethylamines (**4**) were prepared from (*S*)-1-(2-pyridinyl)ethanols (**1**) with complete inversion of the chiral center. Substitution of (*S*)-1-(2-pyridinyl)ethyl methanesulfonate (**2**) with sodium azide gave (*R*)-1-(2-pyridinyl)ethyl azide (**3**) stereospecifically, and reduction of the azide afforded the corresponding amine (**4**) in good yield. When optically pure 2-silyloxy-1-(2-piridinyl)ethanol was used, 2-silyloxy-1-(2-pyridinyl)ethylamine was obtained, and this was converted to optically pure pyridine-substituted 1,3-oxazolidin-2-one at the 4-position.

Introduction

1,3-Oxazolidin-2-one is an important heterocycle in organic synthesis.[1] Particularly, optically active 4- or 5-substituted 1,3-oxazolidin-2-ones have been used effectively as a chiral auxiliary and a ligand for asymmetric reactions including, alkylation,[2] aldol reaction,[3] conjugated addition,[4] Diels-Alder reaction,[5] and carbene insertion.[6] For the synthesis of optically active 1,3-oxazolidin-2-one, optically active ethanolamine, which is conveniently provided from natural amino acids, is an appropriate precursor. Since pyridine-substituted amino acid is not naturally available, pyridine-substituted ethanolamine has rarely been prepared.[7] We recently reported enantioselective acetylation of pyridine-substituted ethyl and allyl alcohols.[8] When 1-(2-pyridinyl)allyl alcohol (**5**) is taken as a starting material, transformations of the chiral alcohol to chiral amine and the double bond to hydroxymethyl function may afford pyridine-substituted chiral ethanolamine, which will lead to the desired 4-(2-pyridinyl)-1,3-oxazolidin-2-one. In this paper, we describe i) the stereospecific replacement of 1-(2-pyridinyl)ethanol (**1**) with the corresponding amine *via* its methanesulfonate (**2**) and azide (**3**), and ii) manipulation of the pyridine-substituted ethanolamines (**4e**) and (**14**) to 4-(2-pyridinyl)-1,3-oxazolidin-2-ones (**9**, **12**, and **17**).

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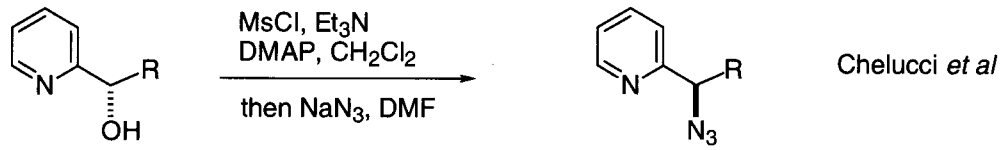
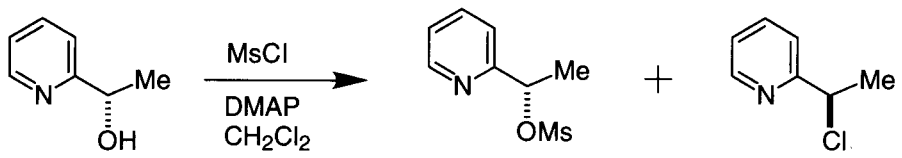
* This paper is dedicated to Professor Teruaki Mukaiyama on the occasion of his 73rd birthday.

Substitution of (2-Pyridinyl)ethyl Methanesulfonate with Azide Anion

The replacement of chiral alcohol with another functional group is a demanding process in organic synthesis and one that may bring a new chiral function to the substrate molecule. Although substitution reactions at the benzylic position have well been documented,[9] there has been little investigation of those at 2-pyridinylmethyl position due to unavailability of the corresponding optically pure 1-(2-pyridinyl)ethyl chloride, mesylate, or tosylate.[10] Chelucci reported the transformation of optically active 1-(2-pyridinyl)ethanols to azides *via* its methanesulfonates.[7] Though the reaction provided the corresponding azides, the specificity was not satisfactory with 66-92% ee, indicating that the enantiomeric purity was lost in the reaction pro-

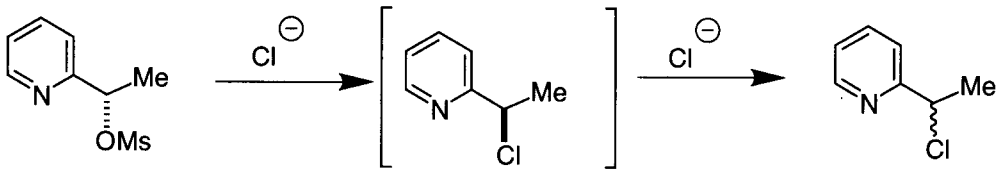


Scheme 1



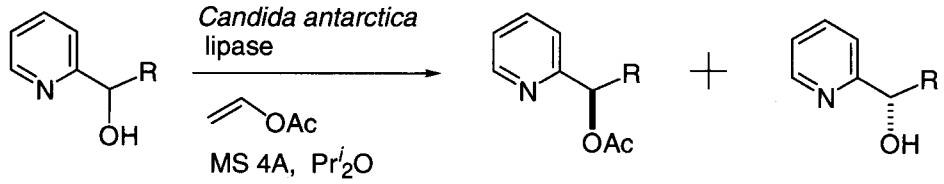
Scheme 2

cesses. The reaction processes involved the mesylation of alcohol and substitution of the mesylate with azide anions. Since they were performed without purification of the mesylate, we have re-examined the reactions and found that the product after the mesylation of **1a** contained 1-(2-pyridinyl)ethyl chloride (**2a'**) having an inverted stereo center (Scheme 2). The chloride must be produced by the reaction of the mesylate with triethylamine hydrochloride produced in the mesylation reaction. In fact, when mesylate was isolated and then treated with chloride anions, 1-(2-pyridinyl)ethyl chloride having an inverted stereocenter was obtained in an enantiomerically pure form in the initial stage of conversion. However, further replacement of the chloride with other chloride anions resulted in epimerization of the chiral center and eventually gave racemate in the final stage (Scheme 3). Obviously, azide formation through chloride decreases the enantio-



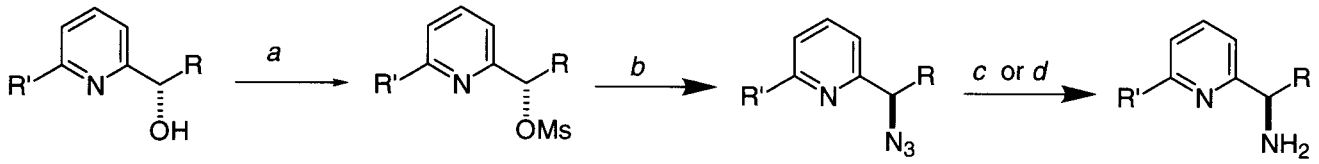
Scheme 3

meric purity of the azide. Therefore, removal of the chloride from the reaction mixture is necessary before the substitution step with azide anions. Although mesylate of 1-phenethyl alcohol is unstable,[11] fortunately that of 1-(2-pyridinyl)ethanol is reasonably stable due to the electron-withdrawing character.



