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An efficient method for the preparation of 3-hydroxyl-5-substituted 2-pyrrolidones and application in the divergent synthesis of (−)-preussin and its analogues

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ABSTRACT

An asymmetric method to (*S*,*R*)-α-hydroxyl-γ-amino alcohols **12** through a diastereoselective addition of Grignard reagents to β-chiral aldimines **11** is described. Subsequent oxidation/cyclization with Sarett reagent provided a novel approach to lactams **14**, a flexible building block whose utility was demonstrated in the divergent synthesis of antifungal agent (−)-preussin **5** and its three analogues **23**, **24**, **25**.

1. Introduction

Functionalized 5-substituted 2-pyrrolidones **1**, **2** and their ring-opened equivalents **3**, **4** (Fig. 1) are found in pharmaceuticals and numerous biologically active natural products.[1,2] They are also valuable chiral building blocks toward the divergent syntheses of other pyrrolidine or indolizidine alkaloids, which include the antifungal (+)-preussin, isolated from the fermentation extracts of *Preussia* sp. and *Aspergillus ochraceus*,[3] and the pheromone (+)-monomorine I **6**.[4] Another example is hapalosin **8**, which was shown to have multidrug-resistance reversing activity in cancer cells.[5] From the practical point of view, one of the most straightforward ways to synthesize these natural products is the asymmetric construction of 2-pyrrolidones **1**, **2**. Although a number of powerful approaches have been reported for the synthesis of **2**,[2a–k] to our best knowledge, only one indirect method could be adapted for the preparation of building block **1**[2l] and several methods for preparation its deprotective amide.[2m–o,15b]

Chiral *N*-*tert*-butanesulfinamide, originally developed by Ellman and Davis, is arguably one of the most efficient auxiliaries applied in modern organic synthesis.[6] One popular application of Ellman's auxiliary is the asymmetric preparation of chiral amines by means of addition to imines with organo-magnesium, lithium, zinc and other anionic reagents.[7] Excellent chemoselectivity was observed in many of these reactions, including the unusual 1,3-migration we

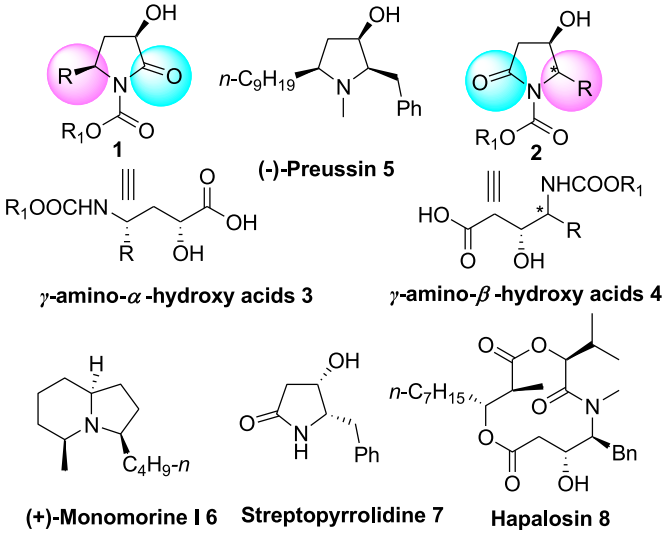

Fig. 1. The structure of several bioactive molecules.

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observed in the reaction of *N-tert*-butanesulfinyl ester with functionalized organo-magnesium reagents.[8] Very recently, our group also studied the chemical selectivity of the imine with aldehydes in the presence of ester, ketone and sterically hindered long-chain alkyl aldehydes.[9]

Encouraged by Ellman's pioneered work of Grignard reagents to α-chiral aldimines[10], we decided to investigate the addition of Grignard reagents to β-chiral aldimines (Fig. 2). we decided to investigate the addition of Grignard reagents to β-chiral aldimines. As part of our continuous interests in pursuing the building blocks used in the synthesis of piperidine alkaloids, depsipeptides, and ceramides,[2k,9,11] our aim is to develop a concise approach to 2,5-disubstituted 3-hydroxy pyrrolidine alkaloids. Herein we report a facile method for the preparation of 5-substituted 3-hydroxy lactam **1** and its application in the divergent syntheses of (−)-preussin **5** and its analogous.

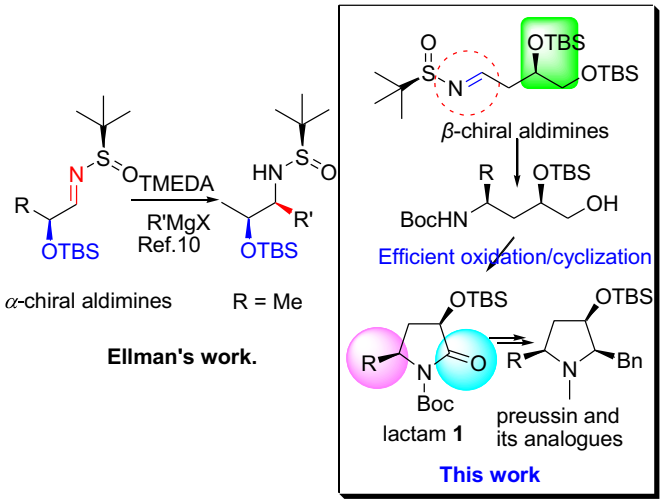
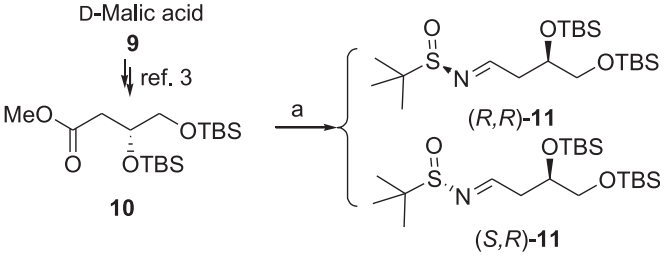


Fig. 2. Addition of nucleophiles to *N-tert*-butanesulfinyl ester.

2. Results and discussion

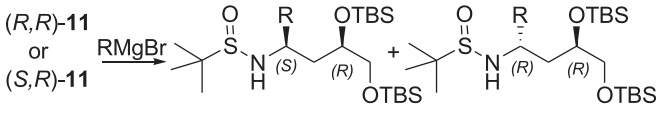
Ester **10** was prepared from D-malic acid via a known method in 73% overall yield.[12] Reduction of **10** with DIBAL-H gave the corresponding aldehyde in quantitative yield without further purification, which was directly reacted with (*R* or *S*)-2-methyl-2-propanesulfinamide in the presence of anhydrous copper sulfate to produce the corresponding β-chiral aldimines **11** in good yields (Scheme 1).[13]



Scheme 1. Reagents and conditions. a. (1) DIBAL-H, toluene, 0.5 h, quantitative yield; (2) (*R* or *S*)-2-methyl-2-propanesulfinamid, $CuSO_4$, PPTS, CH_2Cl_2, 24 h, 91% for (*R*,*R*)-**11**; 70% for (*S*,*R*)-**11**.

Next, several diastereoselective addition reactions to β-chiral aldimines **11** with Grignard reagents were surveyed (Table 1). Treatment of compound **11** with 3.0 equiv of benzylmagnesium bromide in THF at −78 °C followed by warming up the mixture to

Table 1
Addition of Grignard reagents to imines

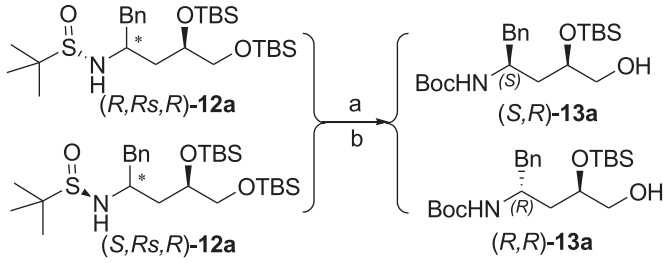


Entry[a]	11	R	12	Y %[b]	(*S*,*R*)/(*R*,*R*)[c]
1[d]	(*R*,*R*)	Bn–	**12a**	70	80:20
2[e]	(*R*,*R*)	Bn–	**12a**	95	87:13
3[e]	(*S*,*R*)	Bn–	**12a**	58	21:79
4[e]	(*R*,*R*)	Allyl–	**12b**	78	88:12
5[d]	(*R*,*R*)	Ph–	**12c**	78	83:17
6[e]	(*R*,*R*)	Ph–	**12c**	89	88:12
7[d]	(*R*,*R*)	4-MePh–	**12d**	77	84:16
8[e]	(*R*,*R*)	4-Me–Ph–	**12d**	94	89:11
9[d]	(*R*,*R*)	CH_2=CH–	**12e**	92	82:18
10[e]	(*R*,*R*)	CH_2=CH–	**12e**	94	89:11
11[d]	(*R*,*R*)	CH≡C–	**12f**	72	73:27
12[e]	(*R*,*R*)	CH≡C–	**12f**	85	83:17
13[d]	(*R*,*R*)	CH_3–	**12g**	87	92:8
14[e]	(*R*,*R*)	CH_3–	**12g**	89	95:5
15[e]	(*R*,*R*)	Et–	**12h**	79	98:2
16[e]	(*R*,*R*)	*n*-C_9H_{19}–	**12i**	89	99:1
17[e]	(*R*,*R*)	*n*-$C_{14}H_{29}$–	**12j**	90	99:1
18[d]	(*R*,*R*)	Isopropyl–	**12k**	83	94:6
19[e]	(*R*,*R*)	Isopropyl–	**12k**	98	98:2
20[e]	(*R*,*R*)	*tert*-Butyl–	**12l**	65	99:1
21[e]	(*R*,*R*)	Cyclopropyl–	**12m**	90	85:15
22[d]	(*R*,*R*)	Cyclopenyl–	**12n**	90	74:26
23[e]	(*R*,*R*)	Cyclopenyl–	**12n**	91	82:18
24[d]	(*R*,*R*)	Cyclohexyl–	**12o**	83	99:1
25[e]	(*R*,*R*)	Cyclohexyl–	**12o**	93	99:1

[a] Reactions were performed with imines **11** (7.93 mmol), Grignard reagents (23.8 mL, 1.0 M in THF) in dry solvent (40 mL) at −78 °C to room temperature for 12 h.
[b] Isolated yield.
[c] *dr* was determined by isolated yields.
[d] THF as solvent (40 mL).
[e] DCM as solvent (40 mL).

room temperature and stirring for 12 h gave **12a** in 70% yield with 80:20 diastereoselectivity (Table 1 entry 1). To improve the diastereoselectivity of the reaction, different conditions were screened (Table 1 entries 1–3). It was discovered that when the solvent was changed to dichloromethane, diastereoselectivity and yields of compounds **12a**, **c**–**g**, **k**, **n**, **o** were slightly improved (Table 1 entries 2, 5–14, 18–19, 22–25). On the other hand, when the diastereomer (*S*,*R*)-**11** was applied to the reaction, (*R*,*R*)-**12a** was generated with 79:21 diastereoselectivity in 58% yield, indicating a mismatch between the chiral auxiliary and the substrate's γ-stereocenter (Table 1 entry 3). When allylmagnesium bromide was used as the nucleophile, similar yield and diastereoselectivity of (*S*,*R*)-**12b** was obtained (Table 1 entry 4). The effect of different Grignard reagents was also investigated, and the result showed that alkyl Grignards in general led to improved diastereoselectivity (up to 99:1, Table 1 entries 13–20, 24, 25). Unexpectedly, cyclopropyl and cyclopentyl magnesium bromide led to moderate diastereoselectivity (Table 1 entries 21–23).

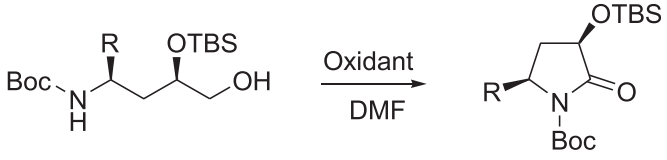
The stereochemistry of **12a** derived from (*R*,*R*)-**11** was ambiguously confirmed by the following synthesis of (−)-preussin **5**. Therefore, the stereochemistry of **12a** derived from (*S*,*R*)-**11** was confirmed by contrast the results of HPLC. The (*S*,*R*) and (*R*,*R*)-**13a** were easily converted from (*Rs*,*S*,*R*) and (*Rs*,*R*,*R*)-**12a**, respectively. The results of HPLC were obviously shown that (*R*,*R*)-**11** mainly produced (*R*,*S*,*R*)-**12a**, while (*S*,*R*)-**11** mainly generated (*S*,*R*,*R*)-**12a** (Scheme 2). According to similar process, treatment of (*S*,*R*)-**12a**–**o** with HCl/Dioxane in ethanol and subsequent protection (Boc_2O/TEA) gave corresponding compounds **13a**–**o** from 54% to 89% yields.



