Fischer carbene catalysis of alkynol cycloisomerization: Application to the synthesis of the altromycin B disaccharide

BonSuk Koo and Frank E. McDonald*
Department of Chemistry, Emory University, Atlanta, GA 30322

SUPPORTING INFORMATION

Experimental procedures and characterization data for new compounds (part 1)

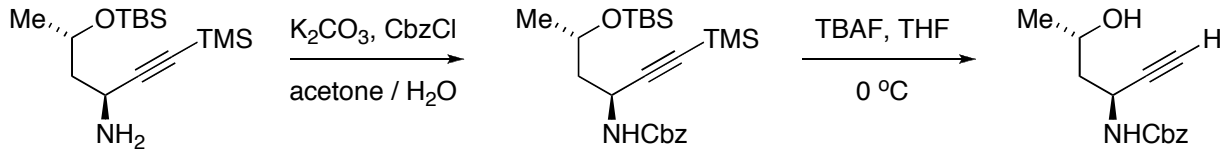
General procedures: ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C), or on an INOVA-600 spectrometer (600 MHz for ^{1}H, 150 MHz for ^{13}C). NMR spectra were recorded on solutions in deuterated chloroform ($CDCl_3$), with residual chloroform (δ 7.26 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR) or deuterated methyl sulfoxide (DMSO-d_6), with residual methyl sulfoxide (δ 2.50 ppm for ^{1}H NMR and δ 35.0 ppm for ^{13}C NMR) taken as the standard, and were reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. IR spectra were collected on a Mattson Genesis II FT-IR spectrometer as neat films. Mass spectra (high resolution FAB or EI) were recorded on a VG 70-S Nier Johason Mass spectrometer or a Thermo Finnigan LTQ FT spectrometer. Melting points were determined with a Fisher-Johns melting point apparatus. Optical rotations were measured at 23°C (concentration in g/100 mL) using a Perkin-Elmer 341 polarimeter. Analytical Thin Layer Chromatography (TLC) was performed on precoated glass backed plates purchased from Whatman (silica gel $60F_{254}$; 0.25mm thickness). Flash column chromatography was carried out with silica gel 60 (230-400 mesh ASTM) from EM Science.

All reactions were carried out with anhydrous solvents in oven-dried or flame-dried and nitrogen- or argon-charged glassware. Anhydrous solvents except as mentioned were dried with 3 or 4 Å molecular sieves (beads) purchased from Aldrich and tested for trace water content with Coulometric KF Titrator from Denver Instruments.

All solvents used in extraction procedures and chromatography were used as received from commercial suppliers without prior purification. During reaction workup, the reaction mixture was usually diluted to three times the original volume, and washed with an equal volume of water and/or aqueous solutions as needed. All reagents were purchased from Aldrich or Strem Chemicals.

Representative examples of alkynyl alcohol synthesis and cycloisomerizations

Preparation of alkynyl alcohol (±)-4



(±)-**A** (±)-**B** (±)-**4**

Cbz protection: The known amine **A**[1] (0.380 g, 1.26 mmol) was dissolved in a mixture of acetone (3 mL) and water (3 mL), K_2CO_3 (17.4 mg, 0.126 mmol) and CbzCl (0.266 mL, 1.89 mmol) were added quickly. The mixture was stirred at room temperature for 10 min, and then water (3 mL) was added and the reaction mixture diluted with CH_2Cl_2 (3 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 15 : 1) gave Cbz protected compound **B** as a white crystal (0.367 g, 81% yield). MP = 100 – 101 ºC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36-7.11 (m, 5H), 5.11 (s, 2H), 4.96 (brs, 1H), 4.64 (brs, 1H), 4.01 (brs, 1H), 1.85 (brs, 1H), 1.60 (ddd, *J* = 3.0, 10.8 Hz, 1H), 1.18 (d, *J* = 6.6 Hz, 3H), 0.84 (s, 9H), 0.08 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.31, 136.61, 128.75, 128.37, 105.16, 88.45, 67.06, 66.23, 46.15, 42.26, 26.11, 24.38, 18.24, 0.14, 0.09, -3.92, -4.67; IR (KBr) 3286, 2958, 2930, 2895, 2857, 2171, 1693, 1538, 1251, 840 cm^{-1}; HRMS [M+H] Calcd. for $C_{23}H_{40}O_3N_1{}^{28}Si_2$, 434.25413, Found. 434.25389.