Scheme 4

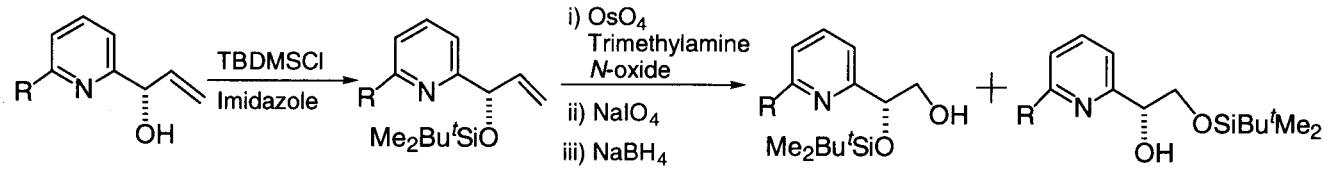
Enantiomerically pure alcohols (**1a-1d**, **5a**, and **5b**) were obtained by lipase-catalyzed enantioselective acetylation (Scheme 4).[8] Alcohols (**1e**) and (**1f**) were derived from (*R*)-1-(2-pyridinyl)allyl alcohols (**5a** and **5b**), as described later. First, alcohol (**1**) was mesylated by the standard method, thus, **1** was treated with methanesulfonyl chloride in the presence of DMAP in CH_2Cl_2. The mesylate can be purified by silica gel column chromatography and stored for a few days in refrigerator. The key substitution was achieved by treatment of the mesylate with sodium azide in DMSO at room temperature. DMSO was critical for this replacement. The reaction rate of other solvents, including DMF, HMPA, acetonitrile, dioxane, ethanol, THF, and others, was much slower than that of DMSO. Reduction of azide (**3**) to amine (**4**) was performed by catalytic hydrogenation in the presence of Pd charcoal, except for **3b**. The yields of each steps are described in the EXPERIMENTAL section. In the case of **3b**, hydrogenolysis of bromide on the pyridine ring took place. Therefore, in this particular case, reduction with triphenylphosphine was employed[12] to give the desired amine (**4b**) in 77% yield. The stereochemistry and enantiomeric purity were confirmed at this stage. Compound (**4a**) was characterized by the spectroscopic data, and the specific rotation, with a fair degree reported in the literature.[13] Enantiomeric purity was confirmed by ^{1}H NMR nmr after deriving to Mosher's MTPA ester.



1a-f **2a-f** **3a-f** **4a-e**

a	R = CH_3	R' = H
b	R = CH_3	R' = Br
c	R = CH_3	R' = $CH_2OSiBu^tMe_2$
d	R = CH_3	R' = 2-pyridinyl
e	R = $CH_2OSiBu^tMe_2$	R' = H
f	R = $CH_2OSiBu^tMe_2$	R' = Br

Scheme 5 *Reagents and Conditions; a*, MsCl, DMAP, CH_2Cl_2, rt ; *b*, NaN_3, DMF, rt ; *c*, 5%-Pd/C, H_2, rt for **3a**, **3c**, **3d**, and **3e** ; *d*, Ph_3P, H_2O, THF, rt.



5a,b **a** , R = H
b, R = Br

6a,b **7a,b** **1e,f**

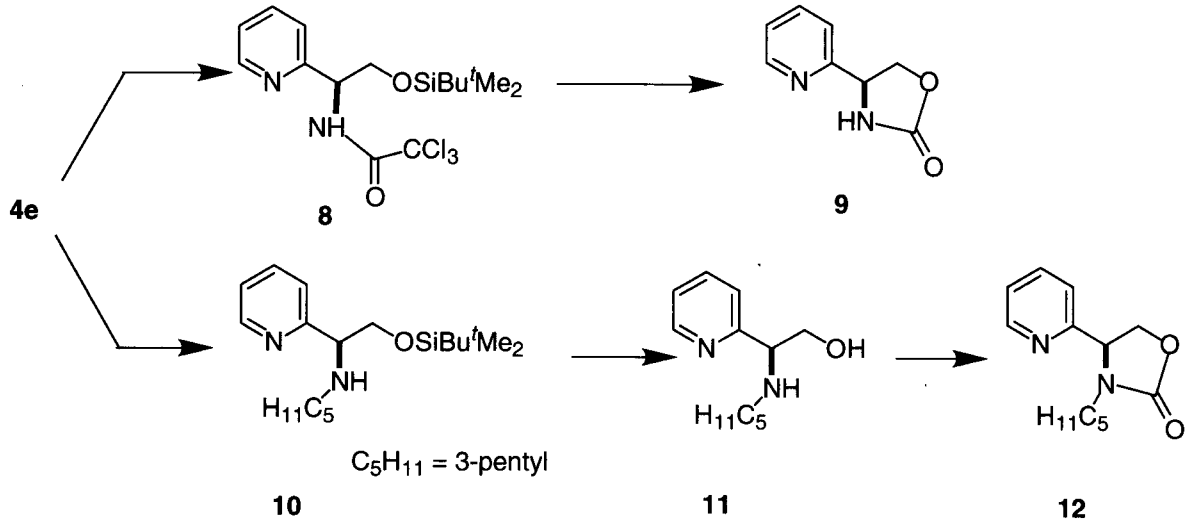
Scheme 6

Preparation of 1e and 1f.

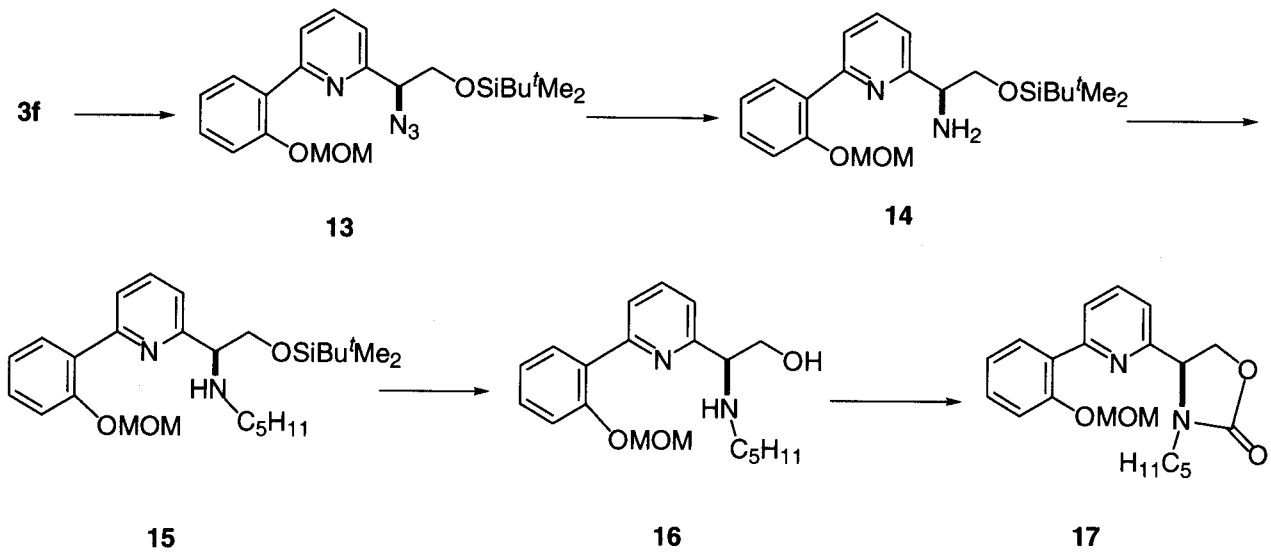
Syntheses of alcohols (**1e**) and (**1f**) are shown in Scheme 6. Silylation of alcohol (**5a**) or (**5b**) with *tert*-butyldimethylsilyl chloride by the standard procedure gave silyl ethers (**6a**) and (**6b**) in 96% and 99% yields, respectively. Since direct ozonolysis of the double bond gave aldehyde in unsatisfactory yield, osmylation and successive oxidative cleavage of the glycol were examined. Catalytic osmylation of alkene with a combination of OsO_4 (5 mol%) and trimethylamine *N*-oxide in aqueous acetone afforded diol, which upon re-oxidation with $NaIO_4$ gave an aldehyde in good yield. The crude aldehyde was directly reduced to alcohol with $NaBH_4$ in one-pot, eventually giving terminal alcohol (**7a**) in 55% yield. However, in the reduction step, a part of the silyl group migrates to the newly generated primary alcohol to form the secondary alcohol (**1e**) in 32% yield. Primary alcohol (**7a**) and secondary alcohol (**1e**) are present in equilibrium at the ratio of 2:1. In fact, when either **7a** or **1e** was treated with K_2CO_3 in methanol for 2 h at room temperature, a mixture of them was obtained in a 2:1 ratio in quantitative yield. In the same reaction sequence, **6b** gave **7b** in 63% yield along with **1f** in 31% yield.

Synthesis of 1,3-Oxazolidin-2-one.

