Article

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Stereoselective Synthesis of Pyrido and Pyrrolo[1,2-c][1,3]oxazin-1-ones *via* Nucleophilic Addition-Cyclization Process of *N*,O-acetal with Ynamides

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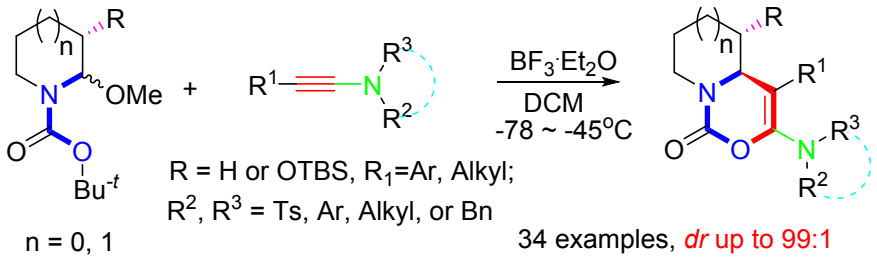
Abstract



An efficient asymmetric approach to access functionalized pyrido and pyrrolo[1,2-c][1,3]oxazin-1-ones has been developed through nucleophilic addition-cyclization process of *N*,O-acetal with ynamides. A number of substituted ynamides **8a-8o** and 3-silyloxypyrrolidine or piperidine *N, O*-acetals **6a**, **7** were amenable to this transformation, and the desired products **9a-9o**, **10a-10m** were obtained with excellent regioselectivities and outstanding diastereoselectivities. Moreover, chiral ynamides **14a-14f** could also experience this addition-cyclization process to afford products **15a-15f** in excellent yields.

Introduction

The development of a versatile approach to divergent skeleton construction is one of the most important tasks in organic and pharmaceutical synthesis.[1] As a prime instance, nitrogen-containing heterocycles exist as subunits in numerous natural products and many biologically active pharmaceuticals.[2] In particular, functionalized piperidine or pyrrolidine and their derived heterocyclic skeletons are very important in synthetic and medicinal chemistry due to their contributions to numerous biologically relevant alkaloids and pharmaceutical agents. Notably, they also serve as useful building blocks.[3] Typical examples include lythramine **1**, hyperaspine **2**,

porantheridine **3**, as well as geissolosimine **4** (Figure 1). The syntheses of these natural products have attracted significant attention from many chemists due to their intriguing structures and biological activities.[4] For example, geissolosimine **4** showed antiparasitic activities against Plasmodium falciparum and Leishmania don ovani, as well as cytotoxic activity against the MRC-5 cell line.[5] Although tremendous efforts were devoted to the construction of the functionalized pyrido or pyrrolo[1,2-c][1,3]oxazin-1-one scaffold,[6] the more straightforward and efficient approach is still in demand.

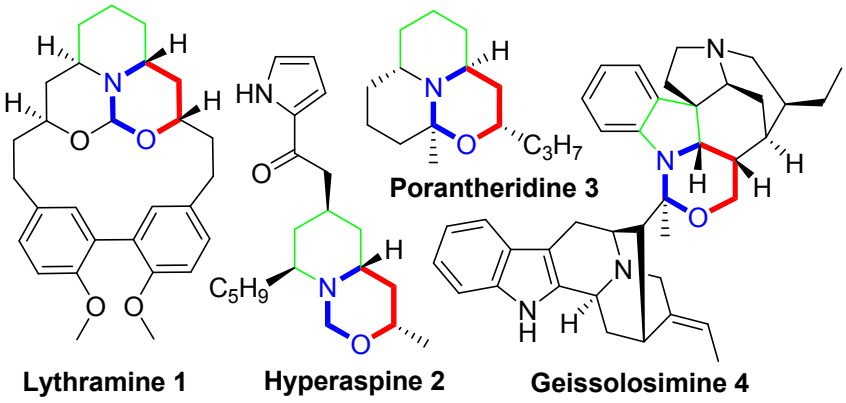


Figure 1. Natural products containing pyrido or pyrrolo [1,2-c][1,3]oxazine skeletons.

In the past decade, ynamides have undoubtedly become one of the most popular synthons in modern organic synthesis, along with the discovery of more efficient methods for accessing ynamides.[7, 8] Many useful transformations from ynamides were successfully realized through the transition-metal catalysis to generate important acyclic and cyclic compounds, such as benzofurans,[9] enamides,[10] amidines,[11] carbolines,[12] oxazoles,[13] quinolines,[14] indoles,[15] and pyridines.[16] More recently, several non-metal catalyzed conversions of ynamides were developed, such as Brønsted acid catalyzed [3,3]-sigmatropic rearrangement[17] and NBS-promoted allyloxyl addition-Claisen rearrangement.[18] On the basis of our efforts in the transformation of *N*,O-acetals,[19] we envisioned that the iminium ion could undergo nucleophilic addition from ynamides and subsequent intramolecular cyclization to give pyrido or pyrrolo[1,2-c][1,3]oxazin-1-ones (Figure 2). As a continuation of our interest in developing diverse building blocks for natural products,[20] herein we present an efficient asymmetric approach from ynamides and *N*,O-acetals **6a, 7** through

nucleophilic addition and subsequent intramolecular cyclization process.

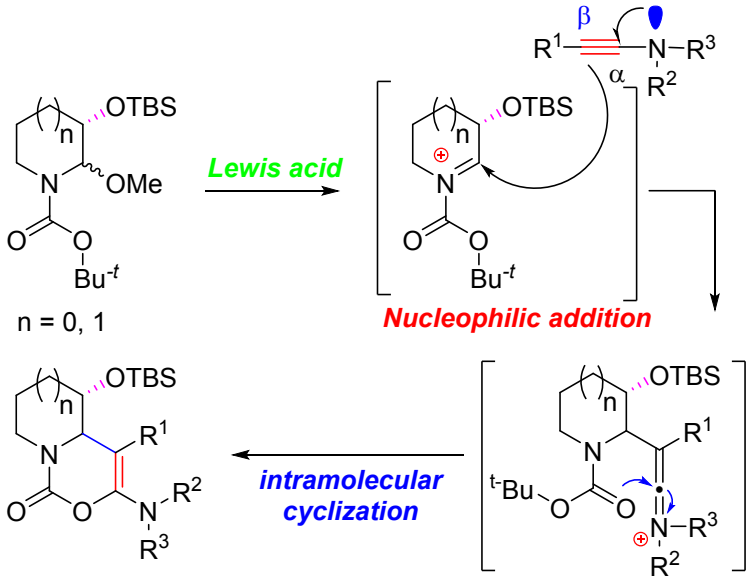
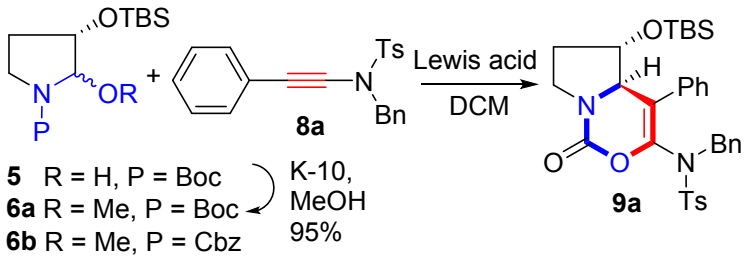


Figure 2. The strategy of addition-cyclization process.

Results and discussions

Our investigation started with the reaction of *N*,O-acetal **6a** with ynamide **8a**[7c]. When **8a** was mixed with either **5** or **6a** and stirred at room temperature for overnight, the desired product **9a** was not produced (Table 1, entries 1-2). When $Sc(OTf)_3$ was used, the mixture was treated at 0 °C for 2 h, the desired product **9a** was obtained with high diastereoselectivity (*dr* > 99:1) in 25% yield (Table 1, entry 3). To improve the reaction yield, various Lewis acids were screened, and the results were summarized in Table 1 (Table 1, entries 4-7). Delightfully, $BF_3{\cdot}Et_2O$ significantly increased the yield of **9a** up to 85% (Table 1, entry 7). Different stoichiometry of $BF_3.OEt_2$ was examined, which resulted in significant drop of the yield of **9a** (Table 1, entries 8-9). When hemiacetal **5** was used in this reaction, the desired product **9a** was obtained with high diastereoselectivity (*dr* > 99:1), but only in 10% yield (Table 1, entry 10). When **6b** was used as substrate, the desired product **9a** was obtained with 28% yield and high diastereoselectivity (*dr* > 99:1) (Table 1, entry 11).

Table 1. Optimization of reaction conditions.

