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Oxyoxazolidinone as an auxiliary for heterocyclic synthesis. Enantioselective formation of *N*-unprotected 2-pyrrolidones from selenocarboxylate and allylamines via radical cyclization

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Abstract—Optically active *N*-unprotected 2-pyrrolidones were prepared in a highly stereoselective manner through radical cyclization reaction of oxyoxazolidinone. Asymmetric induction from the oxyoxazolidinone ring system was generally high and oxazabicyclo[3.3.0]-octanones were obtained in good yields. Treatment of the bicyclic compounds with TBAF resulted in the one-step cleavage of C–O and C–N bond, directly giving secondary 2-pyrrolidones in good yields along with recovery of chiral mandelic acid without loss of optical purity. The use of the present procedure gave optically active 4,5-disubstituted *N*-unprotected 2-pyrrolidone derivatives *trans* selectively.

1. Introduction

The radical cyclization is frequently used as a key reaction for the construction of carbo- or heterocyclic compounds.[1] One of the merits of the reaction is that the cyclization occurs under the neutral conditions as well as bringing high regio- and/or stereoselectivity in the ring construction. 2-Pyrrolidone skeletons are often seen among natural products and the efficient construction of the heterocyclic compounds is sometimes of interest in organic synthesis.[2] Due to the planar structural feature of amide group, simple radical cyclization for secondary amides does not always work successfully; simple radical reduction often competes with the desired cyclization.[3] To overcome this setback, one solution is a strategy that introduces some substituent to make the amide group take on a favorable conformation for the cyclization. For example, existence of a temporary substituent on the amide nitrogen atom allows successful cyclization,[4,5] although this method always requires its removal step in later stage.[6] Recently, we have developed a ready preparation of a new type of chiral orthoester equivalent, oxyoxazolidinones, which is expected to be a potential chiral auxiliary for asymmetric synthesis.[7] So far we have examined 1,3-dipolar cycloaddition and the radical cyclization under the chiral environment brought by this novel heterocyclic structure and have achieved a good level of asymmetric induction. The most useful feature of the present strategy is that treatment with TBAF induces simultaneous cleavage of C–N and C–O bonds, and thus carves the desired secondary amides from the oxyoxazolidinone unit in good yields. Additionally, chiral mandelic acid is also recovered in good yields without loss of its optical purity. In this paper, we will report full details of a new type of synthesis of optically active *N*-unprotected 2-pyrrolidones via radical cyclization with chiral oxyoxazolidinone rings.

2. Results and discussion

The starting materials for the radical cyclization were prepared from EDCI coupling reaction of commercially available (*S*)-mandelic acid **1**, allyl amine, and carboxylic acid (Scheme 1). Obtained *O*-acyl-*N*-allylmandelamides **2** were used for the formation of oxyoxazolidinones **3**. The results are summarized in Table 1.

Treatment of **2a** with TBSOTf resulted in the formation of oxyoxazolidinone **3a** in a quantitative yield. The ring enclosure took 6 h for completion. The diastereoselectivity of the cyclization depended on the α-substituent of the *O*-acyl unit. Simple acetyl derivative, for example, gave **3aX** as an almost single isomer (entry 1). The configuration of **3** was determined by comparison with our previous results.[7] Bromoacetate **2b**, on the other hand, gave a diastereomeric mixture of **3b** although it was formed smoothly (entry 2). We examined phenylselenoacetate **2c** and the diastereoselectivity was improved to about a 6:1 level (entry 3). The major isomer **3cX** was isolated in a diastereomerically pure form by careful chromatographic treatment.

Keywords: radical cyclization; orthoesters; stereoselection; pyrrolidines.
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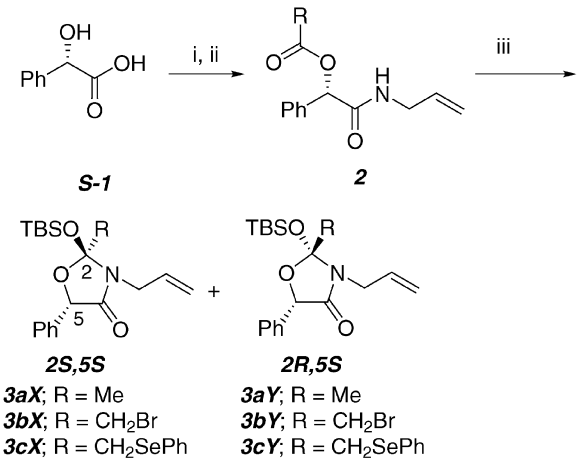
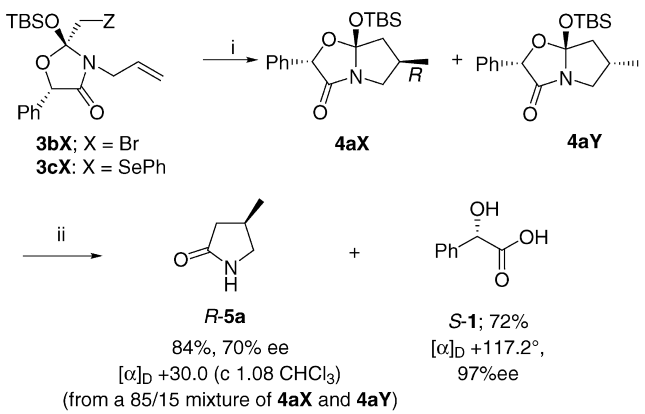


Scheme 1. *Reagents*. (i) $CH_2{=}CHCH_2NH_2$, EDCI; (ii) RCO_2H, EDCI. (iii) TBSOTf, 2,6-lutidine, DMAP, CH_2Cl_2, 0°C.

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

Entry	R	**2**; yield (%)[a]	$[\alpha]_D$	**3**; yield (%)[a]	**X/Y**[b]	$[\alpha]_D$[c]
1	Me	**2a**; 67	+57.8	**3a**; 100	96/4	−13.5
2	$BrCH_2$	**2b**; 90	+78.9	**3b**; 87	63/37	+20.4
3	$PhSeCH_2$	**2c**; 85	+46.5	**3c**; 88	84/16	+51.1

[a] Isolated yield.
[b] Determined by HPLC analyses (Chiral Pak-AD).
[c] Specific rotations for major isomers.



Scheme 2. *Reagents*. (i) Bu_3SnH, AIBN, see Table 2; (ii) TBAF, THF.

Radical cyclization for **3bX** or **3cX** was examined with the use of Bu_3SnH (Scheme 2). The results are summarized in Table 2. Exposure of **3bX** to Bu_3SnH at 110°C resulted in the clean formation of the desired bicyclic compound **4a** in 85% yield (entry 1). No trace of simply reduced product **3aX** was observed in the reaction mixture. The product contained two diastereomers **4aX** and **4aY**, whose ratio was revealed to be 79:21. To improve the stereoselectivity, various reaction conditions were examined. The cyclization initiated by Et_3B at 0°C took long time to finish the reaction, while the diastereoselectivity was improved to 83:17 or 85:15 (entry 2 and 3). Thermal cyclization with **3cX** took place smoothly to give **4a** in a 95% yield, but the diastereoselectivity remained at a moderate level (entry 4). The photo-initiated cyclization for **3cX** at 0°C improved the selectivity as well as the yield of **4a** up to 85:15 and 99%, respectively (entry 5).

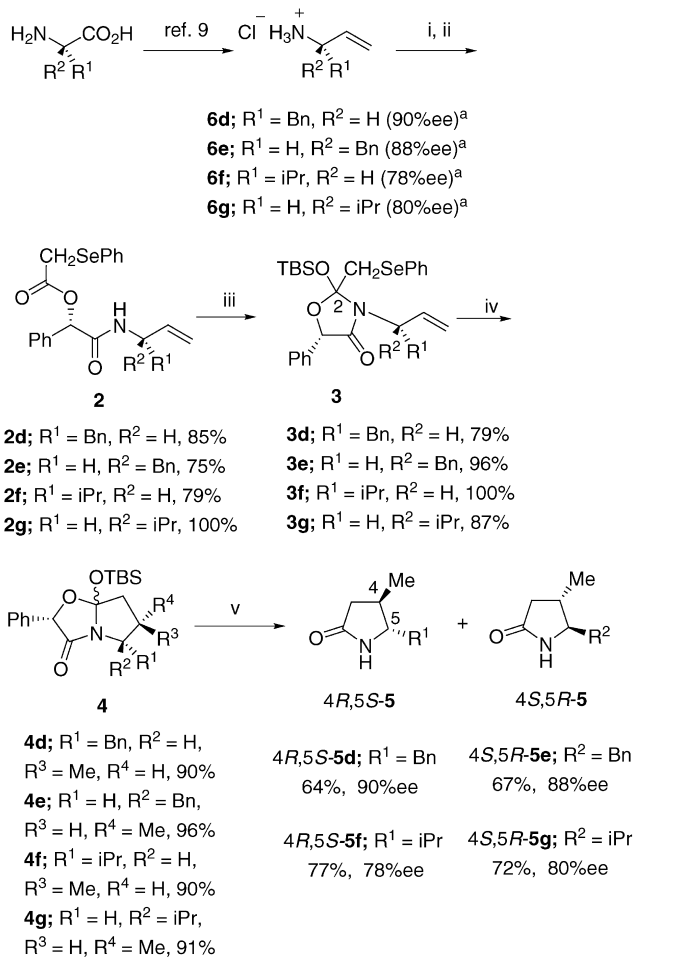
Removal of mandelic acid unit of **4a** was achieved in one-step by treatment with TBAF. Exposure of compound **4a**, inseparable 85:15 mixture of diastereomer **4aX** and **4aY**, to TBAF resulted in the smooth disappearance of **4a** and *N*-unprotected 2-pyrrolidone **5a** was formed in a spot-to-spot manner. Purified **5a** showed dextrorotatory, which indicated that the absolute configuration at the C4 position was *R*.[8] It should be remarked that optically active mandelic acid was recovered in 72% yield. The optical rotation of the recovered mandelic acid was +117.2°, which showed that no significant loss of optical purity at the chiral carbon in mandelic acid unit had happened during the present series of chemical transformation. Hence, this result opens a possibility for recycled use of chiral mandelic acid.