O-Silyl-protected ethanolamine (**1e**) or (**1f**) can be transformed to 1,3-oxazolidin-2-one. In the initial attempt, compound (**4e**) derived from **1e** in Scheme 5, was desilylated and the resulting ethanolamine was cyclized by the reaction with *N,N'*-carbonyldiimidazole. However, the yield was not good in the first step,



Scheme 7



Scheme 8

presumably due to the poor extraction of the intermediary pyridine-substituted ethanolamine from an aqueous phase. Therefore, **4e** was led to trichloroacetamide by treating with trichloroacetic acid anhydride in the presence of DMAP. Then, deprotection of the silyl ether with tetrabutylammonium fluoride and the successive cyclization afforded the desired 1,3-oxazolidin-2-one ring in one-pot.[14] The chemical yield from **4e** to **9** was greatly improved to 92% in two steps. On the other hand, *N*-3-pentenyl derivative (**12**) was prepared by the standard three steps from **4e** (Scheme 7). Amine (**4e**) reacted with 3-pentanone in the presence of $NaBH_3CN$ to give **10** in 79% yield. Desilylation of **10** with tetrabutylammonium fluoride gave **11** in 88% yield. The reaction of this amino alcohol with *N,N'*-carbonyldiimidazole in the presence of potassium *tert*-butoxide in THF at room temperature furnished *N*-3-pentenyl-1,3-oxazolidin-2-one (**12**) in 62% yield. The synthesis of **17** is shown in Scheme 8. An arylation of bromopyridine must be performed before the reduction of azide to amine. The cross-coupling of pyridinyl bromide (**3f**) derived from **1f** shown in Scheme 5, with 2-(methoxymethyloxy)phenylboronic acid was conducted in refluxing benzene and ethanol under the Suzuki coupling conditions in the presence of potassium carbonate and a palladium catalyst. The reaction proceeded slowly but cleanly to give the coupling product (**13**) in 77% yield. Reduction of azide by palladium-catalyzed hydrogenation gave **14** quantitatively. In the same manner described for the preparation of **12**, *N*-alkylation with 3-pentanone and $NaBH_3CN$, desilylation with tetrabutylammonium fluoride and ring formation by *N,N'*-carbonyldiimidazole completed the synthesis of **17** in 83% yield from **14**.

In conclusion, i) substitution of 1-(2-pyridinyl)ethylamine methanesulfonate with sodium azide took place stereospecifically in DMSO with inversion of the chiral center, and ii) 4-(2-pyridinyl)-substituted 1,3-oxazolidin-2-ones were derived from optically pure 1-(2-pyridinyl)allyl alcohol *via* 2-silyloxy-1-(2-pyridinyl)ethylamine.

EXPERIMENTAL

Melting points were taken on a Yanako MP-3 melting point apparatus and are not corrected. ^{1}H NMR were

recorded on a JEOL GXS(400 MHz) and Varian Gemini-300 (300 MHz) spectrometers in $CDCl_3$ with tetramethylsilane as an internal standard. MS spectra were obtained on JMS-MS700 instrument. IR spectra were recorded on JASCO FT/IR-230 instrument. All air- or moisture-sensitive reactions were carried out in flame-dried glassware under an Ar atmosphere. THF and benzene were distilled freshly over sodium/benzophenone ketyl under nitrogen atmosphere. CH_2Cl_2 was dried over P_2O_5, and DMSO and DMF were dried over CaH_2, and they were distilled before the use. Thin layer chromatography (TLC) was performed with Merck $60F_{254}$ precoated silica gel plates. Column chromatography was carried out using Merck silica gel 60 (70-230 mesh) for gravity column.

Preparation of Mesylate (2). To a stirred solution of alcohol (**1**) (2 mmol) and DMAP (489 mg, 4 mmol) in CH_2Cl_2 (8 mL) was added MsCl (186 μL, 2.4 mmol) at 0°C. The mixture was stirred for 10 min at the same temperature and for an additional 30 min at rt. An ice water was added to the reaction mixture and the mixture was extracted with CH_2Cl_2. The organic layer was washed with water and brine, and the residual oil was purified by column chromatography on silica gel eluted with a mixture of EtOAc and hexane. The eluents were 60% EtOAc in hexane for **2a**, 30% for **2b** and **2c**, 40% for **2d** and **2e**, and 20% for **2f**.

2a. Yield 97%. Colorless oil, *Rf* = 0.45 (70% EtOAc in hexane); $[\alpha]_D^{27}$ -90.3° (*c* 1.63, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (1H, dm, *J* = 4.6 Hz), 7.74 (1H, td, *J* = 7.7 and 1.7 Hz), 7.46 (1H, d, *J* = 7.7 Hz), 7.27 (1H, ddd, *J* = 7.7, 5.0 and 0.8 Hz), 5.78 (1H, q, *J* = 6.6 Hz), 2.93 (3H, s), 1.75 (3H, d, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 149.4, 137.2, 123.5, 120.8, 80.6, 38.7, 21.7; IR (film) 1360 and 1175 cm^{-1}; MS (FAB) *m/z* 202 (M^++H); HRMS (FAB) *m/z* Calcd for $C_8H_{12}NO_3S$ (M^++H) 202.0538. Found: 202.0549.

2b. Yield 98%. Colorless oil, *Rf* = 0.65 (CH_2Cl_2); $[\alpha]_D^{28}$ -67.3° (*c* 1.97, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (1H, t, *J* = 7.7 Hz), 7.46 (1H, d, *J* = 7.7 Hz), 7.44 (1H, d, *J* = 7.7 Hz), 5.74 (1H, q, *J* = 6.6 Hz), 3.02 (3H, s), 1.75 (3H, d, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 141.6, 139.5, 127.9, 119.4, 79.3, 38.7, 21.7; IR (film) 1355 and 1175 cm^{-1}; MS (EI) *m/z* (rel intensity) 281 and 279 (M^+, 5 and 5), 202 and 200 (80 and 81), 186 and 184 (base and 91), 158 and 156 (14 and 11), 104 (55); HRMS (EI) *m/z* Calcd for $C_8H_{10}NO_3BrS$ (M^+) 280.9544 and 278.9565. Found: 280.9564 and 278.9579.

2c. Yield 94%. Colorless oil, *Rf* = 0.40 (CH_2Cl_2); $[\alpha]_D^{28}$ -53.7° (*c* 2.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (1H, t, *J* = 7.7 Hz), 7.49 (1H, d, *J* = 7.7 Hz), 7.32 (1H, d, *J* = 7.7 Hz), 5.74 (1H, q, *J* = 6.6 Hz), 4.82 (2H, s), 2.92 (3H, s), 1.74 (3H, d, *J* = 6.6 Hz), 0.96 (9H, s), 0.13 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 157.1, 137.7, 119.9, 118.7, 80.9, 65.9, 38.7, 25.9, 21.9, 18.3, -5.4; IR (film) 1360 and 1180 cm^{-1}; MS (FAB) *m/z* 346 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{15}H_{28}NO_4SSi$ (M^++H) 346.1509. Found: 346.1490.

2d. Yield 72%. Brown crystals; mp 56-58 °C (hexane), *Rf* = 0.36 (50% EtOAc in hexane); $[\alpha]_D^{28}$ +20.3° (*c* 1.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.67 (1H, ddd, *J* = 4.8, 1.8 and 0.9 Hz), 8.45 (1H, dm, *J* = 7.6 Hz), 8.41 (1H, dd, *J* = 7.9 and 1.0 Hz), 7.88 (1H, t, *J* = 7.9 Hz), 7.82 (1H, td, *J* = 7.6 and 1.8 Hz), 7.49 (1H, dd, *J* = 7.9 and 1.0 Hz), 7.32 (1H, ddd, *J* = 7.6, 4.8 and 1.2 Hz), 5.88 (1H, q, *J* = 6.6 Hz), 2.94 (3H, s), 1.84 (3H, d, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 155.7, 155.5, 149.2, 138.1, 136.9, 124.0, 121.2, 120.7, 120.7, 81.0, 38.8, 21.7; IR (film) 1360 and 1180 cm^{-1}; MS (EI) *m/z* (rel intensity) 278 (M^+, 41),183 (base), 155 (72), 130 (14), 78 (33); HRMS (EI) *m/z* Calcd for $C_{13}H_{14}N_2O_3S$ (M^+) 278.0725. Found: 278.0735.

