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Stereoselective formation of optically active 2-oxy-1,3-oxazolidin-4-ones from chiral *O*-acylmandelamides or lactamides

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Abstract—(−)-*O*-Acyllactamides or mandelamides in the presence of TBSOTf underwent cyclization reaction to give optically active 2-oxy-1,3-oxazolidin-4-ones, a novel nitrogen analog of orthoesters, in good yields. An X-ray analysis and NOE studies indicated that the absolute configuration at the newly formed chiral carbon was *S*. For their synthetic application, the 1,3-dipolar cycloaddition of nitrile oxide was examined. The cycloadducts were obtained in a stereoselective manner. Subsequent treatment of the adduct with TBAF resulted in the one-step removal of mandelamide, giving optically active 4,5-dihydroisoxazole and mandelamide in good yields.

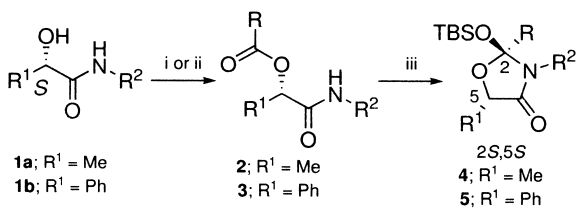
1. Introduction

Acetals serve as a convenient protective group for carbonyl compounds.[1] They have also been recognized as a useful chiral auxiliary for asymmetric synthesis and a number of improvements have been achieved so far.[2] Orthoseters, an analog of acetals with a higher oxidation level, on the other hand, have been rarely used for these purposes.[3] One of the reasons is their instability under acidic conditions; orthoesters usually decompose easily to give corresponding esters.[4] Some acyclic orthoesters, for example, are quickly hydrolyzed during a chromatographic treatment. Additionally, emergence of a new chiral center at the orthoester carbon gives rise to formation of diastereomers so that a facile stereocontrolling method has been desired.[5] Recently, we have found a simple method to prepare a novel nitrogen analogue of chiral orthoesters, 2-oxy-1,3-oxazolidin-4-one, in a highly diastereoselective manner. Here we report the first practical and stereoselective synthesis of optically active nitrogen analogues of cyclic orthoesters from readily available chiral *N*-substituted lactamides or mandelamides. We have also demonstrated its possibility as an auxiliary for asymmetric synthesis.

2. Results and discussion

Optically active *O*-acyl-*N*-substituted lactamides **2** and mandelamides **3**, starting materials of 2-oxy-1,3-oxazolidin-4-ones **4** and **5**, were prepared from commercially available (*S*)-lactic acid or (*S*)-mandelic acid derivatives. *O*-Acylation of lactamide **1** was achieved by their esterification reaction with acyl chloride or carboxylic acid in the presence of DCC. Treatment of **2a** with TBSOTf in the presence of 2,6-lutidine at 0°C, for example, resulted in the rapid disappearance of **2a** and a new compound **4a** was formed in a spot-to-spot manner (Scheme 1). Product **4a** was purified through flash chromatography and isolated in a 90% yield as the sole product (Table 1, entry 1). The results are summarized in Table 1.

The present reaction conditions were examined for various lactamides **2** (entries 1–8). To our surprise, the reaction product usually contained just a single diastereomer so that the stereoselectivity of the reaction should be generally very high. Acetate or substituted acrylate derivatives, for example, underwent a smooth reaction to give a single isomer of their corresponding **4** in good yields (entry 1 and 4–6). For some cases, the yield and the stereoselectivity depended on the structure of lactamides **2**; benzoate **2b** and isobutyrate **2c** took many hours before finishing the reaction and the yields of **4** remained at a poor level (entry 2 and 3).



Scheme 1. *Reagents*: (i) R^1COCl, pyridine, DMAP; (ii) R^1CO_2H, DCC, DMAP; (iii) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0°C.

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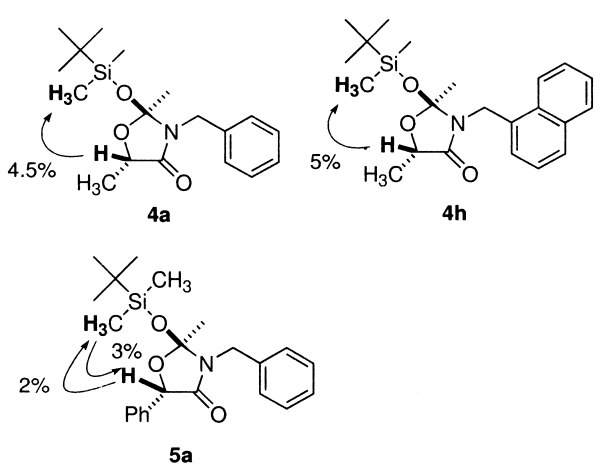
Table 1. Preparation of optically active 2-oxy-1,3-oxazolidin-4-ones **4** and **5**

Entry	R^1	R^2	R	Amide **2** or **3**; yield (%)[a]	$[\alpha]_D$	**4** or **5**; yield (%)[a]	Ratio[b]	$[\alpha]_D$
1	Me	Bn	Me	**2a**; 95	−178.0	**4a**; 90	99:1	−153.9
2	Me	Bn	Ph	**2b**; 84	–[c]	**4b**; 10	84:16	–[c]
3	Me	Bn	Me_2CH–	**2c**; 95	–[c]	**4c**; 0	–	–
4	Me	Bn	CH_2=CH–	**2d**; 88	−60.5	**4d**; 88	92:8	−44.4
5	Me	Bn	MeCH=CH–	**2e**; 67	−156.5	**4e**; 95	94:6	−84.3
6	Me	Bn	PhCH=CH–	**2f**; 74	−112.9	**4f**; 95	95:5	−144.0
7	Me	Bn	EtO_2CCH=CH–	**2g**; 59	−86.5	**4g**; 97	63:37	−86.7
8	Me	1-$C_{10}H_7CH_2$	Me	**2h**; 91	−81.1	**4h**; 93	99:1	−39.0
9	Ph	Bn	Me	**3a**; 79	+115.4	**5a**; 89	>99:1	+57.2
10	Ph	Bn	Ph	**3b**; 95	+57.8	**5b**; 82	>99:1	−13.5
11	Ph	Bn	Me_2CH–	**3c**; 98	+99.8	**5c**; 97	>99:1	+42.4
12	Ph	Bn	C_6H_{13}–	**3d**; 91	+91.6	**5d**; 97	93:7	+54.2
13	Ph	Bn	CH_2=CH–	**3e**; 57	+107.5	**5e**; 84	97:3	+19.0
14	Ph	Bn	PhCH=CH–	**3f**; 40	+47.6	**5f**; 82	>99:1	+95.9
15	Ph	Bn	EtO_2CCH=CH–	**4g**; 41	+68.2	**5g**; 96	82:18	+64.3[d]

[a] Isolated yield.
[b] Determined by HPLC analyses (Chiral Pak-AD).
[c] Racemic lactamide was used.
[d] For major isomer. $[\alpha]_D$ for minor isomer was +30.6.