The merits of the present strategy for the construction of 2-pyrrolidone derivatives **5** are summarized as follows: high yields in each step, smooth radical cyclization without side products, and one-step conversion to *N*-unprotected secondary lactams. We next examined to use chiral amines **6**, derived from commercially available optically active amino acids, for the preparation of 4,5-disubstituted 2-pyrrolidones (Scheme 3).[9] During the conversion, some unavoidable racemization occurred and the optical purities of **6** were indicated in Scheme 3. Mandelamide **2d**, which was prepared from **6d**, underwent the formation of oxyoxazolidinone **3d** in 79% yield using the same treatment. Unfortunately, **3d** consisted of a mixture of diastereomers, in which the major two isomers' ratio is in about 8:2. This result reflected that the stereoselectivity during the formation of **3d** was not as high as the formation of **3a**. Despite our extensive efforts, the present diastereomeric mixture was inseparable so we used this mixture for further conversion. Treatment of **3d** with Bu_3SnH gave bicyclic lactam **4d** in 90% yield. Again no simply reduced product was observed. It should be mentioned that this compound contained basically only two diastereomers; the radical cyclization step was expected to proceed in a very

Table 2. Radical cyclization of **3X**

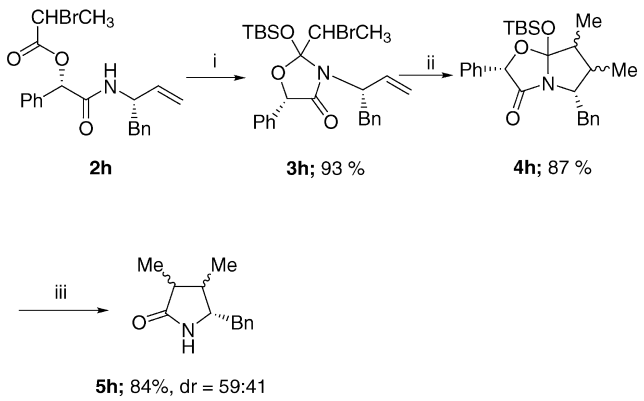
Entry	**3X**	Z	Conditions	**4a**; yield (%)[a]	**X/Y**[b]
1	**3bX**	Br	Toluene, AIBN, Bu_3SnH, reflux 1.5 h	85	79/21
2	**3bX**	Br	Toluene, Et_3B, Bu_3SnH, 0 °C, 3 h then rt, 24 h	38	83/17
3	**3bX**	Br	Toluene, Et_3B, Bu_3SnH, rt, 7 days	68	85/15
4	**3cX**	SePh	Toluene, AIBN, Bu_3SnH, reflux 12 h	95	79/21
5	**3cX**	SePh	Toluene, AIBN, Bu_3SnH, hν, 0°C, 12 h	99	85/15

[a] Isolated yield.
[b] Determined by HPLC analyses (Chiral Pak-AD).



Scheme 3. *Reagents*. (i) (*S*)-mandelic acid, EDCI, Et_3N; (ii) $PhSeCH_2CO_2H$, EDCI, DMAP, CH_2Cl_2, rt, 12 h; (iii) TBSOTf, 2,6-lutidine, DMAP, CH_2Cl_2, 0°C; (iv) Bu_3SnH, AIBN, toluene, 110°C; (v) TBAF, THF (a) enantiomeric excesses of amines **6** are in parentheses.

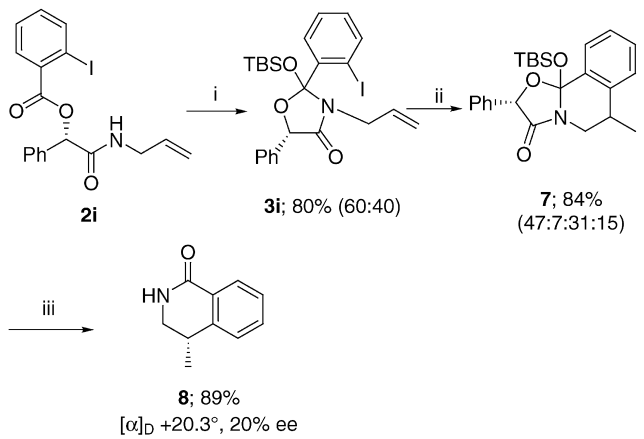
stereoselective manner. The diastereomeric mixture was again inseparable using any methods. Exposure of **4d** to TBAF resulted in the smooth cleavage of C–N and C–O bonds and 2-pyrrolidone **5d** was isolated as a single diastereomer. An NOE experiment for **5d** clearly indicated *trans* configuration between C4 and C5 since 2% of signal enhancement at the C4 methyl group was observed on irradiation at the H5 nuclei. The observed *trans*-selectivity is easily rationalized by comparison with the previous examples.[1,4,5] HPLC analysis of **5d** showed its enantiomeric excess was 90%, which was the same value as the starting amine **6** held. This suggests that 1,2-induction during the radical cyclization step occurred in a highly stereoselective manner regardless of the configuration at C2 position in **3**. From the synthetic point of view, the present method provides a convenient strategy of enantioselective construction of 4,5-disubstituted 2-pyrrolidone. Starting from other chiral amines **6** derived from natural or unnatural amino acids, preparation of optically active 4,5-*trans*-disubstituted 2-pyrrolidones **5** was carried out successfully. In all cases, ee values of **5** reflected the values of the ee for the starting amines **6** so that the 1,2-induction in radical cyclization step took place at almost the perfect level. Although mandelic acid unit failed to give effective chiral bias for the radical cyclization, it provides a suitable configuration that



Scheme 4. *Reagents*. (i) TBSOTf, 2,6-lutidine, DMAP, CH_2Cl_2, 0°C; (ii) Bu_3SnH, AIBN, toluene, 110°C; (iii) TBAF, THF.

encouraged the radical cyclization occurred smoothly without the formation of simple reduced products (Scheme 4).

The present method was applied to the construction of trisubstituted 2-pyrrolidone. The starting material **2h** was readily prepared from mandelic acid, chiral allyl amine **6d**, and racemic 2-bromopropionic acid. The formation of oxyoxazolidinone **3h** was achieved smoothly in the same procedure as mentioned above. Again an inseparable diastereomeric mixture of **3h** was obtained. This whole diastereomeric mixture of **3h** was treated with Bu_3SnH under the standard radical conditions and bicyclic compound **4h** was isolated in 87% yield. Treatment of **4h** with TBAF smoothly converted to trisubstituted 2-pyrrolidones **5h** although they consisted in a pair of diastereomers whose ratios were close to 6:4 (Scheme 5).



Scheme 5. *Reagents*. (i) TBSOTf, 2,6-lutidine, DMAP, CH_2Cl_2, 0°C; (ii) Bu_3SnH, AIBN, toluene, 110°C; (iii) TBAF, THF.

Preparation of *N*-unprotected 2*H*-isoquinolin-1-one was examined with the present procedure. *O*-Acylmandelamide **2i**, derived from *o*-iodobenzoic acid, was converted to oxyoxazolidinone **3i**, which then underwent radical cyclization to give bicyclic lactam **7** in 84% yield. Compound **7** consisted in four diastereomers in the ratio of 47:7:31:15. No simply deharogenated products were observed in the reaction mixture. Addition of TBAF to a solution of **7** induced smooth degradation of the oxyoxazolidinone unit to give mandelic acid and 3,4-dihydro-2*H*-isoquinolin-1-one **8**

in 89% yield. The positive optical rotation of **8** indicated the absolute configuration of **8** was *S*,[10] although the extent of enantiomeric excess of **8** was only 20%.

In conclusion, we have succeeded in developing a useful method to prepare mono- and disubstituted *N*-unprotected 2-pyrrolidones in an optically active form. With the present procedure, the oxyoxazolidinone ring system provides an efficient asymmetric bias for chiral induction. Additionally, one-step removal of mandelic acid from the cyclization product achieves a ready formation of *N*-unprotected 2-pyrrolidone derivatives. All the steps involved in the present sequence can be performed in good yields under neutral and mild conditions. Recovered mandelic acid maintained its optical purity. Thus, the present method will open versatile applicability to the synthesis of *N*-unprotected 2-pyrrolidone derivatives. Further investigation and application for this strategy is now underway in our laboratory.