2e. Yield 99%. Colorless oil, *Rf* = 0.45 (30% EtOAc in hexane); $[\alpha]_D^{25}$ -69.7° (*c* 1.91, $CHCl_3$); ^1H NMR

(400 MHz, $CDCl_3$) δ 8.58 (1H, dm, *J* = 5.0 Hz), 7.73 (1H, td, *J* = 7.7 and 1.7 Hz), 7.51 (1H, d, *J* = 7.7 Hz), 7.26 (1H, ddd, *J* = 7.7, 5.0 and 0.9 Hz), 5.65 (1H, dd, *J* = 7.6 and 3.6 Hz), 4.12 (1H, dd, *J* = 11.4 and 3.6 Hz), 4.00 (1H, dd, *J* = 11.4 and 7.6 Hz), 3.05 (3H, s), 0.86 (9H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 149.3, 136.9, 123.5, 121.9, 84.7, 65.3, 38.7, 25.8, 18.3, -5.5; IR (film) 1360 and 1180 cm^{-1}; MS (FAB) *m/z* 332 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{14}H_{26}NO_4SSi$ (M^++H) 332.1352. Found: 332.1373.

2f. Yield 99%. Colorless oil, *Rf* = 0.30 (20% EtOAc in hexane); $[\alpha]_D^{23}$ -72.6° (*c* 2.22, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (1H, t, *J* = 7.7 Hz), 7.49 (1H, d, *J* = 7.7 Hz), 7.44 (1H, d, *J* = 7.7 Hz), 5.60 (1H, dd, *J* = 7.3 and 3.7 Hz), 4.11 (1H, dd, *J* = 11.4 and 3.7 Hz), 3.96 (1H, dd, *J* = 11.4 and 7.3 Hz), 3.08 (3H, s), 0.85 (9H, s), 0.04 (3H, s), 0.03 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 141.5, 139.1, 127.9, 120.7, 83.5, 65.0, 38.6, 25.7, 18.2, -5.5, -5.5; IR (neat) 1360 and 1180 cm^{-1}; MS (FAB) *m/z* 412 and 410 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{14}H_{25}NO_4BrSSi$ (M^++H) 412.0437 and 410.0457. Found: 412.0440 and 410.0468.

Stereospecific Substitution of Mesylate with Sodium Azide. A mixture of mesylate (**2**) (1 mmol) and sodium azide (260 mg, 4 mmol) was stirred in DMSO (5 mL) at rt. After 1-6 h, the reaction was completed. The mixture was diluted with 30% EtOAc in hexane and washed with water, and brine. The organic layer was dried over $MgSO_4$ and condensed. The residual oil was chromatographed on silica gel eluted with a mixture of EtOAc and hexane. The eluents were 20% EtOAc in hexane for **3a** and **3d**, 5% for **3b**, **3c** and **3f**, and 10% for **3e**.

3a. Colorless oil, *Rf* = 0.45 (40% EtOAc in hexane); $[\alpha]_D^{29}$ +48.6° (*c* 0.75, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (1H, dm, *J* = 4.7 Hz), 7.71 (1H, td, *J* = 7.7 and 1.8 Hz), 7.34 (1H, d, *J* = 7.7 Hz), 7.23 (1H, ddd, *J* = 7.7, 4.7 and 0.9 Hz), 4.67 (1H, q, *J* = 6.8 Hz), 1.60 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 149.4, 137.0, 122.8, 120.5, 61.6, 20.1; IR (film) 2100 cm^{-1}; MS (FAB) *m/z* 149 (M^++H); HRMS (FAB) *m/z* Calcd for $C_7H_9N_4$ (M^++H) 149.0827. Found: 149.0832.

3b Colorless oil, *Rf* = 0.35 (2.5% EtOAc in hexane); $[\alpha]_D^{30}$ +15.6° (*c* 2.01, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (1H, t, *J* = 7.7 Hz), 7.42 (1H, d, *J* = 7.7 Hz), 7.34 (1H, d, *J* = 7.7 Hz), 4.66 (1H, q, *J* = 7.0 Hz), 1.60 (3H, d, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 141.7, 139.3, 127.3, 119.2, 61.0, 20.2; IR (film) 2100 cm^{-1}; MS (EI) *m/z* (rel intensity) 228 and 226 (M^+, 13 and 14), 199 and 197 (25 and 26), 186 and 184 (98 and base), 158 and 156 (69 and 67), 104 (66), 78 (base); HRMS (EI) *m/z* Calcd for $C_7H_7BrN_4$ (M^+) 227.9833 and 225.9854. Found: 227.9837 and 225.9845.

3c Colorless oil, *Rf* = 0.35 (5% EtOAc in hexane); $[\alpha]_D^{28}$ +21.0° (*c* 1.89, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (1H, t, *J* = 7.7 Hz), 7.46 (1H, d, *J* = 7.7 Hz), 7.20 (1H, d, *J* = 7.7 Hz), 4.83 (2H, s), 4.63 (1H, q, *J* = 6.8 Hz), 1.58 (3H, d, *J* = 6.8 Hz), 0.96 (9H, s), 0.13 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 158.9, 137.6, 119.1, 118.4, 66.0, 61.6, 25.9, 20.3, 18.3, -5.4; IR (film) 2110 cm^{-1}; MS (FAB) *m/z* 293 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{14}H_{25}N_4OSi$ (M^++H) 293.1798. Found: 293.1761.

3d Colorless oil, *Rf* = 0.48 (20% EtOAc in hexane); $[\alpha]_D^{29}$ +10.4° (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.68 (1H, ddd, *J* = 4.8, 1.8 and 0.9 Hz), 8.48 (1H, dm, *J* = 7.6 Hz), 8.36 (1H, dd, *J* = 7.8 and 1.0 Hz), 7.84 (1H, t, *J* = 7.8 Hz), 7.83 (1H, td, *J* = 7.6 and 1.8 Hz), 7.32 (1H, dm, *J* = 7.8 Hz), 7.32 (1H, ddd, *J* = 7.6, 4.8 and 1.2 Hz), 4.64 (1H, q, *J* = 6.8 Hz), 1.69 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 155.8, 155.7, 149.0, 137.9, 137.0, 123.8, 121.4, 120.5, 120.0, 61.0, 19.9; IR (film) 2100 cm^{-1}; MS

(FAB) *m/z* 226 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{12}H_{12}N_5$ (M^++H) 226.1093. Found: 226.1091.

3e Colorless oil, *Rf* = 0.35 (10% EtOAc in hexane); $[\alpha]_D^{25}$ +38.7° (*c* 1.83, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (1H, dm, *J* = 5.1 Hz), 7.69 (1H, td, *J* = 7.7 and 1.8 Hz), 7.38 (1H, d, *J* = 7.7 Hz), 7.22 (1H, ddd, *J* = 7.7, 5.1 and 0.9 Hz), 4.68 (1H, dd, *J* = 7.9 and 4.1 Hz), 4.11 (1H, dd, *J* = 10.4 and 4.1 Hz), 3.90 (1H, dd, *J* = 10.4 and 7.9 Hz), 0.87 (9H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 149.0, 136.1, 122.1, 122.0, 68.6, 58.6, 25.8, 18.2, -5.5, -5.6; IR (film) 2100 cm^{-1}; MS (FAB) *m/z* 279 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{13}H_{23}N_4OSi$ (M^++H) 279.1641. Found: 279.1665.

3f Colorless oil, *Rf* = 0.35 (5% EtOAc in hexane); $[\alpha]_D^{24}$ +29.8° (*c* 2.30, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (1H, t, *J* = 7.8 Hz), 7.41 (1H, d, *J* = 7.8 Hz), 7.37 (1H, d, *J* = 7.8 Hz), 4.64 (1H, dd, *J* = 7.6 and 4.0 Hz), 4.12 (1H, dd, *J* = 10.8 and 4.0 Hz), 3.88 (1H, dd, *J* = 10.8 and 7.6 Hz), 0.86 (9H, s), 0.04 (3H, s), 0.03 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 141.5, 138.9, 127.3, 120.7, 66.8, 66.4, 25.7, 18.1, -5.6, -5.6; IR (film) 2105 cm^{-1}; MS (FAB) *m/z* 359 and 357 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{13}H_{22}N_4OBrSi$ (M^++H) 359.0726 and 357.0747. Found: 359.0714 and 357.0751.