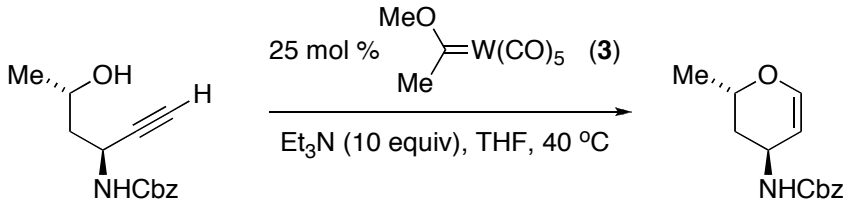
Desilylation: Compound **B** (0.367 g, 1.02 mmol) was dissolved in THF (6 mL), cooled to 0 °C, and TBAF (4.10 mL, 1 M in THF) was added and then stirred for 1 h. The reaction was quenched with water and diluted with EtOAc (5 mL), and then brine (5 mL) was added. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 2 : 1 to 1 : 1) gave the alkynyl alcohol (±)-**4** as a colorless oil (0.229 g, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 5H), 5.19 (brs, 1H), 5.11 (s, 2H), 4.66 (d, *J* = 7.2 Hz, 1H), 4.03 (dqd, *J* =

(1) Davidson, M. H.; McDonald, F. E. *Org. Lett.* **2004**, *6*, 1601.

3.6, 6.0, 10.0 Hz, 1H), 2.34 (d, *J* = 2.0 Hz, 1H), 2.05 (brs, 1H), 1.89-1.76 (m, 2H), 1.24 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.65, 136.36, 128.76, 128.44, 88.14, 72.12, 67.29, 65.57, 44.94, 41.53, 24.12; IR (neat) 3402 (brs), 2965, 2925, 1689, 1530, 1249 cm^{-1}; HRMS Calcd [M+H]. for $C_{14}H_{18}O_3N_1$, 248.12812, Found. 248.12800.

General procedure for alkynyl alcohol cycloisomerizations:

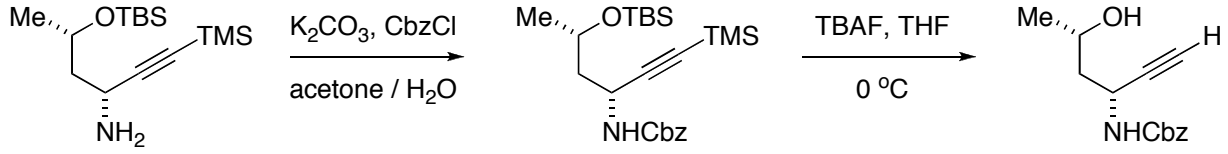
The alkynyl alcohol (0.1 mmol) was dissolved in dry THF (1.0 mL) in a 5 mL conical vial, and then Et_3N (0.14 mL, 1.0 mmol) and tungsten carbene **3** (9.6 mg, 0.025 mmol) were added under argon atmosphere. The vial was sealed with a Teflon cap, and then stirred for 12 h at 40 °C, after which time the reaction mixture was cooled to room temperature. Solvent was removed by rotary evaporation. The yellowish crude oil was purified by chromatography (hexanes : EtOAc = 20 : 1 with 1% Et_3N) to give pure product glycal.