3. Experimental

3.1. General

All ^{1}H and ^{13}C NMR spectra were recorded on a JEOL EX-270 (270 MHz for ^{1}H and 67.5 MHz for ^{13}C) spectrometer. Solvents were dried over the appropriate drying agents (K for TH F, Na for ether, toluene, and benzene, CaH_2 for CH_2Cl_2) and distilled under nitrogen before use. Et_3N was purified by distillation. (*S*)-(−)-Mandelic acid, EDCI, TBSOTf, 2,6-lutidine, Bu_3SnH, AIBN and Et_3B were purchased from Aldrich and used without further purification. Chiral amines **6d** to **6g** were prepared according to the literature method.[9] All the reactions presented here were performed under nitrogen atmosphere unless mentioned. High resolution mass spectra (HRMS) were measured at Advanced Instrumentation Centre, Ehime University, Matsuyama, Japan.

3.1.1. Preparation of (*S*)-(+)-*O*-acetyl-*N*-allylmandelamide (2a). General procedure. To a solution of allylamine (1.178 g, 20.6 mmol), (*S*)-(+)-mandelic acid (1.542 g, 10.1 mmol) and DMAP (0.1 g) in CH_2Cl_2 (10 mL) and was added EDCI (3.8191 g, 20.0 mmol) at room temperature. The reaction mixture was allowed to stir for 12 h. 1 M HCl (20 mL) was added to the solution and the resulting mixture was extracted with CH_2Cl_2 (3×30 mL). The organic phase was combined, washed successively with $NaHCO_3$ and brine, and dried over Na_2SO_4. Filtration and removal of solvent gave *N*-allylmandelamide in 83% yield (1.6048 g, 8.3 mmol). Colorless oil. $[\alpha]_D$=+70.4° (*c* 1.20, $CHCl_3$). ^{1}H NMR δ 3.77 (br, 1H), 3.87 (t, 2H, *J*=5.6 Hz), 5.08 (dd, 1H, *J*=1.5, 18.3 Hz), 5.10 (dd, 1H, *J*=1.3, 9.1 Hz), 5.78 (tdd, 1H, *J*=5.5, 10.9, 16.5 Hz), 6.30 (br, 1H), 7.28–7.42 (m, 5H). ^{13}C NMR δ 41.5, 73.9, 116.3, 126.6, 128.3, 128.5, 133.5, 139.5, 172.4. Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32%. Found: C, 68.94; H, 7.00; N, 7.19.

To a solution of *N*-allylmandelamide (0.4019 g, 2.1 mmol), Et_3N (0.35 mL, 2.4 mmol) and DMAP (0.1 g) in CH_2Cl_2 (10 mL) was added acetyl chloride (0.15 mL, 2.7 mmol) at 0°C over 15 min. The reaction mixture was allowed to stir at the same temperature for 6 h. 1 M HCl (20 mL) was added to the reaction mixture and the resulting biphasic mixture was extracted with CH_2Cl_2 (3×30 mL). The organic phase was combined, washed with $NaHCO_3$ and brine, and dried over Na_2SO_4. Filtration and removal of solvent gave oil residue, which was purified through flash chromatography (silica gel/hexane–ethyl acetate 3:1 v/v) to give **2a** in 67% yield (0.3308 g, 1.4 mmol). Colorless oil. $[\alpha]_D$=+57.8° ($CHCl_3$). ^{1}H NMR δ 2.20 (s, 3H), 3.92 (t, 2H, *J*=5.6 Hz), 5.14 (dd, 1H, *J*=1.3, 11.2 Hz), 5.15 (dd, 1H, *J*=1.5, 16.3 Hz), 5.83 (tdd, 1H, *J*=5.7, 11.0, 16.5 Hz), 6.10 (s, 1H), 6.18 (br, 1H), 7.33–7.47 (m, 5H). ^{13}C NMR δ 20.4, 41.1, 75.1, 115.6, 127.0, 128.2, 128.4, 133.3, 135.2, 168.3, 169.3. IR (ν_{max}, neat) 3300, 2960, 1720, 1650, 1240 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{13}H_{16}NO_3$: 234.1130, found 234.1128.

Other (*S*)-*O*-acyl-*N*-allylmandelamides **2** were prepared in a similar manner.

3.1.2. (*S*)-(+)-*O*-Bromoacetyl-*N*-allylmandelamide (2b). Colorless oil. $[\alpha]_D$=+78.9° (*c* 1.13, $CHCl_3$). ^{1}H NMR δ 3.85–4.00 (m, 4H), 5.17 (dd, 1H, *J*=1.5, 17.2 Hz), 5.19 (dd, 1H, *J*=1.3, 9.6 Hz), 5.83 (tdd, 1H, *J*=5.5, 10.3, 17.2 Hz), 6.14 (s, 1H), 6.30 (br, 1H), 7.37–7.48 (m, 5H). ^{13}C NMR δ 25.4, 41.6, 76.5, 116.5, 127.3, 128.7, 129.1, 133.3, 134.5, 165.5, 167.6. IR (ν_{max}, neat) 3200, 2960, 1720, 1650, 1240 cm^{-1}.

3.1.3. (*S*)-(+)-*O*-(Phenylseleno)acetyl-*N*-allylmandelamide (2c). White solid. Mp 49–50°C. $[\alpha]_D$=+46.5° (*c* 1.06, $CHCl_3$). ^{1}H NMR δ 3.60 (d, 2H, *J*=5.3 Hz), 3.85 (m, 2H, *J*=6.9 Hz), 5.11 (dd, 1H, *J*=1.5, 17.3 Hz), 5.13 (dd, 1H, *J*=1.3, 10.2 Hz), 5.77 (tdd, 1H, *J*=5.5, 10.4, 17.2 Hz), 6.10 (s, 1H), 6.33 (br, 1H), 7.26–7.55 (m, 10H). ^{13}C NMR δ 26.7, 41.4, 75.8, 116.3, 127.2, 127.9, 128.4, 128.7, 129.2, 132.7, 133.3, 135.0, 168.0, 168.8. IR (ν_{max}) 3284, 1727, 1660, 1375, 1253, 1103 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{19}H_{20}NO_3{}^{78}Se$: 390.0608, found 390.0605.

3.1.4. (*S*)-(+)-*O*-(Phenylseleno)acetyl-*N*-(1-(*S*)-benzylallyl)mandelamide (2d). Yellow oil $[\alpha]_D$=+38.8° (*c* 0.59, $CHCl_3$). ^{1}H NMR δ 2.75 (dd, 1H, *J*=7.9, 13.9 Hz), 2.94 (dd, 1H, *J*=5.9, 13.9 Hz), 3.52–3.56 (m, 2H), 4.74–4.82 (m, 1H), 5.06 (dd, 1H, *J*=1.3, 10.2 Hz), 5.08 (dd, 1H, *J*=1.5, 17.3 Hz), 5.77 (ddd, 1H, *J*=5.4, 10.3, 17.2 Hz), 6.06 (s, 1H), 6.38 (d, 1H, *J*=8.6 Hz), 7.06–7.62 (m, 15H). ^{13}C NMR δ 27.2, 40.6, 52.0, 75.8, 115.5, 126.6, 126.7, 127.6, 127.8, 128.3, 128.4, 128.5, 129.2, 129.3, 129.4, 133.1, 136.8, 136.9, 167.8, 168.7. IR (ν_{max}, neat) 3368, 3029, 1658, 1531 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{26}H_{26}NO_3{}^{78}Se$: 478.1086, found 478.1088.

3.1.5. (*S*)-(+)-*O*-(Phenylseleno)acetyl-*N*-(1-(*R*)-benzylallyl)mandelamide (2e). White solid. $[\alpha]_D$=+46.8° (*c* 0.39, $CHCl_3$). ^{1}H NMR δ 2.79 (dd, 1H, *J*=7.3, 13.9 Hz), 2.85 (dd, 1H, *J*=6.6, 13.6 Hz), 3.54 (d, 1H, *J*=17.6 Hz), 3.56 (d, 1H, *J*=17.0 Hz), 4.69–4.80 (m, 1H), 5.05 (dd, 1H, *J*=1.3, 17.2 Hz), 5.08 (dd, 1H, *J*=1.3, 9.6 Hz), 5.79 (ddd, 1H, *J*=5.6, 10.6, 17.2 Hz), 6.04 (s, 1H), 6.20 (d, 1H, *J*=8.3 Hz), 7.06–7.50 (m, 15H). ^{13}C NMR δ 26.7, 40.4, 51.8, 75.7, 115.2, 126.3, 127.1, 127.7, 128.1, 128.4, 128.6, 129.1, 132.5, 134.9, 136.7, 167.2, 168.6. IR (ν_{max}) 1716,

1409, 1251, 1114 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{26}H_{26}NO_3^{78}Se$: 478.1086, found 478.1093.