The reaction with fumaric ester **2g** smoothly gave **4g** in 97% yield but the product contained two diastereomers in about a 2:1 ratio. *N*-1-Naphthylmethyllactamide **2h** also gave a 93% yield of **4h**, which was subjected to X-ray crystallographic analysis for structural elucidation (vide infra).

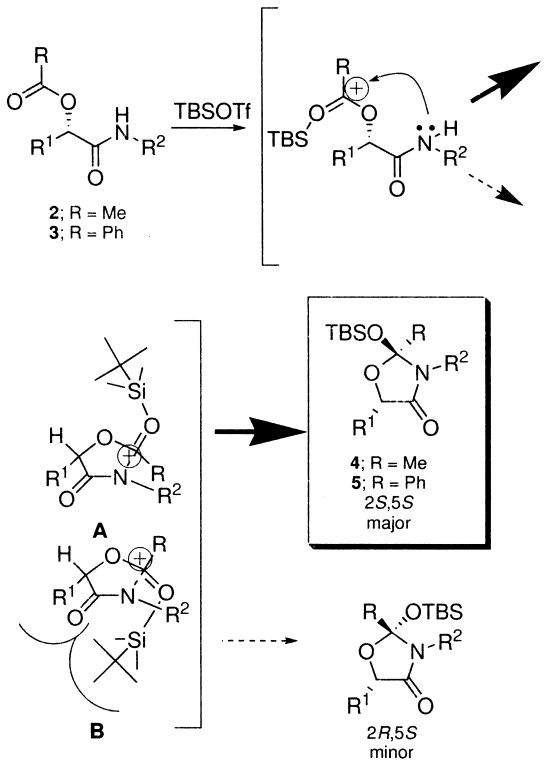
Although the formation of oxyoxazolidinones **4** from lactamides **2** was accomplished stereoselectively, their chemical stability was somewhat problematic. When stored in $CDCl_3$ solution, most of **4a** decomposed into its starting material **2a** within 24 h. This could be serious setback for the further synthetic use of **4**, and so we examined mandelamide to see if we could improve the stability. Preparation of starting materials **3** was carried out in a similar manner to the preparation of **2**. The ring enclosure reactions for **3** progressed again in a spot-to-spot manner and the desired oxyoxazolidinones **5** were isolated in good yields (entries 9–15). The stereoselectivity of the ring formation was usually good to high. Acetate or substituted acrylate as well as benzoate or other alkanoates gave **5** in an excellent stereoselectivity which was in direct contrast to the formation of **4** from lactamides **2**. It should be remarked that all of compounds **5** were stable enough for further chemical treatment or storage. For example, no decomposition was observed for compound **5a** in $CDCl_3$ even after more than several weeks.



Scheme 2. NOE experiments for **4A**-**a** and **4A**-**b**.

The structures of **4** and **5** were determined in the following way: ^{13}C NMR spectrum for compound **4a**, for example, showed one carbonyl carbon and one quaternary carbon that appeared at around 110 ppm. These observations reflected that one of the two carbonyl carbons in **2a** was lost during the conversion to **4a**. The ^1H and ^{13}C NMR spectra suggested that 4a possessed the 2-oxy-1,3-oxazolidin-4-one structure, which was also supported by microanalytical data for **4a**. The structure and the configuration at C2 of **4** were finally confirmed by an X-ray crystallographic analysis for compound **4h**, which clearly indicated the two methyl groups at C2 and C5 positions were located in *cis*.[6] NOE experiments for **4a** and **4h** showed that 5 and 4.5%, respectively, of signal enhancement occurred at the methyl group in TBS when either of the H5 was irradiated (Scheme 2). This observation suggested that **4a** and **4h** held the same configuration at C2 and C5. A similar signal enhancement was also seen in the NOE experiment for **5a**. Based on these results as well as the comparison of NMR and HPLC behavior, the oxyoxazolidinone structure for other **4** and **5** was confirmed.

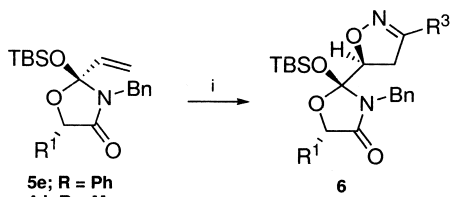
The observed stereoselectivity was very high and it was more than we had expected. If the ring enclosure had taken place through the direct nucleophilic attack of the amide nitrogen to the free-acyl carbonyl carbon, it would be hard to imagine what factor would bring the current high stereoselectivity. We assumed that some activation on the carbonyl must take place before the actual ring enclosure happened because both the acyl carbonyl and the amide nitrogen generally showed very weak reactivity for the nucleophilic addition. The present reaction was affected by the electronic nature of acyl carbonyl carbon; an electron-withdrawing group at the acyl carbon, that usually enhances the nucleophilic addition to the carbonyl, lowered the yield and made the selectivity poor. Additionally, other TBS source such as TBSCl was quite inert to the reaction. Thus, we assume the initial step of the reaction is likely the coordination of the TBS group to the carbonyl group, which



Scheme 3.

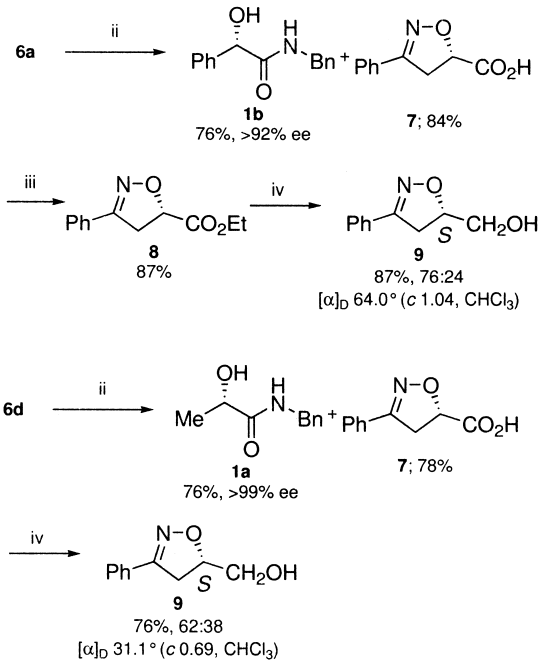
is then activated to the nucleophilic attack by the secondary amide nitrogen. Scheme 3 shows a plausible reaction process. Due to the bulkiness of the TBS group coordinating the carbonyl, intermediate **B** should be less favored than **A**, which leads the 2*S*,5*S* isomers, the major isomer formed in the actual reaction. The electron withdrawing substituent at *R* position, on the other hand, reduces the Lewis basicity of the carbonyl group so that the coordination of the TBS group would be prevented. Thus, the reaction proceeds through the interaction between the non-TBS coordinated carbonyl group and the amide nitrogen and the stereoselectivity and/or reaction rates are spoiled.