(±)-**4** (±)-**5**

Synthesis of glycal (±)-5: Following the general procedure for alkynyl alcohol cycloisomerization, alkynyl alcohol (±)-**4** (25 mg, 0.10 mmol) afforded glycal (±)-**5** as a white crystal (23 mg, 92 % yield). MP = 92-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.30 (m, 5H), 6.49 (d, *J* = 6.4 Hz, 1H), 5.13 (d, *J* = 12.4 Hz, 1H), 5.06 (d, *J* = 12.4 Hz, 1H), 4.83 (brs, 1H), 4.75 (dt, *J* = 1.6, 6.0 Hz, 1H), 4.14 (d, *J* = 6.0 Hz, 1H), 3.86 (dqd, *J* = 1.6, 6.0, 12.4 Hz, 1H), 1.95 (d, *J* = 14.4 Hz, 1H), 1.67 (ddd, *J* = 4.4, 12.4 Hz, 1H), 1.31 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.24, 147.69, 136.61, 128.78, 128.42, 99.75, 68.19, 66.89, 41.82, 36.84, 20.98; IR (KBr) 1680, 1528, 1239 1070 cm^{-1}; HRMS [M+H] Calcd. for $C_{14}H_{18}O_3N_1$, 248.12812, Found. 248.12793.

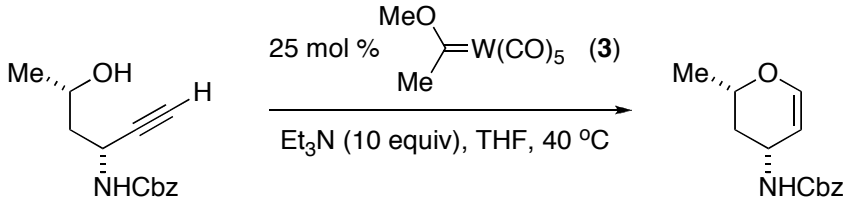
Preparation of alkynyl alcohol (±)-6



(±)-**C** (±)-**D** (±)-**6**

Cbz protection: The procedure as described above for (±)-**4** was followed with the known amine **C**[1] (0.210 g, 0.701 mmol) and CbzCl (0.148 mL, 1.05 mmol), giving Cbz-protected compound **D** as a colorless oil (0.230 g, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.28 (m, 5H), 5.81 (d, *J* = 8.4 Hz, 1H), 5.11 (s, 2H), 4.58 (brs, 1H), 4.25 (brs, 1H), 1.82-1.73 (m, 2H), 1.18 (d, *J* = 6.0 Hz, 3H), 0.90 (s, 9H), 0.15 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.54, 136.87, 128.62, 128.13, 128.04, 104.91, 87.84, 66.92, 66.80, 43.77, 42.40, 26.12, 24.19, 18.19, 0.15, -3.88, -4.75; IR (neat) 3289, 2957, 2930, 2171, 1729, 1500, 1251, 841 cm^{-1}; HRMS [M+H] Calcd. for $C_{23}H_{40}O_3N_1{}^{28}Si_2$, 434.25413, Found. 434.25432.

Desilylation: The procedure as described above for (±)-**4** was followed with compound **D** (0.230 g, 0.701 mmol) and TBAF (2.80 mL, 1 M in THF), giving the alkynyl alcohol (±)-**6** as a colorless oil (0.158 g, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.30 (m, 5H), 5.59 (d, *J* = 8.0 Hz, 1H), 5.11 (s, 2H), 4.71 (m, 1H), 4.01 (m, 1H), 2.97 (d, *J* = 4.0 Hz, 1H), 1H), 2.32 (d, *J* = 2.4 Hz, 1H), 1.83-1.70 (m, 2H) 1.21 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.59, 136.27, 128.76, 128.49, 128.42, 82.88, 71.89, 64.46, 66.44, 44.96, 41.24, 23.41; IR (neat) 3390 (brs), 1704, 1537, 1256 cm^{-1}; HRMS [M+H] Calcd. for $C_{14}H_{18}O_3N_1$, 248.12812, Found. 248.12809.