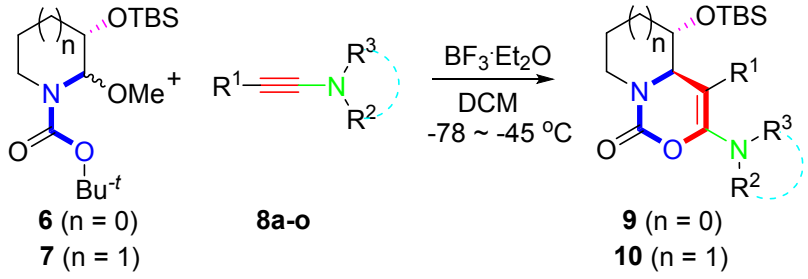


entry[a]	Substrate	P	LA (equiv.)	Y%[b]	*trans:cis*[c]
1	**5**	Boc	--	0	--
2	**6a**	Boc	--	0	--
3[d]	**6a**	Boc	$Sc(OTf)_3$ (0.1)	25	>99:1
4[d]	**6a**	Boc	$In(OTf)_3$ (0.1)	15	>99:1
5[d]	**6a**	Boc	$Cu(OTf)_2$ (0.1)	20	>99:1
6	**6a**	Boc	TMSOTf (2.0)	46	>99:1
7	**6a**	Boc	$BF_3{\cdot}Et_2O$ (2.0)	85	>99:1
8	**6a**	Boc	$BF_3{\cdot}Et_2O$ (2.5)	68	>99:1
9	**6a**	Boc	$BF_3{\cdot}Et_2O$ (1.0)	38	>99:1
10	**5**	Boc	$BF_3{\cdot}Et_2O$ (2.0)	10	>99:1
11	**6b**	Cbz	$BF_3{\cdot}Et_2O$ (2.0)	28	>99:1

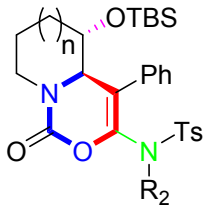
[a] The reactions were performed with $BF_3{\cdot}Et_2O$ (0.6 mmol), **5** or **6** (0.3 mmol) and **8a** (0.36 mmol) in DCM (2 mL) at -78 ~ -45 °C for 2 h. [b] Isolated yield. [c] *dr* were determined by ^1H NMR of crude products. [d] Reaction temperature was 0 °C. K-10 = Montmorillonite K-10.

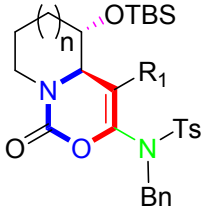
Next, we turned to investigate the scope and limitation of this nucleophilic addition and intramolecular cyclization. Different TsN-substituted ynamides were surveyed under the optimal conditions, as summarized in Scheme 1. In general, the reactions with various TsN-substituted ynamides **8a-8e** proceeded smoothly in moderate yields and with excellent diastereoselectivities (**9a-9e, 10a-10e**). Various ynamides prepared from different alkynes were also screened, and the results showed that most aryl and alkyl substituted ynamides could smoothly lead to the desired products in moderate to excellent yields and with excellent diastereoselectivities (**9f-9j, 10f-10j**). It is worth mentioning that terminal ynamide could successfully provide the product **9o** in 72% yield in spite of low diastereoselectivity (75:25). Other N-substituted ynamides were also screened, affording the desired products in moderate yields and with excellent diastereoselectivities (**9k-9n, 10k-10m**). The stereochemistry of the products pyrrolo[1,2-c][1,3]oxazin-1-ones **9a-9n** were unambiguously assigned as *trans*- form by X-ray crystallographic analysis of compound **9a** (see Supporting Information).

Scheme 1. The reactions with various substituted ynamides [a-c].



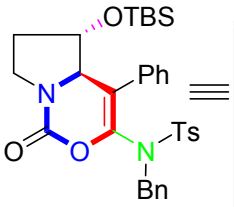
6 (n = 0) **7** (n = 1) **8a-o** **9** (n = 0) **10** (n = 1)



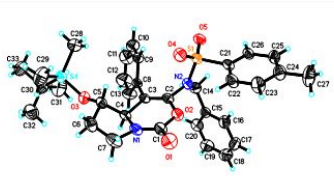


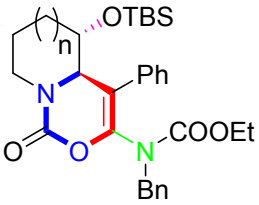
9b n=0, R^2=Allyl, 83%, *dr*>99:1
9c n=0, R^2=*n*-C_4H_9, 67%, *dr*>99:1
9d n=0, R^2=Ph, 54%, *dr*>99:1
9e n=0, R^2=Me, 86%, *dr*>99:1
10a n=1, R^2=Bn, 96%, *dr*>99:1
10b n=1, R^2=Allyl, 80%, *dr*>99:1
10c n=1, R^2=*n*-C_4H_9, 63%, *dr*>99:1
10d n=1, R^2=Ph, 87%, *dr*>99:1
10e n=1, R^2=Me, 83%, *dr*>99:1

9f n=0, R^1=4-BrC_6H_4, 64%, *dr*>99:1
9g n=0, R^1=4-ClC_6H_4, 96%, *dr*>99:1
9h n=0, R^1=4-MeC_6H_4, 91%, *dr*>99:1
9i n=0, R^1=4-MeOC_6H_4, 95%, *dr*>99:1
9j n=0, R^1=2-ClC_6H_4, 94%, *dr*>99:1
10f n=1, R^1=4-BrC_6H_4, 74%, *dr*>99:1
10g n=1, R^1=4-ClC_6H_4, 69%, *dr*>99:1
10h n=1, R^1=4-MeC_6H_4, 58%, *dr*>99:1
10i n=1, R^1=4-MeOC_6H_4, 68%, *dr*>99:1
10j n=1, R^1=2-ClC_6H_4, 51%, *dr*>99:1

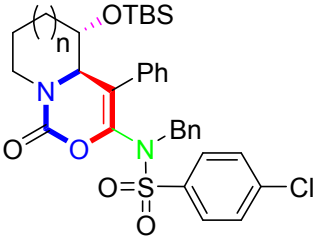


9a 85% *dr*>99:1

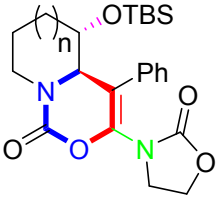




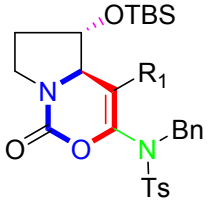
9k n=0, 81%, *dr*>99:1
10k n=1, 61%, *dr*>99:1



9m n=0, 82%, *dr*>99:1
10m n=1, 50%, *dr*>99:1



9l n = 0, 50%, *dr*>99:1
10l n = 1, 41%, *dr*>99:1



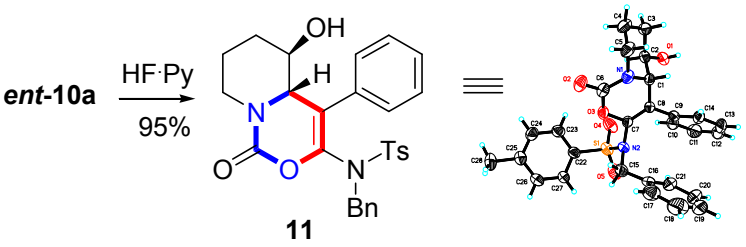
9n R^1=C_6H_{13}, 62% *dr*>99:1
9o R^1=H, 72% *dr*=75:25

[a] The reactions were performed with BF_3·Et_2O (0.6 mmol), *N,O*-acetal (0.3 mmol) and ynamide (0.36 mmol) in dry DCM (2 mL) at -78 ~ -45 °C for 2 h. [b] Isolated yield. [c] *dr* were determined by ^{1}H NMR of crude products.

The structures of pyrido [1,2-c][1,3]oxazin-1-ones **10a-10m** were also unambiguously assigned based on the X-ray crystallographic analysis of

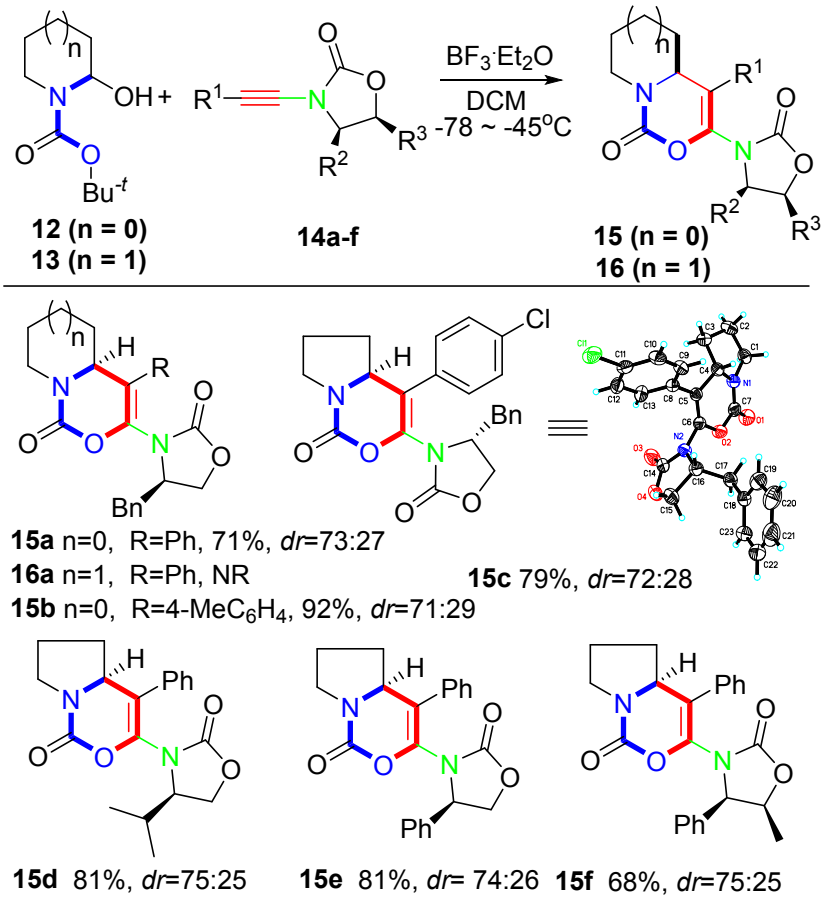
compound **11** derived from *ent*-**10a** (see Scheme 2 and Supporting Information).

Scheme 2. The transformation from *ent*-10a to 11.