Use of oxyoxazolidinone for asymmetric synthesis was examined. The 1,3-dipolar cycloaddition of nitrile oxides is regarded as a useful reaction to construct carbon backbones[7] and its asymmetric modification has been developed so far.[8] The vinyl group in **5e**, for example, underwent cycloaddition with benzonitrile oxide in hexane, giving 4,5-dihydroisoxazole **6a** in a 61% yield (Scheme 4). The diastereomeric ratio of **6a** was found to be 70:30. Use of



6a; R^1 = Ph, R^3 = Ph; 61%, 70:30 (in hexane), 63%, 82:18 (in CH_2Cl_2)
6b; R^1 = Ph, R^3 = p-Cl-C_6H_4-; 56%, 80:20 (in CH_2Cl_2)
6c; R^1 = Ph, R^3 = PhCH=CH-; 29%, 80:20 (in CH_2Cl_2)
6d; R^1 = Me, R^3 = Ph; 64%, 75:25 (in hexane)

Scheme 4. *Reagents*: (i) $R^3CCl{=}NOH$, Et_3N, hexane or CH_2Cl_2, 0°C.



Scheme 5. *Reagents*: (i) TBAF, THF, rt, 10 min; (ii) WSC·EtOH; (iii) L-Selectiride, THF, rt; (iv) BH_3·THF, THF, −10°C.

CH_2Cl_2 as the reaction solvent improved the stereoselectivity to 82:18. Other aromatic nitrile oxides also gave chiral 4,5-dihydroisoxazoles **6b** and **6c** with good diastereoselectivity. The lactamide-derived oxyoxazolidinone **4d** also underwent the dipolar addition in a similar way. To determine the absolute stereogenic center at C5 in the 4,5-dihydroisoxazole, the major isomer of **6a** was separated and treated with TBAF (Scheme 5). To our surprise, mandelamide-free 4,5-dihydroisoxazole-5-carboxylic acid **7** was isolated in an 84% yield along with recovery of mandelamide **1b**. Esterification followed by reductive treatment of **7** resulted in the formation of the corresponding alcohol **9**, which showed dextrorotatory. Comparison of the optical rotation of known **9** unambiguously revealed the absolute configuration at C5 was *S*.[9] Treatment of **6d** in a similar way afforded **9** that also showed dextrorotatory.

In conclusion, we have found the first convenient method to prepare 2-oxy-1,3-oxazolidin-4-one, novel nitrogen analogs of orthoesters, in a highly stereoselective manner. Use of this preparation enables one to construct the orthoester carbon in a stereochemically defined way. Recovery of chiral mandelamide from 2-oxy-1,3-oxazolidin-4-one was readily accomplished by treatment with TBAF. Further investigation on the use of this structure for asymmetric synthesis is now underway in our laboratory.

3. Experimental

3.1. General

All ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ and recorded on JEOL EX-270 (270 MHz for ^1H and 67.5 MHz for ^{13}C) or Brucker Advance 400 (400 MHz for ^1H and 100 MHz for ^{13}C) spectrometer. All the reactions in this paper were performed under nitrogen atmosphere. Solvents

used in the reaction described here were dried over CaH_2 and distilled under nitrogen before use. Optically active lactic acid and mandelic acid were from Aldrich and used without further purification.

3.1.1. Preparation of *O*-benzoyl-*N*-benzyllactamide (2b). General procedure. To a mixture of **1a** (0.5522 g, 3.08 mmol), Et_3N (0.48 mL, 3.25 mmol), and DMAP (0.1236 g, 1.01 mmol) in CH_2Cl_2 (20 mL) at 0°C was added benzoyl chloride (0.52 mL, 3.25 mmol) and the reaction mixture was allowed to stir for 7 h. Aqueous dil HCl was added to the reaction mixture and the resulting biphasic mixture was extracted with CH_2Cl_2 (3×30 mL). The combined organic phase was washed with sat. $NaHCO_3$ and brine, and dried over Na_2SO_4. Filtration and removal of solvent gave a crude product, which was purified through flash chromatography (silica gel/hexane–ethyl acetate 10:1 v/v then 5:1) to give **2b** in 84% yield. White solid. Mp 84°C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.65 (d, 3H, J=6.6 Hz), 4.51 (dd, 2H, J=2.0, 5.9 Hz), 5.54 (q, 1H, J=6.9 Hz), 6.46 (br, 1H), 7.24–8.05 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 17.9, 43.2, 71.1, 127.5, 127.5, 128.4, 128.6, 128.7, 130.1, 133.5, 137.8, 165.3, 170.4. Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94%. Found: C, 72.11; H, 6.05; N, 4.71.

Other chiral or racemic *O*-acyl-*N*-benzyllactamides and mandelamides were prepared in a similar procedure.

3.1.2. (*S*)-*O*-Acetyl-*N*-benzyllactamide (2a). White solid. Mp 65–66°C. $[\alpha]_D$=−178.0° (*c* 1.00, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.51 (d, 3H, J=6.6 Hz), 2.11 (s, 3H), 4.48 (d, 2H, J=5.6 Hz), 5.25 (q, 1H, J=6.8 Hz), 6.39 (br, 1H), 7.27–7.39 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 17.8, 20.9, 43.0, 70.5, 127.5, 128.6, 137.8, 169.4, 170.3. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33%. Found: C, 65.43; H, 6.78; N, 6.26.

3.1.3. (*S*)-*O*-Acryloyl-*N*-benzyllactamide (2d). Colorless oil. $[\alpha]_D$=−60.5° (*c* 1.04, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.55 (d, 3H, J=6.6 Hz), 4.46 (d, 1H, J=9.3 Hz), 4.51 (d, 1H, J=9.8 Hz), 5.36 (q, 1H, J=6.9 Hz), 5.91 (dd, 1H, J=1.3, 10.6 Hz), 6.16 (dd, 1H, J=10.6, 17.2 Hz), 6.40 (br, 1H), 6.48 (dd, 1H, J=1.3, 17.2 Hz), 7.27–7.39 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 17.7, 43.0, 70.5, 127.4, 128.6, 132.1, 137.7, 164.6, 170.4. Exact mass determination: 233.1080 (Calcd $C_{13}H_{15}NO_3$: 233.1052).

3.1.4. (*S*)-*N*-Benzyl-*O*-crtonoyllactamide (2e). White solid. Mp 50°C. $[\alpha]_D$=−156.5° (*c* 0.93, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.53 (d, 3H, J=6.9 Hz), 1.90 (dd, 3H, J=1.7, 6.9 Hz), 4.48 (d, 2H, J=6.6 Hz), 5.34 (q, 1H, J=6.8 Hz), 5.88 (qd, 1H, J=1.7, 15.6 Hz), 6.42 (br, 1H), 7.05 (qd, 1H, J=6.9, 15.5 Hz), 7.25–7.38 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 17.9, 18.0, 43.0, 70.2, 121.7, 127.5, 128.6, 137.8, 146.5, 164.9, 170.5. Exact mass determination: 247.1232 (Calcd $C_{14}H_{17}NO_3$: 247.1208).