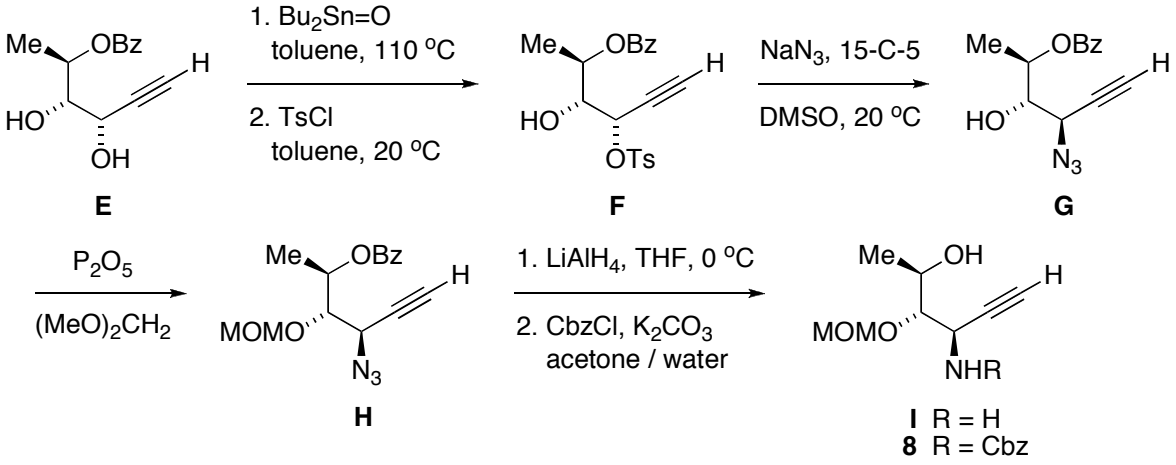


(±)-**6** (±)-**7**

Synthesis of glycal (±)-7: Following the general procedure for alkynyl alcohol cycloisomerization, substrate (±)-**6** (25 mg, 0.1 mmol) afforded glycal (±)-**7** as a white crystal (24 mg, 95% yield). MP = 92-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 5H), 6.38 (dd, *J* = 1.2, 6.0 Hz, 1H), 5.10 (s, 2H), 4.65 (d, *J* = 7.2 Hz, 1H), 4.58 (dt, *J* =

2.0, 6.4 Hz, 1H), 4.30 (ddd, *J* = 8.8 Hz, 1H), 4.08 (dqd, *J* = 6.0 Hz, 1H), 2.26 (dd, *J* = 6.4, 12.8 Hz, 1H), 1.41 (ddd, *J* = 11.2, 13.2 Hz, 1H) 1.28 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.09, 146.27, 136.65, 128.77, 128.39, 102.58, 71.77, 66.92, 44.26, 37.59, 21.18; IR (KBr) 1683, 1234, 746 cm^{-1}; HRMS [M+H] Calcd. for $C_{14}H_{18}O_3N_1$, 248.12812, Found. 248.12801.

Preparation of alkynyl alcohol 8



Selective tosylation: A Dean-Stark column was fitted into a 50 mL round bottom flask containing a solution of known diol **E**[2] (1.00 g, 4.27 mmol) and dibutyltin oxide (1.34 g, 1.34 mmol) in toluene (20 mL). The reaction mixture was refluxed for 5 h, and then cooled to room temperature. *p*-Toluenesulfonyl chloride (1.22 g, 6.40 mmol) was added, and the reaction mixture was stirred vigorously for 24 h at room temperature. Solvent was removed by rotary evaporation, and chromatography (hexanes : EtOAc = 4 : 1) gave monotosylated compound **F** as a colorless oil (1.08 g, 65% yield). $[\alpha]^{23}_D$ = +39.2 (*c* = 2.07, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02-7.99 (m, 2H), 7.82-7.80 (m, 2H), 7.59 (dt, *J* = 2.4, 7.6 Hz, 1H), 7.46 (dt, *J* = 1.6, 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.31 (dd, *J* = 2.0, 3.6 Hz, 1H), 5.18 (dt, *J* = 6.4, 13.6 Hz, 1H), 4.11 (dq, *J* = 3.6, 6.4 Hz, 1H), 2.71 (d, *J* = 6.4 Hz, 1H), 2.46 (d, *J* = 2.4 Hz, 1H), 2.43 (s, 3H), 1.46 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.64, 145.57, 133.54, 133.34, 130.03, 129.90, 128.70, 128.39, 78.95, 75.23, 75.18, 72.02, 71.16, 21.93, 16.65; IR (neat) 3503 (brs), 3281, 2127, 1717, 1275, 1177 cm^{-1}; HRMS [M+H] Calcd. for $C_{20}H_{21}O_6{}^{32}S_1$ 389.10534, Found 389.10454.