Then, several chiral ynamides[7c] were also explored. As summarized in **Scheme 3**, the desired products **15a-15f** were successfully obtained from various substituted chiral ynamides in moderatate yields, albeit with low diastereoselectivities due to the lack of stereocontrol by OTBS group. To our surprise, piperidine hemiacetal **13** did not react with ynamide **14a** or **14e**. The stereochemistries of the major isomers **15a-15f** were unambiguously assigned based on the X-ray crystallographic analysis of compound **15c** (see Supporting Information).

Scheme 3. The reactions with different chiral ynamides [a-c].



[a] The reactions were performed with $BF_3{\cdot}Et_2O$ (0.6 mmol), hemiacetal (0.3 mmol) and chiral ynamide (0.36 mmol) in DCM (2 mL) at -78 ~ -45 °C for 2 h. [b] Isolated yield. [c] *dr* were determined by ^1H NMR of crude products or column chromatography.

A possible mechanism for this nucleophilic addition-cyclization process was illustrated in Figure 3. When *N*,O-acetal **7** reacted with ynamide **8a**, imide onium was first generated under Lewis acid conditions. Conformation **a** is more stable than **b** due to allylic strain considerations where it is preferred to have the alpha-H coplanar to the double bond.[21] The axial OTBS stereocenter is disposed for a Felkin type attack where ynamide **8a** is preferred to attack from axial orientation. Finally, the carbonyl of Boc group would attack the α position of intermediate **c** to form the cyclization product **10a**.[22]

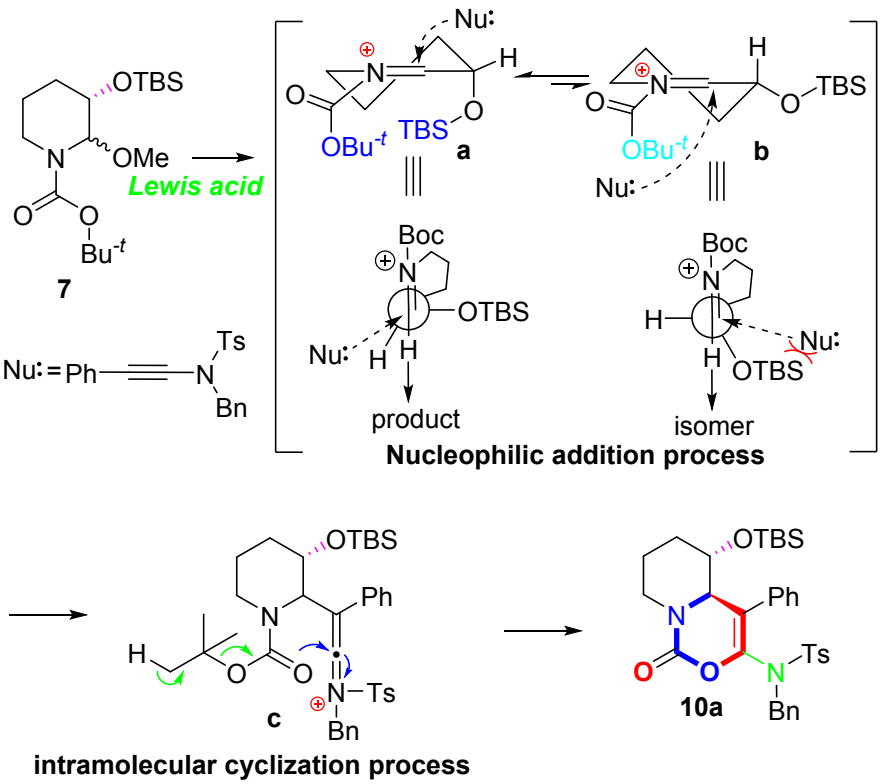


Figure 3. Proposed mechanism of the addition-cyclization.

Conclusion

In summary, we established a novel and efficient approach for highly regio- and diastereoselective synthesis of functionalized pyrido and pyrrolo[1,2-c][1,3]oxazin-1-ones **9a-9o, 10a-10m** by treatment of *N*,O-acetals **6**, **7** with ynamides **8a-8n**. In addition, chiral ynamides **14a-14f** were also investigated. The reaction experienced a one-pot sequence of nucleophilic addition and subsequent intramolecular cyclization process, providing an efficient synthesis of chiral pyrido and pyrrolo[1,2-c][1,3]oxazin-1-ones in moderate to excellent yields and with excellent diastereoselectivities.

Experimental Section

General Considerations 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) with Petroleum/EtOAc or DCM/MeOH as eluent. Optical rotations were

measured on a polarimeter with a sodium lamp. HRMS were measured on a LTQ-Orbit. IR spectra were recorded using film on a Fourier Transform Infrared Spectrometer. NMR spectra were recorded at 400 MHz or 600 MHz, and chemical shifts are reported in δ (ppm) referenced to an internal TMS standard for ^{1}H NMR and $CDCl_3$ (77.16 ppm) for $^{13}C\{^1H\}$ NMR.

General Procedure for Synthesis of 6 and 7. To a solution of **SM**[19a, 23] (8 mmol) in dry THF (20 mL) was added solution of $LiHBEt_3$ in THF (1 M, 1.1 eq, 8.8 mL) at -78^{o}C. The reaction mixture was stirred for 1 h at the same temperature, and the reaction was quenched with water (5 mL) and warmed to room temperature. To the mixture were added saturated aqueous $NaHCO_3$ (20 mL) and 30% H_2O_2 solution (5 mL). After stirring for 1 h, the mixture was extracted with ethyl acetate (20 × 3), 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 = 10:1). The product was dissolved in methol (15 ml) and Montmorillonite K 10 (400 mg) was added to the solution. After stirring for 1 h, filtered, concentrated, the residue was purified by flash chromatography on silica gel (PE/EA = 25:1).

tert-Butyl-(3*S*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methoxypyrrolidine-1-carboxylate (**6a**). Colorless oil (2.39 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.90-4.87 (m, 0.5H), 4.78-4.75 (m, 0.5H), 4.10 (d, J = 3.6 Hz, 1H), 3.63-3.55 (m, 0.5H), 3.51-3.44 (m, 0.5H), 3.40-3.32 (m, 4H), 2.12-2.00 (m, 1H), 1.79-1.70 (m, 1H), 1.48 (s, 9H), 0.92-0.84 (m, 9H), 0.12-0.06 (m, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.4 (156.0), 94.4, 80.1 (79.8), 75.2 (74.4), 55.6 (56.1), 44.1 (44.7), 31.0 (31.8), 28.5, 25.8 (26.0), 18.1, -4.7 (-4.6) ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{34}NO_4Si$, 332.2246; found, 332.2247.

tert-Butyl-(3*S*)-3-((*tert*-butyldimethylsilyl)oxy)-2-methoxypiperidine-1-carboxylate (**7**).Colorless oil (1.80 g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.30-5.00 (m, 1H), 4.03-3.59 (m, 2H), 3.34-3.22 (m, 3H), 2.92-2.72 (m, 1H), 1.93-1.73 (m, 2H), 1.56-1.49 (m, 1H), 1.47 (s, 9H), 1.35-1.25 (m, 1H), 0.93-0.86 (m, 9H), 0.12-0.03 (m, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.6, 85.7 (84.6), 79.8 (80.2), 71.3 (71.0), 66.8, 54.4 (55.2), 37.6 (36.8), 28.5 (27.8), 26.9, 25.8 (26.0), 18.1 (19.0), -4.8

(-4.5), -5.0 (-4.6) ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{36}NO_4Si$, 346.2403; found, 346.2403.

General Procedure for Synthesis of 8a-8o and 14a-14f.[7c] To a mixture of an amide (2 mmol), K_3PO_4 (4 mmol), $CuSO_4•5H_2O$ (0.2mmol,) and 1,10-phenanthroline (0.4 mmol,) in toluene at N_2 atmosphere was added a solution 1-bromoalkyne (2.2 mmol) in toluene. The reaction was stirred at 75 °C for 24 h at N_2 atmosphere. The reaction mixture was cooled to room temperature and diluted with EtOAc and filtered through Celite and the filtrate was concentrated in vacuo. The crude products were purified by silica gel flash chromatography to afford the desired ynamide.

The data for new compounds of ynamides.

(*R*)-4-benzyl-3-(p-tolylethynyl)oxazolidin-2-one (**14b**). Pale yellow solid (495 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.32 (m, 4H), 7.31-7.26 (m, 1H), 7.26-7.22 (m, 2H), 7.15-7.11 (m, 2H), 4.38-4.31 (m, 2H), 4.19-4.12 (m, 1H), 3.28 (dd, J = 14.0, 3.6 Hz, 1H), 3.04-2.97 (m, 1H), 2.35 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.7, 138.6, 134.4, 131.8, 129.5, 129.2, 129.1, 127.6, 119.1, 77.3, 73.4, 67.5, 58.6, 38.1, 21.6 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{18}NO_2$, 292.1327; found, 292.1330.

(*R*)-4-benzyl-3-((4-chlorophenyl)ethynyl)oxazolidin-2-one (**14c**). Pale yellow solid (511 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 4H), 7.32-7.27 (m, 3H), 7.26-7.21 (m, 2H), 4.42-4.32 (m, 2H), 4.22-4.14 (m, 1H), 3.27 (dd, J = 14.0, 3.6 Hz, 1H), 3.04-2.97 (m, 1H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.5, 134.4, 134.2, 132.9, 129.5, 129.2, 128.8, 127.7, 120.8, 79.0, 72.4, 67.7, 58.6, 38.2 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{15}ClNO_2$, 312.0780; found, 312.0785.