3.1.5. (*S*)-*N*-Benzyl-*O*-cinnamoyllactamide (2f). White solid. Mp 101°C. $[\alpha]_D$=−112.9° (*c* 1.03, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.59 (d, 3H, J=6.6 Hz), 4.47 (dd, 1H, J=5.9, 14.9 Hz), 4.54 (dd, 1H, J=5.9, 14.9 Hz), 5.42 (q, 1H, J=6.8 Hz), 6.46 (d, 1H, J=15.8 Hz), 6.47 (br, 1H), 7.27–7.56 (m, 10H), 7.74 (d, 1H, J=16.2 Hz). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 17.8, 42.9, 70.4, 116.8, 127.3, 127.3, 128.0, 128.5, 128.2, 130.5, 133.7, 137.8, 146.0, 165.4, 170.4. Exact mass determination: 309.1367 (Calcd $C_{19}H_{19}NO_3$: 309.1365).

3.1.6. (*S*)-*N*-Benzyl-*O*-(3-ethoxycarbonylacryloyl)lactamide (2g). White solid. Mp 65°C. $[\alpha]_D$=−86.5° (*c* 0.96, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.32 (t, 3H, J=7.1 Hz), 1.57 (d, 3H, J=6.9 Hz), 4.27 (q, 2H, J=7.2 Hz), 4.49 (d, 2H, J=5.6 Hz), 5.37 (q, 1H, J=6.8 Hz), 6.38 (br, 1H), 6.86 (d, 1H, J=15.5 Hz), 6.93 (d, 1H, J=15.8 Hz), 7.27–7.39 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 14.4, 18.2, 43.5, 61.9, 71.8, 127.9, 129.1, 132.7, 135.3, 138.0, 163.9, 164.9, 170.1. Exact mass determination: 305.1241 (Calcd $C_{16}H_{19}NO_5$: 305.1263).

3.1.7. (*S*)-*O*-Acetyl-*N*-(1-naphtylmethyl)lactamide (2h). White solid. Mp 185°C. $[\alpha]_D$=−81.1° (*c* 1.10, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.50 (d, 1H, J=6.9 Hz), 2.03 (s, 1H), 4.88 (dd, 1H, J=5.3, 14.5 Hz), 4.97 (dd, 1H, J=5.3, 14.5 Hz), 5.24 (q, 1H, J=6.8 Hz), 6.34 (br, 1H), 7.41–7.99 (m, 7H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 17.9, 21.0, 41.5, 70.7, 123.3, 125.4, 126.1, 126.7, 128.8, 131.3, 133.0, 133.9, 169.4, 170.0. Exact mass determination: 271.1224 (Calcd $C_{16}H_{17}NO_3$: 271.1208).

3.1.8. (*S*)-*O*-Acetyl-*N*-benzylmandelamide (3a). White solid. Mp 75°C. $[\alpha]_D$=+115.4° (*c* 1.03, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.17 (s, 1H), 4.45 (dd, 1H, J=5.6, 14.8 Hz), 4.52 (dd, 1H, J=5.6, 14.8 Hz), 6.12 (s, 1H), 6.40 (br, 1H), 7.22–7.47 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 20.7, 43.0, 75.4, 127.2, 127.3, 127.3, 128.5, 128.5, 128.8, 135.4, 137.7, 168.3, 169.3. Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94%. Found: C, 72.13; H, 6.20; N, 4.95.

3.1.9. (*S*)-*O*-Benzoyl-*N*-benzylmandelamide (3b). White solid. Mp 104–105°C. $[\alpha]_D$=+57.8° (*c* 1.27, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.48 (dd, 1H, J=5.9, 15.2 Hz), 4.56 (dd, 1H, J=5.8, 15.2 Hz), 6.39 (s, 1H), 6.46 (br, 1H), 7.21–8.19 (m, 15H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 43.7, 76.4, 127.7, 127.9, 128.9, 129.1, 129.2, 129.4, 129.5, 129.8, 130.5, 134.0, 135.8, 138.0, 165.4, 168.9, 172.1. Anal. Calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06%. Found: C, 76.37; H, 5.54; N, 3.60.

3.1.10. (*S*)-*N*-Benzyl-*O*-isobutyroylmandelamide (3c). White solid. Mp 61–62°C. $[\alpha]_D$=+99.8° (*c* 1.22, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.17 (d, 3H, J=6.9 Hz), 1.19 (d, 1H, J=7.3 Hz), 2.66 (m, 1H, J=7.0 Hz), 4.42 (dd, 1H, J=5.9, 15.2 Hz), 4.49 (dd, 1H, J=5.9, 15.2 Hz), 6.11 (s, 1H), 6.46 (br, 1H), 7.19–7.46 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 18.8, 33.8, 43.3, 75.2, 127.1, 127.5, 127.6, 128.7, 128.9, 135.6, 137.6, 168.4, 175.2. Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50%. Found: C, 73.01; H, 6.81; N, 4.21.

3.1.11. (*S*)-*N*-Benzyl-*O*-heptanoylmandellactamide (3d). Yellow oil. $[\alpha]_D$=+91.6° (*c* 1.01, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (t, 3H, J=6.8 Hz), 1.24–1.28 (m, 6H), 1.56–1.65 (m, 2H), 2.43 (t, 2H, J=7.2 Hz), 4.49 (d, 2H, J=5.9 Hz), 6.14 (s, 1H), 6.41 (br, 1H), 7.22–7.46 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 13.9, 22.3, 24.7,

28.6, 31.3, 34.1, 43.2, 75.2, 127.2, 127.5, 128.5, 128.6, 128.9, 135.6, 137.6, 168.4, 172.0. Anal. Calcd for $C_{22}H_{27}NO_3$: C, 74.76; H, 7.70; N, 3.96%. Found: C, 74.70; H, 7.70; N, 3.96.

3.1.12. (*S*)-*O*-Acryroyl-*N*-benzylmandelamide (3e). Colorless oil. $[\alpha]_D$=+107.1° (*c* 1.10, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.45 (dd, 1H, *J*=5.8, 15.2 Hz), 4.53 (dd, 1H, *J*=5.8, 15.2 Hz), 5.93 (dd, 1H, *J*=1.3, 10.6 Hz), 6.22 (dd, 1H, *J*=10.2, 17.2 Hz), 6.43 (br, 1H), 6.51 (dd, 1H, *J*=1.3, 17.5 Hz), 7.22–7.49 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 43.1, 75.5, 127.0, 127.2, 127.3, 127.4, 128.5, 128.6, 128.8, 132.4, 135.3, 137.6, 164.4, 168.2.

3.1.13. (*S*)-*N*-Benzyl-*O*-cinnamoylmandelamide (3f). White solid. Mp 136°C. $[\alpha]_D$=+47.6° (*c* 1.10, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.52 (dd, 1H, *J*=6.2, 14.8 Hz), 4.56 (dd, 1H, *J*=6.6, 14.8 Hz), 6.29 (s, 1H), 6.50 (br, 1H), 6.53 (d, 1H, *J*=16.2 Hz), 7.24–7.54 (m, 15H), 7.77 (d, 1H, *J*=15.9 Hz). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 43.4, 75.5, 116.6, 127.4, 127.6, 127.7, 128.2, 128.7, 128.8, 128.9, 129.9, 130.7, 133.9, 135.6, 137.7, 146.7, 165.2, 168.4. Anal. Calcd for $C_{24}H_{21}NO_3$: C, 77.61; H, 5.70; N, 3.77%. Found: C, 77.45; H, 5.98; N, 3.32.