Scheme 2. Reagents and conditions: (a). HCl/dioxane, EtOH; (b). Boc_2O, TEA, DCM, 57% for (*S*,*R*)-**13a** and 53% for (*R*,*R*)-**13a**.

Next, we turned our attention to the preparation of lactams **14** from **13**. Initially, the known intramolecular oxidative cyclization of **13** with pyridinium dichromate (PDC) was attempted.[14] The alcohol **13c** was treated with PDC in DMF to give lactam **14c** in low yield (Table 2, entry 1). To improve the yield of **14a**–**l**, different conditions and substrates were screened, but the results showed that the yields of **14c**, **e**, **h**–**i** were not improved (Table 2 entries 1–4). Compared to the Oxidation/cyclization process of lactam **2**,[14] the formation of lactams **14a**–**l** was more difficult. We speculated that the bulky OTBS group of compound **13a**–**g**, **i**, **k**–**m**, **o** limited the yield of the oxidative cyclization reaction. To improve the yield of lactams **14**, various conditions were investigated. Ultimately, when Sarett reagent[21] [$CrO_3{\cdot}(C_5H_5)_2$] was used, the reaction proceeded with good to excellent yield (Table 2 entries 5–16). To the best of our knowledge, this is the first example for the synthesis of lactams by oxidation/cyclization with Sarett reagent.

Table 2
Preparation of **14a**–**l** by oxidation/cyclization

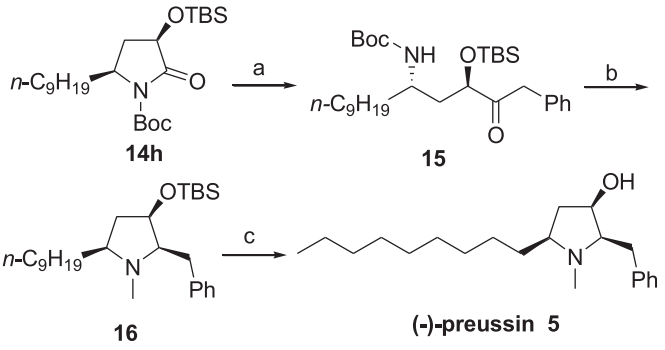


13a-g, 13i, 13k-m, 13o **14 a-l**

Entry[a]	R	Oxidant	14	Yield %[b]
1	Ph–	PDC	**14c**	41
2	CH_2=CH–	PDC	**14e**	35
3	*n*-C_9H_{19}–	PDC	**14h**	53
4	Isopropyl–	PDC	**14i**	48
5	Bn	$CrO_3{\cdot}(C_5H_5)_2$	**14a**	58
6	Allyl–	$CrO_3{\cdot}(C_5H_5)_2$	**14b**	34
7	Ph–	$CrO_3{\cdot}(C_5H_5)_2$	**14c**	72
8	4-MePh–	$CrO_3{\cdot}(C_5H_5)_2$	**14d**	81
9	CH_2=CH–	$CrO_3{\cdot}(C_5H_5)_2$	**14e**	45
10	CH≡C–	$CrO_3{\cdot}(C_5H_5)_2$	**14f**	57
11	Me–	$CrO_3{\cdot}(C_5H_5)_2$	**14g**	52
12	*n*-C_9H_{19}–	$CrO_3{\cdot}(C_5H_5)_2$	**14h**	72
13	Isopropyl–	$CrO_3{\cdot}(C_5H_5)_2$	**14i**	81
14	*tert*-Butyl–	$CrO_3{\cdot}(C_5H_5)_2$	**14j**	76
15	Cyclopropyl–	$CrO_3{\cdot}(C_5H_5)_2$	**14k**	70
16	Cyclohexyl–	$CrO_3{\cdot}(C_5H_5)_2$	**14l**	55

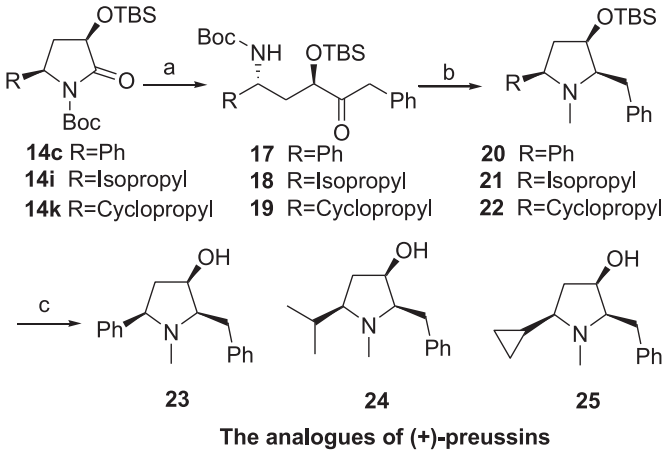
[a] The reactions were performed with amines **13** (2.44 mmol), Sarett reagent (5 equiv) in dry DMF (5 mL) at rt for 24 h.
[b] Isolated yield.

With the chiral 2-pyridones **14a**–**l** in hand, we turned our attention to the synthesis of (+)-preussin,[14–16] a pyrrolidinol alkaloid. Recently, it was reported that (−)-preussin **5** could inhibit growth of the bacteria *Candida* and filamentous fungi,[3,17] induce apoptosis in human tumor cells[18] and inhibit cell growth of the fission yeast *ts* mutants defective on *cdc*2-regulatory genes.[16b,19] All of these reported biological activities rendered preussin an attractive synthetic target.[14–16] Our synthesis started with the treatment of compound **14h** with benzylmagnesium bromide to generate ring-opened compound **15** in 82% yield (Scheme 3). The addition/ring-opening process to convert pyrrolidones to its open chain form is known to require rather harsh reaction conditions.[20] We were pleased to find that lactam **14h** smoothly underwent addition/ring-opening process to provide **15** in good yield. The coordination of a magnesium cation with the *ortho* oxygen in **14** may account for the success of this reaction. Deprotection of the Boc group in **15** with 2,2,2-trifluoroacetic acid and subsequent one-pot cyclization/hydrogenation/methylation generated intermediate **16** in 59% overall yield. Finally, **16** was treated with tetrabutylammonium fluoride (TBAF) in tetrahydrofuran to give (−)-preussin **5** {$[\alpha]_D^{25}$ −34.7 (*c* 0.5, $CHCl_3$); lit.[15l] $[\alpha]_D^{25}$ +32 (*c* 1.1, $CHCl_3$)} in 95% yield. The spectroscopic and physical data of the synthetic **5** were identical to the reported data.[15l]



Scheme 3. Reagents and conditions: (a) BnMgBr, −78 °C, 3 h, 72%; (b) 1. CF_3COOH, rt, 3 h; NaOH, pH=10–12; 2. H_2, Pd/C, $Pd(OH)_2$, $(HCHO)_n$, rt, 16 h, two steps 59%; (c) TBAF, THF, rt, 8 h, 95%.

In light of our interest in diversity-oriented synthesis,[11f] we prepared several analogues of (−)-preussin (Scheme 4). Following the synthetic sequence described above, three analogues of (−)-preussin **23** {$[\alpha]_D^{25}$ +6.98 (*c* 0.38, $CHCl_3$)}, **24** {$[\alpha]_D^{26}$ −25.42 (*c* 0.63, $CHCl_3$)}, **25** {$[\alpha]_D^{25}$ −36.53 (*c* 0.79, $CHCl_3$)} were successfully prepared in 19%, 34%, 8% respectively yields. The structures of analogues **23**, **24** and **25** were unambiguously confirmed by spectroscopic data.



Scheme 4. Reagents and conditions. (a) BnMgBr, −78 °C, 3 h, 64% for **17**, 80% for **18**, 39% for **19**; (b) 1. CF_3COOH, rt, 3 h; NaOH, rt, pH=10–12; 2. H_2, Pd/C, $Pd(OH)_2$, $(HCHO)_n$, rt, 16 h, two steps 55% for **20**, 69% for **21**, 37% for **22**; (c) TBAF, THF, rt, 24 h, 55% for **23**, 61% for **24**, 57% for **25**.

3. Conclusions

In summary, an efficient method for the preparation of (*S*,*R*)-α-hydroxy-γ-amino **12** by a diastereoselective addition of Grignard reagents to β-chiral aldimines **11** has been developed. Moreover,

a novel approach for the synthesis of flexible building blocks **14** has been achieved by oxidation/cyclization with Sarett reagent in moderate to excellent yields. Using this strategy, (−)-preussin **5** and its three analogues **23**, **24** and **25** have been synthesized. Further studies on this methodology's application in the diversity-oriented synthesis of other bioactive compounds are now in progress in our laboratory.

4. Experimental section

4.1. General

THF was distilled from sodium/benzophenone. Reactions were monitored by thin layer chromatography (TLC) on glass plates coated with silica gel with fluorescent indicator. Flash chromatography was performed on silica gel (300–400 mesh) with Petroleum/EtOAc as eluent. Optical rotations were measured on a polarimeter with a sodium lamp. HRMS were measured on an LCMS-IT-TOF apparatus. IR spectra were recorded using film on a Fourier Transform Infrared Spectrometer. NMR spectra were recorded at 400 MHz or 500 MHz, and chemical shifts are reported in δ (parts per million) referenced to an internal TMS standard for ^{1}H NMR and $CDCl_3$ (77.0 ppm) for ^{13}C NMR.

*4.1.1. (R,E)-N-((R/S)-3,4-Bis(tert-butyldimethylsilyloxy)butylidene)-2-methylpropane-2-sulfinamide (**11**).* A solution of **10** (30.54 g, 84.28 mmol) in toluene (200 mL) was cooled to −78 °C and stirred for 10 min. To this solution was added a solution of diisobutylaluminium hydride (101.2 mL, 101.2 mmol, 20% in hexane) dropwise and the reaction mixture was stirred for 20 min. The mixture was quenched with a solution of potassium sodium tartrate (1 M) and warmed to room temperature. The crude aldehyde, which was dissolved in DCM (200 mL). (*R*)-2-Methyl-2-propanesulfinamide (7.89 g, 65.15 mmol), cupric sulfate anhydrous (23.11 g, 144.78 mmol), and PPTS (0.91 g, 3.62 mmol) were added to the solution in one portion and the mixture was stirred for 19 h. The resulting mixture was filtrated and the filtrate was concentrated to give the crude product, which was purified by flash chromatography on silica gel (PE/EA=20/1) to give **11** (28.42 g) in 91% yield as a yellow oil.

(*R,R*)-**11** $[\alpha]_D^{25}$ −121.29 (*c* 2.16, $CHCl_3$); IR (film): ν_{max} 3433, 2956, 2929, 2854, 1638, 1473, 1459, 1387, 1368, 1253, 1084, 1004, 939, 835, 806, 776 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (t, *J*=4.8 Hz, 1H), 4.02–4.07 (m, 1H), 3.62 (dd, *J*=5.4, 10.2 Hz, 1H), 3.48 (dd, *J*=7.0, 10.2 Hz, 1H), 2.85–2.75 (m, 1H), 2.72–2.60 (m, 1H), 1.25–1.15 (m, 9H), 0.85–0.85 (m, 18H), 0.10–0.05 (m, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 70.9, 66.8, 56.5, 41.1, 25.9, 25.8, 22.4, 18.3, 18.1, −4.4, −4.8, −5.4 ppm; HRMS (ESI) calcd for $[C_{20}H_{45}NO_3SSi_2+H^+]$: 436.2737, found: 436.2737.

4.2. General procedure for the synthesis of 12a–o

A solution of **11** (3.45 g, 7.93 mmol) in dry DCM (40 mL) was treated with a solution of Grignard reagent (23.78 mL, 23.78 mmol, 1 M in THF) at −78 °C. The reaction mixture was allowed to warm to room temperature and stirred for 12 h. The mixture was quenched with a solution of saturated NH_4Cl and extracted with DCM (50 mL×3). The combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (PE/EA=6/1) to give **12a**–**o**.