General Procedure for Synthesis of 9 and 10. To a solution of **6a** (0.3 mmol) or **7** (0.3 mmol) and **8**[7c] (0.36 mmol) in dry DCM (2 mL) was added dropwise $BF_3·Et_2O$ (76 μL, 0.6 mmol) at -78°C. The reaction was allowed to warm to -45 °C slowly and stirred for 2 h at -45 °C. Saturated aqueous $NaHCO_3$ (2 mL) was added to quench the reaction. The mixture was extracted with DCM (5 × 3) 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 = 5:1) to give **9** or **10**.

N-benzyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**9a**). White solid (154 mg, 85%), mp 140-142 °C. $[\alpha]_D^{24}$ +89.1 (*c* 1.78, $CHCl_3$); IR (film): ν_{max} 3030, 2952, 2927, 2854, 1743, 1682, 1649, 1354, 1164, 1012, 773, 675 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88-7.64 (m, 2H), 7.33-7.29 (m, 2H), 7.26-7.17 (m, 4H), 7.15-7.07 (m, 2H), 7.06-6.89 (m, 2H), 6.88-6.72 (m, 2H), 4.28-4.18 (m, 1H), 4.12-3.94 (m, 3H), 3.93-3.83 (m, 1H), 3.50-3.42 (m, 1H), 2.43 (s, 3H), 2.11-1.97 (m, 1H), 1.70-1.60 (m, 1H), 0.66 (s, 9H), -0.22 (s, 3H), -0.60 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.6, 144.3, 138.0, 135.7, 133.8, 129.7, 129.4, 128.7, 128.3, 128.1, 128.0, 127.9, 75.3, 65.1, 51.8, 44.1, 32.7, 25.7, 21.7, 17.6, -4.5, -5.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{33}H_{41}N_2O_5SSi$, 605.2500; found, 605.2504.

N-allyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**9b**). White solid (138 mg, 83%), mp 129-130 °C. $[\alpha]_D^{24}$ +101 (*c* 0.815, $CHCl_3$); IR (film): ν_{max} 3066, 2952, 2928, 2855, 1741, 1681, 1355, 1165, 868, 746, 677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82-7.72 (m, 2H), 7.44-7.35 (m, 4H), 7.34-7.28 (m, 3H), 5.38-5.21 (m, 1H), 5.03-4.93 (m, 2H), 4.45 (d, *J* = 6.4 Hz, 1H), 4.14 (dd, *J* = 12.8, 6.0 Hz, 1H), 3.93-3.85 (m, 1H), 3.63-3.56 (m, 1H), 3.55-3.47 (m, 1H), 3.45-3.36 (m, 1H), 2.42 (m, 3H), 2.19-2.09 (m, 1H), 1.77-1.67 (m, 1H), 0.70 (s, 9H), -0.16 (s, 3H), -0.54 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.5, 144.3, 138.7, 136.0, 132.1, 131.6, 129.7, 129.6, 128.6, 128.5, 128.2, 119.8, 75.4, 65.0, 51.3, 44.1, 32.8, 25.8, 21.7, 17.7, -4.4, -5.7 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{29}H_{39}N_2O_5SSi$, 555.2344; found, 555.2346.

N-butyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**9c**). White solid (115 mg, 67%), mp 133-135 °C. $[\alpha]_D^{24}$ +116 (*c* 2.23, $CHCl_3$); IR (film): ν_{max} 3057, 2959, 2929, 2856, 1738, 1681, 1355, 1167, 837, 775, 678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81-7.73 (m, 2H), 7.48-7.43 (m, 2H), 7.39-7.33 (m, 2H),

7.33-7.27 (m, 3H), 4.48 (d, J = 6.4 Hz, 1H), 4.19-4.12 (m, 1H), 3.95-3.87 (m, 1H), 3.55-3.47 (m, 1H), 2.96-2.87 (m, 1H), 2.85-2.74 (m, 1H), 2.40 (s, 3H), 2.20-2.10 (m, 1H), 1.77-1.68 (m, 1H), 1.18-1.05 (m, 2H), 0.97-0.82 (m, 2H), 0.70 (s, 9H), 0.67-0.61 (m, 3H), -0.17 (s, 3H), -0.55 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 148.6, 144.1, 138.7, 136.0, 132.2, 129.6, 129.4, 128.7, 128.5, 128.2, 116.1, 75.5, 65.2, 48.1, 44.1, 32.8, 29.7, 25.8, 21.7, 19.7, 17.7, 13.6, -4.4, -5.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{43}N_2O_5SSi$, 571.2656; found, 571.2657.

N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methyl-N-phenylbenzenesulfonamide (**9d**). White solid (96 mg, 54%), mp 158-160 °C. $[\alpha]_D^{24}$ +44.0 (*c* 1.32, $CHCl_3$); IR (film): ν_{max} 3063, 2953, 2928, 2856, 1747, 1682, 1361, 1156, 838, 772, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.52 (m, 2H), 7.35-7.27 (m, 5H), 7.21-7.17 (m, 2H), 7.16-7.12 (m, 1H), 7.08-7.02 (m, 2H), 6.70-6.63 (m, 2H), 4.33 (d, *J* = 6.4 Hz, 1H), 4.16 (dd, *J* = 6.4, 13.2 Hz, 1H), 3.93-3.85 (m, 1H), 3.55-3.47 (m, 1H), 2.37 (s, 3H), 2.22-2.10 (m, 1H), 1.76-1.66 (m, 1H), 0.65 (s, 9H), -0.18 (s, 3H), -0.58 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, CDCl3) δ 148.5, 144.2, 140.6, 138.2, 135.5, 132.0, 129.6, 129.3, 128.8, 128.6, 128.5, 128.3, 128.1, 115.4, 75.2, 65.1, 44.1, 32.7, 25.7, 21.7, 17.7, -4.4, -5.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{39}N_2O_5SSi$, 591.2343; found, 591.2347.

N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-N,4-dimethylbenzenesulfonamide (**9e**). White solid (136 mg, 86%), mp 167-169 °C. $[\alpha]_D^{24}$ +98.7 (*c* 0.905, $CHCl_3$); IR (film): ν_{max} 3055, 2953, 2928, 2856, 1743, 1682, 1355, 1159, 837, 772, 678 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.65 (m, 2H), 7.40-7.36 (m, 4H), 7.36-7.30 (m, 2H), 7.28 (s, 1H), 4.47 (d, J = 6.4 Hz, 1H), 4.13 (dd, J = 13.2, 6.4 Hz, 1H), 3.94-3.86 (m, 1H), 3.55-3.47 (m, 1H), 2.70 (s, 3H), 2.41 (s, 3H), 2.18-2.08 (m, 1H), 1.78-1.68 (m, 1H), 0.71 (s, 9H), -0.16 (s, 3H), -0.53 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 148.6, 144.2, 140.7, 135.2, 132.3, 129.7, 129.2, 128.6, 128.5, 128.3, 114.6, 75.4, 65.1, 44.1, 35.8, 32.7, 25.8, 21.7, 17.7, -4.4, -5.7 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{37}N_2O_5SSi$, 529.2187; found: 529.2186.

N-Benzyl-N-((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**10a**). Foam solid (178 mg, 96%). $[\alpha]_D^{24}$ -56.3 (*c* 1.38, $CHCl_3$); IR (film): ν_{max} 3030, 2951, 2927, 2856, 1731, 1682, 836, 773 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95-7.70 (m, 2H), 7.35-7.27 (m, 2H), 7.25-7.16 (m, 6H), 7.15-6.95 (m, 3H), 6.75 (s, 1H), 4.25-4.16 (m, 2H), 4.05-3.80 (m, 2H), 3.76-3.66 (m, 1H), 2.75-2.65 (m, 1H), 2.43 (s, 3H), 2.11-2.06 (m, 1H), 1.78-1.65 (m, 2H), 1.49-1.40 (m, 1H), 0.53 (s, 9H), -0.13 (s, 3H), -0.23 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.8, 144.3, 135.8, 134.1, 133.6, 129.7, 129.2, 128.7, 128.3, 127.9, 127.5, 72.4, 65.2, 52.1, 46.0, 35.6, 25.6, 23.1, 21.8, 17.8, -4.3 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{43}N_2O_5SSi$, 619.2656; found, 619.2659.

N-Allyl-N-((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**10b**). Foam solid (136 mg, 80%). $[\alpha]_D^{24}$ +27.0 (*c* 1.91, $CHCl_3$); IR (film): ν_{max} 3033, 2949, 2927, 2855, 1735, 1731, 1219, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88-7.76 (m, 2H), 7.62-7.57 (m, 2H), 7.38-7.34 (m, 2H), 7.34-7.27 (m, 3H), 5.05-4.85 (m, 2H), 4.29-4.20 (m, 1H), 4.10 (d, *J* = 9.2 Hz, 1H), 3.83-3.73 (m, 1H), 3.70-3.50 (m, 2H), 2.84-2.75 (m, 1H), 2.43 (s, 3H), 2.17-2.09 (m, 1H), 1.85-1.69 (m, 2H), 1.62-1.59 (m, 1H), 1.58-1.46 (m, 1H), 0.60 (s, 9H), -0.06 (s, 3H), -0.14 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 149.9, 143.3, 135.1, 133.3, 130.4, 128.7, 127.7, 127.6, 127.2, 126.8, 118.9, 71.6, 64.2, 50.4, 45.2, 34.8, 24.7, 22.2, 20.8, 16.8, -5.2, -5.3 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{41}N_2O_5SSi$, 569.2500; found, 569.2504.