3.1.14. (*S*)-*N*-Benzyl-*O*-(3-ethoxycarbonylacryloyl)-mandelmaide (3g). White solid. Mp 96–97°C. $[\alpha]_D$=+68.2° (*c* 1.14, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.31 (t, 3H, *J*=7.1 Hz), 4.26 (q, 2H, *J*=7.3 Hz), 4.45 (dd, 1H, *J*=5.3, 14.9 Hz), 4.53 (dd, 1H, *J*=5.6, 14.8 Hz), 6.21 (s, 1H), 6.37 (br, 1H), 6.93 (s, 2H), 7.21–7.48 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 13.9, 43.3, 61.4, 76.1, 127.4, 127.5, 128.6, 128.8, 129.2, 132.2, 134.8, 135.0, 137.5, 163.4, 164.5, 167.8. Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81%. Found: C, 68.33; H, 5.72; N, 3.77.

3.1.15. Preparation of (2*S*,5*S*)-*N*-benzyl-2-(*tert*-butyldimethylsilyloxy)-2,5-dimethyl-1,3-oxazolidine-4-one (4a). General procedure. 2,6-Lutidine (0.54 mL, 3.77 mmol), DMAP (0.0834 g, 0.68 mmol), and TBSOTf (0.51 mL, 1.78 mmol) were added to a solution of lactamide **2a** (0.2251 g, 1.01 mmol) in CH_2Cl_2 at 0°C in this order. After 23 h, pyridine was added and the solvent was removed in vacuo. The residue was subjected through flash chromatography (silica gel/hexane–ethyl acetate 10:1 v/v) to give **4a** in 90% yield as colorless oil (0.3078 g). $[\alpha]_D$=−153.9° (*c* 1.19, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.05 (s, 3H), 0.11 (s, 3H), 0.82 (s, 9H), 1.39 (s, 3H), 1.43 (d, 3H, *J*=6.6 Hz), 4.15 (d, 1H, *J*=15.2 Hz), 4.44 (q, 1H, *J*=6.6 Hz), 4.75 (d, 1H, *J*=15.6 Hz), 7.22–7.31 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.7, −3.6, 17.7, 18.0, 25.6, 29.2, 43.3, 72.9, 110.2, 127.4, 127.8, 128.5, 137.4, 172.8. Anal. Calcd for $C_{18}H_{29}NO_3Si$: C, 64.44; H, 8.71; N, 4.17%. Found: C, 64.15; H, 8.57; N, 4.15.

Other chiral oxyoxazolidinones **4** and **5** were prepared in a similar procedure. Their physical data are listed below.

3.1.16. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-5-methyl-2-phenyl-1,3-oxazolidine-4-one (4b). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.07 (s, 3H), 0.07 (s, 3H), 0.83 (s, 9H), 1.63 (d, 3H, *J*=6.8 Hz), 4.10 (d, 1H, *J*=15.2 Hz), 4.39 (d, 1H, *J*=15.2 Hz), 4.71 (q, 1H, *J*=6.7 Hz), 6.99–7.48 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ −3.7, −3.3, 17.7, 18.0, 25.9, 43.6, 73.3, 110.5, 125.8, 127.0, 128.1, 128.2, 128.3, 129.3, 136.9, 139.8, 172.1.

3.1.17. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-5-methyl-2-vinyl-1,3-oxazolidine-4-one (4d). Colorless oil. $[\alpha]_D$=−44.4° (*c* 0.78, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.05 (s, 3H), 0.09 (s, 3H), 0.83 (s, 9H), 1.47 (d, 3H, *J*=6.9 Hz), 4.31 (d, 1H, *J*=15.5 Hz), 4.50 (d, 1H, *J*=15.2 Hz), 4.55 (q, 1H, *J*=6.9 Hz), 5.18 (dd, 1H, *J*=3.3, 8.6 Hz), 5.58 (d, 1H, *J*=2.6 Hz), 5.59 (d, 1H, *J*=8.6 Hz), 7.21–7.31 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.6, −3.5, 17.8, 18.2, 25.6, 43.2, 73.2, 108.5, 118.1, 127.2, 128.2, 128.3, 137.0, 137.6, 172.2. MS (FAB) *m/z* 348 [(M+H)$^+$, 55%].

3.1.18. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-5-methyl-2-(1-propenyl)-1,3-oxazolidine-4-one (4e). Colorless oil. $[\alpha]_D$=−84.3° (*c* 1.37, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.08 (s, 3H), 0.82 (s, 9H), 1.46 (d, 3H, *J*=6.9 Hz), 1.58 (dd, 3H, *J*=1.7, 6.9 Hz), 4.26 (d, 1H, *J*=15.2 Hz), 4.51 (d, 1H, *J*=15.2 Hz), 4.52 (q, 1H, *J*=6.5 Hz), 5.21 (dd, *J*=1.7, 15.2 Hz), 5.98 (qd, 1H, *J*=6.7, 15.2 Hz), 7.20–7.30 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ −3.5, −3.4, 17.0, 18.0, 18.3, 25.8, 43.4, 73.2, 108.7, 127.2, 128.3, 128.4, 130.2, 131.4, 137.4, 172.2.

3.1.19. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-5-methyl-2-[1-(2-phenylethenyl)]-1,3-oxazolidine-4-one (4f). Colorless oil. $[\alpha]_D$=−144.4° (*c* 1.15, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.09 (s, 3H), 0.12 (s, 3H), 0.88 (s, 9H), 1.52 (d, 3H, *J*=6.6 Hz), 4.30 (d, 1H, *J*=15.2 Hz), 4.59 (q, 1H, *J*=6.7 Hz), 4.63 (d, 1H, *J*=15.2 Hz), 5.78 (d, 1H, *J*=15.5 Hz), 6.82 (d, 1H, *J*=15.8 Hz), 7.10–7.29 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.6, −3.5, 17.9, 18.2, 25.7, 43.3, 73.2, 108.9, 126.8, 126.9, 127.2, 128.3, 128.4, 128.5, 128.8, 132.7, 135.3, 137.2, 172.1.

3.1.20. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-[1-(2-ethoxycarbonylethenyl)]-5-methyl-1,3-oxazolidine-4-one (4g). Colorless oil. $[\alpha]_D$=−86.7° (*c* 1.54, $CHCl_3$). For major isomer ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.06 (s, 3H), 0.10 (s, 3H), 0.85 (s, 9H), 1.23 (t, 3H, *J*=7.1 Hz), 1.50 (d, 3H, *J*=6.9 Hz), 4.12 (q, 1H, *J*=7.1 Hz), 4.25 (d, 1H, *J*=15.2 Hz), 4.57 (q, 1H, *J*=6.8 Hz), 4.64 (d, 1H, *J*=15.2 Hz), 6.07 (d, 1H, *J*=15.2 Hz), 6.39 (d, 1H, *J*=15.5 Hz), 7.21–7.30 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.7, −3.5, 14.1, 18.2, 25.6, 43.3, 60.7, 73.6, 107.5, 123.1, 127.5, 128.3, 128.5, 136.5, 144.5, 165.4, 171.7.