Reduction of Azide; Catalytic Hydrogenation. A solution of azide (**3**) (1 mmol) in ethanol (10 mL) was stirred in the presence of 5% Pd charcoal (50 mg) under a hydrogen atmosphere. After the reaction was completed (1-10 h), Pd catalyst was removed by filtration through a celite pad and the pad was washed with ethanol. The combined filtrates were condensed to give amine (**4**) almost quantitatively.

4a Yellow oil, *Rf* = 0.32 (50% MeOH in EtOAc); $[\alpha]_D^{26}$ +24.3° (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.55 (1H, dm, *J* = 4.8 Hz), 7.65 (1H, td, *J* = 7.6 and 1.8 Hz), 7.30 (1H, d, *J* = 7.6 Hz), 7.15 (1H, ddd, *J* = 7.6, 4.8 and 1.2 Hz), 4.15 (1H, q, *J* = 6.6 Hz), 1.91 (2H, s), 1.43 (3H, d, *J* = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 149.1, 136.6, 121.8, 120.1, 52.5, 24.5; IR (film) 3360 and 3280 cm^{-1}; MS (FAB) *m/z* 123 (M^++H); HRMS (FAB) *m/z* Calcd for $C_7H_{11}N_2$ (M^++H) 123.0922. Found: 123.0923.

4c Yellow oil, *Rf* = 0.18 (30% MeOH in EtOAc); $[\alpha]_D^{28}$ +9.6° (*c* 2.38, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (1H, t, *J* = 7.7 Hz), 7.32 (1H, d, *J* = 7.7 Hz), 7.11 (1H, d, *J* = 7.7 Hz), 4.78 (2H, s), 4.09 (1H, q, *J* = 6.6 Hz), 1.98 (2H, s), 1.37 (3H, d, *J* = 6.6 Hz), 0.93 (9H, s), 0.09 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 160.6, 137.1, 117.9, 117.8, 66.1, 52.3, 25.8, 24.4, 18.3, -5.4; IR (film) 3360 and 3290 cm^{-1}; MS (FAB) *m/z* 267 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{14}H_{27}N_2OSi$ (M^++H) 267.1893. Found: 267.1878.

4d Yellow oil, *Rf* = 0.12 (50% MeOH in EtOAc); $[\alpha]_D^{29}$ +7.9° (*c* 1.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.67 (1H, dm, *J* = 4.9 Hz), 8.49 (1H, dm, *J* = 7.6 Hz), 8.26 (1H, dd, *J* = 7.8 and 1.0 Hz), 7.82 (1H, td, *J* = 7.6 and 1.8 Hz), 7.78 (1H, t, *J* = 7.8 Hz), 7.33 (1H, ddd, *J* = 7.6, 4.9 and 1.2 Hz), 7.30 (1H, dd, *J* = 7.8 and 1.0 Hz), 4.22 (1H, q, *J* = 6.7 Hz), 1.70 (2H, br s), 1.50 (3H, d, *J* = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 156.2, 155.2, 149.0, 137.4, 136.7, 123.6, 121.1, 120.1, 119.0, 52.3, 24.4; IR (film) 3360 and 3280 cm^{-1}; MS (EI) *m/z* (rel intensity) 199 (M^+, 14),184 (base), 156 (55), 130 (16), 78 (21), 59 (18); HRMS (EI) *m/z* Calcd for $C_{12}H_{13}N_3$ (M^+) 199.1109. Found: 199.1078.

4e Yellow oil, *Rf* = 0.20 (10% MeOH in EtOAc); $[\alpha]_D^{28}$ +13.3° (*c* 2.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (1H, dm, *J* = 5.0 Hz), 7.59 (1H, td, *J* = 7.6 and 1.8 Hz), 7.32 (1H, d, *J* = 7.6 Hz), 7.11 (1H, ddd, *J* = 7.6, 5.0 and 1.0 Hz), 4.05 (1H, dd, *J* = 7.2 and 4.9 Hz), 3.80 (1H, dd, *J* = 9.6 and 4.9 Hz), 3.63 (1H, dd, *J* = 9.6 and 7.2 Hz), 1.92 (2H, s), 0.81 (9H, s), -0.07 (3H, s), -0.07 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7,

149.0, 136.1, 122.1, 122.0, 68.6, 58.6, 25.8, 18.2, -5.5, -5.6; IR (film) 3375 and 3290 cm^{-1}; MS (FAB) *m/z* 253 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{13}H_{25}N_2OSi$ (M^++H) 253.1736. Found: 253.1757.

14 Colorless oil, *Rf* = 0.20 (EtOAc); $[\alpha]_D^{24}$ -5.3° (*c* 2.01, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (1H, dd, *J* = 7.7 and 1.8 Hz), 7.70 (1H, dd, *J* = 8.4 and 1.1 Hz), 7.65 (1H, t, *J* = 7.7 Hz), 7.34 (1H, ddd, *J* = 8.4, 7.7 and 1.8 Hz), 7.28 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.22 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.13 (1H, td, *J* = 7.7 and 1.1 Hz), 5.18 (2H, s), 4.14 (1H, dd, *J* = 7.0 and 4.8 Hz), 3.89 (1H, dd, *J* = 9.5 and 4.8 Hz), 3.73 (1H, dd, *J* = 9.5 and 7.0 Hz), 3.43 (3H, s), 2.03 (2H, s), 0.86 (9H, s), -0.02 (3H, s), -0.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 155.1, 154.7, 135.7, 131.2, 130.3, 129.7, 123.4, 122.2, 120.0, 115.4, 95.0, 68.8, 58.7, 56.1, 25.8, 18.2, -5.5, -5.5; IR (neat) 3380 and 3300 cm^{-1}; MS (FAB) *m/z* 389 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{21}H_{33}N_2O_3Si$ (M^++H) 389.2261. Found: 389.2238.

Reduction of Azide by Triphenylphosphine. A mixture of azide (**3b**) (165 mg, 0.73 mmol), triphenylphosphine (276 mg, 1.45 mmol), and water (26 μL, 1.45 mmol) was stirred in THF (20 mL) for 24 h. The mixture was condensed and the residual oil was chromatographed on silica gel eluted with EtOAc to give **4b** (113 mg) in 77% yield. Yellow oil, *Rf* = 0.25 (50% MeOH in EtOAc); $[\alpha]_D^{28}$ +14.8° (*c* 2.37, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (1H, t, *J* = 7.6 Hz), 7.22 (1H, d, *J* = 7.6 Hz), 7.17 (1H, d, *J* = 7.6 Hz), 4.01 (1H, q, *J* = 6.7 Hz), 1.90 (2H, s), 1.30 (3H, d, *J* = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 141.5, 138.9, 126.0, 118.7, 52.0, 24.1; IR (film) 3360 and 3280 cm^{-1}; MS (FAB) *m/z* 203 and 201 (M^++H); HRMS (FAB) *m/z* Calcd for $C_7H_{10}BrN_2$ (M^++H) 203.0007 and 201.0027. Found: 202.9991 and 201.0014.

Silylation of 5a and 5b. To a mixture of **5** (1 mmol) and imidazole (136 mg, 2 mmol) in DMF (2 mL) was added *tert*-butyldimethylsilyl chloride (166 mg, 1.1 mmol) and the mixture was stirred for 1 h at rt. The reaction mixture was diluted with 30% EtOAc in hexane (20 mL), washed with water and brine, and dried over $MgSO_4$. The solvent was removed and the residue was purified by column chromatography on silica gel eluted with 10% EtOAc in hexane to give **6**.

6a. Yield 96%. Colorless oil, *Rf* = 0.40 (10% EtOAc in hexane); $[\alpha]_D^{29}$ -93.1° (*c* 1.98, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (1H, dm, *J* = 5.1 Hz), 7.67 (1H, td, *J* = 7.7 and 1.7 Hz), 7.50 (1H, d, *J* = 7.7 Hz), 7.13 (1H, ddd, *J* = 7.7, 5.1 and 0.8 Hz), 6.03 (1H, ddd, *J* = 17.1, 10.3 and 5.2 Hz), 5.40 (1H, dt, *J* = 17.1 and 1.6 Hz), 5.29 (1H, dm, *J* = 5.2 Hz), 5.11 (1H, dt, *J* = 10.3 and 1.6 Hz), 0.92 (9H, s), 0.09 (3H, s), 0.01 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 148.5, 140.2, 136.8, 122.0, 120.0, 114.0, 76.8, 25.8, 18.3, -4.8, -5.0; MS (FAB) *m/z* 250 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{14}H_{24}NOSi$ (M^++H) 250.1627. Found: 250.1625.