N-Butyl-N-((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**10c**). Foam solid (110 mg, 63%). $[\alpha]_D^{24}$ +39.5 (*c* 1.17, $CHCl_3$); IR (film): ν_{max} 3055, 2955, 2928, 2875, 1738, 1731, 1166, 837, 766 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86-7.79 (m, 2H), 7.67-7.63 (m, 2H), 7.38-7.30 (m, 4H), 7.28-7.24 (m, 1H), 4.27 (dd, *J* = 11.6, 2.4 Hz, 1H), 4.12 (d, *J* = 9.2 Hz, 1H), 3.86-3.79 (m, 1H), 3.02-2.90 (m, 2H), 2.86-2.77 (m, 1H), 2.42 (s, 3H), 2.20-2.10 (m, 1H), 1.89-1.70 (m, 2H), 1.60-1.48 (m,

1H), 1.20-0.80 (m, 4H), 0.66-0.58 (m, 12H), -0.05 (s, 3H), -0.12 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 151.1, 144.1, 138.9, 136.0, 134.3, 129.7, 128.7, 128.7, 128.2, 127.8, 117.6, 72.5, 65.3, 48.5, 46.2, 35.8, 25.7, 23.2, 21.7, 19.8, 17.8, 13.7, -4.3 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{31}H_{45}N_2O_5SSi$, 585.2813; found, 585.2816.

N-((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,7,8-tetrahydro -1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methyl-N-phenylbenzenesulfonamide (**10d**). Foam solid (158 mg, 87%). $[\alpha]_D^{24}$ -6.35 (*c* 1.28, $CHCl_3$); IR (film): ν_{max} 2993, 29511, 2927, 2856, 1738, 1731, 1361, 1159, 836, 756, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.56 (m, 4H), 7.38-7.31 (m, 2H), 7.30-7.25 (m, 1H), 7.23-7.18 (m, 2H), 7.19-7.13 (m, 1H), 7.12-7.05 (m, 2H), 6.94-6.83 (m, 2H), 4.30-4.24 (m, 1H), 4.00 (d, *J* = 9.6 Hz, 1H), 3.84-3.76 (m, 1H), 2.84-2.74 (m, 1H), 2.38 (s, 3H), 2.15-2.08 (m, 1H), 1.87-1.69 (m, 2H), 1.57-1.46 (m, 1H), 0.58 (s, 9H), -0.13 (s, 3H), -0.34 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 150.9, 144.3, 140.7, 138.8, 135.3, 134.0, 129.3, 129.1, 129.0, 129.0, 128.3, 128.1, 127.9, 127.6, 116.9, 72.2, 65.2, 46.3, 35.7, 25.6, 23.2, 21.7, 17.8, -4.5 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{33}H_{41}N_2O_5SSi$, 605.2500; found, 605.2502.

N-((4*aS*,5*R*)-5-((tert-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,7,8-tetrahydro -1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-N,4-dimethylbenzenesulfonamide (**10e**). Foam solid (135 mg, 83%). $[\alpha]_D^{24}$ +3.2 (*c* 1.62, $CHCl_3$); IR (film): ν_{max} 2950, 2928, 2856, 1738, 1731,1361, 1160, 837, 768, 672 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7,77-7.72 (m, 2H), 7.60-7.56 (m, 2H), 7.37-7.23 (m, 5H), 4.29-4.22 (m, 1H), 4.10 (d, *J* = 9.2 Hz, 1H), 3.80-3.73 (m, 1H), 2.85-2.76 (m, 4H), 2.42 (s, 3H), 2.17-2.09 (m, 1H), 1.86-1.69 (m, 2H), 1.60-1.49 (m, 1H), 0.62 (s, 9H), -0.07 (s, 3H), -0.17 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 151.0, 144.2, 140.9, 135.3, 134.0, 129.7, 128.5, 128.3, 127.8, 115.5, 72.4, 64.8, 46.3, 35.8, 35.8, 25.7, 23.2, 21.7, 17.9, -4.3, -4.4 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{28}H_{39}N_2O_5SSi$, 543.2344; found, 543.2346.

N-benzyl-N-((4*aR*,5*S*)-4-(4-bromophenyl)-5-((*tert*-butyldimethylsilyl)oxy)-1-ox o-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamid

e (**9f**). White solid (131 mg, 64%), mp 123-125 °C. $[\alpha]_D^{24}$ +69.8 (*c* 1.06, $CHCl_3$); IR (film): ν_{max} 2955, 2929, 2856, 1740, 1654, 1354, 1253, 1164, 837, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88-7.68 (m, 2H), 7.38-7.28 (m, 5H), 7.25-7.07 (m, 3H), 6.98-6.74 (m, 3H), 4.20-4.12 (m, 2H), 4.06-3.79 (m, 3H), 3.52-3.44 (m, 1H), 2.45 (s, 3H), 2.17-2.02 (m, 1H), 1.72-1.63 (m, 1H), 0.65 (s, 9H), -0.19 (s, 3H), -0.56 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.4, 144.6, 138.1, 135.4, 133.6, 131.2, 131.1, 130.7, 129.8, 129.4, 128.8, 128.4, 128.2, 122.1, 116.2, 75.3, 64.5, 51.8, 43.9, 32.5, 25.6, 21.8, 17.6, -4.3, -5.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{33}H_{40}BrN_2O_5SSi$, 683.1605; found, 683.1602.

N-benzyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-4-(4-chlorophenyl)-1-oxo-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**9g**). White solid (184 mg, 96%), mp 134-136 °C. $[\alpha]_D^{24}$ +72.4 (*c* 1.76, $CHCl_3$); IR (film): ν_{max} 3030, 2952, 2928, 2856, 1747, 1682, 1355, 1256, 1164, 837, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90-7.68 (m, 2H), 7.38-7.32 (m, 2H), 7.28-7.19 (m, 2H), 7.19-7.08 (m, 4H), 7.00-6.70 (m, 3H), 4.25-4.11 (m, 2H), 4.08-3.88 (m, 2H), 3.88-3.80 (m, 1H), 3.52-3.44 (m, 1H), 2.45 (s, 3H), 2.16-2.03 (m, 1H), 1.72-1.65 (m, 1H), 0.66 (s, 9H), -0.18 (s, 3H), -0.56 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.4, 144.5, 138.1, 135.4, 133.8, 133.6, 130.8, 130.2, 129.8, 129.5, 128.7, 128.4, 128.2, 116.1, 77.4, 75.2, 64.6, 51.8, 43.9, 32.5, 25.6, 21.7, 17.6, -4.3, -5.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{33}H_{40}ClN_2O_5SSi$, 639.2110; found, 639.2110.

N-benzyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-(p-tolyl)-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**9h**). White solid (169 mg, 91%), mp 138-140 °C. $[\alpha]_D^{24}$ +81.4 (*c* 1.02, $CHCl_3$); IR (film): ν_{max} 3030, 2952, 2928, 2855, 1743, 1649, 1164, 837, 777, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87-7.66 (m, 2H), 7.33-7.27 (m, 2H), 7.22-7.06 (m, 3H), 7.06-6.98 (m, 3H), 6.92-6.70 (m, 3H), 4.23-4.13 (m, 1H), 4.10-3.93 (m, 3H), 3.89-3.80 (m, 1H), 3.48-3.40 (m, 1H), 2.43 (s, 3H), 2.34 (s, 3H), 2.10-1.95 (m, 1H), 1.69-1.63 (m, 1H), 0.66 (s, 9H), -0.22 (s, 3H), -0.58 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.7, 144.3, 137.7, 135.9, 134.0, 129.7, 129.2, 128.9, 128.7, 128.3, 128.0, 75.3, 65.1,

51.8, 44.1, 32.8, 25.7, 21.8, 21.3, 17.7, -4.4, -5.8 ppm; HRMS (ESI-Orbitrap) *m/z*: [M + H]$^+$ calcd for $C_{34}H_{43}N_2O_5SSi$, 619.2656; found, 619.2658.

N-benzyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-4-(4-methoxyphenyl)-1-oxo-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**9i**). White solid (181 mg, 95%), mp 64-66 °C. $[\alpha]_D^{24}$ +73.7 (*c* 1.98, $CHCl_3$); IR (film): ν_{max} 3032, 2953, 2929, 2855, 1740, 1609, 1164, 836, 779, 666 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.73 (m, 2H), 7.35-7.29 (m, 3H), 7.24-7.05 (m, 3H), 6.90-6.70 (m, 5H), 4.21-4.14 (m, 1H), 4.08-3.99 (m, 3H), 3.90-3.83 (m, 1H), 3.82 (s, 3H), 3.49-3.40 (m, 1H), 2.44 (s, 3H), 2.10-1.98 (m, 1H), 1.66-1.60 (m, 1H), 0.68 (s, 9H), -0.20 (s, 3H), -0.54 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.4, 148.7, 144.3, 137.8, 135.8, 133.9, 130.6, 129.7, 129.3, 128.7, 128.3, 128.0, 124.1, 113.7, 75.4, 65.1, 55.4, 51.8, 44.1, 32.8, 25.7, 21.7, 17.7, -4.4, -5.7 ppm; HRMS (ESI-Orbitrap) *m/z*: [M + H]$^+$ calcd for $C_{34}H_{43}N_2O_6SSi$, 635.2606; found, 635.2604.