*4.2.1. (R)-N-((2S,4R)-4,5-Bis(tert-butyldimethylsilyloxy)-1-phenylpentan-2-yl)-2-methylpropane-2-sulfinamide ((S,R)-**12a**).* (*S,R*)-**12a** (3.48 g, 95%) as a colorless oil. $[\alpha]_D^{24}$ +47.38 (*c* 0.82, $CHCl_3$); IR (film): ν_{max} 3136, 2954, 2928, 2856, 1655, 1460, 1363, 1251, 1138, 1098, 1044, 1033, 1004, 833, 777, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.26 (m, 4H), 7.25–7.20 (m, 1H), 3.82–3.72 (m, 2H), 3.51 (dd, *J*=4.8, 10.0 Hz, 1H), 3.32 (dd, *J*=6.8, 10.0 Hz, 1H), 3.23 (d, *J*=9.6 Hz, 1H), 3.11 (dd, *J*=4.2,13.4 Hz, 1H), 3.04 (dd, *J*=7.4,13.4 Hz, 1H), 1.57–1.47 (m, 2H), 1.25–1.15 (m, 9H), 0.92–0.86 (m, 9H), 0.86–0.82 (m, 9H), 0.10–0.05 (m, 6H), 0.05–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.1, 130.3, 128.3, 126.4, 70.4, 67.3, 56.2, 54.4, 43.7, 40.6, 25.9, 25.9, 22.8, 18.2, 18.1, −3.84, −4.42, −5.35, −5.39 ppm; HRMS (ESI) calcd for $[C_{27}H_{53}NO_3SSi_2+H^+]$: 528.3363, found: 528.3344.

(*R,R*)-**12a** (1.92 g, 58%) as a white solid. Mp 95–96 °C. $[\alpha]_D^{25}$ +17.37 (*c* 1.26, $CHCl_3$); IR (film): ν_{max} 3274, 2954, 2930, 2856, 1495, 1473, 1463, 1251, 1134, 1110, 1088, 1048, 1007, 955, 895, 834, 862, 814, 773, 753, 703 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.21 (m, 5H), 3.92–3.82 (m, 1H), 3.82–3.72 (m, 1H), 3.58 (dd, *J*=5.2, 10.0 Hz, 1H), 3.45 (dd, *J*=6.0, 10.4 Hz, 1H), 3.25 (d, *J*=8.0 Hz, 1H), 3.04 (dd, *J*=6.4, 13.6 Hz, 1H), 2.97 (dd, *J*=5.2, 13.6 Hz, 1H), 1.86–1.74 (m, 1H), 1.63–1.53 (m, 1H), 1.18 (s, 9H), 0.94–0.86 (m, 18H), 0.10–0.01 (m, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 130.3, 128.4, 126.5, 70.5, 67.5, 55.8, 53.7, 42.1, 40.3, 29.7, 25.9, 25.8, 22.6, 18.4, 18.1, −4.2, −4.7, −5.4 ppm; HRMS (ESI) calcd for $[C_{27}H_{53}NO_3SSi_2+H^+]$: 528.3363, found: 528.3372.

*4.2.2. (R)-N-((2R,4S)-1,2-Bis(tert-butyldimethylsilyloxy)hept-6-en-4-yl)-2-methylpropane-2-sulfinamide (**12b**).* **12b** (2.69 g, 78%) as a white solid. Mp 71–72 °C; $[\alpha]_D^{26}$ −9.01 (*c* 1.12, $CHCl_3$); IR (film): ν_{max} 3153, 2929, 2857, 1471, 1419, 1389, 1362, 1255, 1099, 1043, 1055, 941, 912 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.90–5.78 (m, 1H), 5.24 (d, *J*=5.2 Hz, 1H), 5.21 (br s, 1H), 3.92–3.82 (m, 1H), 3.65–3.52 (m, 2H), 3.41 (dd, *J*=6.8, 10.0 Hz, 1H), 3.31 (d, *J*=8.8 Hz, 1H), 2.63–2.46 (m, 2H), 1.76–1.67 (m, 1H), 1.67–1.55 (m, 1H), 1.35–1.25 (m, 9H), 1.07–0.85 (m, 18H), 0.22–0.17 (m, 6H), 0.17–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.8, 119.0, 70.4, 67.3, 56.0, 53.1, 41.8, 40.8, 25.9, 22.8, 18.3, 18.1, −3.9, −4.5, −5.3 ppm; HRMS (ESI) calcd for $[C_{23}H_{51}NO_3SSi_2+H^+]$: 478.3206, found: 478.3208.

*4.2.3. (R)-N-((1R,3R)-3,4-Bis(tert-butyldimethylsilyloxy)-1-phenylbutyl)-2-methylpropane-2-sulfinamide (**12c**).* **12c** (3.19 g, 89%) as a colorless oil. $[\alpha]_D^{25}$ −29.91 (*c* 0.99, $CHCl_3$); IR (film): ν_{max} 3399, 2954, 2928, 2857, 1664, 1655, 1648, 1638, 1459, 1400, 1071, 835, 766, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.34 (m, 4H), 7.32–7.25 (m, 1H), 4.60–4.52 (m, 1H), 3.82–3.74 (m, 1H), 3.64 (d, *J*=6.0 Hz, 1H), 3.57 (dd, *J*=5.2, 10.0 Hz, 1H), 3.43 (dd, *J*=6.4, 10.0 Hz, 1H), 2.24 (ddd, *J*=5.1, 8.3, 13.9 Hz, 1H), 1.85 (ddd, *J*=5.9, 6.7, 14.1 Hz, 1H), 1.24–1.21 (m, 9H), 0.91–0.88 (m, 9H), 0.94–0.91 (m, 9H), 0.05–0.02 (m, 6H), 0.10–0.05 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 128.7, 127.6, 127.0, 70.7, 67.1, 56.6, 56.0, 43.1, 26.0, 25.9, 22.7, 18.3, 18.1, −4.1, −4.6, −5.4 ppm; HRMS (ESI) calcd for $[C_{26}H_{51}NO_3SSi_2+H^+]$: 514.3206, found: 514.3201.

*4.2.4. (R)-N-((1R,3R)-3,4-Bis(tert-butyldimethylsilyloxy)-1-p-tolylbutyl)-2-methylpropane-2-sulfinamide (**12d**).* **12d** (3.50 g, 94%) as a colorless oil. $[\alpha]_D^{27}$ −12.39 (*c* 0.89, $CHCl_3$); IR (film): ν_{max} 3351, 2945, 2833, 2601, 2519, 2043, 1450, 1410, 1108, 1031 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.19 (m, 2H), 7.18–7.08 (m, 2H), 4.48 (dd, *J*=6.4, 13.2 Hz, 1H), 3.80–3.70 (m, 1H), 3.60–3.50 (m, 2H), 3.38 (dd, *J*=7.0, 9.4 Hz, 1H), 2.36–2.27 (m, 3H), 2.24–2.15 (m, 1H), 1.85–1.75 (m, 1H), 1.29–1.17 (m, 9H), 0.88–0.74 (m, 18H), 0.16–0.03 (m, 6H), 0.03–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 137.2, 129.3, 126.9, 70.6, 67.1, 56.4, 55.9, 42.9, 25.9, 25.9, 22.7, 21.1, 18.3, 18.1, −4.1, −4.6, −5.4 ppm; HRMS (ESI) calcd for $[C_{27}H_{53}NO_3SSi_2+H^+]$: 528.3363, found: 528.3361.

*4.2.5. (R)-N-((3R,5R)-5,6-Bis(tert-butyldimethylsilyloxy)hex-1-en-3-yl)-2-methylpropane-2-sulfinamide (**12e**).* **12e** (3.07 g, 94%) as a white solid. Mp 115–116 °C; $[\alpha]_D^{25}$ −20.23 (*c* 0.30, $CHCl_3$); IR (film): ν_{max} 3145, 2929, 2858, 1473, 1389, 1362, 1257, 1050, 998, 915, 835,

777, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.10–5.95 (m, 1H), 5.33 (dd, *J*=0.8,17.2 Hz, 1H), 5.21 (dd, *J*=1.2, 10.4 Hz, 1H), 4.05–3.95 (m, 1H), 3.95–3.85 (m, 1H), 3.63 (dd, *J*=5.2, 10.0 Hz, 1H), 3.47 (dd, *J*=6.8, 10.0 Hz, 1H), 3.33 (d, *J*=8.0 Hz, 1H), 1.95–1.85 (m, 1H), 1.72–1.65 (m, 1H), 1.42–1.20 (m, 9H), 1.12–0.75 (m, 18H), 0.35–0.15 (m, 6H), 0.15–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 115.6, 70.2, 67.1, 56.2, 56.0, 41.3, 25.9, 25.9, 22.7, 18.3, 18.1, −4.0, −4.5, −5.4 ppm; HRMS (ESI) calcd for $[C_{22}H_{49}NO_3SSi_2+H^+]$: 464.3050, found: 464.3049.

*4.2.6. (R)-N-((3R,5R)-5,6-Bis(tert-butyldimethylsilyloxy)hex-1-yn-3-yl)-2-methylpropane-2-sulfinamide (**12f**).* **12f** (2.58 g, 85%) as a white solid. Mp 65–66 °C. $[\alpha]_D^{26}$ +5.26 (*c* 1.02, $CHCl_3$); IR (film): ν_{max} 3313, 3220, 2956, 2930, 2897, 2858, 1473, 1463, 1389, 1362, 1255, 1092, 1005, 939, 810 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.30–4.25 (m, 1H), 4.02–3.95 (m, 1H), 3.70–3.57 (m, 2H), 3.50 (dd, *J*=6.8, 10.0 Hz, 1H), 2.51–2.50 (m, 1H), 2.14–2.06 (m, 1H), 1.94–1.86 (m, 1H), 1.33–1.27 (m, 9H), 1.01–0.87 (m, 18H), 0.27–0.14 (m, 6H), 0.14–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 84.4, 72.8, 70.0, 67.0, 56.4, 44.4, 42.5, 25.9, 25.9, 22.6, 18.3, 18.0, −4.2, −4.5, −5.4 ppm; HRMS (ESI) calcd for $[C_{22}H_{47}NO_3SSi_2+H^+]$: 462.2893, found: 462.2885.

*4.2.7. (R)-N-((2S,4R)-4,5-Bis(tert-butyldimethylsilyloxy)pentan-2-yl)-2-methylpropane-2-sulfinamide (**12g**).* **12g** (3.03 g, 89%) as a white solid. Mp 104–105 °C; $[\alpha]_D^{26}$ +3.67 (*c* 1.12, $CHCl_3$); IR (film): ν_{max} 3344, 2944, 2832, 2600, 2514, 2043, 1459, 1449, 1420 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) : δ 3.82–3.75 (m, 1H), 3.56–3.47 (m, 2H), 3.33 (dd, *J*=7.2, 9.2 Hz, 1H), 2.93 (d, *J*=8.8 Hz, 1H), 1.73–1.64 (m, 1H), 1.49–1.40 (m, 1H), 1.32 (d, *J*=6.0 Hz, 3H), 1.25–1.14 (m, 9H), 0.86–0.70 (m, 9H), 1.05–0.86 (m, 9H), 0.12–0.04 (m, 6H), 0.04–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.4, 67.3, 55.9, 50.3, 44.1, 25.9, 24.8, 22.7, 18.3, 18.1, −4.0, −4.5, −5.4 ppm; HRMS (ESI) calcd for $[C_{21}H_{49}NO_3SSi_2+H^+]$: 452.3050, found: 452.3048.

*4.2.8. (R)-N-((3S,5R)-5,6-Bis(tert-butyldimethylsilyloxy)hexan-3-yl)-2-methylpropane-2-sulfinamide (**12h**).* **12h** (2.86 g, 79%) as a white solid. Mp 92–93 °C; $[\alpha]_D^{25}$ +5.79 (*c* 1.46, $CHCl_3$); IR (film): ν_{max} 3349, 2945, 2833, 2601, 2515, 2228, 2051, 1654, 1447, 1420, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.85–3.76 (m, 1H), 3.55 (dd, *J*=5.0, 9.8 Hz, 1H), 3.38 (dd, *J*=3.0, 8.6 Hz, 1H), 3.35–3.30 (m, 1H), 3.07 (d, *J*=8.8 Hz, 1H), 1.85–1.75 (m, 1H), 1.67–1.50 (m, 3H), 1.25–1.20 (m, 9H), 0.95 (t, *J*=7.2 Hz, 3H), 0.92–0.87 (m, 18H), 0.10–0.07 (m, 6H), 0.07–0.05 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) : δ 70.5, 67.4, 56.0, 55.8, 40.9, 30.5, 25.9, 22.8, 18.3, 18.1, 9.9, −3.8, −4.4, −5.4 ppm; HRMS (ESI) calcd for $[C_{22}H_{51}NO_3SSi_2+H^+]$: 466.3206, found: 466.3187.