(2) McDonald, F. E.; Reddy, K. S.; Díaz, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4304.

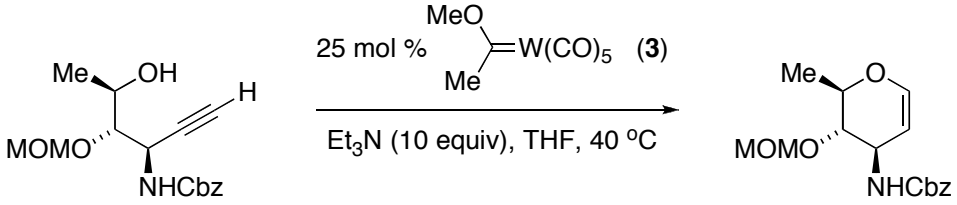
Azide substitution: The tosylate **F** (0.480 g, 1.24 mmol) was dissolved in dry DMSO (4 mL), 15-Crown-5 (0.4 mL) and NaN_3 (0.403 g, 6.20 mmol) were added, and the reaction mixture was stirred overnight at room temperature. The reaction mixture was diluted with Et_2O (5 mL) and quenched with water (5 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 5 : 1) provided azido alcohol **G** as a white solid (0.240 g, 75% yield). MP = 69-70 ^oC; $[\alpha]^{23}_D$ = -123.8 (*c* = 1.47, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05-8.01 (m, 2H), 7.58 (dt, *J* = 2.4, 7.2 Hz, 1H), 7.47-7.43 (m, 2H), 5.31 (dq, *J* = 6.4, 12.8 Hz, 1H), 4.25 (dd, *J* = 2.4, 5.2 Hz, 1H), 3.97 (t, *J* = 5.2 Hz, 1H), 2.70 (d, *J* = 2.4 Hz, 1H), 2.58 (brs, 1H), 1.46 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.78, 133.48, 130.13, 129.88, 128.68, 77.56, 76.52, 75.68, 70.95, 54.57, 15.93; IR (KBr) 3467 (brs), 3295, 2112, 1713, 1275, 713 cm^{-1}; HRMS [M+H] Calcd. for $C_{13}H_{14}O_3N_3$ 260.10297, Found 260.10251.

MOM protection: The azido alcohol **G** (0.216 g, 0.833 mmol) was dissolved in dimethoxymethane (4 mL), and P_2O_5 (0.125 g, 0.833 mmol) was added. The reaction mixture was stirred for 30 min at room temperature, and additional P_2O_5 (0.125 g, 0.833 mmol) was added and then stirred for 30 min. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and poured into a solution of cold saturated aq. $NaHCO_3$ (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 10 : 1) gave MOM-protected compound **H** as a colorless oil (0.180 g, 71% yield). $[\alpha]^{23}_D$ = -58.95 (*c* = 3.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05-8.02 (m, 2H), 7.56 (dt, *J* = 2.8, 7.2 Hz, 1H), 7.47-7.42 (m, 2H), 5.40 (dq, *J* = 4.8, 6.4 Hz, 1H), 4.93 (d, *J* = 6.8 Hz, 1H), 4.81 (d, *J* = 5.6 Hz, 1H), 4.20 (dd, *J* = 2.4, 5.2 Hz, 1H), 4.00 (dd, *J* = 4.8, 5.2 Hz, 1H), 3.44 (s, 3H), 2.70 (d, *J* = 2.0 Hz, 1H), 1.45 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.70, 133.35, 130.24, 129.81, 128.62, 98.02, 80.56, 77.57, 76.79, 70.95, 56.62, 53.78, 15.54; IR (neat) 2112, 1720, 1273, 1037 cm^{-1}; HRMS [M+H] Calcd. for $C_{15}H_{18}O_4N_3$ 304.12918, Found 304.12836.