3.1.6. (*S*)-(+)-*O*-(Phenylseleno)acetyl-*N*-(1-(*S*)-isopropylallyl)mandelamide (2f). White solid. Mp 60–61°C. $[\alpha]_D$=+46.8° (*c* 0.39, $CHCl_3$). ^1H NMR δ 0.87 (d, 3H, *J*=6.9 Hz), 0.88 (d, 3H, *J*=6.9 Hz), 1.73–1.86 (m, 1H), 3.58 (d, 1H, *J*=17.2 Hz), 3.62 (d, 1H, *J*=16.9 Hz), 4.29–4.37 (m, 1H), 5.07 (dd, 1H, *J*=1.3, 17.5 Hz), 5.08 (dd, 1H, *J*=1.3, 10.3 Hz), 5.68 (ddd, 1H, *J*=5.9, 10.2, 17.2 Hz), 6.13 (s, 1H), 6.35 (d, 1H, *J*=8.9 Hz), 7.26–7.53 (m, 10H). ^{13}C NMR δ 18.5, 19.1, 27.4, 32.4, 57.0, 76.5, 116.5, 127.8, 128.4, 129.0, 129.3, 129.8, 133.1, 135.8, 136.4, 167.9, 169.1. IR (ν_{max}) 3275, 3085, 1735, 1660, 1560, 1405, 1251, 1105 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{22}H_{26}NO_3^{80}Se$: 432.1078, found 432.1070.

3.1.7. (*S*)-(+)-*O*-(Phenylseleno)acetyl-*N*-(1-(*R*)-isopropylallyl)mandelamide (2g). White solid. $[\alpha]_D$=+25.7° (*c* 0.62, $CHCl_3$). ^1H NMR δ 0.85 (d, 3H, *J*=6.9 Hz), 0.86 (d, 3H, *J*=6.9 Hz), 1.71–1.83 (m, 1H, *J*=6.9 Hz), 3.58 (d, 1H, *J*=14.8 Hz), 3.65 (d, 1H, *J*=13.8 Hz), 4.29–4.37 (m, 1H), 5.08 (dd, 1H, *J*=1.3, 11.2 Hz), 5.08 (dd, 1H, *J*=1.5, 17.2 Hz), 5.73 (ddd, 1H, *J*=6.0, 10.8, 16.9 Hz), 6.13 (s, 1H), 6.28 (d, 1H, *J*=9.7 Hz), 7.26–7.62 (m, 10H). ^{13}C NMR δ 18.1, 18.6, 26.8, 31.9, 56.6, 75.9, 115.9, 127.3, 127.9, 128.6, 128.8, 129.1, 129.3, 132.5, 135.1, 136.0, 167.7, 168.9. IR (ν_{max}) 3300, 2960, 1735, 1662, 1639, 1527, 1253, 1105 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{22}H_{26}NO_3^{78}Se$: 430.1086, found 430.1091.

3.1.8. (*S*)-(+)-*O*-(2-Bromo)propionyl-*N*-(1-(*S*)-benzylallyl)mandelamide (2h). Colorless oil. $[\alpha]_D$=+76.8° (*c* 0.56, $CHCl_3$). ^1H NMR δ 1.68 (d, 3H, *J*=6.9 Hz), 2.76–3.02 (m, 2H), 4.41–4.50 (m, 1H), 4.77–4.87 (m, 1H), 5.02–5.15 (m, 2H), 5.77–5.91 (m, 1H), 6.06 (s, 1H for minor isomer), 6.11 (s, 1H for major isomer), 6.15 (d, 1H, *J*=7.6 Hz for minor isomer), 6.30 (d, 1H, *J*=7.9 Hz for major isomer), 7.01–7.51 (m, 10H). ^{13}C NMR δ 21.3, 21.5, 40.7, 40.8, 51.8, 52.0, 74.2, 115.2, 115.4, 126.7, 126.8, 127.3, 127.5, 127.6, 127.7, 128.4, 128.5, 128.6, 128.9, 129.2, 129.3, 129.4, 129.5, 134.5, 136.8, 136.9, 139.0, 167.2, 167.2, 171.8, 173.6. IR (ν_{max}, neat) 3300, 3000, 1747, 1648, 1527, 1454, 1180 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{21}H_{23}^{79}BrNO_3$: 416.0861, found 416.0865.

3.1.9. (*S*)-(+)-*O*-(2-Iodo)benzoyl-*N*-allylmandelamide (2i). Colorless oil. $[\alpha]_D$=+77.7° (*c* 1.11, $CHCl_3$). ^1H NMR δ 3.96 (t, 2H, *J*=5.8 Hz), 5.14 (dd, 1H, *J*=1.3, 10.2 Hz), 5.18 (dd, 1H, *J*=1.3, 17.2 Hz), 5.84 (tdd, 1H, *J*=5.4, 10.6, 17.2 Hz), 6.34 (s, 1H), 6.47 (br, 1H), 7.17–8.03 (m, 9H). ^{13}C NMR δ 41.6, 76.7, 93.8, 116.5, 127.5, 128.0, 128.6, 128.9, 131.4, 133.0, 133.4, 134.1, 135.0, 141.2, 164.8, 167.8. IR (ν_{max}, neat) 3300, 3000, 1731, 1662, 1567, 1247, 1135, 1103, 1018, 925 cm^{-1}. Anal.Calcd for $C_{18}H_{16}INO_3$: C, 51.32; H, 3.83; N, 3.33%. Found: C, 51.52; H, 4.15; N, 3.24.

3.1.10. Preparation of (2*S*,5*S*)-*N*-allyl-2-(*tert*-butyldimethylsilyl)oxy-2-methyl-5-phenyl-1,3-oxazolidin-4-one (3aX). General procedure. To a solution of **2a** (0.1169 g, 0.5 mmol) in CH_2Cl_2 at 0°C was added 2,6-lutidine (0.15 mL, 1.3 mmol), DMAP (0.1 g), and TBSOTf (0.30 mL, 1.3 mmol) in this order. The reaction mixture was allowed to stir for 6 h. Pyridine (0.5 mL) was added to the solution and the solvent was remove in *vacuo*. The residue was subjected to through flash chromatography (silica gel/hexane–ethyl acetate 10:1 v/v) to give **3a** in 100% yield (0.1804 g, 0.5 mmol). Colorless oil. $[\alpha]_D$=−13.5° (*c* 1.06, $CHCl_3$). ^1H NMR δ 0.16 (s, 3H), 0.21 (s, 3H), 0.90 (s, 9H), 1.78 (s, 3H), 3.82 (dd, 1H, *J*=6.6, 15.8 Hz), 4.09 (dd, 1H, *J*=5.3, 15.8 Hz), 5.14 (dd, 1H, *J*=1.3, 10.2 Hz), 5.21 (dd, 1H, *J*=1.3, 17.2 Hz), 5.29 (s, 1H), 5.76–5.90 (m, 1H), 7.33–7.46 (m, 5H). ^{13}C NMR δ −3.6, −3.5, 17.9, 25.5, 28.6, 42.5, 76.5, 110.4, 117.3, 126.2, 128.4, 128.5, 133.2, 135.9, 169.8. IR (ν_{max}, neat) 2950, 1720, 1400, 1210, 1080 cm^{-1}.

Other optically active oxyoxazolidinones **3** were prepared in a similar procedure. The diastereomers of **3bX**, **3bY**, and **3cX** were separated by careful flash chromatography eluted with hexane–ether 20:1 v/v.

3.1.11. (2*S*,5*S*)-*N*-Allyl-2-(*tert*-butyldimethylsilyl)oxy-2-bromomethyl-5-phenyl-1,3-oxazolidin-4-one (3bX). Colorless oil. $[\alpha]_D$=+20.4° (*c* 0.96, $CHCl_3$). ^1H NMR δ 0.18 (s, 3H), 0.25 (s, 3H), 0.92 (s, 9H), 3.57 (d, 1H, *J*=11.5 Hz), 3.71 (d, 1H, *J*=11.9 Hz), 3.94 (dd, 1H, *J*=6.9, 15.5 Hz), 4.06 (dd, 1H, *J*=5.9, 15.5 Hz), 5.18 (dd, 1H, *J*=1.2, 10.1 Hz), 5.27 (dd, 1H, *J*=1.3, 17.1 Hz), 5.37 (s, 1H), 5.85–5.98 (m, 1H), 7.31–7.62 (m, 5H). ^{13}C NMR δ −3.2, −2.9, 18.2, 26.0, 36.4, 43.5, 78.3, 109.7, 118.7, 127.0, 128.8, 129.0, 133.2, 135.0, 170.0. IR (ν_{max}, neat) 2930, 1720, 1400, 1210, 1080 cm^{-1}.

3.1.12. (2*R*,5*S*)-*N*-Allyl-2-(*tert*-butyldimethylsilyl)oxy-2-bromomethyl-5-phenyl-1,3-oxazolidin-4-one (3bY). Colorless oil. $[\alpha]_D$=+22.7° (*c* 0.99, $CHCl_3$). ^1H NMR δ −0.06 (s, 3H), 0.15 (s, 3H), 0.88 (s, 9H), 3.68 (d, 1H, *J*=11.2 Hz), 3.75 (d, 1H, *J*=11.6 Hz), 3.96 (dd, 1H, *J*=7.4, 15.3 Hz), 4.09 (dd, 1H, *J*=5.6, 15.5 Hz), 5.22 (dd, 1H, *J*=1.2, 10.1 Hz), 5.31 (dd, 1H, *J*=1.7, 17.2 Hz), 5.52 (s, 1H), 5.80–6.06 (m, 1H), 7.31–7.48 (m, 5H). ^{13}C NMR δ −3.6, −3.1, 17.7, 25.5, 37.7, 42.8, 80.9, 109.1, 118.4, 127.5, 128.4, 128.7, 132.6, 135.4, 169.3. IR (ν_{max}, neat) 2950, 1720, 1400, 1210, 1080 cm^{-1}.