*4.2.9. (R)-N-((2R,4S)-1,2-Bis(tert-butyldimethylsilyloxy)tridecan-4-yl)-2-methylpropane-2-sulfinamide (**12i**).* **12i** (3.94 g, 89%) as a colorless oil. $[\alpha]_D^{27}$ +2.96 (*c* 0.47, $CHCl_3$); IR (film): ν_{max} 3386, 2944, 2949, 2836, 1655, 1459, 1449, 1407 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.85–3.76 (m, 1H), 3.65–3.60 (m, 0.4H), 3.53 (dd, *J*=5.2, 10.0 Hz, 1H), 3.42–3.30 (m, 2H), 3.04 (d, *J*=8.8 Hz, 1H), 1.85–1.67 (m, 2H), 1.62–1.47 (m, 3H), 1.42–1.22 (m, 16H), 1.22–1.17 (m, 8H), 0.87–0.82 (m, 10H), 0.90–0.87 (m, 8H), 0.20–0.05 (m, 6H), 0.05–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.4, 67.4, 56.0, 54.4, 41.3, 37.8, 31.8, 29.5, 29.5, 29.4, 29.3, 25.9, 25.6, 22.8, 22.6, 18.3, 18.0, 14.1, −3.9, −4.5, −5.4 ppm; HRMS (ESI) calcd for $[C_{29}H_{65}NO_3SSi_2+H^+]$: 564.4302, found: 564.4294.

*4.2.10. (R)-N-((2R,4S)-1,2-Bis(tert-butyldimethylsilyloxy)octadecan-4-yl)-2-methylpropane-2-sulfinamide (**12j**).* **12j** (4.47 g, 90%) as a colorless oil. $[\alpha]_D^{25}$ −3.49 (*c* 0.98, $CHCl_3$); IR (film): ν_{max} 3351, 2945, 2833, 2600, 2521, 2219, 2039, 1452, 1412, 1117, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.90–3.76 (m, 1H), 3.55 (dd, *J*=5.0, 9.8 Hz, 1H), 3.45–3.37 (m, 1H), 3.35 (dd, *J*=3.0, 8.2 Hz, 1H), 3.04 (d, *J*=8.4 Hz, 1H), 1.85–1.74 (m, 1H), 1.65–1.50 (m, 4H), 1.29–1.26 (m, 21H), 1.24–1.21 (m, 11H), 0.93–0.87 (m, 21H), 0.12–0.07 (m, 6H), 0.07–0.04 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 70.5, 67.4, 61.6, 41.4, 37.8, 35.0, 31.9, 29.7, 29.6, 29.5, 29.4, 26.2, 25.9, 25.7, 22.8, 22.8, 22.7, 18.3, 18.1, 14.1, −3.8, −4.4, 5.4 δ ppm; HRMS (ESI) calcd for $[C_{34}H_{75}NO_3SSi_2+H^+]$: 634.5084, found: 634.5042.

*4.2.11. (R)-N-((3R,5R)-5,6-Bis(tert-butyldimethylsilyloxy)-2-methylhexan-3-yl)-2-methylpropane-2-sulfinamide (**12k**).* **12i** (3.66 g, 98%) as a white solid, mp 66–67 °C. $[\alpha]_D^{25}$ +24.51 (*c* 1.06, $CHCl_3$); IR (film): ν_{max} 3399, 2949, 2855, 2841, 2382, 1653, 1457, 1252, 1021 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.82–3.75 (m, 1H), 3.57 (dd, *J*=5.0, 9.8 Hz, 1H), 3.38–3.34 (m, 1H), 3.34–3.28 (m, 1H), 3.19 (d, *J*=9.6 Hz, 1H), 2.20–2.08 (m, 1H), 1.56–1.38 (m, 2H), 1.24 (s, 9H), 0.95–0.87 (m, 24H), 0.12–0.04 (m, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.6, 67.5, 59.3, 56.2, 36.8, 33.4, 25.9, 22.9, 19.0, 18.3, 18.1, 16.3, −3.7, −4.4, −5.3, −5.4 ppm; HRMS (ESI) calcd for $[C_{23}H_{53}NO_3SSi_2+H^+]$: 480.3363, found: 480.3325.

*4.2.12. N-((3R,5R)-5,6-Bis(tert-butyldimethylsilyloxy)-2,2-dimethylhexan-3-yl)-2-methylpropane-2-sulfinamide (**12l**).* **12l** (2.51 g, 65%) as a white solid, mp 95–96 °C. $[\alpha]_D^{27}$ +3.84 (*c* 1.06, $CHCl_3$); IR (film): ν_{max} 3344, 2946, 2833, 2603, 2519, 2229, 2044, 1658, 1452, 1417, 1118, 1031 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.90–3.80 (m, 1H), 3.58 (dd, *J*=5.0, 9.8 Hz, 1H), 3.32 (dd, *J*=7.2, 9.6 Hz, 1H), 3.23 (d, *J*=8.0 Hz, 1H), 3.16–3.08 (m, 1H), 1.64–1.48 (m, 2H), 1.30–1.22 (m, 9H), 0.98 (s, 9H), 0.92–0.87 (m, 18H), 0.16–0.08 (m, 6H), 0.08–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.8, 67.7, 62.8, 56.6, 38.3, 34.5, 29.7, 27.0, 26.0, 25.9, 23.1, 18.3, 18.1, −3.7, −4.2, −5.4 ppm; HRMS (ESI) calcd for $[C_{24}H_{55}NO_3SSi_2+H^+]$: 494.3519, found: 494.3515.

*4.2.13. (R)-N-((1R,3R)-3,4-Bis(tert-butyldimethylsilyloxy)-1-cyclopropylbutyl)-2-methylpropane-2-sulfinamide (**12m**).* **12m** (2.90 g, 90%) as a white solid, mp 101–102 °C. $[\alpha]_D^{27}$ −26.31 (*c* 0.92, $CHCl_3$); IR (film): ν_{max} 3152, 3002, 2957, 2928, 2901, 2857, 1472, 1361, 1251, 1128, 1095, 1050, 998 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.95–3.87 (m, 1H), 3.61 (dd, *J*=5.2, 10.0 Hz, 1H), 3.44 (dd, *J*=7.0, 9.8 Hz, 1H), 3.27 (d, *J*=8.0 Hz, 1H), 2.71–2.61 (m, 1H), 1.91–1.81 (m, 1H), 1.78–1.70 (m, 1H), 1.34–1.25 (m, 9H), 0.99–0.87 (m, 18H), 0.79–0.69 (m, 1H), 0.69–0.61 (m, 1H), 0.61–0.53 (m, 1H), 0.34–0.25 (m, 1H), 0.18–0.00 (m, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.3, 67.3, 59.5, 55.9, 42.1, 25.9, 25.9, 22.8, 18.6, 18.3, 18.1, 5.5, 4.4, −3.9, −4.6, −5.4 ppm; HRMS (ESI) calcd for $[C_{23}H_{51}NO_3SSi_2+H^+]$: 478.3206, found: 478.3207.

*4.2.14. N-((1R,3R)-3,4-Bis(tert-butyldimethylsilyloxy)-1-cyclopentylbutyl)-2-methylpropane-2-sulfinamide (**12n**).* **12n** (2.99 g, 91%) as a white solid, mp 92–93 °C. $[\alpha]_D^{25}$ +4.03 (*c* 0.79, $CHCl_3$); IR (film): ν_{max} 3251, 2954, 2928, 2858, 1252, 1131, 1097, 1052, 834 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.88–3.78 (m, 1H), 3.55 (dd, *J*=5.2, 10.0 Hz, 1H), 3.40–3.28 (m, 2H), 3.16 (d, *J*=8.0 Hz, 1H), 2.25–2.12 (m, 1H), 1.85–1.70 (m, 2H), 1.67–1.50 (m, 6H), 1.40–1.27 (m, 2H), 1.22 (s, 9H), 0.95–0.85 (m, 18H), 0.12–0.02 (m, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.7, 67.6, 57.9, 56.1, 45.8, 39.8, 29.7, 28.6, 25.9, 25.7, 25.5, 22.9, 18.3, 18.1, −3.7, −4.4, −5.4 ppm; HRMS (ESI) calcd for $[C_{25}H_{55}NO_3SSi_2+H^+]$: 506.3519, found: 506.3518.

*4.2.15. (R)-N-((1R,3R)-3,4-BIS(tert-butyldimethylsilyloxy)-1-cyclohexylbutyl)-2-methyl-propane-2-sulfinamide (**12o**).* **12o** (3.79 g, 93%) as a white solid, mp 91–92 °C. $[\alpha]_D^{25}$ +18.36 (*c* 0.89, $CHCl_3$); IR (film): ν_{max} 3258, 2955, 2929, 2856, 2739, 2709, 2662, 1472, 1450, 1414, 1389, 1362, 1252, 1230, 1181, 1095, 1051, 994, 974, 940, 893, 835, 775, 742, 714, 662 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.78–3.70 (m, 1H), 3.59 (dd, *J*=5.2, 10.0 Hz, 1H),

3.32–3.22 (m, 2H), 3.18 (d, *J*=9.6 Hz, 1H), 1.78–1.68 (m, 3H), 1.68–1.58 (m, 3H), 1.55–1.38 (m, 2H), 1.32–1.22 (m, 2H), 1.19 (s, 9H), 1.16–0.97 (m, 3H), 0.86 (s, 9H), 0.85 (s, 9H), 0.07–0.00 (m, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.6, 67.5, 59.0, 56.1, 43.8, 37.9, 29.5, 27.2, 26.6, 26.3, 26.2, 25.9, 22.8, 18.2, 18.0, −3.8, −4.4, −5.4 ppm; HRMS (ESI) calcd for [$C_{26}H_{57}NO_3SSi_2$+H^+]: 520.3676, found: 520.3681.

4.3. General procedure for synthesis of 13a–o

A solution of **12** (3.79 mmol) in EtOH (5 mL) was cooled to 0 °C. A solution of HCl/dioxane (3.8 mL) was added and the reaction was stirred for 30 min. The mixture was concentrated and the residue was dissolved in DCM (50 mL). Boc_2O (0.99 g, 4.55 mmol) and TEA (2.6 mL, 18.95 mmol) were added to the solution and the mixture was stirred overnight. The mixture was quenched with a saturated aqueous solution of NH_4Cl and resulting layers were separated. The aqueous layer was extracted with DCM for three times and the combined organic layers were washed with brine, dried, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (PE/EA=4/1) to give **13a–o**.

*4.3.1. tert-Butyl (2S,4R)-4-(tert-butyldimethylsilyloxy)-5-hydroxy-1-phenylpentan-2-yl-carbamate ((S,R)-**13a**).* (*S*,*R*)-**13a** (0.885 g, 57%) as a colorless oil. $[\alpha]_D^{24}$ +17.23 (*c* 1.50, $CHCl_3$); IR (film): ν_{max} 3400, 2929, 2857, 1691, 1498, 1391, 1366, 1253, 1171, 1047, 836, 777, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.27 (m, 2H), 7.25–7.16 (m, 3H), 4.67 (d, *J*=6.8 Hz, 1H), 3.98–3.79 (m, 2H), 3.60–3.40 (m, 2H), 2.95 (dd, *J*=3.8, 13.0 Hz, 1H), 2.71 (dd, *J*=7.8, 13.0 Hz, 1H), 1.95 (br s, 1H), 1.86–1.62 (m, 2H), 1.46–1.40 (m, 9H), 0.90 (m, 9H), 0.10–0.05 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 138.1, 129.6, 128.3, 126.3, 79.1, 70.3, 66.7, 49.1, 41.9, 37.7, 28.4, 25.9, 18.0, −4.5, −4.9 ppm; HRMS (ESI) calcd for [$C_{22}H_{39}NO_4Si$+Na^+]: 432.2546, found: 432.2545. The results of HPLC (Waters 2535 Quaternary Gradient Module, Waters 2707 Autosampler and Waters 2489 UV/Visible Detector; PC-3 column (19×250 mm), *n*-hexane/*i*-propanol=90/10, 0.7 mL/min, rt: 5.23 min).