For minor isomer ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.11 (s, 3H), 0.88 (s, 9H), 1.23 (t, 3H, *J*=7.1 Hz), 1.54 (d, 3H, *J*=6.9 Hz), 4.12 (q, 1H, *J*=7.1 Hz), 4.31 (d, 1H, *J*=15.2 Hz), 4.50 (q, 1H, *J*=6.8 Hz), 4.61 (d, 1H, *J*=14.8 Hz), 5.99 (d, 1H, *J*=15.5 Hz), 6.42 (d, 1H, *J*=15.2 Hz), 7.21–7.30 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.2, −3.2, 17.5, 17.9, 25.6, 43.3, 60.7, 74.2, 107.3, 121.7, 127.6, 128.3, 128.5, 136.5, 142.9, 165.4, 170.8. MS (FAB) *m/z* 420 [(M+H)$^+$, 90%].

3.1.21. (2*S*,5*S*)-2-(*tert*-Butyldimethylsilyloxy)-2,5-dimethyl-*N*-(1-naphthylmethyl)-1,3-oxazolidine-4-one (4h).

White plate. $[\alpha]_D=-39.0°$ (*c* 1.10, $CHCl_3$). Mp 82–83°C. ^1H NMR (270 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.10 (s, 3H), 0.81 (s, 9H), 1.25 (s, 3H), 1.46 (d, 3H, *J*=6.6 Hz), 4.50 (q, 1H, *J*=6.8 Hz), 4.71 (d, 1H, *J*=15.5 Hz), 5.25 (d, 1H, *J*=15.5 Hz), 7.22–8.11 (m, 7H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.7, −3.6, 17.6, 18.0, 25.5, 28.8, 41.5, 72.7, 110.3, 123.4, 125.0, 125.8, 126.5, 126.8, 128.5, 128.6, 131.4, 132.3, 133.7, 172.6. MS (FAB) *m/z* 386 [$(M+H)^+$, 50%].

3.1.22. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-2-methyl-5-phenyl-1,3-oxazolidine-4-one (5a). White solid. $[\alpha]_D=+57.2°$ (*c* 1.27, $CHCl_3$). Mp 87–88°C. ^1H NMR (270 MHz, $CDCl_3$) δ 0.14 (s, 3H), 0.17 (s, 3H), 0.87 (s, 9H), 1.54 (s, 3H), 4.20 (d, 1H, *J*=15.5 Hz), 4.68 (d, 1H, *J*=15.5 Hz), 5.33 (s, 1H), 7.22–7.46 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.6, 17.7, 25.5, 28.8, 43.6, 78.0, 110.3, 126.3, 127.4, 127.8, 128.6, 128.6, 136.0, 137.3, 170.5. Anal. Calcd for $C_{23}H_{31}NO_3Si$: C, 69.48; H, 7.86; N, 3.52%. Found: C, 69.39; H, 8.11; N, 3.49.

3.1.23. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-2,5-diphenyl-1,3-oxazolidine-4-one (5b). Colorless oil. $[\alpha]_D=-13.5°$ (*c* 1.24, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 0.02 (s, 3H), 0.15 (s, 3H), 0.88 (s, 9H), 4.21 (d, 1H, *J*=15.2 Hz), 4.43 (d, 1H, *J*=15.2 Hz), 5.60 (s, 1H), 7.00–7.61 (m, 15H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.7, −3.2, 18.0, 25.6, 25.8, 43.9, 77.7, 110.6, 126.8, 127.0, 127.2, 128.0, 128.1, 128.2, 128.3, 128.5, 129.3, 135.2, 136.6, 139.4, 169.8.

3.1.24. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-2-isopropyl-5-phenyl-1,3-oxazolidine-4-one (5c). Colorless oil. $[\alpha]_D=+42.4°$ (*c* 1.00, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 0.12 (s, 3H), 0.22 (s, 3H), 0.41 (d, 3H, *J*=6.9 Hz), 0.93 (s, 9H), 0.99 (d, 3H, *J*=6.6 Hz), 2.00 (m, 1H, *J*=6.7 Hz), 4.17 (d, 1H, *J*=14.8 Hz), 4.80 (d, 1H, *J*=14.8 Hz), 5.43 (s, 1H), 7.21–7.58 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.9, −3.2, 16.2, 16.9, 18.0, 25.7, 36.9, 44.2, 77.2, 114.5, 126.4, 127.5, 127.6, 128.2, 128.4, 128.7, 135.4, 136.9, 170.6.

3.1.25. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-2-hexyl-5-phenyl-1,3-oxazolidine-4-one (5d). Colorless oil. $[\alpha]_D=+54.2°$ (*c* 1.11, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.20 (s, 3H), 0.80 (t, 3H, *J*=6.3 Hz), 0.90 (s, 9H), 0.77–1.29 (m, 8H), 1.58–1.89 (m, 2H), 4.17 (d, 1H, *J*=15.2 Hz), 4.82 (d, 1H, *J*=15.2 Hz), 5.36 (s, 1H), 7.23–7.51 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.6, −3.3, 13.9, 17.8, 22.3, 23.6, 25.6, 28.6, 31.4, 40.2, 43.9, 77.7, 112.5, 126.6, 127.5, 128.3, 128.4, 128.5, 128.7, 135.6, 137.1, 170.9.

3.1.26. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-5-phenyl-2-vinyl-1,3-oxazolidine-4-one (5e). Colorless oil. $[\alpha]_D=+19.0°$ (*c* 1.42, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 0.14 (s, 3H), 0.15 (s, 3H), 0.87 (s, 9H), 4.35 (d, 1H, *J*=15.2 Hz), 4.57 (d, 1H, *J*=15.2 Hz), 5.27 (dd, 1H, *J*=2.0, 9.6 Hz), 5.42 (s, 1H), 5.64 (dd, 1H, *J*=1.7, 16.8 Hz), 5.76 (dd, 1H, *J*=9.6, 16.8 Hz), 7.21–7.49 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.5, −3.4, 18.0, 25.7, 43.6, 78.2, 108.9, 118.9, 126.5, 127.3, 128.3, 128.6, 128.7, 135.9, 137.0, 137.1, 170.0. Anal. Calcd for $C_{24}H_{31}NO_3Si$: C, 70.38; H, 7.63; N, 3.42%. Found: C, 70.13; H, 7.82; N, 3.37.