6b. Yield 99%. Colorless oil, *Rf* = 0.33 (5% EtOAc in hexane); $[\alpha]_D^{26}$ -105.2° (*c* 2.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (1H, t, *J* = 7.7 Hz), 7.46 (1H, d, *J* = 7.7 Hz), 7.33 (1H, d, *J* = 7.7 Hz), 6.03 (1H, ddd, *J* = 17.2, 10.3 and 4.8 Hz), 5.41 (1H, dt, *J* = 17.2 and 1.8 Hz), 5.28 (1H, dt, *J* = 4.8 and 1.8 Hz), 5.11 (1H, dt, *J* = 10.3 and 1.8 Hz), 0.93 (9H, s), 0.09 (3H, s), 0.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 140.8, 139.5, 139.1, 126.2, 118.7, 114.2, 75.9, 25.8, 18.3, -4.9, -5.0; MS (FAB) *m/z* 330 and 328 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{14}H_{23}NOBrSi$ (M^++H) 330.0712 and 328.0732. Found: 330.0700 and 328.0715.

Transformation of Alkene to Alcohol; Conversion of 6a to 1e and 6b to 1f. A mixture of alkene (**6a**) or

(**6b**) (1 mmol), trimethylamine *N*-oxide (445 mg, 4 mmol), and a catalytic amount of OsO_4 (13 mg, 5 mol%) was stirred in a mixture of acetone (8 mL) and water (1 mL) for 2 h at rt. Then, saturated $NaHSO_3$ solution (1 mL) was added to the reaction mixture and it was stirred for 30 min. The mixture was filtered through a celide pad and the pad was washed with acetone. The combined filtrates were condensed and the residue was extracted with EtOAc. The organic extract was washed with water and brine, and dried over $MgSO_4$. After the solvent was removed, the residual oil was dissolved in a mixture of methanol (7.5 mL) and water (2.5 mL). $NaIO_4$ (257 mg, 1.2 mmol) was added to the mixture by several portions at 0°C, and the mixture was stirred for 2 h at the same temperature. Then, an excess of $NaBH_4$ was added at rt and the mixture was stirred for 10 min. Acetone (0.5 mL) was added and the solvent was evaporated. The residue was extracted with 50% EtOAc in hexane (30 mL), and wased with water and brine. The extract was dried over $MgSO_4$ and the crude product was purified by column chromatography on silica gel. The eluents and yields were following; **7a** 30% EtOAc in hexane, 55% yield and **1e** 40% EtOAc in hexane, 30% yield; **7b** 15% EtOAc in hexane, 63% yield and **1f** 20% EtOAc in hexane, 31% yield. **Isomerization of Alcohols.** A mixture of **7a** or **7b** (1 mmol) and K_2CO_3 (14 mg, 0.1 mmol) in methanol (10 mL) was stirred for 2 h at rt. The same purification described above gave about a 2:1 ratio of primary and secondary alcohols in quiantitative yields.

7a Colorless oil, *Rf* = 0.33 (30% EtOAc in hexane); $[\alpha]_D^{31}$ -84.0° (*c* 1.52, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (1H, dm, *J* = 4.9 Hz), 7.71 (1H, td, *J* = 7.7 and 1.8 Hz), 7.51(1H, d, *J* = 7.7 Hz), 7.19 (1H, ddd, *J* = 7.7, 4.9 and 0.9 Hz), 4.86 (1H, t, *J* = 5.5 Hz), 3.82-3.74 (2H, m), 3.25 (1H, br s), 0.94 (9H, s), 0.12 (3H, s), 0.03 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 148.4, 136.8, 122.3, 120.5, 74.8, 67.6, 25.8, 18.2, -4.8, -4.9; IR (film) 3290 cm^{-1}; MS (FAB) *m/z* 254 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{13}H_{24}NO_2Si$ (M^++H) 254.1576. Found: 254.1588.

1e Colorless oil, *Rf* = 0.50 (30% EtOAc in hexane); $[\alpha]_D^{31}$ -16.5° (*c* 1.98, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (1H, dm, *J* = 4.9 Hz), 7.67 (1H, td, *J* = 7.7 and 1.6 Hz), 7.44 (1H, d, *J* = 7.7 Hz), 7.19 (1H, ddd, *J* = 7.7, 4.9 and 0.7 Hz), 4.77 (1H, m), 3.95 (1H, d, *J* = 4.9 Hz), 3.84 (1H, dd, *J* = 10.0 and 5.3 Hz), 3.80 (1H, dd, *J* = 10.0 and 6.0 Hz), 0.84 (9H, s), -0.01 (3H, s), -0.03 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 148.3, 136.3, 122.4, 121.2, 73.6, 67.6, 25.8, 18.2, -5.5, -5.5; IR (film) 3400 cm^{-1}; MS (FAB) *m/z* 254 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{13}H_{24}NO_2Si$ (M^++H) 254.1576. Found: 254.1548.

7b Colorless oil, *Rf* = 0.43 (20% EtOAc in hexane); $[\alpha]_D^{26}$ -69.9° (*c* 1.92, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (1H, t, *J* = 7.7 Hz), 7.46 (1H, d, *J* = 7.7 Hz), 7.36 (1H, d, *J* = 7.7 Hz), 4.85 (1H, t, *J* = 4.8 Hz), 3.83 (1H, m), 3.73 (1H, m), 2.43 (1H, br s), 0.93 (9H, s), 0.11 (3H, s), 0.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 140.9, 138.9, 126.6, 119.4, 75.0, 67.3, 25.8, 18.1, -4.9, -4.9; IR (film) 3410 cm^{-1}; MS (FAB) *m/z* 334 and 332 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{13}H_{23}NO_2BrSi$ (M^++H) 334.0661 and 332.0681. Found: 334.0647 and 332.0681.

1f Colorless oil, *Rf* = 0.50 (20% EtOAc in hexane); $[\alpha]_D^{26}$ -33.8° (*c* 1.89, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (1H, t, *J* = 7.7 Hz), 7.45 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.38 (1H, dd, *J* = 7.7 and 1.1 Hz), 4.76 (1H, m), 3.90 (1H, dd, *J* = 9.9 and 4.8 Hz), 3.80 (1H, dd, *J* = 9.9 and 5.9 Hz), 3.44 (1H, br s), 0.84 (9H, s), 0.00 (3H, s), -0.03 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 141.0, 138.7, 126.7, 119.9, 73.5, 67.0, 25.8, 18.2, -5.5, -5.6; IR (film) 3440 cm^{-1}; MS (FAB) *m/z* 334 and 332 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{13}H_{23}O_2BrNSi$ (M^++H) 334.0661 and 332.0681. Found: 334.0681 and 332.0672.

Synthesis of 8. To a solution of amine (**4e**) (2.83 g, 11.21 mmol) and DMAP (2.74 g, 22.42 mmol) in CH_2Cl_2 (56 mL) was dropped trichloroacetic acid anhydride (2.46 mL, 13.45 mmol) at 0°C. The mixture was stirred for 10 min at the same temperature and for an additional 10 min at rt. An ice cooled water (5 mL) was added and the mixture was extracted with CH_2Cl_2 (120 mL). The extract was washed with water and brine, dried over $MgSO_4$ and condensed. The crude product was purified by column chromatography on silica gel eluted with 15% EtOAc in hexane to give **8** (4.23 g) in 95% yield. Colorless oil; *Rf* = 0.25 (10% EtOAc in hexane); $[\alpha]_D^{25}$ +7.2° (*c* 2.13, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (1H, dm, *J* = 4.9 Hz), 8.36 (1H, d, *J* = 6.7 Hz), 7.68 (1H, td, *J* = 7.6 and 1.8 Hz), 7.29 (1H, d, *J* = 7.6 Hz), 7.23 (1H, ddd, *J* = 7.6, 4.9 and 0.9 Hz), 5.02 (1H, ddd, *J* = 6.7, 6.4 and 4.3 Hz), 4.05 (1H, dd, *J* = 9.8 and 4.3 Hz), 3.82 (1H, dd, *J* = 9.8 and 6.4 Hz), 0.78 (9H, s), -0.10 (3H, s), -0.13 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 156.3, 149.0, 136.4, 122.8, 122.4, 92.7, 64.8, 56.8, 25.6, 18.0, -5.7, -5.8; IR (film) 3360 and 1715 cm^{-1}; MS (FAB) *m/z* 397 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{15}H_{24}N_2O_2Cl_3Si$: 397.0673 (M^++1). Found: 397.0671.