3.1.13. (2*S*,5*S*)-*N*-Allyl-2-(*tert*-butyldimethylsilyl)oxy-5-phenyl-2-(phenylseleno)acetyl-1,3-oxazolidin-4-one (3cX). Colorless oil. $[\alpha]_D$=+51.1° (*c* 1.15, $CHCl_3$). ^1H NMR δ 0.17 (s, 3H), 0.27 (s, 3H), 0.92 (s, 9H), 3.32 (d, 1H, *J*=12.9 Hz), 3.53 (d, 1H, *J*=12.9 Hz), 3.83 (dd, 1H, *J*=6.8, 15.7 Hz), 4.01 (dd, 1H, *J*=5.6, 15.5 Hz), 5.13 (dd, 1H, *J*=1.3, 10.2 Hz), 5.20 (dd, 1H, *J*=1.3, 17.1 Hz), 5.34 (s, 1H), 5.74–5.92 (m, 1H), 7.19–7.51 (m, 10H). ^{13}C NMR δ −3.7, −3.4, 17.7, 25.5, 38.1, 42.8, 78.0, 110.8, 117.9, 126.5, 127.0, 128.2, 128.3, 128.9, 129.1, 132.7, 132.8, 134.8, 169.5. IR (ν_{max}, neat) 2910, 1720, 1400, 1240 cm^{-1}. Anal. Calcd for $C_{25}H_{33}NO_3SeSi$: C, 59.75; H, 6.62; N, 2.79%. Found: C, 59.52; H, 6.67; N, 2.83.

3.1.14. (5*S*)-*N*-(1-(*S*)-Benzylallyl)-2-(*tert*-butyldimethylsilyl)oxy-5-phenyl-2-(phenylseleno)acetyl-1,3-oxazolidin-4-one (3d). Colorless oil. $[\alpha]_D$=+53.1° (*c* 1.18 $CHCl_3$). ^1H NMR δ −0.03 (s, 3H for minor isomer), 0.01 (s, 3H for

minor isomer), 0.10 (s, 3H for major isomer), 0.24 (s, 3H for major isomer), 0.88 (s, 9H for minor isomer), 1.02 (s, 9H, for major isomer), 3.17–3.63 (m, 4H), 4.02–4.13 (m, 1H), 4.02–4.13 (m, 1H), 4.76 (d, 1H, J=17.5 Hz for major isomer), 4.96 (d, 1H, J=10.2 Hz for major isomer), 5.05 (d, 1H, J=12.2 Hz for minor isomer), 5.10 (d, 1H, J=10.2 Hz for minor isomer), 5.20 (s, 1H for minor isomer), 5.38 (s, 1H for major isomer), 6.04–6.18 (m, 1H), 7.18–7.57 (m, 15H). ^{13}C NMR δ −3.6, −3.5, −3.3, −3.0, 14.0, 17.5, 22.5, 25.6, 25.7, 38.2, 38.3, 58.5, 58.9, 76.5, 79.7, 111.8, 111.4, 117.8, 126.4, 126.6, 126.9, 127.1, 127.5, 127.5, 127.7, 128.3, 128.4, 128.5, 128.7, 128.9, 129.0, 129.1, 129.4, 129.5, 130.8, 132.4, 132.8, 133.2, 133.9, 134.6, 134.9, 135.5, 137.9, 138.2, 169.1, 169.3. IR (ν_{max}, neat) 3000, 1720, 1672, 1251, 1105 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{32}H_{40}NO_3Si^{80}Se$: 592.1950, found 592.1953.

3.1.15. (5*S*)-*N*-(1-(*R*)-Benzylallyl)-2-(*tert*-butyldimethylsilyl)oxy-5-phenyl-2-(phenylseleno)acetyl-1,3-oxazolidin-4-one (3e). Colorless oil. $[\alpha]_D$=+3.6° (*c* 0.55 $CHCl_3$). ^{1}H NMR δ −0.09 (s, 3H for major isomer), 0.14 (s, 3H for minor isomer), 0.18 (s, 3H for major isomer), 0.29 (s, 3H for minor isomer), 0.88 (s, 9H for minor isomer), 0.92 (s, 9H for major isomer), 2.88–2.99 (m, 1H), 3.36–3.51 (m, 3H), 3.91–4.02 (m, 1H), 4.96 (d, 1H, J=17.2 Hz), 5.10 (d, 1H, J=10.1 Hz for major isomer), 5.16 (d, 1H, J=5.9 Hz for minor isomer), 5.21 (s, 1H for minor isomer), 5.28 (s, 1H for major isomer), 6.29–6.44 (m, 1H), 6.89–7.60 (m, 15H). ^{13}C NMR δ −3.6, −3.3, −3.2, −2.9, 13.9, 17.7, 22.4, 25.6, 25.7, 31.4, 37.6, 37.8, 38.4, 38.7, 59.1, 59.4, 77.7, 80.6, 110.9, 111.0, 117.1, 117.8, 125.5, 126.2, 126.3, 126.4, 126.5, 126.7, 126.7, 127.5, 127.9, 128.1, 128.4, 128.7, 128.9, 129.5, 131.5, 132.7, 135.2, 135.2, 135.3, 135.9, 137.6, 137.8, 169.0, 169.2. IR (ν_{max}, neat) 3000, 1716, 1409, 1251, 1072 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{32}H_{40}NO_3Si^{78}Se$: 592.1950, found 592.1950.

3.1.16. (5*S*)-2-(*tert*-Butyldimethylsilyl)oxy-5-*N*-(1-(*S*)-isopropylallyl)-phenyl-2-(phenylseleno)acetyl-1,3-oxazolidin-4-one (3f). Colorless oil. $[\alpha]_D$=+65.0° (*c* 1.13 $CHCl_3$). ^{1}H NMR δ 0.00 (s, 3H for minor isomer), 0.10 (s, 3H for minor isomer), 0.21 (s, 3H for major isomer), 0.31 (s, 3H for major isomer), 0.90 (s, 9H for minor isomer), 0.93 (d, 6H, J=6.6 Hz for major isomer), 0.94 (s, 9H for major isomer), 1.00 (d, 6H, J=6.6 Hz for minor isomer), 2.36–2.44 (m, 1H for minor isomer), 2.66–2.79 (m, 1H for major isomer), 3.32 (t, 1H, J=9.7 Hz for major isomer), 3.42–3.48 (m, 2H), 3.84 (t, 1H, J=9.1 Hz for minor isomer), 5.06–5.21 (m, 2H), 5.25 (s, 1H for minor isomer), 5.36 (s, 1H for major isomer), 6.00–6.18 (m, 1H), 7.14–7.62 (m, 10H). ^{13}C NMR δ −3.6, −3.1, −2.8, −2.7, 18.0, 20.0, 20.5, 20.6, 20.7, 25.6, 25.7, 26.0, 28.1, 30.5, 38.2, 40.4, 63.1, 65.2, 77.7, 80.5, 111.3, 111.7, 118.0, 119.7, 126.7, 127.1, 127.6, 128.3, 128.5, 128.9, 129.1, 131.1, 131.3, 131.6, 132.0, 132.9, 134.4, 134.8, 135.6, 136.2, 168.8, 169.8. IR (ν_{max}, neat) 3050, 2920, 1720, 1560, 1450, 1400, 1240 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{28}H_{40}NO_3Si^{80}Se$: 546.1942, found 546.1935.

3.1.17. (5*S*)-2-(*tert*-Butyldimethylsilyl)oxy-5-*N*-(1-(*R*)-isopropylallyl)-phenyl-2-(phenylseleno)acetyl-1,3-oxazolidin-4-one (3g). Colorless oil. $[\alpha]_D$=−30.6° (*c* 1.21 $CHCl_3$). ^{1}H NMR δ 0.06 (s, 3H for major isomer), 0.15 (s, 3H for minor isomer), 0.23 (s, 3H for major isomer), 0.31 (s, 3H for minor isomer), 0.88–0.96 (m, 6H), 0.91 (s, 9H for major isomer), 0.94 (s, 9H for minor isomer), 2.42–2.55 (m, 1H for minor isomer), 2.64–2.78 (m, 1H for major isomer), 3.14–3.59 (m, 3H), 5.08–5.26 (m, 2H), 5.26 (s, 1H for minor isomer), 5.31 (s, 1H for major isomer), 6.26–6.39 (m, 1H), 7.18–7.62 (m, 10H). ^{13}C NMR δ (ppm) −3.3, −3.0, −2.8, 14.0, 17.9, 18.0, 20.0, 20.2, 20.6, 22.6, 25.4, 25.6, 25.7, 25.9, 27.5, 29.2, 31.5, 38.8, 39.0, 64.8, 65.3, 77.9, 80.9, 111.2, 111.3, 118.1, 118.5, 126.3, 126.8, 127.0, 127.3, 128.3, 128.4, 129.0, 130.7, 131.2, 131.7, 132.8, 132.8, 134.2, 135.4, 136.3, 168.9, 169.4. IR (ν_{max}, neat) 3000, 1718, 1253, 1230, 1108 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{28}H_{40}NO_3Si^{80}Se$: 546.1942, found 546.1935.