*4.3.2. tert-Butyl (2R,4S)-2-(tert-butyldimethylsilyloxy)-1-hydroxyhept-6-en-4-yl-carbamate (**13b**).* **13b** (0.858 g, 57%) as a colorless oil. $[\alpha]_D^{25}$ +18.90 (*c* 0.45, $CHCl_3$); IR (film): ν_{max} 3353, 2945, 2833, 2601, 2526, 2343, 2231, 2048, 1450, 1425, 1110, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers): δ 5.82–5.70 (m, 1H), 5.15–5.00 (m, 2H), 4.55 (d, *J*=7.8 Hz, 1/5H), 4.64 (d, *J*=7.8 Hz, 4/5H), 3.98–3.92 (m, 1/5H), 3.88–3.82 (m, 4/5H), 3.79–3.63 (m, 1H), 3.58 (d, *J*=10.4 Hz, 1H), 3.46 (d, *J*=9.6 Hz, 1H), 2.35–2.16 (m, 2H), 2.12–1.92 (m, 1H), 1.77–1.68 (m, 1H), 1.60–1.35 (m, 9H), 1.10–0.75 (m, 9H), 0.25–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 134.3, 117.8, 79.0, 71.9, 70.2, 66.6, 47.3, 40.1, 38.3, 28.4, 25.8, 18.0, −4.5, −4.6, −4.8 ppm; HRMS (ESI) calcd for [$C_{18}H_{37}NO_4Si$+Na^+]: 382.2390, found: 382.2390.

*4.3.3. tert-Butyl (1R,3R)-3-(tert-butyldimethylsilyloxy)-4-hydroxy-1-phenylbutyl-carbamate (**13c**).* **13c** (1.34 g, 87%) as a colorless oil. $[\alpha]_D^{25}$ +25.25 (*c* 0.93, $CHCl_3$); IR (film): ν_{max} 3349, 2945, 2833, 2597, 2520, 2228, 2044, 1684, 1450, 1418, 1114, 1031 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers): δ 7.25–7.20 (m, 1H), 7.38–7.26 (m, 4H), 5.54 (s, 1/5H), 5.29 (s, 3/5H), 4.74 (br s, 4/5H), 4.58 (br s, 1/5H), 3.85 (br s, 1H), 3.65–3.50 (m, 2H), 2.06 (d, *J*=13.2 Hz, 1H), 2.00–1.90 (m, 1H), 1.42 (s, 9H), 1.27 (t, *J*=13.2, 2H), 0.95 (s, 9H), 0.16–0.10 (m, 3H), 0.10–0.06 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 143.3, 128.5, 127.1, 126.0, 79.3, 70.2, 66.4, 52.0, 41.4, 28.3, 25.9, 18.0, −4.5, −4.9 ppm; HRMS (ESI) calcd for [$C_{21}H_{37}NO_4Si$+Na^+]: 418.2390, found: 418.2396.

*4.3.4. tert-Butyl (1R,3R)-3-(tert-butyldimethylsilyloxy)-4-hydroxy-1-p-tolylbutyl-carbamate (**13d**).* **13d** (0.838 g, 54%) as a colorless oil. $[\alpha]_D^{24}$ +34.70 (*c* 0.64, $CHCl_3$); IR (film): ν_{max} 3346, 2945, 2833, 2597, 2515, 2343, 2339, 2039, 1653, 1462, 1450, 1430, 1029 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers): δ 7.20–7.10 (m, 4H), 5.30–5.10 (s, 9/10H), 5.10–5.00 (s, 1/10H), 4.75–4.60 (s, 9/10H), 4.60–4.50 (s, 1/10H), 3.85–3.75 (m, 1H), 3.65–3.58 (m, 1H), 3.58–3.50 (m, 1H), 2.35 (s, 3H), 1.98–1.90 (m, 2H), 0.97–0.92 (m, 9H), 0.95 (s, 9H), 0.10–0.07 (m, 3H), 0.15–0.10 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 140.2, 136.7, 129.3, 125.9, 79.3, 70.3, 66.3, 51.8, 41.3, 28.4, 25.9, 21.1, 18.0, −4.5, −4.8 ppm; HRMS (ESI) calcd for [$C_{22}H_{39}NO_4Si$+Na^+]: 432.2546, found: 432.2543.

*4.3.5. tert-Butyl (3R,5R)-5-(tert-butyldimethylsilyloxy)-6-hydroxyhex-1-en-3-yl-carbamate (**13e**).* **13e** (1.16 g, 78%) as a colorless oil. $[\alpha]_D^{25}$ −2.51 (*c* 0.60, $CHCl_3$); IR (film): ν_{max} 3349, 2945, 2833, 2597, 2520, 2228, 2044, 1684, 1450, 1418, 1114, 1031 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers): δ 6.05–5.90 (m, 1/5H), 5.85–5.70 (m, 3/5H), 5.30–5.08 (m, 3/2H), 5.00–4.75 (m, 1/2H), 4.25–4.10 (m, 1/2H), 4.05–3.80 (m, 1H), 3.65–3.45 (m, 13/10H), 3.42 (dd, *J*=6.8, 10.0 Hz, 1/5H), 3.20 (d, *J*=8.4 Hz, 1/5H), 2.10–1.95 (m, 3/5H), 1.88–1.75 (m, 1H), 1.75–1.60 (m, 1H), 1.55–1.35 (m, 6H), 1.35–1.05 (m, 3H), 0.95–0.85 (m, 9H), 0.15–0.05 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 139.0, 115.6, 79.2, 70.3, 66.5, 50.2, 41.4, 38.9, 28.4, 25.9, 22.7, 18.0, −4.0, −4.4, −4.8, −5.4 ppm; HRMS (ESI) calcd for [$C_{17}H_{35}NO_4Si$+Na^+]: 368.2233, found: 368.2232.

*4.3.6. tert-Butyl (3R,5R)-5-(tert-butyldimethylsilyloxy)-6-hydroxyhex-1-yn-3-yl-carbamate (**13f**).* **13f** (1.32 g, 89%) as a colorless oil. $[\alpha]_D^{25}$ +73.55 (*c* 1.01, $CHCl_3$); IR (film): ν_{max} 3346, 2945, 2833, 2600, 2526, 2225, 2048, 1476, 1452, 1415, 1032 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.17 (br s, 1H), 4.50 (br s, 1H), 4.15–4.05 (m, 1H), 3.68–3.60 (m, 1H), 3.58–3.50 (m, 1H), 2.30 (d, *J*=2.4 Hz, 1H), 1.98–1.90 (m, 3H), 1.46–1.43 (m, 9H), 0.95–0.88 (m, 9H), 0.17–0.15 (m, 3H), 0.14–0.13 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8, 83.4, 79.8, 71.1, 70.3, 66.2, 40.2, 39.1, 28.3, 25.9, 18.0, −4.4, −4.7 ppm; HRMS (ESI) calcd for [$C_{17}H_{33}NO_4Si$+Na^+]: 366.2077, found: 366.2075.

*4.3.7. tert-Butyl (2S,4R)-4-(tert-butyldimethylsilyloxy)-5-hydroxypentan-2-yl-carbamate (**13g**).* **13g** (1.09 g, 74%) as a colorless oil. $[\alpha]_D^{26}$ +8.10 (*c* 0.84, $CHCl_3$); IR (film): ν_{max} 3345, 2944, 2593, 2509, 2227, 2039, 1684, 1455, 1415, 1031 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.82–4.70 (m, 1H), 4.00–3.88 (m, 1H), 3.79 (br s, 1H), 3.70–3.60 (m, 1H), 3.60–3.58 (m, 1H), 1.80–1.60 (m, 1H), 1.50 (s, 9H), 1.25 (d, *J*=6.4 Hz, 3H), 0.98 (s, 9H), 0.25–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 78.9, 70.3, 66.5, 43.8, 41.0, 28.4, 25.8, 21.9, 18.0, −4.5, −4.8 ppm; HRMS (ESI) calcd for [$C_{17}H_{33}NO_4Si$+Na^+]: 356.2233, found: 356.2232.

*4.3.8. tert-Butyl (2R,4S)-2-(tert-butyldimethylsilyloxy)-1-hydroxytridecan-4-ylcarbamate (**13i**).* **13i** (1.17 g, 74%) as a colorless oil. $[\alpha]_D^{25}$ +9.30 (*c* 1.08, $CHCl_3$); IR (film): ν_{max} 3369, 2920, 2855, 1719, 1691, 1500, 1460, 1366, 1252, 1173, 1055, 837, 777 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.60 (d, *J*=8.8 Hz, 9/10H), 4.52 (d, *J*=8.8 Hz, 1/10H), 3.85 (dd, *J*=4.4, 7.6 Hz, 1H), 3.68–3.54 (m, 2H), 3.52–3.45 (m, 1H), 2.32–2.15 (m, 1H), 1.75–1.65 (m, 1H), 1.46–1.40 (m, 11H), 1.35–1.20 (m, 15H), 0.95–0.85 (m, 12H), 0.14–0.10 (m, 3H), 0.10–0.08 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.5, 78.9, 72.4, 70.4, 66.8, 59.4, 48.0, 39.2, 36.2, 31.9, 29.6, 29.6, 29.3, 28.4, 25.9, 25.8, 22.7, 18.0, 14.1, −4.4, −4.6, −4.8 ppm; HRMS (ESI) calcd for [$C_{24}H_{51}NO_4Si$+Na^+]: 468.3485, found: 468.3489.

*4.3.9. tert-Butyl (3R,5R)-5-(tert-butyldimethylsilyloxy)-6-hydroxy-2-methylhexan-3-yl-carbamate (**13k**).* **13k** (1.22 g, 81%) as a colorless oil. $[\alpha]_D^{25}$ +19.85 (*c* 1.10, $CHCl_3$); IR (film): ν_{max} 3399, 2949, 2927, 2855, 2841, 1655, 1459, 1252, 1110, 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers): δ 4.48 (d, *J*=8.8 Hz, 4/5H), 4.35–4.25 (m, 1/5H), 3.90–3.80 (m, 1H), 3.64–3.44 (m, 3H), 2.05–1.95 (m, 1H), 1.87–1.75

(m, 1H), 1.74–1.65 (m, 1H), 1.50–1.42 (m, 9H), 0.95–0.90 (m, 9H), 0.90–0.85 (m, 6H), 0.16–0.12 (m, 3H), 0.12–0.09 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.5, 78.8, 70.5, 66.8, 52.4, 35.9, 32.5, 29.6, 28.3, 25.8, 18.1, 17.9, 17.8, −4.6, −4.9 ppm; HRMS (ESI) calcd for [$C_{18}H_{39}NO_4Si$+Na^+]: 384.2546, found: 384.2535.

*4.3.10. tert-Butyl (3R,5R)-5-(tert-butyldimethylsilyloxy)-6-hydroxy-2,2-dimethylhexan-3-ylcarbamate (**13l**).* **13l** (1.11 g, 73%) as a white solid, mp 81–83 °C. $[\alpha]_D^{27}$ +12.97 (*c* 0.64, $CHCl_3$); IR (film): ν_{max} 3358, 2946, 2834, 2593, 2517, 2225, 2043, 1689, 1652, 1642, 1457, 1415, 1028 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers): δ 4.30 (d, *J*=9.8 Hz, 4/5H), 4.18 (d, *J*=9.8 Hz, 1/5H), 3.82–3.74 (m, 1H), 3.62–3.54 (m, 1H), 3.50–3.42 (m, 9/5H), 3.36–3.28 (m, 1/5H), 2.01–1.90 (m, 1H), 1.79 (ddd, *J*=14.4, 7.6, 1.6 Hz, 1H), 1.71 (br s, 1H), 1.50–1.20 (m, 9H), 1.10–0.60 (m, 18H), 0.25–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 155.8, 78.8, 71.0, 67.0, 55.8, 35.6, 35.2, 29.7, 28.4, 26.2, 25.9, 18.0, −4.6, −4.7 ppm; HRMS (ESI) calcd for [$C_{19}H_{41}NO_4Si$+Na^+]: 398.2703, found: 398.2710.