3.1.27. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-5-phenyl-2-[1-(2-phenylethenyl)]-1,3-oxazolidine-4-one (5f). Colorless oil. $[\alpha]_D=+95.9°$ (*c* 1.95, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 0.18 (s, 6H), 0.93 (s, 9H), 4.34 (d, 1H, *J*=15.2 Hz), 4.70 (d, 1H, *J*=15.2 Hz), 5.46 (s, 1H), 5.91 (d, 1H, *J*=15.5 Hz), 6.91 (d, 1H, *J*=15.5 Hz), 7.13–7.53 (m, 15H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.7, −3.4, 17.9, 25.7, 43.6, 78.2, 109.3, 126.5, 126.9, 127.2, 127.4, 127.9, 128.1, 128.4, 128.5, 128.6, 128.9, 133.4, 135.2, 135.8, 137.1, 169.8. Anal. Calcd for $C_{30}H_{35}NO_3Si$: C, 74.19; H, 7.26; N, 2.88%. Found: C, 73.85; H, 7.55; N, 2.79.

3.1.28. (2*S*,5*S*)-*N*-Benzyl-2-(*tert*-butyldimethylsilyloxy)-5-phenyl-2-[1-(2-ethoxycarbonylethenyl)]-1,3-oxazolidine-4-one (5g). For major isomer: Colorless oil. $[\alpha]_D=+64.3°$ (*c* 0.69, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 3H), 0.10 (s, 3H), 0.90 (s, 9H), 1.24 (t, 3H, *J*=7.1 Hz), 4.13 (q, 2H, *J*=7.2 Hz), 4.28 (d, 1H, *J*=15.2 Hz), 4.68 (d, 1H, *J*=15.2 Hz), 5.44 (s, 1H), 6.14 (d, 1H, *J*=15.4 Hz), 6.51 (d, 1H, *J*=15.4 Hz), 7.13–7.53 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.5, −3.5, 14.1, 17.9, 25.7, 43.7, 60.7, 78.3, 107.8, 123.9, 126.4, 127.6, 128.2, 128.4, 128.5, 128.6, 135.2, 136.4, 143.8, 165.3, 169.6. Anal. Calcd for $C_{27}H_{35}NO_5Si$: C, 67.33; H, 7.32; N, 2.91%. Found: C, 67.09; H, 7.45; N, 2.93.

For minor isomer: colorless oil. $[\alpha]_D=+30.6°$ (*c* 0.217, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.07 (s, 3H), 0.83 (s, 9H), 1.26 (t, 3H, *J*=7.1 Hz), 4.13 (q, 2H, *J*=7.2 Hz), 4.45 (d, 1H, *J*=15.2 Hz), 4.65 (d, 1H, *J*=15.2 Hz), 5.37 (s, 1H), 6.13 (d, 1H, *J*=16.4 Hz), 6.56 (d, 1H, *J*=15.4 Hz), 7.21–7.49 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.3, −3.1, 14.1, 17.9, 25.6, 43.6, 60.8, 79.4, 107.4, 121.8, 127.5, 127.7, 128.3, 128.5, 128.6, 128.9, 135.0, 136.6, 142.8, 165.5, 168.8.

3.2. 1,3-Dipolar cycloaddition to 5e

To a mixture of **5e** (0.4320 g, 1.05 mmol) and benzohydroximic chloride (0.2462 g, 1.58 mmol) in CH_2Cl_2 (1.1 mL) at 0°C was added Et_3N (0.23 mL, 1.58 mmol) over 24 h. Water (20 mL) was added to the reaction mixture and the resulting biphasic mixture was extracted with CH_2Cl_2 (30 mL×3). The organic phase was combined and dried over $MgSO_4$. Removal of solvent gave the crude product that was purified through flash chromatography (silica gel/hexane–ether 30:1 v/v then 20:1 to 10:1) to give 4,5-dihydroisoxazole **6a** in 63% yield (0.3513 g, 0.67 mmol) along with the recovery of the starting material **5e** (0.0409 g, 0.1 mmol). The diastereomeric ratio of the crude product was determined by HPLC analysis (chiral pak AD, hexane/2-PrOH 92:8, v/v) to be 82:18. The two of diastereomers were separated by careful chromatographic treatment.

3.2.1. For major isomer of 6a. Colorless oil. $[\alpha]_D=+161.0°$ (*c* 0.55, $CHCl_3$). ^1H NMR (270 MHz, $CDCl_3$) δ 0.24 (s, 3H), 0.25 (s, 3H), 0.92 (s, 9H), 3.26 (dd, 1H, *J*=11.4, 17.0 Hz), 3.43 (dd, 1H, *J*=7.9, 17.2 Hz), 4.37 (d, 1H, *J*=15.2 Hz), 4.68 (dd, 1H, *J*=8.1, 11.4 Hz), 4.88 (d, 1H,

J=15.2 Hz), 5.41 (s, 1H), 7.20–7.56 (m, 15H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −4.0, −3.1, 17.8, 25.5, 35.9, 44.0, 79.9, 81.5, 110.5, 126.5, 127.1, 127.6, 128.2, 128.3, 128.4, 128.5, 128.6, 129.1, 130.0, 134.7, 135.9, 155.8, 170.4. Anal. Calcd for $C_{31}H_{36}N_2O_4Si$: C, 70.42; H, 6.86; N, 5.30%. Found: C, 70.32; H, 7.22; N, 4.90.

For minor isomer of **6a**: $[\alpha]_D$=+25.6° (c 0.68, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.09 (s, 3H), 0.16 (s, 3H), 0.77 (s, 9H), 2.70 (dd, 1H, J=11.2, 17.5 Hz), 2.96 (dd, 1H, J=5.9, 17.2 Hz), 4.25 (d, 1H, J=14.9 Hz), 4.53 (dd, 1H, J=6.1, 11.4 Hz), 4.85 (d, 1H, J=15.2 Hz), 5.33 (s, 1H), 7.04–7.38 (m, 15H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −3.8, −3.3, 18.0, 25.5, 37.0, 44.2, 77.3, 84.2, 109.9, 125.6, 126.6, 127.7, 128.4, 128.5, 128.6, 128.9, 130.0, 134.9, 136.7, 155.9, 170.4. Anal. Calcd for $C_{31}H_{36}N_2O_4Si$: C, 70.42; H, 6.86; N, 5.30%. Found: C, 70.46; H, 7.09; N, 5.10.

Other cycloadducts **6b**, **6c** and **6d** were obtained in a similar procedure. Their physical data are listed below.

3.2.2. Cycloadduct (6b). Colorless oil. $[\alpha]_D$=+117.0° (c 0.38, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.16 (s, 3H), 0.25 (s, 3H), 0.93 (s, 9H), 3.21 (dd, 1H, J=11.6, 17.2 Hz), 3.37 (dd, 1H, J=7.9, 17.2 Hz), 4.34 (d, 1H, J=15.5 Hz), 4.66 (dd, 1H, J=7.9, 11.6 Hz), 4.90 (d, 1H, J=15.5 Hz), 5.41 (s, 1H), 7.20–7.52 (m, 14H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −4.1, −3.2, 17.8, 25.5, 35.7, 44.0, 78.7, 81.1, 110.4, 126.5, 127.1, 127.5, 127.6, 127.7, 128.2, 128.3, 128.5, 128.6, 128.8, 134.6, 135.8, 154.9, 170.4. Anal. Calcd for $C_{31}H_{35}ClN_2O_4Si$: C, 66.11; H, 6.26; N, 4.97%. Found: C, 65.95; H, 6.48; N, 4.77.