3.1.18. (5*S*)-*N*-(1-(*S*)-Benzylallyl)-2-(*tert*-butyldimethylsilyl)oxy-2-(1-bromo)propionyl-5-phenyl-1,3-oxazolidin-4-one (3h). Colorless oil. $[\alpha]_D$=+37.4° (*c* 0.37 $CHCl_3$). ^{1}H NMR δ −0.20 (s, 3H for isomer A), 0.10 (s, 3H for isomer B), 0.16 (s, 3H for isomer C), 0.26 (s, 3H for isomer B), 0.27 (s, 3H for isomer D), 0.33 (s, 3H for isomer C), 0.35 (s, 3H for isomer A), 0.36 (s, 3H for isomer D), 0.84 (s, 9H for isomer C), 0.88 (s, 9H for isomer A), 1.02 (s, 9H for isomer B), 1.04 (s, 9H for isomer D), 1.41 (d, 3H, J=6.9 Hz for isomer D), 1.63 (d, 3H, J=6.6 Hz for isomer C), 1.69 (d, 3H, J=6.9 Hz for isomer B), 1.73 (d, 3H, J=6.6 Hz for isomer A), 3.09 (m, 1H), 3.66–3.75 (m, 1H), 4.11–4.22 (m, 2H), 4.72–4.96 (m, 2H), 5.46 (s, 1H), 6.10–6.27 (m, 1H), 7.17–7.64 (m, 10H). ^{13}C NMR δ −3.8, −3.6, −3.4, −3.3, −3.2, −2.9, −2.8, −2.7, 14.1, 14.2, 18.0, 18.1, 19.2, 20.1, 20.3, 20.5, 22.6, 25.4, 25.6, 25.7, 25.8, 25.9, 31.5, 38.2, 38.5, 39.8, 59.1, 59.3, 59.5, 60.3, 60.8, 61.2, 76.2, 76.8, 77.3, 77.6, 79.9, 110.9, 111.4, 111.9, 118.4, 118.5, 118.7, 126.1, 126.2, 126.4, 126.5, 126.6, 127.0, 127.4, 127.8, 127.9, 128.0, 128.2, 128.2, 128.3, 128.4, 128.6, 128.8, 128.8, 129.4, 129.6, 133.4, 133.6, 134.5, 134.8, 135.0, 137.7, 137.9, 138.4, 169.0, 169.1. IR (ν_{max}, neat) 3000, 1735, 1666, 1527, 1450, 1227, 1178, 1074 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{27}H_{37}BrNO_3Si$: 530.1726, found 530.1719.

3.1.19. (2*S*)-*N*-Allyl-2-(*tert*-butyldimethylsilyl)oxy-2-(iodo)phenyl-5-phenyl-1,3-oxazolidin-4-one (3i). Colorless oil. $[\alpha]_D$=+12.9° (*c* 1.57, $CHCl_3$). ^{1}H NMR δ −0.58 (s, 3H for major isomer), −0.23 (s, 3H for major isomer), 0.22 (s, 3H for minor isomer), 0.27 (s, 3H for minor isomer), 0.91 (s, 9H for minor isomer), 1.04 (s, 9H for major isomer), 3.47 (dd, 1H, J=6.6 Hz, 15.5 Hz for minor isomer), 3.68 (dd, 1H, J=6.4, 15.3 Hz for major isomer), 3.95 (dd, 1H, J=6.3, 15.5 Hz for major isomer), 3.97 (dd, 1H, J=5.9, 14.7 Hz for minor isomer),4.91–5.02 (m, 2H), 5.62 (s, 1H for minor isomer), 5.66–5.82 (m, 1H), 5.99 (s, 1H for major isomer), 7.00–8.02 (m, 9H). ^{13}C NMR δ −3.7, −3.0, −2.8,−2.6, 14.0, 14.1, 18.4, 22.6, 25.6, 26.0, 26.1, 31.5, 42.9, 43.4, 75.9, 80.8, 93.0, 94.8, 110.2, 110.9, 117.8, 118.0, 126.3, 127.1, 127.3, 127.6, 127.9, 128.5, 128.9, 129.0, 130.5, 130.7, 130.9, 131.1, 132.0, 133.5, 135.5, 138.8, 140.1, 142.9, 169.4, 170.1. IR (ν_{max}, neat) 2900, 1710, 1420, 1240, 1200 cm^{-1}. MS (FAB) *m*/*z* 536 [(M+H)$^+$, 11%].

3.1.20. Preparation of (2*S*)-7a-(*tert*-butyldimethylsilyl)-oxy-6-methyl-2-phenyltetrahydropyrrolo[2,1-*b*]oxazol-3-one (4a) through radical cyclization. General procedure. To a solution of **3c** (1.1473 g, 2.28 mmol) in

toluene (34 mL) at 0 °C was added a solution of Bu_3SnH (1.25 mL, 4.50 mmol) and AIBN (0.052 g, 0.32 mmol) in toluene (80 mL) over 12 h under UV irradiation conditions. The solvent was removed in vacuo and the residue was subjected to flash chromatography to give **4a** in 76% yield (0.6017 g, 1.73 mmol). The diastereomer ratio was 85:15 which was determined by HPLC analysis (Chiral Pak-AD). Colorless oil. ^{1}H NMR δ 0.18 (s, 3H for minor isomer), 0.20 (s, 3H for major isomer), 0.22 (s, 3H for minor isomer), 0.23 (s, 3H for major isomer), 0.92 (s, 9H for minor isomer), 0.94 (s, 9H for major isomer), 1.12 (d, 1H, J=6.6 Hz for minor isomer), 1.17 (d, 1H, J=6.6 Hz for major isomer), 1.82–1.92 (m, 1H), 2.42–2.51 (m, 2H), 2.80 (dd, 1H, J=6.9, 11.6 Hz for major isomer), 3.10 (dd, 1H, J=8.1, 11.4 Hz for minor isomer), 3.43 (dd, 1H, J=8.1, 11.4 Hz for minor isomer), 3.91 (dd, 1H, J=7.8, 12.0 Hz for major isomer), 5.57 (s, 1H for major isomer), 5.67 (s, 1H for minor isomer), 7.33–7.41 (m, 5H). ^{13}C NMR δ −3.7, −3.5, −3.4, −3.3, 17.6, 19.3, 25.4, 25.6, 33.9, 33.2, 45.5, 45.7, 48.7, 49.3, 81.5, 82.8, 117.7, 118.1, 126.4, 126.5, 128.5, 135.6, 172.2. IR (ν_{max}, neat) 3000, 1750, 1650, 1300, 1250 cm^{-1}. Anal.Calcd for $C_{19}H_{29}NO_3Si$: C, 65.67; H, 8.41; N, 4.03%. Found: C, 65.78; H, 8.67; N, 3.92.

3.1.21. Preparation of (2*S*,5*S*)-5-benzyl-7a-(*tert*-butyldimethylsilyl)oxy-6-methyl-2-phenyltetrahydropyrrolo[2,1-*b*]oxazol-3-one (4d). General procedure. A solution of **3d** (0.9777 g, 1.65 mmol), Bu_3SnH (0.55 mL, 2.05 mmol) and AIBN (0.0491 g, 0.30 mmol) in toluene (17 mL), purged by nitrogen, was heated at refluxing temperature for 4 h. The solvent was removed in vacuo and the residue was subjected through flash chromatography (silica gel/hexane–ether 20:1 then 5:1 v/v) to give **4d** in 90% yield (0.6497 g, 1.48 mmol). Colorless oil. The diastereomer ratio was determined by HPLC analyses (Chiral Pak-AD). The ratio was=70:29:1:>0. $[\alpha]_D$= +47.8° (c 0.34, $CHCl_3$). ^{1}H NMR δ −0.14 (s, 3H for minor isomer), 0.10 (s, 3H for major isomer), 0.13 (s, 3H for minor isomer), 0.19 (s, 3H for major isomer), 0.74 (d, 3H, J=6.9 Hz for major isomer), 0.82 (d, 3H, J=6.9 Hz for minor isomer), 0.90 (s, 9H for minor isomer), 0.92 (s, 9H for major isomer), 1.27–1.36 (m, 1H), 1.79 (m, 1H), 2.22–2.38 (m, 1H), 2.64 (dd, 1H, J=9.2, 13.8 Hz for major isomer), 2.84 (dd, 1H, J=8.2, 13.2 Hz for minor isomer), 3.58–3.61 (m, 1H), 3.75–3.87 (m, 1H), 5.32 (s, 1H for minor isomer), 5.55 (s, 1H for major isomer), 7.21–7.47 (m, 10H). ^{13}C NMR δ −3.7, −3.6, −3.5, −3.4, 13.5, 14.0, 17.6, 19.1, 20.7, 22.6, 23.3, 25.6, 25.7, 27.7, 29.0, 31.5, 35.7, 38.2, 39.0, 39.8, 42.0, 43.8, 46.8, 62.6, 63.3, 83.5, 83.6, 117.2, 117.9, 126.3, 126.5, 128.3, 128.4, 129.3, 129.4, 135.8, 137.7, 169.1, 171.6. IR (ν_{max}, neat) 3000, 1743, 1687, 1290, 1257, 1214, 1186 cm^{-1}. HRMS (EI) calcd for (M+) $C_{26}H_{35}NO_3Si$: 437.2386, found 437.2390.