Synthesis of 9. To a solution of **8** (423 mg, 1 mmol) in THF (5 mL) was added tetrabutylammonium fluoride (1.12 mL, 1M in THF solution). After the mixture was stirred for 3 h at rt, solvent was removed and the residue was chromatographed on silica gel eluted with EtOAc to give **9** (168 mg) in 97% yield. Colorless crystals; mp 86-87 °C (hexane), *Rf* = 0.45 (10% MeOH in EtOAc); $[\alpha]_D^{20}$ +80.1° (*c* 1.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (1H, ddd, *J* = 4.8, 1.5 and 0.9 Hz), 7.74 (1H, ddd, *J* = 7.9, 7.6 amd 1.5 Hz), 7.49 (1H, s), 7.42 (1H, dm, *J* = 7.9 Hz), 7.26 (1H, ddd, *J* = 7.6, 4.8 and 1.2 Hz), 5.08 (1H, ddm, *J* = 8.8 and 5.8 Hz), 4.80 (1H, td, *J* = 8.8 and 1.8 Hz), 5.08 (1H, ddd, *J* = 8.8, 5.8 and 1.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 158.9, 149.6, 137.3, 123.2, 120.0, 70.7, 56.8; IR (KBr) 3240, 1735 and 1700 cm^{-1}; MS (FAB) *m/z* 165 (M^++H); HRMS (FAB) *m/z* Calcd for $C_8H_9N_2O_2$ (M^++H) 165.0664. Found: 165.0667. Anal. Calcd for $C_8H_8N_2O_2$: C, 58.53; H, 4.91; N, 17.06. Found: C, 58.53; H, 4.80; N, 16.96.

Synthesis of 13. A mixture of **3f** (4.3 g, 12.03 mmol), 2-(methoxymethyloxy)phenylboronic acid (2.01 g, 13.24 mmol), sodium carbonate (13.2 mL, 2M aqueous solution, 26.4 mmol), and a catalytic amount of $Pd(PPh_3)_4$ (278 mg, 2 mol%) was heated in a mixture of benzene (225 mL) and ethanol (9 mL) at the refluxing temperature for 36 h. After cooling, the mixture was quenched with brine (10 mL) and extracted with EtOAc (300 mL). The organic layer was washed with water and brine, dried over $MgSO_4$ and condensed. The residue was purified by column chromatographed on silica gel eluted with 10% EtOAc in hexane to give **13** (3.84 g) in 77% yield. Colorless oil, *Rf* = 0.23 (5% EtOAc in hexane); $[\alpha]_D^{25}$ +25.7° (*c* 2.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (1H, dd, *J* = 7.7 and 1.8 Hz), 7.77 (1H, dd, *J* = 8.4 and 1.1 Hz), 7.71 (1H, t, *J* = 7.7 Hz), 7.36 (1H, ddd, *J* = 8.4, 7.7 and 1.8 Hz), 7.31 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.23 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.15 (1H, td, *J* = 7.7 and 1.1 Hz), 5.19 (2H, s), 4.73 (1H, dd, *J* = 7.7 and 4.0 Hz), 4.20 (1H, dd, *J* = 10.6 and 4.0 Hz), 3.96 (1H, dd, *J* = 10.6 and 7.7 Hz), 3.44 (3H, s), 0.89 (9H, s), 0.05 (3H, s), 0.05 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 155.5, 154.7, 136.2, 131.2, 130.0, 129.7, 124.2, 122.3, 119.7, 115.4, 95.0, 67.8, 66.8, 56.2, 25.7, 18.2, -5.6; IR (film) 2100 cm^{-1}; MS (FAB) *m/z* 415 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{21}H_{31}N_4O_3Si$ (M^++H) 415.2165. Found: 415.2148.

Synthesis of 14. Compound (**14**) was obtained quantitatively by the catalytic hydrogenation described for the preparation of **4** similarly. Colorless oil, *Rf* = 0.20 (EtOAc); $[\alpha]_D^{24}$ -5.3° (*c* 2.01, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (1H, dd, *J* = 7.7 and 1.8 Hz), 7.70 (1H, dd, *J* = 8.4 and 1.1 Hz), 7.65 (1H, t, *J* = 7.7 Hz), 7.34 (1H, ddd, *J* = 8.4, 7.7 and 1.8 Hz), 7.28 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.22 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.13 (1H, td, *J* = 7.7 and 1.1 Hz), 5.18 (2H, s), 4.14 (1H, dd, *J* = 7.0 and 4.8 Hz), 3.89 (1H, dd, *J* = 9.5 and 4.8 Hz), 3.73 (1H, dd, *J* = 9.5 and 7.0 Hz), 3.43 (3H, s), 2.03 (2H, s), 0.86 (9H, s), -0.02 (3H, s), -0.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 155.1, 154.7, 135.7, 131.2, 130.3, 129.7, 123.4, 122.2, 120.0, 115.4, 95.0, 68.8, 58.7, 56.1, 25.8, 18.2, -5.5, -5.5; IR (neat) 3380 and 3300 cm^{-1}; MS (FAB) *m/z* 389 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{21}H_{33}N_2O_3Si$ (M^++H) 389.2261. Found: 389.2238.

3-Pentylation of Primary Amine; Synthesis of 10 and 15. To a mixture of amine (**4e** or **14**, 1 mmol) and 3-pentanone (151 μL, 1.5 mmol) in methanol (5 mL) was added $NaBH_3CN$ (75 mg, 1.2 mmol). The mixture was stirred for 3 days at rt, and then condensed. The residue was extracted with 50% EtOAc in hexane (40 mL), and the extract was washed with water and brine, and dried over $MgSO_4$. The solvent was removed and the residue was purified by column chromatography on silica gel eluted with 20% EtOAc in hexane to give the desired amine (**10** or **15**).

Compound (10). Yield 79%. Colorless oil, *Rf* = 0.18 (10% EtOAc in hexane); $[\alpha]_D^{29}$ +51.9° (*c* 2.67, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (1H, dm, *J* = 5.0 Hz), 7.62 (1H, td, *J* = 7.7 and 1.8 Hz), 7.44 (1H, d, *J* = 7.7 Hz), 7.13 (1H, ddd, *J* = 7.7, 5.0 and 1.0 Hz), 3.96 (1H, dd, *J* = 7.4 and 5.3 Hz), 3.77 (1H, dd, *J* = 9.6 and 5.3 Hz), 3.65 (1H, dd, *J* = 9.6 and 7.4 Hz), 2.25 (1H, m), 1.83 (1H, br s), 1.48-1.41 (2H, m), 1.38-1.25 (2H, m), 0.86 (3H, t, *J* = 7.4 Hz), 0.83 (9H, s), 0.79 (3H, t, *J* = 7.4 Hz), -0.06 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 149.0, 135.9, 122.8, 122.0, 67.1, 63.4, 57.4, 26.9, 25.8, 25.0, 18.2, 10.3, 9.0, -5.5, -5.6; IR (film) 3340 cm^{-1}; MS (FAB) *m/z* 323 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{18}H_{35}N_2OSi$ (M^++H) 323.2519. Found: 323.2519.