Reduction of azide: The azide **H** (0.180 g, 0.590 mmol) was dissolved in dry THF (4 mL) and the solution was cooled to 0 ^oC. Lithium aluminum hydride (1.80 mL, 1 M in

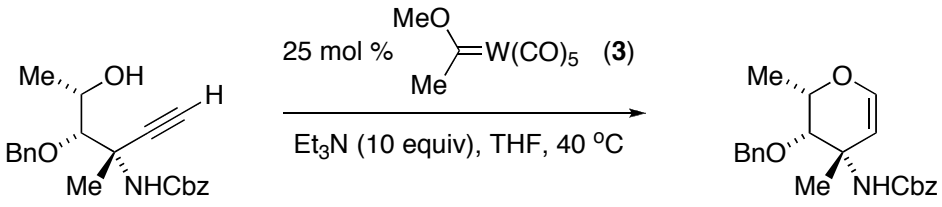
THF, 1.8 mmol) was added dropwise to the 0 °C solution, and the reaction mixture was stirred for 3 h at 0 °C. The reaction mixture was quenched by careful addition of water (0.1 mL) and 15% NaOH (0.3 mL), and then stirred for 1 h at room temperature. The resulting clear solution with white solid was treated with $MgSO_4$ and filtered through Celite. After rotary evaporation of the organic layer, the amino alcohol **I** was obtained as a yellowish oil, which was directly used for the next step without further purification.

Cbz protection: The procedure as described above for (±)-**4** and (±)-**6** was followed with crude amino alcohol **I,** K_2CO_3 (17.4 mg, 0.126 mmol) and CbzCl (0.266 mL, 1.89 mmol) in a mixture of acetone (3 mL) / water (3 mL), and gave alkynyl alcohol **8** as a colorless oil (0.120 g, 67 % yield over 2 steps) after chromatography (hexanes : EtOAc = 5 : 1). $[\alpha]^{23}_D$ = +21.4 (*c* = 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.31 (m, 5H), 5.54 (d, *J* = 8.4 Hz, 1H), 4.88 (d, *J* = 6.8 Hz, 2H), 3.88 (brd, *J* = 6.0 Hz, 1H), 3.50 (dd, *J* = 3.2, 5.2 Hz, 1H), 3.42 (s, 3H), 3.11 (d, *J* = 4.4 Hz, 1H), 2.33 (d, *J* = 3.6 Hz, 1H), 1.27 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.55, 136.19, 128.78, 128.53, 128.45, 98.21, 84.38, 81.43, 72.63, 67.62, 67.08, 56.68, 44.61, 19.55; IR (neat) 3410 (brs), 2926, 1709, 1514, 1252, 1030 cm^{-1}; HRMS [M+H] Calcd. for $C_{16}H_{22}O_5N_1$ 308.14925, Found 308.14896.



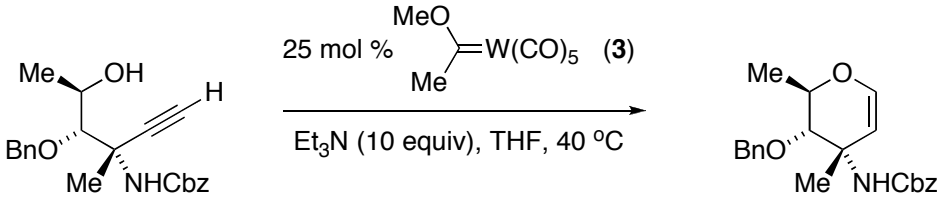
8 **9**

<u>Synthesis of glycal 9:</u> Following the general procedure for alkynyl alcohol cycloisomerization, substrate **8** (30.7 mg, 0.10 mmol) afforded glycal **9** as a white crystal (29.4 mg, 95% yield). MP = 102-103 °C; $[\alpha]^{23}_D$ = -74.2 (*c* = 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 5H), 6.31 (dd, *J* = 1.6, 6.4 Hz, 1H), 5.11 (s, 2H), 5.06 (brs, 1H), 4.73 (s, 1H), 4.72 (d, *J* = 6.8 Hz, 1H), 4.67 (d, *J* = 6.8 Hz, 1H), 4.29 (m, 1H), 3.98 (dq, *J* = 6.4, 8.4 Hz, 1H), 3.36 (dd, *J* = 8.4, 1H), 3.21 (s, 3H), 1.35 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.33, 144.44, 136.67, 128.73, 128.37, 101.51, 97.38, 78.85, 74.55, 66.94, 56.12, 50.36, 17.41; IR (KBr) 1693, 1553, 1234, 1047 cm^{-1}; HRMS [M+H] Calcd. for $C_{16}H_{22}O_5N_1$, 308.14925, Found. 308.14847.