Other bicyclic lactams **4e** to **4h** were prepared in a similar procedure.

3.1.22. (2*S*,5*R*)-5-Benzyl-7a-(*tert*-butyldimethylsilyl)oxy-6-methyl-2-phenyltetrahydropyrrolo[2,1-*b*]oxazol-3-one (4e). Colorless oil. ^{1}H NMR δ −0.27 (s, 3H for minor isomer), −0.14 (s, 3H for minor isomer), 0.22 (s, 6H for major isomer), 0.80 (d, 3H, J=7.2 Hz for minor isomer), 0.82 (s, 9H for minor isomer), 0.89 (d, 3H, J=6.3 Hz for major isomer), 0.95 (s, 9H for major isomer), 1.64–1.80 (m, 1H), 2.26–2.29 (m, 1H), 2.46–2.52 (m, 1H), 2.75–2.88 (m, 1H), 3.19–3.62 (m, 1H), 4.11–4.20 (m, 1H), 5.38 (s, 1H for major isomer), 5.64 (s, 1H for minor isomer), 7.17–7.51 (m, 10H). ^{13}C NMR δ −3.8, −3.6, −3.2, 14.0, 17.5, 18.7, 20.2, 22.5, 25.6, 25.8, 31.4, 35.4, 39.4, 39.8, 41.4, 44.2, 47.3, 62.2, 64.9, 82.3, 83.6, 116.5, 118.1, 126.2, 128.0, 128.1, 128.2, 129.0, 129.2, 137.3, 138.4, 169.3, 170.6. IR (ν_{max}, neat) 3000, 1687, 1257, 1228 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{26}H_{36}NO_3Si$: 438.2464, found 438.2467.

3.1.23. (2*S*,5*S*)-7a-(*tert*-Butyldimethylsilyl)oxy-5-isopropyl-6-methyl-2-phenyltetrahydropyrrolo[2,1-*b*]oxazol-3-one (4f). Colorless oil. ^{1}H NMR δ −0.14, 0.10 (s, 3H for minor isomer), 0.12 (s, 3H for minor isomer), 0.21 (s, 6H for major isomer), 0.68 (d, 3H, J=6.9 Hz for major isomer), 0.84 (d, 3H, J=6.6 Hz for minor isomer), 0.86 (s, 9H for minor isomer), 0.92 (d, 3H, J=7.3 Hz for major isomer), 0.94 (s, 9H for major isomer), 1.03 (d, 3H, J=6.6 Hz for minor isomer), 1.18 (d, 3H, J=6.6 Hz for minor isomer), 1.26 (d, 3H, J=7.3 Hz for major isomer), 2.24–2.32 (m, 1H), 2.35–2.51 (m, 1H), 2.89–3.00 (m, 1H), 3.22 (t, 1H, J=7.1 Hz for minor isomer), 3.35 (t, 1H, J=3.3 Hz for major isomer), 5.34 (s, 1H for minor isomer), 5.56 (s, 1H for major isomer), 7.31–7.49 (m, 5H). ^{13}C NMR δ −4.8, −3.8, −3.6, 15.7, 16.5, 17.9, 18.6, 18.9, 19.5, 20.4, 22.6, 25.2, 25.5, 25.6, 26.0, 29.3, 33.8, 38.2, 38.7, 40.7, 68.1, 69.2, 82.3, 83.6, 117.3, 126.3, 127.6, 127.9, 128.3, 128.4, 128.5, 130.0, 130.1, 175.1. IR (ν_{max}, neat) 3000, 11733, 1375, 1247, 1047 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{22}H_{36}NO_3Si$: 390.2465, found 390.2462.

3.1.24. (2*S*,5*R*)-7a-(*tert*-Butyldimethylsilyl)oxy-5-isopropyl-6-methyl-2-phenyltetrahydropyrrolo[2,1-*b*]oxazol-3-one (4g). Colorless oil. ^{1}H NMR δ −0.34 (s, 3H for minor isomer), 0.07 (s, 3H for minor isomer), 0.19 (s, 3H for major isomer), 0.22 (s, 3H for major isomer), 0.82 (s, 9H for minor isomer), 0.90 (d, 3H, J=6.9 Hz for minor isomer), 0.91 (d, 3H, J=6.9 Hz for minor isomer), 0.92 (s, 3H for major isomer), 1.01 (d, 3H, J=6.9 Hz for major isomer), 1.02 (d, 3H, J=6.9 Hz for major isomer), 1.12 (d, 3H, J=7.3 Hz for minor isomer), 1.23 (d, 3H, J=7.3 Hz for major isomer), 1.65–1.88 (m, 2H), 2.11 (dd, 1H, J=10.4, 12.3 Hz for minor isomer), 2.31 (dd, 1H, J=6.9, 11.9 Hz for major isomer), 2.43–2.54 (m, 1H), 2.87–3.30 (m, 1H), 5.43 (s, 1H for major isomer), 5.66 (s, 1H for minor isomer), 7.25–7.50 (m, 5H). ^{13}C NMR δ −3.8, −3.5, −3.4, −2.8, 16.5, 17.7, 17.8, 19.7, 19.8, 20.1, 20.3, 22.5, 23.4, 25.3, 25.6, 25.8, 25.9, 33.2, 34.0, 37.8, 44.0, 47.9, 68.1, 68.9, 82.3, 84.7, 117.0, 118.8, 126.4, 128.3, 128.4, 128.5, 128.6, 128.7, 135.8, 135.9, 168.5, 171.4. IR (ν_{max}, neat) 2960, 1741, 1689, 1463, 1375, 1288, 1255, 1216, 1184 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{22}H_{36}NO_3Si$: 390.2465, found 390.2462.

3.1.25. (2*S*,5*S*)-5-Benzyl-7a-(*tert*-butyldimethylsilyl)oxy-6,7-dimethyl-2-phenyltetrahydropyrrolo[2,1-*b*]oxazol-3-one (4h). Colorless oil. $[\alpha]_D$=+39.2° (c 0.72 $CHCl_3$). ^{1}H NMR δ −0.15 (s, 3H for one isomer), −0.10 (s, 3H for one isomer), 0.09 (s, 3H for one isomer), 0.11 (s, 3H for one isomer), 0.18 (s, 3H for one isomer), 0.19 (s, 3H for one isomer), 0.21 (s, 3H for one isomer), 0.22 (s, 3H for one isomer), 0.89 (s, 9H for one isomer), 0.92 (s, 9H for one isomer), 0.93 (s, 9H for one isomer), 0.94 (s, 9H for one

isomer), 0.74–1.03 (m, 6H), 2.05–2.32 (m, 1H), 2.49–3.00 (m, 1H), 3.12–3.19 (m, 1H), 3.52–3.67 (m, 1H), 3.99–4.04 (m, 1H), 5.27 (s, 1H for one isomer), 5.35 (s, 1H for one isomer), 5.47 (s, 1H for one isomer), 5.64 (s, 1H for one isomer), 7.13–7.49 (m, 10H). ^{13}C NMR δ −4.0, −3.8, −3.7, −3.5, −3.4, −3.2, −3.1, 8.5, 9.0, 13.9, 14.1, 15.1, 15.9, 17.2, 17.6, 17.9, 19.8, 22.4, 23.1, 25.4, 25.6, 25.7, 25.8, 31.4, 35.9, 36.7, 39.0, 41.2, 41.8, 43.8, 45.4, 47.4, 60.0, 62.9, 64.5, 74.0, 83.5, 84.8, 118.1, 118.5, 119.1, 126.0, 126.1, 126.2, 126.2, 126.3, 126.4, 126.5, 126.6, 126.7, 127.5, 127.6, 127.9, 128.2, 128.2, 128.3, 128.4, 128.6, 128.6, 128.8, 129.1, 129.3, 129.3, 129.5, 129.8, 130.0, 134.2, 135.3, 135.9, 136.3, 136.4, 137.6, 137.6, 168.4, 171.2, 174.7, 178.0. IR (ν_{max}, neat) 3000, 1730, 1253, 1186 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{27}H_{38}NO_3Si$: 452.2621, found 452.2616.