N-benzyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-4-(2-chlorophenyl)-1-oxo-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**9j**). Foam solid (180 mg, 94%). $[\alpha]_D^{24}$ +48.9 (*c* 1.59, $CHCl_3$); IR (film): ν_{max} 3066, 3032, 2953, 2925, 2849, 1738, 1689, 1649, 1361, 1219, 838, 771, 673 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers) δ 7.75-7.70 (m, 1.78H), 7.57-7.53 (m, 0.22H), 7.38-7.23 (m, 5H), 7.22-7.15 (m, 2H), 7.11-7.05 (m, 2H), 6.90-6.84 (m, 2H), 4.66-4.62 (m, 0.88H), 4.33-4.31 (m, 0.12H), 4.18-4.04 (m, 2H), 4.02-3.93 (m, 1H), 3.85-3.76 (m, 1H), 3.57-3.49 (m, 1H), 2.41 (s, 2.70H), 2.38 (s, 0.30H), 2.15-2.02 (m, 1H), 1.76-1.66 (m, 1H), 0.67 (s, 8.09H), 0.63 (s, 0.91H), -0.18 (s, 3H), -0.49 (s, 0.22H), -0.55 (s, 2.78H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.6, 144.3, 136.0, 135.1, 134.4, 132.4, 131.3, 129.8, 129.7, 129.6, 128.8, 128.7, 128.4, 128.3, 127.9, 127.1, 74.8, 63.0, 52.6, 43.9, 32.6, 25.7, 21.7, 17.6, -4.2, -5.6 ppm; HRMS (ESI-Orbitrap) *m/z*: [M + H]$^+$ calcd for $C_{33}H_{40}ClN_2O_5SSi$, 639.2110; found, 639.2111.

N-benzyl-N-((4*aS*,5*R*)-4-(4-bromophenyl)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**10f**). Foam solid (155 mg, 74%). $[\alpha]_D^{24}$ +38.1 (*c* 1.94, $CHCl_3$); IR (film): ν_{max} 3029, 2951, 2928, 2855, 1731, 1682, 1361, 1258, 1164, 837, 753, 676 cm^{-1}; ^{1}H NMR

(400 MHz, $CDCl_3$) δ 8.00-7.70 (m, 2H), 7.36-7.28 (m, 5H), 7.20-6.96 (m, 6H), 4.32-4.20 (m, 2H), 3.90-3.60 (m, 3H), 2.76-2.66 (m, 1H), 2.45 (s, 3H), 2.12-2.05 (m, 1H), 1.79-1.68 (m, 2H), 1.46-1.38 (m, 1H), 0.54 (s, 9H), -0.07--0.20 (m, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.5, 144.5, 135.5, 133.3, 131.0, 130.4, 129.8, 129.4, 128.8, 128.3, 121.5, 72.5, 65.1, 52.0, 46.1, 35.7, 25.5, 23.2, 21.8, 17.7, -4.2 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{42}BrN_2O_5SSi$, 697.1762; found, 697.1766.

N-benzyl-N-((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-4-(4-chlorophenyl)-1-oxo-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**10g**). Foam solid (135 mg, 69%). $[\alpha]_D^{23}$ +46.9 (*c* 1.48, $CHCl_3$); IR (film): ν_{max} 3032, 2952, 2928, 2857, 1747, 1689, 1649, 1219, 772, 674 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95-7.67 (m, 2H), 7.37-7.30 (m, 2H), 7.20-7.96 (m, 8H), 6.80 (s, 1H), 4.31-4.20 (m, 2H), 3.98-3.62 (m, 3H), 2.75-2.66 (m, 1H), 2.45 (s, 3H), 2.13-2.05 (m, 1H), 1.82-1.66 (m, 2H), 1.48-1.39 (m, 1H), 0.54 (s, 9H), -0.0--0.36 (m, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.6, 144.5, 135.5, 133.3, 132.8, 130.0, 129.8, 129.4, 128.7, 128.3, 128.1, 128.0, 72.5, 65.1, 52.0, 46.1, 35.7, 25.5, 23.2, 21.8, 17.7, -4.3 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{42}ClN_2O_5SSi$, 653.2267; found, 653.2268.

N-benzyl-N-((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-(p-tolyl)-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**10h**). Foam solid (110 mg, 58%). $[\alpha]_D^{24}$ +39.6 (*c* 1.86, $CHCl_3$); IR (film): ν_{max} 3029, 2952, 2927, 2855, 1731, 1682, 1649, 1219, 1163, 772, 686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95-7.65 (m, 2H), 7.35-7.24 (m, 2H), 7.19-7.10 (m, 4H), 7.08-6.98 (m, 4H), 6.78 (s, 1H), 4.30-4.15 (m, 2H), 4.12-3.93 (m, 1H), 3.90-3.81 (m, 1H), 3.75-3.64 (m, 1H), 2.75-2.65 (m, 1H), 2.43 (s, 3H), 2.32 (s, 3H), 2.11-2.03 (m, 1H), 1.82-1.64 (m, 2H), 1.49-1.39 (m, 1H), 0.54 (s, 9H), -0.12 (s, 3H), -0.24 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.9, 144.2, 137.2, 136.0, 131.1, 129.7, 129.2, 128.7, 128.6, 128.5, 128.2, 127.9, 72.3, 65.2, 52.1, 46.0, 35.7, 25.6, 23.1, 21.8, 21.2, 17.7, -4.4, -4.4 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{35}H_{45}N_2O_5SSi$, 633.2813; found, 633.2815.

N-benzyl-N-((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-4-(4-methoxyphenyl)-1-oxo-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**10i**). Foam solid (132 mg, 68%). $[\alpha]_D^{24}$ +41.9 (*c* 1.62, $CHCl_3$); IR (film): ν_{max} 3033, 2952, 2927, 2855, 1731, 1682, 1649, 1219, 1163, 772, 686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94-7.73 (m, 2H), 7.34-7.28 (m, 2H), 7.24-7.18 (m, 3H), 7.16-6.96 (m, 3H), 6.82-6.72 (m, 3H), 4.30-4.16 (m, 2H), 4.15-3.90 (m, 1H), 3.88-3.78 (m, 4H), 3.76-3.62 (m, 1H), 2.75-2.64 (m, 1H), 2.44 (s, 3H), 2.11-2.03 (m, 1H), 1.83-1.64 (m, 2H), 1.50-1.36 (m, 1H), 0.56 (s, 9H), -0.11 (s, 3H), -0.22 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 151.0, 144.3, 135.9, 129.9, 129.7, 129.2, 128.8, 128.7, 128.2, 128.1, 128.0, 127.9, 127.3, 126.5, 113.4, 72.3, 65.2, 55.5, 52.2, 46.0, 35.7, 25.6, 23.2, 21.8, 17.8, -4.4, -4.4 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{35}H_{45}N_2O_6SSi$, 649.2762; found, 649.2763.

N-benzyl-N-((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-4-(2-chlorophenyl)-1-oxo-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**10j**). Foam solid (100 mg, 51%). $[\alpha]_D^{24}$ +87.9 (*c* 1.38, $CHCl_3$); IR (film): ν_{max} 3055, 2962, 2934, 2879, 1682, 1649, 1397, 1213, 1065, 768, 706 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84-7.78 (m, 2H), 7.34-7.29 (m, 2H), 7.28-7.21 (m, 2H), 7.20-7.13 (m, 2H), 7.12-7.08 (m, 1H), 7.09-7.00 (m, 2H), 6.86-6.78 (m, 2H), 4.26-4.11 (m, 3H), 4.05-3.95 (m, 1H), 3.90-3.81 (m, 1H), 2.80-2.69 (m, 1H), 2.43 (s, 3H), 2.15-2.06 (m, 1H), 1.83-1.72 (m, 1H), 1.72-1.64 (m, 1H), 1.46-1.34 (m, 1H), 0.62 (s, 9H), -0.04 (s, 3H), -0.12 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.5, 144.4, 140.1, 135.6, 133.9, 133.0, 132.8, 129.8, 129.2, 129.0, 128.7, 128.4, 128.0, 126.6, 117.6, 72.7, 63.7, 52.1, 46.0, 35.4, 25.9, 23.0, 21.8, 18.0, -3.3, -3.7 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{42}ClN_2O_5SSi$, 653.2267; found, 653.2269.

Ethylbenzyl((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)carbamate (**9k**). White solid (127 mg, 81%), mp 83-84 °C. $[\alpha]_D^{24}$ +85.1 (*c* 1.33, $CHCl_3$); IR (film): ν_{max} 3033, 2953, 2929, 2855, 1742, 1649, 1377, 1219, 772, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rotamers) δ 7.37-7.27 (m, 3H), 7.22-6.98 (m, 6H), 6.68-6.54 (m, 1H), 4.55-4.39 (m, 1H), 4.38-4.22 (m, 2H), 4.10-3.98 (m, 1H), 3.97-3.83 (m, 2H), 3.74-3.61 (m, 1H),

3.56-3.40 (m, 1H), 2.18-1.95 (m, 1H), 1.94-1.65 (m, 1H), 1.74-1.65 (m, 1H), 1.43-1.32 (m, 1H), 1.30-1.15 (m, 1H), 1.10-0.98 (m, 1H), 0.68 (s, 9H), -0.19 (s, 3H), -0.58 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, rotamers) δ 155.7, 149.1, 140.9, 136.1, 132.4, 129.8, 128.7, 128.4, 128.2, 127.8, 127.6, 111.1, 75.5, 64.2 (65.2), 62.8 (62.4), 51.2, 43.9 (44.2), 32.6 (32.8), 25.8, 17.7, 14.8 (14.4), -4.4, -5.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{29}H_{39}N_2O_5Si$, 523.2623; found, 523.2621.