(±)-**10** (±)-**11**

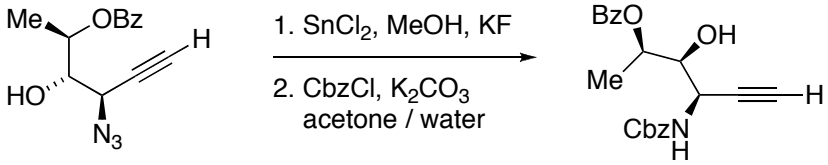
Synthesis of glycal (±)-11: Following the general procedure for alkynyl alcohol cycloisomerization, the known alkynyl alcohol substrate (±)-**10** (37 mg, 0.10 mmol) afforded known glycal (±)-**11** as a white crystal (31 mg, 84% yield). All spectroscopic data for compounds (±)-**10** and (±)-**11** match the reported data.[3]



(±)-**12** (±)-**13**

Synthesis of glycal (±)-13: Following the general procedure for alkynyl alcohol cycloisomerization, the known alkynyl alcohol substrate (±)-**12** (37 mg, 0.10 mmol) afforded known glycal (±)-**13** as a white crystal (35 mg, 94% yield). All spectroscopic data for compounds (±)-**12** and (±)-**13** match the reported data.[3]

Preparation of alkynyl alcohol 14



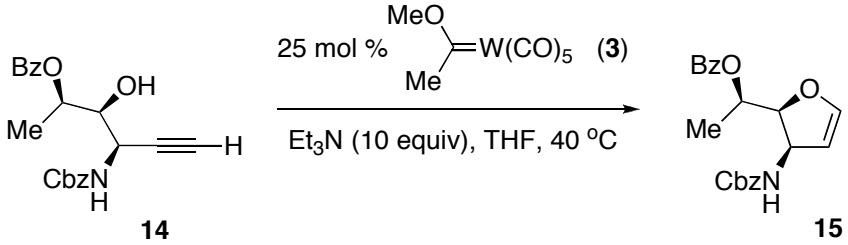
G **14**

Reduction of azide: The azido alcohol **G** (0.16 g, 0.62 mmol) was dissolved in MeOH (6 mL), and $SnCl_2$ (0.18 g, 0.93 mmol) was added. The reaction mixture was stirred at room temperature for 24 h. Solvent was removed by rotary evaporation, and the crude material was dissolved in EtOAc (6 mL). Aqueous KF (3 mL, 5 M) was added and the reaction mixture was stirred at room temperature for 5 h. The organic layer was

(3) Cutchins, W. W.; McDonald, F. E. *Org. Lett.* **2002**, 4, 749.

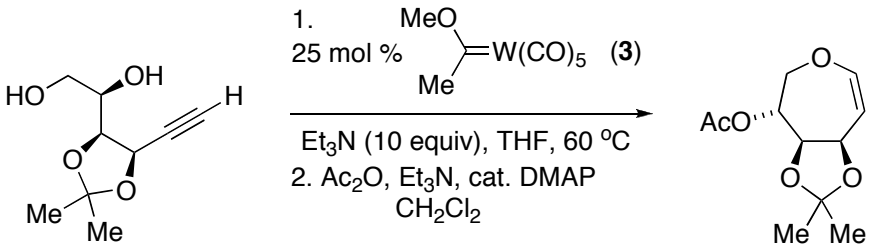
separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over $MgSO_4$, and solvents removed by rotary evaporation. The yellowish crude amino alcohol was used for the next step without further purification.