3.1.26. Preparation of (*R*)-(+)-4-methylpyrrolidin-2-one (5a).[8] **General procedure.** To a solution of **4a** (0.6017 g, 1.73 mmol) in THF (2 mL) was added TBAF (2 mL, 1.0 M in THF solution) at room temperature. The reaction mixture was allowd to stir for 30 min. The solvent was removed in vacuo and the residue was subjected to flash chromatography (silica gel/hexane–ethyl acetate 3:1 then ethyl acetate–acetone 3:1, 1:1, ethyl acetate–AcOH 9:1 v/v) to give **5a** in 84% yield (0.1441 g, 1.45 mmol). $[\alpha]_D$=+30.0° (*c* 1.08, $CHCl_3$). ^{1}H NMR δ 1.15 (d, 3H, *J*=6.6 Hz), 1.95 (dd, 1H, *J*=7.1, 15.3 Hz), 2.43 (d, 1H, *J*=8.3 Hz), 2.48–2.64 (m, 2H), 2.97 (dd, 1H, *J*=5.9, 9.2 Hz), 3.51 (t, 1H, *J*=8.4 Hz), 5.64 (br, 1H). ^{13}C NMR δ 19.9, 29.7, 38.8, 50.0, 179.2. IR (ν_{max}, neat) 3287, 1679, 1274 cm^{-1}. (*S*)-(+)-Mandelic acid **1** was also recovered in 72% yield (0.1895 g, 1.2 mmol). $[\alpha]_D$=+117.2° ($CHCl_3$).

Other mandelic-acid free pyrrolidones **5** were prepared in a similar manner.

3.1.27. (4*R*,5*S*)-5-Benzyl-4-methylpyrrolidin-2-one (5d). The enantiomeric ratio of **5d** or **e** was determined by HPLC analysis (Chiral Cel OJ, hexane/2-PrOH 95:5 v/v; flow rate, 0.5 mL/min; 4*R*, 5*S*-**5d**; t_R=31.8 min, 4*S*, 5*R*-**5e**; t_R=39.1 min) to be 95:5. Yellow oil. $[\alpha]_D$=−46.1° (*c* 0.71, $CHCl_3$). ^{1}H NMR δ 1.13 (d, 3H, *J*=6.6 Hz), 2.00 (dd, 1H, *J*=7.8, 16.7 Hz), 2.14–2.17 (m, 1H), 2.52 (dd, 1H, *J*=8.4, 16.7 Hz), 2.59 (dd, 1H, *J*=9.2, 13.5 Hz), 2.96 (dd, 1H, *J*=4.3, 13.5 Hz), 3.38–3.45 (m, 1H), 5.44 (br, 1H), 7.16–7.36 (m, 5H). ^{13}C NMR δ 18.9, 35.3, 38.6, 41.7, 63.0, 126.8, 128.7, 128.9, 137.5, 177.0. IR (ν_{max}, neat) 3200, 1685, 1456 cm^{-1}. HRMS (EI) calcd for (M+) $C_{12}H_{15}NO$: 189.1154, found 189.1183.

3.1.28. (4*R*,5*S*)-5-Isopropyl-4-methylpyrrolidin-2-one (5f). The enantiomeric ratio of **5f** or **5g** was determined by HPLC analysis for its *N*-Boc derivative (chiral Pak AD, hexane/2-PrOH 99:1 v/v; flow rate, 0.5 mL/min; 4*R*, 5*S*-*N*-Boc-**5f**; t_R=21.9 min, 4*S*, 5*R*-*N*-Boc-**5g**; t_R=20.4 min) to be 89:11. Yellow oil $[\alpha]_D$=+5.0° (*c* 0.42 $CHCl_3$). ^{1}H NMR δ 0.91 (d, 3H, *J*=6.9 Hz), 0.94 (d, 3H, *J*=6.6 Hz), 1.14 (d, 3H, *J*=6.9 Hz), 1.57–1.76 (m, 1H), 1.94 (dd, 1H, *J*=5.6, 17.2 Hz), 2.18–2.27 (m, 1H), 2.55 (dd, 1H, *J*=8.9, 17.2 Hz), 2.97 (t, 1H, *J*=5.1 Hz), 5.97 (br, 1H). ^{13}C NMR δ 18.1, 19.2, 21.4, 31.9, 32.6, 39.2, 68.4, 178.4. IR (ν_{max}, neat) 3220, 1693, 1465, 1388, 1280 cm^{-1}. HRMS (EI) calcd for (M+) $C_{17}H_{23}NO_3$: 289.1678, found 289.1673.

3.1.29. 5-(*S*)-Benzyl-3,4-dimethylpyrrolidin-2-one (5h). The diastereomeric ratio of **5h** was determined by HPLC analysis for its *N*-Boc derivative (Chiral Pak AD, hexane/2-PrOH 99:1 v/v; flow rate, 0.5 mL/min; major-*N*-Boc-**5h**; t_R=20.4 min, minor-*N*-Boc-**5h**; t_R=18.6 min) to be 59:41. Yellow oil $[\alpha]_D$=−23.9° (*c* 0.61 $CHCl_3$). ^{1}H NMR δ 1.03 (d, 3H, *J*=6.9 Hz for major isomer), 1.09 (d, 3H, *J*=7.6 Hz for major isomer), 1.14 (d, 3H, *J*=6.6 Hz for minor isomer), 1.18 (d, 3H, *J*=7.3 Hz for minor isomer), 1.62–1.76 (m, 1H for minor isomer), 2.00–2.19 (m, 1H for major isomer), 2.22–2.35 (m, 1H), 2.47–2.64 (m, 1H), 2.92–3.06 (m, 1H), 3.31–3.47 (m, 1H), 5.44 (br, 1H), 7.16–7.35 (m, 5H). ^{13}C NMR δ 10.3, 13.7, 13.8, 16.2, 38.0, 39.2, 40.9, 41.1, 44.5, 44.6, 60.9, 61.0, 126.5, 126.6, 128.5, 128.6, 128.8, 128.9, 137.5, 137.6, 179.0, 180.0. IR (ν_{max}, neat) 3245, 1700, 1658, 1454, 1268 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{13}H_{18}NO$: 204.1388, found 204.1386.

3.1.30. Preparation of 10b-(*tert*-Butyldimethylsilyl)oxy-6-methyl-2-(*S*)-phenyl-6,10b-dihydro-5*H*-oxazolo[2,3-*a*]isoquinolin-3-one (7). This compound was prepared in a similar procedure to the preparation of **4**. The diastereomeric ratio of **7** was determined by HPLC analysis (Chiral Pak AD, hexane/2-PrOH 95:5 v/v; flow rate, 0.5 mL/min; retention times for 4 diastereomers were; 23.4, 26.9, 27.7, and 32.6 min) to be 46:7:31:15. Colorless oil. $[\alpha]_D$=+64.5° (*c* 1.18 $CHCl_3$). ^{1}H NMR δ −0.20 (s, 3H for major isomer), 0.07 (s, 3H for major isomer), 0.19 (s, 3H for minor isomer), 0.20 (s, 3H for minor isomer), 0.84 (s, 9H for major isomer), 0.89 (s, 9H for minor isomer), 1.34 (d, 3H, *J*=6.6 Hz for minor isomer), 1.38 (d, 3H, *J*=6.6 Hz for major isomer), 3.02–3.31 (m, 2H), 4.21 (dd, 1H, *J*=5.3, 11.9 Hz for minor isomer), 4.31 (dd, 1H, *J*=6.1, 12.4 Hz for major isomer), 5.17 (s, 1H for major isomer), 5.53 (s, 1H for minor isomer), 7.03–7.67 (m, 9H). ^{13}C NMR δ −3.8, −3.7, −3.4, −3.3, 14.1, 17.8, 18.0, 18.1, 18.8, 22.6, 23.4, 25.5, 25.6, 30.9, 31.5, 42.5, 42.8, 79.9, 80.1, 106.1, 124.8, 126.2, 126.3, 126.4, 126.5, 126.7, 127.0, 127.1, 127.2, 127.3, 128.3, 128.4, 128.8, 129.1, 135.7, 136.1, 136.8, 136.9, 137.7, 137.8, 168.4. IR (ν_{max}, neat) 3050, 2950, 1730, 1450, 1240 cm^{-1}.

3.1.31. Preparation of 4-methyl-3,4-dihydro-2*H*-isoquinolin-1-one (8).[10] This compound was prepared in a similar procedure to the preparation of **5**. The enantiomeric ratio of **8** was determined by HPLC analysis (Chiral Pak AD, hexane/2-PrOH 97:3 v/v; flow rate, 0.5 mL/min; *S*-**8**; t_R=45.1 min, *R*-**8**; t_R=46.9 min) to be 60:40. Colorless oil. $[\alpha]_D$=+20.3° (*c* 1.10, $CHCl_3$). ^{1}H NMR δ 1.36 (d, 3H, *J*=6.9 Hz), 3.07–3.19 (m, 1H), 3.29 (ddd, 1H, *J*=3.4, 6.3, 8.6 Hz), 3.65 (ddd, 1H, *J*=2.6, 4.8, 8.4 Hz), 6.02 (br, 1H), 7.26 (d, 1H, *J*=7.6 Hz), 7.37 (dt, 1H, *J*=1.0, 7.5 Hz), 7.47 (dt, 1H, *J*=1.3, 7.6 Hz), 8.08 (dd, 1H, *J*=1.7, 7.9 Hz). ^{13}C NMR δ 17.9, 31.7, 45.8, 125.4, 126.4, 127.4, 127.7, 131.9, 143.6, 166.3. IR (ν_{max}, neat) 3300, 2950, 1720, 1580 cm^{-1}. HRMS (FAB) calcd for (M+H) $C_{10}H_{12}NO$: 162.0919, found 162.0923.

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