Ethylbenzyl((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)carbamate (**10k**). Foam solid (98 mg, 61%). $[\alpha]_D^{24}$ +51.7 (*c* 1.62, $CHCl_3$); IR (film): ν_{max} 3030, 2951, 2929, 2856, 1731, 1682, 1649, 1252, 1108, 775, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, rotamers) δ 7.44-7.30 (m, 1H), 7.25-7.17 (m, 3H), 7.16-7.10 (m, 4H), 6.95 (s, 1H), 4.75-4.16 (m, 4H), 4.02-3.88 (m, 2H), 3.76-3.64 (m, 1H), 2.84-2.66 (m, 1H), 2.10 (d, *J* = 10.0 Hz, 1H), 1.88-1.68 (m, 2H), 1.52-1.32 (m, 3H), 1.06-0.96 (m, 1H), 0.64-0.50 (m, 9H), -0.13 (s, 3H), -0.20--0.37 (m, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, rotamers) δ 156.0, 151.2, 140.3 (141.2), 135.5 (136.7), 134.4 (134.8), 128.8, 128.4, 128.2, 127.9, 127.5, 113.6, 72.5, 64.3 (64.8), 62.8 (62.6), 51.5 (52.0), 46.0 (46.3), 35.7, 25.6, 23.2, 17.8, 14.8 (14.3), -4.4 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{41}N_2O_5Si$, 537.2779; found, 537.2788.

(4*aR*,5*S*)-5-((*tert*-Butyldimethylsilyl)oxy)-3-(2-oxooxazolidin-3-yl)-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-1-one (**9l**). White solid (65 mg, 50%), mp 89-91 ^{o}C. $[\alpha]_D^{24}$ +83.0 (*c* 1.51, $CHCl_3$); IR (film): ν_{max} 3033, 2952, 2927, 2855, 1736, 1649, 1253, 1126, 775, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.28 (m, 3H), 7.27-7.23 (m, 2H), 4.46 (d, *J* = 6.8 Hz, 1H), 4.29-4.22 (m, 1H), 4.22-4.14 (m, 1H), 4.14-4.08 (m, 1H), 3.93-3.85 (m, 1H), 3.68-3.61 (m, 1H), 3.58-3.48 (m, 2H), 2.19-2.09 (m, 1H), 1.77-1.68 (m, 1H), 0.68 (s, 9H), -0.18 (s, 3H), -0.57 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 155.6, 148.4, 136.9, 132.0, 128.8, 128.6, 128.5, 113.5, 75.3, 64.8, 62.7, 44.6, 44.1, 32.6, 25.7, 17.7, -4.4, -5.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{31}N_2O_5Si$, 431.1997; found: 431.1995.

(4*aS*,5*R*)-5-((*tert*-Butyldimethylsilyl)oxy)-3-(2-oxooxazolidin-3-yl)-4-phenyl-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-1-one (**10l**). Foam solid (55 mg,

41%). $[\alpha]_D^{24}$ +61.0 (*c* 1.11, $CHCl_3$); IR (film): ν_{max} 2952, 2928, 2856, 1730, 1647, 1398, 1219, 1162, 1104, 836, 771, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.31 (m, 2H), 7.35-7.29 (m, 2H), 7.26-7.22 (m, 1H), 4.39-4.22 (m, 3H), 4.12 (d, J = 9.2 Hz, 1H), 3.86-3.74 (m, 2H), 3.53-3.46 (m, 1H), 2.86-2.78 (m, 1H), 2.18-2.10 (m, 1H), 1.84-1.72 (m, 2H), 1.60-1.48 (m, 1H), 0.59 (s, 9H), -0.08 (s, 3H), -0.18 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 156.2, 150.7, 136.9, 134.1, 128.5, 128.0, 127.9, 115.2, 72.8, 64.8, 62.9, 46.3, 44.4, 35.7, 25.7, 23.3, 17.8, -4.2, -4.4 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{33}N_2O_5Si$, 445.2153; found, 445.2156.

N-benzyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-chlorobenzenesulfonamide (**9m**). Foam solid (154 mg, 82%). $[\alpha]_D^{24}$ +85.2 (*c* 1.14, $CHCl_3$); IR (film): ν_{max} 3030, 2952, 2928, 2855, 1743, 1682, 1649, 1361, 1166, 772, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88-7.64 (m, 2H), 7.49-7.43 (m, 2H), 7.30-7.17 (m, 5H), 7.16-7.06 (m, 2H), 6.99 (s, 1H), 6.86-6.74 (m, 2H), 4.29-4.20 (m, 1H), 4.14-3.94 (m, 3H), 3.90-3.82 (m, 1H), 3.51-3.43 (m, 1H), 2.12-2.00 (m, 1H), 1.72-1.64 (m, 1H), 0.67 (s, 9H), -0.22 (s, 3H), -0.60 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.6, 144.2, 140.7, 135.2, 132.3, 129.7, 129.2, 128.6, 128.5, 128.3, 114.6, 75.4, 65.1, 44.1, 35.8, 32.7, 25.8, 21.7, 17.7, -4.4, -5.7 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{38}ClN_2O_5SSi$, 625.1954; found, 625.1957.

N-benzyl-N-((4*aS*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4-phenyl-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-chlorobenzenesulfonamide (**10m**). Foam solid (96 mg, 50%). $[\alpha]_D^{24}$ +53.4 (*c* 1.18, $CHCl_3$); IR (film): ν_{max} 3030, 2951, 2928, 2856, 1731, 1682, 1647, 1362, 1219, 1167, 772, 656 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02-7.68 (m, 2H), 7.53-7.41 (m, 2H), 7.28-7.20 (m, 6H), 7.18-7.00 (m, 3H), 6.78 (s, 1H), 4.28-4.17 (m, 2H), 4.12-3.94 (m, 1H), 3.92-3..86 (m, 1H), 3.77-3.68 (m, 1H), 2.77-2.67 (m, 1H), 2.13-2.05 (m, 1H), 1.80-1.67 (m, 2H), 1.51-1.41 (m, 1H), 0.55 (s, 9H), -0.12 (s, 3H), -0.23 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.7, 140.0, 137.4, 133.9, 130.1, 129.3, 129.1, 128.7, 128.4, 128.1, 127.6, 72.4, 65.3, 52.5, 46.1, 35.7, 25.6, 23.1, 17.8, -4.3 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{33}H_{40}ClN_2O_5SSi$, 639.2110; found, 639.2114.

N-benzyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-4-hexyl-1-oxo-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**9n**). Colorless Oil (114 mg, 62%). $[\alpha]_D^{24}$ +31.8 (*c* 2.00, $CHCl_3$); IR (film): ν_{max} 3033, 2955, 2929, 2857, 17335, 1640, 1219, 1165, 838, 772, 673 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, rotamers) δ 7.84-7.73 (m, 2H), 7.36-7.24 (m, 7H), 4.68-4.58 (m, 1H), 4.00-3.86 (m, 2H), 3.82-3.74 (m, 1H), 3.47-3.29 (m, 2H), 2.43 (m, 3H), 2.24-2.12 (m, 1H), 2.06-1.93 (m, 1H), 1.74-1.46 (m, 2H), 1.45-1.34 (m, 1H), 1.34-1.14 (m, 5H), 1.03-0.86 (m, 5H), 0.84 (s, 9H), 0.10--0.10 (m, 6H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.9, 144.4, 135.6, 134.8, 134.6, 130.1, 129.9, 129.8, 129.7, 128.7, 128.6, 128.3, 128.2, 118.0, 75.8, 62.5, 50.8 (51.8), 43.3 (43.1), 32.0 (32.2), 29.8 (29.9), 27.8 (28.0), 27.4 (27.2), 25.8, 22.8, 21.7, 17.8, 14.2, -4.0, -4.6 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{33}H_{49}N_2O_5SSi$, 613.3126; found, 613.3121.

N-benzyl-N-((4*aR*,5*S*)-5-((*tert*-butyldimethylsilyl)oxy)-1-oxo-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**9o**). Colorless oil (114 mg, 72%). The data of major product: IR (film): ν_{max} 3032, 2952, 2928, 2854, 1738, 1645, 1219, 1166, 838, 773, 672 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79-7.75 (m, 2H), 7.35-7.27 (m, 7H), 5.16 (d, *J* = 2.0 Hz, 1H), 4.63 (d, *J* = 13.6 Hz, 1H), 4.30 (d, J = 14.0 Hz, 1H), 3.74 (dd, J = 1.6, 8 Hz, 1H), 3.61-3.47 (m, 2H), 3.47-3.39 (m, 1H), 2.44 (s, 3H), 2.09-2.00 (m, 1H), 1.72-1.63 (m, 1H), 0.84 (s, 9H), -0.02 (s, 3H), -0.03 (s, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.6, 144.5, 140.9, 135.8, 134.8, 130.0, 129.1, 128.6, 128.2, 127.9, 102.8, 75.7, 61.0, 50.9, 43.5, 31.1, 25.8, 21.8, 18.0, -4.6, -4.7 ppm;

General Procedure for Synthesis of 15 and 16. To a solution of **12** (0.3 mmol) or **13** (0.3 mmol) and **14**[3] (0.36 mmol) in dry DCM (2 mL) was added dropwise $BF_3{\cdot}Et_2O$ (76 μL, 0.6 mmol) at -78°C. The reaction was allowed to warm to -45 °C slowly and stirred for 2 h at -45 °C. Saturated aqueous $NaHCO_3$ (2 mL) was added to quench the reaction. The mixture was extracted with DCM (5 × 3) 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 = 2:1) to give **15** or **16**.