3.2.3. Cycloadduct (6c). Colorless oil. $[\alpha]_D$=+156.4° (c 0.20, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.15 (s, 3H), 0.27 (s, 3H), 0.92 (s, 9H), 3.07 (dd, 1H, J=11.5, 16.5 Hz), 3.29 (dd, 1H, J=8.6, 16.8 Hz), 4.38 (d, 1H, J=15.5 Hz), 4.65 (dd, 1H, J=8.4, 11.4 Hz), 4.84 (d, 1H, J=15.5 Hz), 5.41 (s, 1H), 6.60 (d, 1H, J=16.5 Hz), 6.89 (d, 1H, J=16.5 Hz), 7.22–7.56 (m, 15H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −4.0, −3.1, 17.8, 25.5, 34.4, 44.0, 78.8, 81.2, 110.3, 117.5, 126.9, 127.1, 127.6, 127.7, 128.2, 128.4, 128.7, 128.8, 128.9, 134.7, 135.6, 136.0, 136.3, 157.0, 170.5. Anal. Calcd for $C_{33}H_{38}N_2O_4Si$: C, 71.45; H, 6.90; N, 5.05%. Found: C, 71.43; H, 7.52; N, 4.49.

3.2.4. Cycloadduct (6d). Colorless oil. $[\alpha]_D$=+71.5° (c 0.39, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.18 (s, 3H), 0.83 (s, 9H, for minor isomer), 0.91 (s, 9H, for major isomer),1.43 (d, 3H, J=6.9 Hz, for minor isomer), 1.48 (d, 3H, J=6.9 Hz, for major isomer), 2.87 (dd, 1H, J=10.4, 16.7 Hz, for minor isomer), 3.11 (dd, 1H, J=6.4, 17.3 Hz, for minor isomer), 3.23 (dd, 1H, J=11.4, 17.0 Hz, for major isomer), 3.39 (dd, 1H, J=6.9, 17.2 Hz, for major isomer), 4.24 (d, 1H, J=15.5 Hz, for major isomer), 4.33 (d, 1H, J=15.2 Hz, for minor isomer), 4.46 (dd, 1H, J=7.1, 11.4 Hz, for major isomer), 4.52 (q, 1H, J=6.8 Hz, for major isomer), 4.55 (q, 1H, J=6.1 Hz, for minor isomer), 4.85 (d, 1H, J=15.5 Hz, for major isomer), 7.24–7.62 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ −4.5, −4.1, −3.5, −3.3, 17.4, 17.7, 17.8, 18.0, 25.4, 25.5, 25.7, 35.7, 36.7, 43.3, 43.9, 73.2, 74.4, 80.2, 84.3, 109.5, 110.7, 126.4, 126.5, 126.6, 127.5, 127.6, 128.2, 128.3, 128.4, 128.5, 128.6, 128.9, 129.1, 130.0, 135.9, 136.9, 155.7, 156.0, 172.4, 172.8. MS (FAB) m/z 467 [$(M+H)^+$, 80%].

3.2.5. Preparation of (*S*)-4,5-dihydroisoxazole-5-carboxylic acid (7). To a solution of **6a** (0.320 g, 0.60 mmol) in THF (1.1 mL) at room temperature was added TBAF (1.0 M in THF, 0.7 mL). The reaction mixture was allowed to stir at 0°C for 30 min. Solvent was removed in vacuo and the residue was subjected to flash chromatography (silica gel/hexane–ethyl acetate 10:1 v/v then 1:1 to 1:2 and ethyl acetate–acetic acid 96:4 v/v) to give carboxylic acid **7** in 85% yield (0.0969 g, 0.51 mmol) and mandelamide (0.1247 g, 0.52 mmol).

$[\alpha]_D$=+67.0° (c 0.41, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.70 (dd, 1H, J=7.3, 17.4 Hz), 3.76 (dd, 2H, J=10.2, 17.1 Hz), 5.24 (dd, 1H, J=7.6, 9.9 Hz), 7.43–7.47 (m, 3H), 7.66–7.70 (m, 2H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 39.3, 77.2, 127.0, 128.5, 128.9, 130.2, 133.9, 156.5.

3.2.6. Preparation of (*S*)-5-ethoxycarbonyl-3-phenyl-4,5-dihydroisoxazole (8). To a solution of **7** (0.0969 g, 0.51 mmol), ethyl alcohol (0.07 mL, 1.23 mmol), and DMAP (1 mg) in CH_2Cl_2 at room temperature was added EDCI (0.1981 g, 1.04 mmol). The reaction mixture was allowed to stir at room temperature for 24 h. The reaction was quenched with dil HCl (1 M, 5 mL) and the mixture was extracted with CH_2Cl_2 (20 mL×3). The organic phase was combined and dried over $MgSO_4$. Removal of solvent gave the crude ethyl ester **8** in 87% yield. Yellow oil. $[\alpha]_D$=+105.0° (c 0.49, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.33 (t, 3H, J=7.1 Hz), 3.61 (dd, 1H, J=10.6, 16.8 Hz), 3.68 (dd, 2H, J=7.9, 17.1 Hz), 4.28 (q, 2H, J=7.2 Hz), 5.17 (dd, 1H, J=7.9, 10.2 Hz), 7.41–7.43 (m, 3H), 7.67–7.71 (m, 2H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 14.0, 38.8, 61.9, 76.5, 126.8, 128.5, 128.7, 130.4, 155.9, 170.1.

3.2.7. Preparation of (*S*)-5-hydroxymethyl-3-phenyl-4,5-dihydroisoxazole (9). To a solution of **8** (0.0601 g, 0.27 mmol) in THF (2 mL) at room temperature was added L-selectride (1.0 M in THF, 0.80 mL). Resulting solution was allowed to stir at ambient temperature for 30 min. The reaction was quenched with water (0.5 mL), KOH (20%, 0.5 mL) and H_2O_2 (30 wt%, 0.5 mL). The mixture was concentrated and the residue was subjected to flash chromatography (silica gel/hexane–ethyl acetate 1:1 v/v) to give **9** in 86% yield (0.0419 g, 0.24 mmol). $[\alpha]_D$=+64.0° (c 1.04, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.28 (dd, 1H, J=7.9, 16.8 Hz), 3.41 (dd, 1H, J=11.6, 17.5 Hz), 3.69 (dd, 1H, J=5.0, 12.2 Hz), 3.89 (dd, 1H, J=3.3, 12.2 Hz), 4.80 (m, 1H), 7.40–7.44 (m, 3H), 7.66–7.69 (m, 2H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 36.3, 63.5, 81.2, 126.6, 128.6, 129.2, 130.1, 157.0.

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