Compound (15). Yield 98%. Colorless oil, *Rf* = 0.50 (20% EtOAc in hexane); $[\alpha]_D^{24}$ +38.1° (*c* 1.56, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (1H, dd, *J* = 7.7 and 1.8 Hz), 7.66 (1H, dd, *J* = 8.4 and 1.1 Hz), 7.64 (1H, t, *J* = 7.7 Hz), 7.38 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.33 (1H, ddd, *J* = 8.4, 7.7 and 1.8 Hz), 7.21 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.13 (1H, td, *J* = 7.7 and 1.1 Hz), 5.18 (2H, s), 4.04 (1H, dd, *J* = 7.0 and 5.5 Hz), 3.84 (1H, dd, *J* = 9.5 and 5.5 Hz), 3.72 (1H, dd, *J* = 9.5 and 7.0 Hz), 3.42 (3H, s), 2.34 (1H, m), 2.12 (1H, br s), 1.51-1.30 (4H, m), 0.86 (3H, t, *J* = 7.3 Hz), 0.85 (3H, t, *J* = 7.3 Hz), 0.84 (9H, s), -0.06 (3H, s), -0.06 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 155.1, 154.7, 135.4, 131.2, 130.5, 129.6, 123.2, 122.3, 120.8, 115.5, 95.0, 67.3, 63.3, 57.4, 56.1, 26.9, 25.8, 25.1, 18.2, 10.4, 9.1, -5.5, -5.6; IR (film) 3340 cm^{-1}; MS (FAB) *m/z* 459 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{26}H_{43}N_2O_3Si$: 459.3043 (M^++1). Found: 459.3043.

Deprotection of Silyl Group; Synthesis of 11 and 16. To a solution of silyl ether (**10** or **15**, 1 mmol) in THF (10 mL) was added tetrabutylammonium fluoride (1.2 mL, 1.0 M solution in THF, 1.2 mmol), and the mixture was stirred for 2 h at rt. The reaction mixture was diluted with CH_2Cl_2 (100 mL), washed with water and brine, and dried over $MgSO_4$. The solvent was removed and the residue was chromatographed on silica gel eluted with EtOAc to give **11** or **16**.

Compound (11). Yield 88%. Slight yellow crystals; mp 62-63 °C (hexane), *Rf* = 0.15 (10% MeOH in EtOAc); $[\alpha]_D^{29}$ +72.0° (*c* 2.22, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (1H, dm, *J* = 5.0 Hz), 7.63 (1H, td, *J* = 7.7 and 1.8 Hz), 7.27 (1H, dm, *J* = 7.7 Hz), 7.16 (1H, ddd, *J* = 7.7, 5.0 and 0.9 Hz), 3.85 (1H, dd, *J* = 7.6 and 4.6 Hz), 3.80 (1H, br s), 3.73 (1H, dd, *J* = 10.5 and 4.6 Hz), 3.57 (1H, dd, *J* = 10.5 and 7.6 Hz), 2.27 (1H, m), 2.18 (1H, br s), 1.47-1.27 (4H, m), 0.88 (3H, t, *J* = 7.5 Hz), 0.77 (3H, t, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 149.2, 136.4, 122.6, 122.2, 65.5, 61.9, 57.7, 26.5, 25.8, 9.9, 9.4; IR (KBr) 3340 and 3180 cm^{-1}; MS (FAB) *m/z* 209 (M^++H); Anal. Calcd for $C_{12}H_{20}N_2O$: C, 69.19; H, 9.68; N, 13.45. Found: C, 69.31; H, 9.88; N, 13.58.

Comopund (16). Yield 94%. Colorless oil, *Rf* = 0.25 (EtOAc); $[\alpha]_D^{24}$ +76.2° (*c* 2.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (1H, dd, *J* = 7.7 and 1.8 Hz), 7.71 (1H, dd, *J* = 8.1 and 1.1 Hz), 7.68 (1H, t, *J* = 7.9 Hz), 7.35 (1H, ddd, *J* = 8.1, 7.7 and 1.8 Hz), 7.23 (1H, dd, *J* = 7.9 and 1.1 Hz), 7.20 (1H, dd, *J* = 7.9 and 1.1 Hz), 7.13 (1H, td, *J* = 7.7 and 1.1 Hz), 5.19 (2H, s), 3.91 (1H, dd, *J* = 7.0 and 4.8 Hz), 3.81 (1H, dd, *J* = 10.6 and 4.8 Hz), 3.68 (1H, dd, *J* = 10.6 and 7.0 Hz), 3.43 (3H, s), 2.96 (1H, br s), 2.39 (1H, m), 1.52-1.32 (4H, m), 0.90 (3H, t, *J* = 7.7 Hz), 0.81 (3H, t, *J* = 7.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 155.4, 154.7, 136.2, 131.0, 129.9, 129.8, 123.5, 122.2, 120.5, 115.4, 95.0, 65.5, 61.4, 57.8, 56.1, 26.5, 25.8, 9.9, 9.5; IR (film) 3360 cm^{-1}; MS (FAB) *m/z* 345 (M^++H); HRMS (FAB) *m/z* Calcd for $C_{20}H_{29}N_2O_3$: 345.2178 (M^++1). Found: 345.2155.

Synthesis of 12 and 17. A mixture of amino alcohol (**11** or **16**, 1 mmol), *N,N'*-carbonyldiimidazole (195 mg, 1.2 mmol), and *t*-BuOK (112 mg, 1 mmol) in THF (10 mL) was stirred for 48 h at rt. The reaction mixture was diluted with EtOAc (80 mL), washed with water and brine, and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluted with EtOAc for **12** and 40% EtOAc in hexane for **17** to give 1,3-oxazolidin-2-one.

Compound (12). Yield 62%. Yellow oil, *Rf* = 0.65 (10% MeOH in EtOAc); $[\alpha]_D^{25}$ -9.8° (*c* 2.22, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (1H, dm, *J* = 4.7 Hz), 7.73 (1H, td, *J* = 7.7 and 1.7 Hz), 7.43 (1H, dm, *J* = 7.7 Hz), 7.28 (1H, ddd, *J* = 7.7, 4.7 and 1.0 Hz), 4.85 (1H, dd, *J* = 8.7 and 5.4 Hz), 4.62 (1H, t, *J* = 8.7 Hz), 4.36 (1H, dd, *J* = 8.7 and 5.4 Hz), 3.47 (1H, m), 1.67-1.57 (2H, m), 1.04 (1H, m), 0.96 (1H, m), 0.86 (3H, t, *J* = 7.4 Hz), 0.74 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 158.6, 149.6, 137.1, 123.7, 122.0, 68.7, 59.7, 58.8, 26.5, 24.4, 11.1, 11.1; IR (film) 1740 cm^{-1}; MS (EI) *m/z* (rel intensity) 234 (M^+, 3), 205 (base); HRMS (EI) *m/z* Calcd for $C_{13}H_{18}N_2O_2$ (M^+) 234.1368. Found: 234.1362.

Compound (17). Yield 91%. Colorless crystals; mp 78-79 °C (hexane), *Rf* = 0.30 (40% EtOAc in hexane); $[\alpha]_D^{28}$ -0.8° (*c* 1.99, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (1H, dd, *J* = 7.7 and 0.9 Hz), 7.81 (1H, dd, *J* = 7.7 and 1.8 Hz), 7.75 (1H, t, *J* = 7.7 Hz), 7.37 (1H, ddd, *J* = 8.0, 7.7 and 1.8 Hz), 7.35 (1H, dd, *J* = 7.7 and 0.9 Hz), 7.23 (1H, dd, *J* = 7.7 and 0.9 Hz), 7.14 (1H, ddd, *J* = 8.0, 7.7 and 0.9 Hz), 5.20 (2H, s), 4.94 (1H, dd, *J* = 9.1 and 5.5 Hz), 4.64 (1H, dd, *J* = 9.1 and 8.6 Hz), 4.46 (1H, dd, *J* = 8.6 and 5.5 Hz), 3.52 (1H, m), 3.43 (3H, s), 1.79-1.58 (2H, m), 1.15-1.02 (2H, m), 0.89 (3H, t, *J* = 7.4 Hz), 0.76 (3H, t, *J* = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 158.8, 155.9, 154.8, 136.7, 131.1, 130.3, 129.2, 124.9, 122.4, 119.9, 115.3, 94.9, 68.8, 59.9, 58.9, 56.2, 26.5, 24.4, 11.2, 11.1; IR (film) 1740 cm^{-1}; MS (EI) *m/z* (rel intensity) 370 (M^+, base); Anal. Calcd for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07; N, 7.56. Found: C, 68.11; H, 7.25; N, 7.75.

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