*4.3.11. tert-Butyl (1R,3R)-3-(tert-butyldimethylsilyloxy)-1-cyclopropyl-4-hydroxybutyl-carbamate (**13m**).* **13m** (1.19 g, 79%) as a colorless oil. $[\alpha]_D^{27}$ −24.39 (*c* 0.64, $CHCl_3$); IR (film): ν_{max} 3354, 2945, 2833, 2598, 2512, 2344, 2226, 2047, 1473, 1449, 1413, 1117, 1029 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.95–3.85 (m, 1H), 3.61 (dd, *J*=5.0, 9.4 Hz, 1H), 3.43 (dd, *J*=7.0, 9.8 Hz, 1H), 3.27 (d, *J*=8.0 Hz, 1H), 2.70–2.62 (m, 1H), 1.92–1.82 (m, 1H), 1.77–1.68 (m, 1H), 1.35–1.22 (m, 9H), 0.97–0.92 (m, 11H), 0.80–0.70 (m, 1H), 0.68–0.60 (m, 1H), 0.60–0.52 (m, 1H), 0.35–0.25 (m, 1H), 0.14–0.12 (m, 3H), 0.12–0.11 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.3, 67.3, 59.5, 55.9, 42.1, 25.9, 25.8, 22.8, 18.6, 5.5, 4.4, −3.9, −4.6, −5.4 ppm; HRMS (ESI) calcd for [$C_{18}H_{37}NO_4Si$+Na^+]: 382.2390, found: 382.2389.

*4.3.12. tert-Butyl (1R,3R)-3-(tert-butyldimethylsilyloxy)-1-cyclohexyl-4-hydroxybutyl-carbamate (**13o**).* **13o** (1.34 g, 87%) as a colorless oil. $[\alpha]_D^{25}$ +13.76 (*c* 1.29, $CHCl_3$); IR (film): ν_{max} 3358, 2928, 2854, 1686, 1528, 1509, 1450, 1391, 1366, 1251, 1173 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.57 (d, *J*=9.2 Hz, 1H), 3.85–3.77 (m, 1H), 3.60–3.40 (m, 3H), 2.15–2.05 (m, 1H), 1.78–1.60 (m, 6H), 1.47–1.37 (m, 11H), 1.27–1.05 (m, 4H), 1.00–0.93 (m, 1H), 0.88 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6, 78.8, 70.6, 66.7, 52.1, 42.9, 36.4, 28.4, 26.5, 26.3, 25.9, 18.0, −4.6, −4.8, ppm; HRMS (ESI) calcd for [$C_{21}H_{43}NO_4Si$+Na^+]: 402.3040, found: 402.3028.

4.4. General procedure for synthesis of 14a–l

To a solution of compound **13** (2.44 mmol) in anhydrous DMF (5 mL) was added $CrO_3 \cdot 2Py$ (3.15 g, 12.22 mmol). After being stirred for 24 h at room temperature, the mixture was diluted with water, and extracted with EtOAc (30 mL×5). The combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (PE/EA=2/1) to give **14a–l**.

*4.4.1. (3R,5S)-tert-Butyl 5-benzyl-3-(tert-butyldimethylsilyloxy)-2-oxopyrrolidine-1-carboxylate (**14a**).* **14a** (574 mg, 58%) as a colorless oil. $[\alpha]_D^{27}$ +48.66 (*c* 1.00, $CHCl_3$); IR (film): ν_{max} 3338, 2945, 2832, 2594, 2517, 2235, 1448, 1408, 1111, 1028 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.28 (m, 2H), 7.26–7.17 (m, 3H), 4.25–4.12 (m, 2H), 3.45 (dd, *J*=3.2, 12.8 Hz, 1H), 2.80 (dd, *J*=10.0, 13.2 Hz, 1H), 2.05–1.95 (m, 1H), 1.77–1.70 (m, 1H), 1.65–1.50 (m, 9H), 0.95–0.80 (m, 9H), 0.20–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 150.1, 137.6, 129.4, 128.6, 126.6, 83.2, 71.5, 57.6, 41.0, 31.8, 29.7, 28.1, 25.7, 18.2, −4.6, −5.3 ppm; HRMS (ESI) calcd for [$C_{22}H_{35}NO_4Si$+Na^+]: 428.2233, found: 428.2234.

*4.4.2. (3R,5S)-tert-Butyl 5-allyl-3-(tert-butyldimethylsilyloxy)-2-oxo-pyrrolidine-1-carboxylate (**14b**).* **14b** (336 mg, 34%) as a colorless oil. $[\alpha]_D^{25}$ +99.6 (*c* 0.72, $CHCl_3$); IR (film): ν_{max} 3056, 2956, 2930, 2857, 1788, 1755, 1720, 1473, 1463, 1370, 1346, 1306, 1265, 1155, 1088, 974 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers): δ 5.80–5.65 (m, 1H), 5.30–5.25 (m, 1/5H), 5.15–5.05 (m, 9/5H), 4.30–4.25 (m, 1/10H), 4.25–4.15 (m, 9/10H), 4.05–3.95 (m, 1H), 2.77–2.67 (m, 1H), 2.47–2.37 (m, 1H), 2.27–2.17 (m, 1H), 1.80–1.70 (m, 1H), 1.62–1.40 (m, 9H), 0.89 (s, 9H), 0.25–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 150.1, 133.1, 118.6, 83.1, 71.2, 54.9, 39.0, 32.2, 28.0, 25.7, 18.1, −4.6, −5.3 ppm; HRMS (ESI) calcd for [$C_{18}H_{33}NO_4Si$+Na^+]: 378.2077, found: 378.2078.

*4.4.3. (3R,5R)-tert-Butyl 3-(tert-butyldimethylsilyloxy)-2-oxo-5-phenylpyrrolidine-1-carboxylate (**14c**).* **14c** (723 mg, 73%) as a colorless oil. $[\alpha]_D^{25}$ +66.14 (*c* 0.92, $CHCl_3$); IR (film): ν_{max} 3357, 2945, 2833, 2585, 2519, 2223, 2046, 1782, 1655, 1450, 1417, 1111, 1031 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.23 (m, 5H), 4.81 (dd, *J*=6.2, 9.4 Hz, 1H), 4.39 (dd, *J*=7.0, 10.2 Hz, 1H), 2.75–2.65 (m, 1H), 1.88–1.78 (m, 1H), 1.28–1.22 (m, 2H), 1.20–1.15 (m, 7H), 0.90–0.82 (m, 9H), 0.22–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 149.2, 142.4, 128.6, 127.6, 125.7, 82.9, 70.9, 58.2, 38.3, 29.7, 27.5, 25.6, 18.2, −4.5, −5.3 ppm; HRMS (ESI) calcd for [$C_{21}H_{33}NO_4Si$+Na^+]: 414.2077, found: 414.2078.

*4.4.4. (3R,5R)-tert-Butyl 3-(tert-butyldimethylsilyloxy)-2-oxo-5-p-tolylpyrrolidine-1-carboxylate (**14d**).* **14d** (802 mg, 81%) as a white solid; mp 94–96 °C. $[\alpha]_D^{24}$ +55.44 (*c* 1.05, $CHCl_3$); IR (film): ν_{max} 3408, 3338, 2954, 2928, 2856, 1697, 1514, 1461, 1390, 1366, 1253, 1172, 1108, 1045, 1010, 838, 808, 777, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20–7.08 (m, 4H), 4.77 (dd, *J*=6.2, 9.4 Hz, 1H), 4.37 (dd, *J*=7.4, 10.2 Hz, 1H), 2.72–2.60 (m, 1H), 2.33 (s, 3H), 1.85–1.75 (m, 1H), 1.28–1.18 (m, 9H),0.90–0.85 (m, 9H), 0.20–0.05 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 149.3, 139.4, 137.2, 129.2, 125.7, 82.9, 70.9, 57.9, 38.4, 27.6, 25.7, 21.1, 18.2, −4.5, −5.3 ppm; HRMS (ESI) calcd for [$C_{22}H_{35}NO_4Si$+Na^+]: 428.2233, found: 428.2234.

*4.4.5. (3R,5R)-tert-Butyl 3-(tert-butyldimethylsilyloxy)-2-oxo-5-vinylpyrrolidine-1-carboxylate (**14e**).* **14e** (445 mg, 45%) as a colorless oil. $[\alpha]_D^{27}$ +10.53 (*c* 1.14, $CHCl_3$); IR (film): ν_{max} 3086, 2956, 2931, 2887, 2858, 1790, 1725, 1648, 1473, 1463, 1423, 1393, 1305, 1156, 1078 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.98–5.85 (m, 1H), 5.28 (d, *J*=17.2 Hz, 1H), 5.21 (d, *J*=10.0 Hz, 1H), 4.45 (dd, *J*=7.4, 14.2 Hz, 1H), 4.31 (dd, *J*=6.8, 7.6 Hz, 1H), 2.54–2.44 (m, 1H), 1.82–1.72 (m, 1H), 1.56 (s, 9H), 0.97 (s, 9H), 0.28–0.12 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 149.8, 138.5, 116.2, 83.1, 70.9, 57.7, 35.1, 28.0, 25.7, 18.2, −4.6, −5.3 ppm; HRMS (ESI) calcd for [$C_{17}H_{31}NO_4Si$+Na^+]: 364.1920, found: 364.1919.

*4.4.6. (3R,5R)-tert-Butyl 3-(tert-butyldimethylsilyloxy)-5-ethynyl-2-oxopyrrolidine-1-carboxylate (**14f**).* **14f** (563 mg, 57%) as a colorless oil. $[\alpha]_D^{25}$ +105.35 (*c* 1.32, $CHCl_3$); IR (film): ν_{max} 3429, 3310, 2957, 2931, 2887, 2841, 2858, 1701, 1499, 1392, 1367, 1254, 1170, 1109, 1047, 1007 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers): δ 4.60–4.52 (m, 9/10H), 4.32 (d, *J*=5.2 Hz, 1/10H), 4.23 (t, *J*=7.2 Hz, 4/5H), 2.92 (dd, *J*=5.2, 17.2 Hz, 1/5H), 2.64–2.53 (m, 4/5H), 2.43 (d, *J*=2.0 Hz, 1/5H), 2.42–2.32 (m, 4/5H), 2.10–2.00 (m, 1H), 1.74–1.35 (m, 9H), 0.97–0.75 (m, 9H), 0.20–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 149.2, 83.8, 81.8, 72.0, 70.3, 45.3, 35.0, 29.6, 27.9, 25.6, 18.1, −4.6, −5.3 ppm; HRMS (ESI) calcd for [$C_{17}H_{29}NO_4Si$+Na^+]: 362.1764, found: 362.1761.

*4.4.7. (3R,5S)-tert-Butyl 3-(tert-butyldimethylsilyloxy)-5-methyl-2-oxopyrrolidine-1-carboxylate (**14g**).* **14g** (514 mg, 52%) as a colorless oil. $[\alpha]_D^{27}$ +47.36 (*c* 1.08, $CHCl_3$); IR (film): ν_{max} 3406, 2955, 2923, 2841, 1652, 1014 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.25–4.15 (m, 1H), 4.05–3.95 (m, 1H), 2.45–2.30 (m, 1H), 1.60–1.45 (m, 10H), 1.45–1.35 (m, 3H), 0.92–0.80 (m, 9H), 0.18–0.00 (m, 6H) ppm; ^{13}C

NMR (100 MHz, $CDCl_3$): δ 172.9, 150.2, 82.9, 71.2, 51.3, 35.7, 28.0, 25.7, 21.7, 18.1, −4.6, −5.3 ppm; HRMS (ESI) calcd for $[C_{16}H_{31}NO_4Si+H^+]$: 352.1920, found: 352.1917.

*4.4.8. (3R,5R)-tert-Butyl 3-(tert-butyldimethylsilyloxy)-2-oxo-5-vinylpyrrolidine-1-carboxylate (**14h**).* **14h** (713 mg, 72%) as a colorless oil. $[\alpha]_D^{25}$ +10.35 (*c* 0.91, $CHCl_3$); IR (film): ν_{max} 3433, 2958, 2925, 2849, 2102, 1640, 1250, 1172, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.50 (d, *J*=8.4 Hz, 1H), 3.87–3.80 (m, 1H), 3.65–3.52 (m, 2H), 3.50–3.40 (m, 1H), 1.72–1.60 (m, 1H), 1.45–1.37 (m, 10H), 1.25–1.20 (m, 13H), 0.90–0.80 (m, 12H), 0.10–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 155.5, 78.9, 70.4, 66.8, 47.9, 39.2, 36.2, 31.9, 29.6, 29.5, 29.3, 28.4, 25.9, 22.7, 18.0, 14.1, −4.5, −4.8 ppm; HRMS (ESI) calcd for $[C_{24}H_{47}NO_4Si+Na^+]$: 464.3172, found: 464.3176.