(*S*)-3-((*R*)-4-Benzyl-2-oxooxazolidin-3-yl)-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrr

olo[1,2-c][1,3]oxazin-1-one (**15a**). Foam solid (83 mg, 71%, *d.r.* = 73:27). The data of major product: $[\alpha]_D^{24}$ +14.4 (*c* 1.03, $CHCl_3$); IR (film): ν_{max} 3024, 2951, 2918, 1897, 1731, 1649, 1217, 1066, 769, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.34 (m, 3H), 7.34-7.28 (m, 3H), 7.19-7.16 (m, 2H), 7.13-7.09 (m, 2H), 4.36 (dd, *J* = 10.8, 4.4 Hz, 1H), 4.17-4.12 (m, 1H), 4.06-3.97 (m, 1H), 3.95-3.90 (m, 1H), 3.76-3.68 (m, 1H), 3.56-3.49 (m, 1H), 3.10 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.72 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.01-1.92 (m, 1H), 1.90-1.84 (m, 1H), 1.80-1.74 (m, 1H), 1.54-1.44 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.3, 148.3, 135.8, 135.2, 132.9, 129.0, 128.9, 128.5, 127.9, 127.4, 113.9, 68.3, 59.2, 55.9, 46.3, 39.6, 32.4, 22.2 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{23}N_2O_4$, 391.1652; found, 391.1654.

(*S*)-3-((*R*)-4-Benzyl-2-oxooxazolidin-3-yl)-4-(p-tolyl)-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-1-one (**15b**). Foam solid (112 mg, 92%, *d.r.* = 71:29). The data of major product: $[\alpha]_D^{24}$ +19.1 (*c* 1.04, $CHCl_3$); IR (film): ν_{max} 3029, 2961, 2919, 1731, 1647, 1214, 1066, 750, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33-7.27 (m, 2H), 7.27-7.25 (m, 1H), 7.19-7.14 (m, 2H), 7.14-7.09 (m, 2H), 7.08-7.03 (m, 2H), 4.33 (dd, *J* = 11.2, 4.8 Hz, 1H), 4.18-4.13 (m, 1H), 4.07-3.96 (m, 1H), 3.96-3.90 (m, 1H), 3.76-3.67 (m, 1H), 3.56-3.48 (m, 1H), 3.10 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.72 (dd, *J* = 13.6, 7.6 Hz, 1H), 2.35 (s, 3H), 2.00-1.90 (m, 1H), 1.90-1.74 (m, 2H), 1.52-1.41 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.3, 148.3, 138.4, 135.6, 135.3, 129.9, 129.6, 129.1, 128.9, 127.7, 127.3, 113.9, 68.3, 59.2, 55.9, 46.3, 39.7, 32.4, 22.2, 21.4 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{25}N_2O_4$, 405.1809; found, 405.1809.

(*S*)-3-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-4-(4-chlorophenyl)-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-1-one (**15c**). Foam solid (101 mg, 79%, *d.r.* = 72:28), mp, 210-212. The data of major product: $[\alpha]_D^{24}$ +35.2 (*c* 1.59, $CHCl_3$); IR (film): ν_{max} 3029, 2953, 2919, 2850, 1731, 1682, 1647, 1217, 1065, 770, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H), 7.17-7.09 (m, 4H), 4.34 (dd, *J* = 10.8, 4.0 Hz, 1H), 4.26-4.20 (m, 1H), 4.20-4.10 (m, 1H), 3.99-3.91 (m, 1H), 3.76-3.67 (m, 1H), 3.57-3.50 (m, 1H), 3.12 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.74 (dd, *J* = 13.6, 7.6 Hz, 1H),

2.03-1.93 (m, 1H), 1.89-1.76 (m, 2H), 1.50-1.40 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.1, 148.0, 136.2, 135.1, 134.4, 131.5, 129.4, 129..2, 129.1, 129.0, 127.5, 112.8, 68.4, 59.1, 55.9, 46.4, 39.7, 32.4, 22.3 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{22}ClN_2O_4$, 425.1263; found, 425.1264.

(*S*)-3-((*R*)-4-Isopropyl-2-oxooxazolidin-3-yl)-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-1-one (**15d**). Foam solid (83 mg, 81%, *d.r.* = 75:25). IR (film): ν_{max} 3032, 2954, 2928, 2854, 1731, 1682, 1649, 1219, 1063, 771, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *d.r.* = 75:25) δ 7.40-7.32 (m, 4H), 7.29-7.27 (m, 1H), 4.61-4.55 (m, 1H), 4.15-4.09 (m, 1H), 3.99-3.94 (m, 1H), 3.82-3.74 (m, 1H), 3.64-3.52 (m, 2H), 2.06-1.97 (m, 1H), 1.97-1.85 (m, 3H), 1.68-1.56 (m, 1H), 0.90 (d, J = 7.2 Hz, 3H), 0.79 (d, J = 6.8 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, *d.r.* = 75:25) δ 156.1, 148.5, 136.9, 133.0, 128.9, 128.8, 128.7, 128.6, 128.2, 128.1, 113.5, 65.0 (64.3), 60.1 (61.2), 59.5 (59.8), 46.4 (46.3), 32.5 (32.4), 30.3 (29.1), 22.3 (22.2), 18.2, 15.8 (14.7) ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{23}N_2O_4$, 343.1652; found, 343.1654.

(*S*)-3-((*R*)-2-oxo-4-Phenyloxazolidin-3-yl)-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-1-one (**15e**). Foam solid (91 mg, 81%, *d.r.* = 74:26). The data of major product: $[\alpha]_D^{24}$ -39.3 (*c* 1.50, $CHCl_3$); IR (film): ν_{max} 3032, 3023, 1731, 1682, 1649, 1219, 771, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.36 (m, 3H), 7.36-7.32 (m, 3H), 7.19-7.15 (m, 2H), 7.02-6.97 (m, 2H), 4.80-4.70 (m, 1H), 4.54-4.48 (m, 1H), 4.40 (dd, J = 11.2, 4.4 Hz, 1H), 4.17-4.11 (m, 1H), 3.72-3.63 (m, 1H), 3.52-3.44 (m, 1H), 1.96-1.87 (m, 1H), 1.82-1.70 (m, 2H), 1.47-1.36 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.3, 148.4, 136.0, 135.9, 132.7, 129.5, 129.2, 128.7, 128.5, 128.4, 128.0, 113.7, 70.3, 59.5, 59.3, 46.2, 32.3, 22.2 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_4$, 377.1495; found, 377.1500.

(*S*)-3-((4*R*,5*S*)-5-Methyl-2-oxo-4-phenyloxazolidin-3-yl)-4-phenyl-4a,5,6,7-tetrahydro-1H-pyrrolo[1,2-c][1,3]oxazin-1-one (**15f**). Foam solid (80 mg, 68%, *d.r.* = 75:25). IR (film): ν_{max} 3033, 2954, 2928, 2899, 1735, 1649, 1065, 759, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *d.r.* = 75:25) δ 7.40-7.36 (m, 4H), 7.32-7.26 (m, 4H), 6.91-6.86 (m, 2H), 5.44 (d, J = 8.4 Hz, 1 H), 4.63 (dd, J = 11.6, 5.2 Hz, 1H),

4.43-4.33 (m, 1H), 3.82-3.73 (m, 1H), 3.60-3.51 (m, 1H), 2.06-1.91 (m, 3H), 4.43-4.33 (m, 1H), 0.83 (d, J = 6.4 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, *d.r.* = 75:25) δ 154.9 (156.3), 148.4 (148.5), 135.8 (135.2), 134.6 (134.4), 133.0 (133.1), 129.2, 128.9, 128.8, 128.5, 128.4, 128.3, 127.8, 126.5, 126.5, 114.4 (116.9), 79.6 (80.0), 59.5 (59.9), 54.7 (55.9), 46.4 (46.3), 32.5 (32.3), 22.2, 14.9 (14.6) ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{23}N_2O_4$, 391.1652; found, 391.1652.

N-benzyl-N-((4*aS*,5*R*)-5-Hydroxy-1-oxo-4-phenyl-4a,5,7,8-tetrahydro-1H,6H-pyrido[1,2-c][1,3]oxazin-3-yl)-4-methylbenzenesulfonamide (**11**). To a solution of ***ent*-10a** in THF (1 mL) was added HF·Py (2 mL) at room temperature. The reaction was stirred for 2 h at the same temperature. Saturated aqueous solution of $NaHCO_3$ was carefully added to quench the reaction and extracted with EtOAc (10 mL × 3), and the combined organic layers were washed with brine. Dried, filtered, and concentrated, the resides was purified by flash chromatography on silica gel (PE: EA = 1:1) to give white solid **11** (77 mg, 95%), mp 168-170 °C. $[\alpha]_D^{24}$ -91.9 (*c* 1.04, $CHCl_3$); IR (film): ν_{max} 3029, 2944, 2932, 2863, 1715, 1682, 1649, 1163, 768, 671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85-7.76 (m, 2H), 7.36-7.31 (m, 2H), 7.29-7.25 (m, 3H), 7.24-7.18 (m, 1H), 7.16-7.06 (m, 4H), 6.89-6.79 (m, 2H), 4.32-4.21 (m, 2H), 4.12-3.92 (m, 1H), 3.76 (d, J = 9.2 Hz, 1H), 3.72-3.53 (m, 1H), 2.73-2.64 (m, 1H), 2.45 (s, 3H), 2.10-2.02 (m, 1H), 1.80-1.72 (m, 1H), 1.45-1.25 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 149.8, 144.6, 137.8, 135.5, 134.0, 133.7, 129.8, 129.4, 128.7, 128.6, 128.4, 128.2, 116.6, 72.4, 65.3, 51.7, 45.9, 33.4, 23.3, 21.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ calcd for $C_{28}H_{29}N_2O_5S$, 505.1792; found, 505.1794.

Supporting Information: Copies of ^1H, $^{13}C\{^1H\}$ NMR spectra and X-ray structural data (CIF) (**9a**; **11**; **15c**). The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org.

Accession Codes

CCDC 1873700, 1873701, 1873704 contain the supplementary crystallographic data

for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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