*4.4.9. (3R,5R)-tert-Butyl 3-(tert-butyldimethylsilyloxy)-5-isopropyl-2-oxopyrrolidine-1-carboxylate (**14i**).* **14i** (801 mg, 81%) as a white solid; mp 63–64 °C. $[\alpha]_D^{25}$ +156.27 (*c* 0.77, $CHCl_3$); IR (film): ν_{max} 3348, 2945, 2833, 2600, 2231, 2046, 1774, 1447, 1412, 1108, 1031 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.26 (dd, *J*=6.8, 10.0 Hz, 1H), 3.96–3.88 (m, 1H), 2.60–2.45 (m, 1H), 2.25–2.15 (m, 1H), 1.70–1.57 (m, 1H), 1.58–1.48 (m, 9H), 0.95–0.87 (m, 12H), 0.79 (d, *J*=6.8 Hz, 3H), 0.20–0.15 (m, 3H), 0.15–0.10 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 150.5, 83.0, 70.6, 58.6, 29.7, 28.4, 28.0, 27.5, 25.8, 18.5, 18.3, 14.7, −4.5, −5.2 ppm; HRMS (ESI) calcd for $[C_{18}H_{35}NO_4Si+Na^+]$: 380.2233, found: 380.2227.

*4.4.10. (3R,5R)-tert-Butyl 5-tert-butyl-3-(tert-butyldimethylsilyloxy)-2-oxopyrrolidine-1-carboxylate (**14j**).* **14j** (752 mg, 76%) as a colorless oil. $[\alpha]_D^{25}$ +31.84 (*c* 0.84, $CHCl_3$); IR (film): ν_{max} 3422, 2955, 2925, 2847, 1647, 1371, 1288, 1260, 1157 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rotamers): δ 4.37–4.31 (m, 1/10H), 4.28 (dd, *J*=3.2, 10.0 Hz, 9/10H), 4.08 (dd, *J*=2.8, 9.6 Hz, 1H), 2.43–2.32 (m, 4/5H), 2.23–2.14 (m, 1/5H), 1.80–1.72 (m, 1H), 1.56–1.53 (m, 7H), 1.51–1.48 (m, 2H), 0.95–0.94 (m, 9H), 0.93–0.89 (m, 9H), 0.18–0.11 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 151.2, 83.1, 82.8, 70.3, 63.0, 36.1, 29.0, 28.3, 27.9, 27.3, 26.5, 25.7, 18.2, −4.5, −5.3 ppm; HRMS (ESI) calcd for $[C_{19}H_{37}NO_4Si+Na^+]$: 394.2390, found: 394.2392.

*4.4.11. (3R,5R)-tert-Butyl 3-(tert-butyldimethylsilyloxy)-5-cyclopropyl-2-oxopyrrolidine-1-carboxylate (**14k**).* **14i** (692 mg, 70%) as a colorless oil. $[\alpha]_D^{25}$ +43.15 (*c* 2.00, $CHCl_3$); IR (film): ν_{max} 2955, 2931, 2887, 2857, 1786, 1755, 1724, 1369, 1342, 1301, 1257, 1159, 1082, 843, 781, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.18 (dd, *J*=5.2, 7.6 Hz, 1H), 3.55–3.47 (m, 1H), 2.30–2.18 (m, 1H), 1.72–1.64 (m, 1H), 1.55–1.48 (m, 9H), 1.27–1.17 (m, 1H), 0.90–0.85 (m, 9H), 0.62–0.52 (m, 2H), 0.50–0.40 (m, 1H), 0.23–0.15 (m, 1H), 0.15–0.09 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 149.5, 81.9, 70.1, 58.5, 32.6, 27.0, 24.7, 17.1, 15.2, 4.9, 0.0, −5.6, −6.3 ppm; HRMS (ESI) calcd for $[C_{18}H_{33}NO_4Si+Na^+]$: 378.2077, found: 378.2072.

*4.4.12. (3R,5R)-tert-Butyl-3-(tert-butyldimethylsilyloxy)-5-cyclohexyl-2-oxopyrrolidine-1-carboxylate (**14l**).* **14l** (544 mg, 55%) as a colorless oil. $[\alpha]_D^{25}$ +55.67 (*c* 1.66, $CHCl_3$); IR (film): ν_{max} 3346, 2945, 2833, 2606, 2517, 2048, 1450, 1417, 1118, 1031 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.21 (t, *J*=8.0 Hz, 1H), 3.87 (dd, *J*=7.2, 12.4 Hz, 1H), 2.24–2.08 (m, 2H), 1.80–1.63 (m, 4H), 1.60–1.45 (m, 11H), 1.27–1.07 (m, 3H), 1.05–0.92 (m, 2H), 0.89 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 150.5, 82.9, 70.8, 58.5, 39.4, 29.2, 28.0, 26.5, 26.4, 25.9, 25.7, 25.7, 18.2, −4.5, −5.3. ppm; HRMS (ESI) calcd for $[C_{21}H_{39}NO_4Si+Na^+]$: 420.2546, found: 420.2553.

4.5. General procedure for synthesis of 15, 17–19

To a solution of compound **14** (2.27 mmol) in anhydrous Et_2O (12 mL) was cooled to −78 °C. Then a solution of Grignard reagent (6.80 mL, 1 M in Et_2O) was slowly added. After being stirred for 3 h at room temperature, the mixture was quenched with saturated aqueous solution of NH_4Cl and warmed to room temperature. The resulted mixture was extracted with EtOAc (20 mL×3) and the combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (PE/EA=2/1) to give **15**, **17**–**19**.

*4.5.1. tert-Butyl (3R,5S)-3-(tert-butyldimethylsilyloxy)-2-oxo-1-phenyltetradecan-5-ylcarbamate (**15**).* **15** (991 mg, 82%) as a colorless oil. $[\alpha]_D^{27}$ +47.36 (*c* 1.08, $CHCl_3$); IR (film): ν_{max} 3338, 2944, 2833, 2599, 2515, 2232, 2043, 1450, 1415, 1112, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rotamers): δ 7.39–7.31 (m, 2H), 7.31–7.27 (m, 1H), 7.24–7.19 (m, 1H), 4.55 (d, *J*=8.4 Hz, 1H), 4.30 (dd, *J*=3.0,9.0 Hz, 1H), 3.94 (d, *J*=16.8 Hz, 1H), 3.82 (d, *J*=16.8 Hz, 1H), 3.76–3.62 (m, 1H), 1.84–1.74 (m, 4/5H), 1.72–1.68 (m, 1/5H), 1.64–1.57 (m, 1H), 1.47–1.42 (m, 9H), 1.32–1.22 (m, 16H), 1.02–0.95 (m, 9H), 0.92–0.85 (m, 3H), 0.19–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.5, 155.3, 133.9, 129.8, 128.5, 127.0, 78.9, 76.3, 47.8, 44.3, 39.5, 36.1, 31.9, 29.7, 29.6, 29.5, 29.5, 29.3, 28.4, 25.8, 22.7, 18.0, 14.1, −4.8, −5.3 ppm; HRMS (ESI) calcd for $[C_{31}H_{55}NO_4Si+Na^+]$: 556.3798, found: 556.3734.

*4.5.2. tert-Butyl (1R,3R)-3-(tert-butyldimethylsilyloxy)-4-oxo-1,5-diphenylpentyl-carbamate(**17**).* **17** (791 mg, 64%) as a colorless oil. $[\alpha]_D^{25}$ −7.98 (*c* 1.09, $CHCl_3$); IR (film): ν_{max} 3441, 3029, 2928, 2856, 1713, 1367, 1310, 1255, 1147, 1088, 1029, 837, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rotamers): δ 7.47–7.28 (m, 8H), 7.26–7.22 (m, 1H), 7.17–7.07 (m, 1H), 4.70–4.58 (m, 4/5H), 4.55–4.45 (m, 1/5H), 4.12–4.02 (m, 4/5H), 3.98–3.88 (m, 1/5H), 3.82–3.70 (m, 4/5H), 3.68–3.58 (m, 1/5H), 3.34 (d, *J*=13.6 Hz, 1H), 2.52–2.40 (m, 1/5H), 2.17 (d, *J*=13.6 Hz, 7/10H), 2.07 (dd, *J*=4.8,14.0 Hz, 4/5H), 1.58 (br s, 4/5H), 1.45–1.38 (m, 1H), 1.34–1.26 (m, 1H), 1.26–1.18 (m, 1H), 1.16 (s, 6H), 1.05–0.95 (m, 6H), 0.95–0.77 (m, 3H), 0.22–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.0, 154.9, 141.9, 137.7, 130.9, 129.4, 128.7, 128.4, 128.0, 127.8, 127.1, 126.3, 126.1, 93.2, 80.4, 73.2, 45.3, 41.1, 28.3, 28.0, 26.0, 25.8, 25.7, 18.2, −4.7, −4.7 ppm; HRMS (ESI) calcd for $[C_{28}H_{41}NO_4Si+Na^+]$: 506.2703, found: 506.2703.

*4.5.3. tert-Butyl (3R,5R)-5-(tert-butyldimethylsilyloxy)-2-methyl-6-oxo-7-phenylheptan-3-ylcarbamate (**18**).* **18** (1.01 g, 80%) as a colorless oil. $[\alpha]_D^{25}$ −26.08 (*c* 1.35, $CHCl_3$); IR (film): ν_{max} 3356, 2959, 2930, 2895, 2858, 1697, 1497, 1472, 1390, 1365, 1253, 1172, 1088, 1009, 838, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.32 (m, 2H), 7.31–7.27 (m, 1H), 7.24–7.19 (m, 2H), 4.47 (d, *J*=9.2 Hz, 1H), 4.25 (dd, *J*=2.4, 8.8 Hz, 1H), 3.96 (d, *J*=16.4 Hz, 1H), 3.82 (d, *J*=16.4 Hz, 1H), 3.65–3.57 (m, 1H), 1.88–1.78 (m, 1H), 1.74–1.66 (m, 1H), 1.48–1.43 (m, 9H), 0.99 (s, 9H), 0.90–0.82 (m, 6H), 0.12–0.05 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.8, 155.5, 133.9, 129.8, 128.5, 127.0, 78.9, 76.3, 52.2, 44.4, 36.5, 32.5, 28.4, 28.0, 25.8, 18.1, 18.0, 18.0, 14.2, −4.8, −5.3 ppm; HRMS (ESI) calcd for $[C_{25}H_{43}NO_4Si+H^+]$: 450.3040, found: 450.3033.

*4.5.4. tert-Butyl (1R,3R)-3-(tert-butyldimethylsilyloxy)-1-cyclo-propyl-4-oxo-5-phenyl-pentylcarbamate (**19**).* **19** (491 mg, 39%) as a colorless oil. $[\alpha]_D^{25}$ −47.86 (*c* 1.00, $CHCl_3$); IR (film): ν_{max} 3361, 3005, 2955, 2930, 2857, 1716, 1497, 1472, 1391, 1366, 1253, 1172, 1092, 1044, 838, 780, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38–7.32 (m, 2H), 7.31–7.26 (m, 1H), 7.23–7.19 (m, 2H), 4.67–4.53 (m, 1H), 4.32 (dd, *J*=3.6, 8.8 Hz, 1H), 3.94 (d, *J*=16.8 Hz, 1H), 3.85 (d, *J*=16.8 Hz, 1H), 2.00–1.88 (m, 1H), 1.82–1.70 (m, 1H), 1.46 (s, 9H), 0.99–0.92 (m, 9H), 0.85–0.75 (m, 1H), 0.52–0.38 (m, 3H), 0.25–0.17 (m, 1H), 0.12–0.07 (m, 3H), 0.07–0.04 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.4, 155.5, 133.9, 129.8, 128.5, 126.9, 79.0, 76.1, 51.5, 44.2, 40.1, 29.7, 28.7, 28.6, 28.4, 28.1, 25.8,

25.6, 21.1, 18.0, 17.0, 14.2, 3.0, −4.8, −5.2 ppm; HRMS (ESI) calcd for [$C_{25}H_{41}NO_4Si+Na^+$]: 470.2703, found: 470.2712.

4.6. General procedure for synthesis of 16, 20–22

Compound **15** (or **17**–**19**) (0.47 mmol) was dissolved in CF_3COOH (6 mL) and stirred for 1 h, then the mixture was alkalized with 30% aqueous solution of NaOH to pH to 10–12. The resulted mixture was extracted with $CHCl_3$ (20 mL×5) and the combined organic layers were washed with brine. The solvent was dried and concentrated to give crude intermediate. The crude material along with 10% (wt) Pd/C and 20% (wt) $Pd(OH)_2$/C were stirred in MeOH (20 mL) under H_2 atmosphere for 8 h. The reaction mixture was then treated with paraformaldehyde (250 mg). After being stirred for 3 h, the mixture was filtered and purified by flash chromatography on silica gel (CH_2Cl_2/CH_3OH=40/1) to give **16**, **20**–**22**.

*4.6.1. (2R,3R,5S)-2-Benzyl-3-(tert-butyldimethylsilyloxy)-1-methyl-5-nonylpyrrolidine(**16**).* **16** (119 mg, two steps 59%) as a colorless oil. $[\alpha]_D^{24}$ −45.99 (*c* 1.05, $CHCl_3$); IR (film): ν_{max} 3344, 2944, 2833, 2600, 2512, 2225, 2038, 1455, 1417, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.24 (m, 4H), 7.22–7.15 (m, 1H), 4.22–4.12 (m, 1H), 3.09 (dd, *J*=8.0, 14.4 Hz, 1H), 2.81 (d, *J*=4.0, 14.0 Hz, 1H), 2.57–2.45 (m, 1H), 3.25 (s, 3H), 2.14–2.04 (m, 1H), 1.80–1.68 (m, 1H), 1.50–1.42 (m, 1H), 1.35–1.25 (m, 16H), 0.92–0.87 (m, 12H), 0.03–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 129.1, 128.1, 125.7, 73.4, 71.2, 66.0, 40.7, 40.4, 34.6, 34.1, 31.9, 30.0, 29.7, 29.6, 29.6, 29.4, 26.7, 26.0, 22.7, 18.2, 14.1, −4.3, −5.0 ppm; HRMS (ESI) calcd for [$C_{27}H_{49}NOSi+H^+$]: 432.3662, found: 432.3645.

*4.6.2. (2R,3R,5R)-2-Benzyl-3-(tert-butyldimethylsilyloxy)-1-methyl-5-phenylpyrrolidine(**20**).* **20** (108 mg, two steps 55%) as a colorless oil. $[\alpha]_D^{25}$ −10.19 (*c* 1.26, $CHCl_3$); IR (film): ν_{max} 3297, 3027, 2955, 2928, 2856, 1495, 1455, 1254, 1068, 836, 775, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.44–7.29 (m, 4H), 7.26–7.21 (m, 4H), 7.20–7.16 (m, 1H), 7.10 (d, *J*=6.8 Hz, 1H), 3.78–3.70 (m, 1H), 2.88 (d, *J*=6.0 Hz, 1H), 2.84–2.77 (m, 1H), 2.64–2.54 (m, 1H), 2.54–2.46 (m, 1H), 2.41 (s, 3H), 2.25–2.14 (m, 1H), 1.80–1.70 (m, 1H), 1.02–0.95 (m, 9H), 0.12–0.01 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4, 141.7, 129.2, 129.1, 128.5, 128.3, 128.2, 126.3, 125.8, 125.6, 73.1, 67.7, 43.1, 35.8, 32.4, 30.0, 26.1, 18.2, −3.9, −4.5 ppm; HRMS (ESI) calcd for [$C_{24}H_{35}NOSi+NH_3^+$]: 398.2753, found: 398.2883.

*4.6.3. (2R,3R,5R)-2-Benzyl-3-(tert-butyldimethylsilyloxy)-5-isopropyl-1-methylpyrroli-dine (**21**).* **21** (133 mg, two steps 69%) as a colorless oil. $[\alpha]_D^{26}$ −13.63 (*c* 2.03, $CHCl_3$); IR (film): ν_{max} 3370, 2956, 2929, 2894, 2857, 2783, 1463, 1386, 1361, 1253, 1127, 1044, 972, 837, 775, 742, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30–7.26 (m, 4H), 7.22–7.16 (m, 1H), 4.19 (dd, *J*=6.0, 11.6 Hz, 1H), 3.01 (dd, *J*=7.2, 14.0 Hz, 1H), 2.71 (d, *J*=6.0, 14.0 Hz, 1H), 2.58 (dd, *J*=6.4, 12.8 Hz, 1H), 2.20–2.14 (m, 1H), 2.13 (s, 3H), 1.95–1.85 (m, 1H), 1.60–1.50 (m, 1H), 0.95–0.91 (m, 11H), 0.91–0.87 (m, 4H), 0.06–0.00 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.1, 129.3, 128.0, 125.5, 72.9, 71.1, 70.3, 41.1, 35.1, 34.1, 28.7, 26.0, 25.9, 20.5, 18.2, 16.0, −4.2, −5.1 ppm; HRMS (ESI) calcd for [$C_{21}H_{37}NOSi+H^+$]: 348.2723, found: 348.2749.

*4.6.4. (2R,3R,5R)-2-Benzyl-3-(tert-butyldimethylsilyloxy)-5-cyclopropyl-1-methylpyrrolidine(**22**).* **22** (71 mg, two steps 37%) as a colorless oil. $[\alpha]_D^{26}$ −47.69 (*c* 1.40, $CHCl_3$); IR (film): ν_{max} 3445, 2955, 2922, 2851, 2359, 1738, 1464, 1377 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.32–7.23 (m, 4H), 7.22–7.15 (m, 1H), 4.19–4.11 (m, 1H), 3.10 (dd, *J*=8.4, 14.4 Hz, 1H), 2.83 (dd, *J*=4.4, 14.4 Hz, 1H), 2.52–2.42 (m, 1H), 2.35 (s, 3H), 2.26 (dd, *J*=6.8, 13.6 Hz, 1H), 1.70–1.60 (m, 1H), 1.38–1.22 (m, 2H), 0.90 (s, 9H), 0.67–0.57 (m, 1H), 0.47–0.37 (m, 1H), 0.30–0.20 (m, 1H), 0.06–0.01 (m, 1H), −0.02 (s, 3H), −0.09 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 128.8, 127.9, 125.5, 73.2, 71.1, 70.7, 41.3, 40.3, 33.7, 29.5, 25.9, 20.9, 18.3, 18.0, 5.0, 0.0, −4.5, −5.2 ppm; HRMS (ESI) calcd for [$C_{21}H_{35}NOSi+H^+$]: 346.2566, found: 346.2588.

4.7. General procedure for synthesis of *ent*-5, 23–25

Compound **16** (or **20**–**22**) (0.12 mmol) was dissolved in THF (1 mL) and stirred for 10 min at 0 °C. Then, a solution of TBAF (0.2 mL, 1 M in THF) was added in one portion. After being stirred for overnight, the mixture was diluted with water and extracted with EtOAc (20 mL×3). The combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (CH_2Cl_2/CH_3OH=40/1) to give (−)-preussin *ent*-**5**, **23**–**25**.

*4.7.1. (2R,3R,5S)-2-Benzyl-1-methyl-5-nonylpyrrolidin-3-ol((+)-preussin ent-**5**).* (+)-**preussin** *ent*-**5** (35 mg, 95%) as a pale yellow oil. $[\alpha]_D^{24}$ −34.71 (*c* 0.51, $CHCl_3$); IR (film): ν_{max} 3357, 2944, 2833, 2598, 2517, 2227, 2048, 1655, 1460, 1449, 1420, 1402, 1113, 1031 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.29 (m, 4H), 7.26–7.20 (m, 1H), 3.87–3.81 (m, 1H), 2.93 (dd, *J*=10.0, 13.2 Hz, 1H), 2.87 (dd, *J*=5.0, 13.4 Hz, 1H), 2.38 (s, 3H), 2.34–2.28 (m, 1H), 2.26–2.18 (m, 1H), 2.11–2.01 (m, 1H), 1.78–1.70 (m, 1H), 1.48–1.42 (m, 1H), 1.35–1.26 (m, 16H), 0.92–0.87 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 129.4, 128.4, 126.1, 73.7, 70.4, 65.9, 39.3, 38.6, 31.9, 31.9, 29.9, 29.7, 29.7, 29.6, 29.4, 29.3, 26.3, 22.7, 14.1 ppm; HRMS (ESI) calcd for [$C_{21}H_{35}NO+H^+$]: 318.2797, found: 318.2806.

*4.7.2. (2R,3R,5R)-2-Benzyl-1-methyl-5-phenylpyrrolidin-3-ol (**23**).* **23** (19 mg, 55%) as a pale yellow oil. $[\alpha]_D^{25}$ +6.98 (*c* 0.38, $CHCl_3$); IR (film): ν_{max} 3375, 3026, 2926, 2375, 1651, 1455, 1098, 745, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.26 (m, 5H), 7.24–7.16 (m, 4H), 7.10 (d, *J*=7.6 Hz, 1H), 3.49–3.42 (m, 1H), 2.89 (dd, *J*=6.2, 14.2 Hz, 1H), 2.79–2.75 (m, 1H), 2.74–2.70 (m, 1H), 2.54–2.46 (m, 1H), 2.39 (dd, *J*=10.4 Hz, 1H), 2.30 (s, 3H), 1.87–1.77 (m, 1H), 1.60–1.45 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5, 140.6, 129.0, 128.6, 128.5, 128.4, 128.3, 128.2, 126.1, 125.6, 69.9, 43.2, 40.7, 36.1, 31.9, 31.5, 26.1 ppm; HRMS (ESI) calcd for [$C_{18}H_{21}NO+NH_3^+$]: 284.1889, found: 284.2006.

*4.7.3. (2R,3R,5R)-2-Benzyl-5-isopropyl-1-methylpyrrolidin-3-ol(**24**).* **24** (20 mg, 61%) as a pale yellow oil. $[\alpha]_D^{26}$ −25.42 (*c* 0.63, $CHCl_3$); IR (film): ν_{max} 3419, 2957, 2871, 2784, 1495, 1454, 1386, 1125, 1110, 1030, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.27 (m, 4H), 7.25–7.17 (m, 1H), 3.80–3.70 (m, 1H), 2.83 (m, 2H), 2.31 (s, 3H), 2.23–2.15 (m, 1H), 2.00–1.85 (m, 2H), 1.54–1.44 (m, 1H), 1.32–1.25 (m, 1H), 0.97–0.92 (m, 1H), 0.92–0.84 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.6, 129.5, 128.3, 126.0, 73.7, 70.3, 70.0, 38.4, 33.7, 32.9, 27.8, 20.0, 15.1 ppm; HRMS (ESI) calcd for [$C_{15}H_{23}NO+H^+$]: 234.1858, found: 234.1861.

*4.7.4. (2R,3R,5R)-2-Benzyl-5-cyclopropyl-1-methylpyrrolidin-3-ol (**25**).* **25** (19 mg, 57%) as a pale yellow solid, mp 98–100 °C. $[\alpha]_D^{25}$ −36.53 (*c* 0.79, $CHCl_3$); IR (film): ν_{max} 3334, 3027, 2999, 2559, 2931, 2850, 2768, 1670, 1495, 1454, 1427, 1347, 1198, 1144, 1122, 1030, 929, 748, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.32–7.26 (m, 4H), 7.23–7.17 (m, 1H), 3.85–3.75 (m, 1H), 2.92–2.85 (m, 2H), 2.44 (s, 3H), 2.30–2.20 (m, 2H), 2.15 (d, *J*=8.8 Hz, 1H), 1.65–1.55 (m, 1H), 1.45–1.35 (m, 1H), 0.85–0.75 (m, 1H), 0.65–0.55 (m, 1H), 0.45–0.35 (m, 1H), 0.30–0.20 (m, 1H), 0.05–0.00 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 129.4, 128.4, 126.1, 73.7, 70.9, 70.2, 39.9,

39.0, 33.5, 15.3, 5.2, 0.0 ppm; HRMS (ESI) calcd for [$C_{15}H_{21}NO+H^+$]: 232.1701, found: 232.1730.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.05.037.

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