Cbz protection: The procedure as described above for (±)-**4,** (±)-**6** and **8** was followed with crude amino alcohol**,** K_2CO_3 (8.7 mg, 0.062 mmol) and CbzCl (0.13 mL, 0.93 mmol) in a mixture of acetone (2 mL) / water (2 mL), and gave the alkynyl alcohol **14** as a colorless oil (0.146 g, 64% yield over 2 steps) after chromatography (hexanes : EtOAc = 5 : 1). $[\alpha]^{23}_D$ = +45.4 (*c* = 2.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.6 Hz, 2H), 7.55 (dt, *J* = 2.8, 7.6 Hz 1H), 7.43-7.39 (m, 2H), 7.31 (brs, 5H), 5.41 (d, *J* = 9.2 Hz, 1H), 5.24 (ddd, *J* = 2.4, 4.8 Hz, 1H), 5.05 (s, 2H), 4.75 (d, *J* = 3.2 Hz, 1H), 3.98 (d, *J* = 4.4 Hz, 1H), 3.07 (d, *J* = 3.6 Hz, 1H), 2.39 (d, *J* = 2.0 Hz, 1H), 1.45 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166. 02, 156.12, 136.14, 133.35, 130.21, 129.86, 128.71, 128.62, 128.41, 80.95, 75.74, 73.18, 71.03, 67.52, 45.57, 16.28; IR (neat) 3406 (brs), 2926, 2252, 2120, 1968, 1713, 1524, 1275, 1116 cm^{-1}; HRMS [M+H] Calcd. for $C_{21}H_{22}O_5N_1$ 368.14925, Found 368.14822.



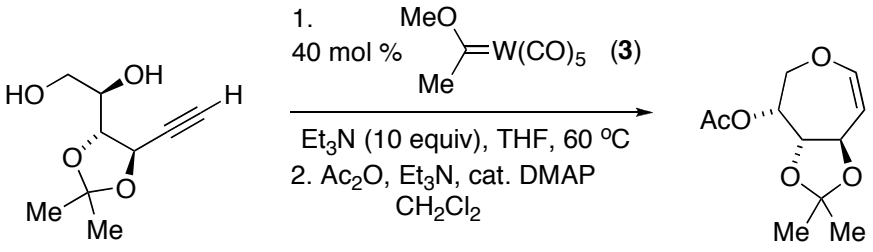
14 **15**

Synthesis of glycal 15: Following the general procedure for alkynyl alcohol cycloisomerization, substrate **14** (37 mg, 0.10 mmol) afforded glycal **15** as colorless oil (28 mg, 77% yield). $[\alpha]^{23}_D$ = +77.3 (*c* = 1.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04-8.02 (m, 2H), 7.55 (dt, *J* = 2.8, 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.33-7.28 (m, 3H), 7.23-7.22 (m, 2H), 6.52 (dd, *J* = 1.2, 2.4 Hz, 1H), 5.46 (dq, *J* = 6.4 Hz, 1H), 5.18-5.14 (m, 1H), 5.08 (t, *J* = 3.2 Hz, 1H), 4.85 (d, *J* = 12.4 Hz, 1H), 4.76 (d, *J* = 10.0 Hz, 1H), 4.66 (d, *J* = 12.4 Hz, 1H), 4.44 (dd, *J* = 7.6 Hz, 1H), 1.48 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166. 12, 155.50, 149.45, 136.74, 133.55, 130.69, 130.32, 129.01, 128.69, 128.65, 102.98, 84.59, 68.71, 67.35, 54.50, 18.09; IR (KBr) 2925, 1716, 1524, 1266, 1059, 712 cm^{-1}; HRMS [M+H] Calcd. for $C_{21}H_{22}O_5N_1$ 368.14925, Found 368.14801.



16 **17**

Synthesis of glycal 17: Following the general procedure for alkynyl alcohol cycloisomerization, the known substrate **16** (15 mg, 0.10 mmol) underwent reaction at 60 °C. Upon completion, volatile components were removed by rotary evaporation. The crude mixture was dissolved in dry CH_2Cl_2 (1.5 mL), and acetic anhydride (19 μL, 0.2 mmol), triethylamine (62 μL, 0.4 mmol), and dimethylaminopyridine (1 crystal) were added, and the reaction mixture was stirred for 3 h at room temperature. After removal of volatiles by rotary evaporation, chromatography of the crude material (hexanes : EtOAc = 20 : 1) gave the known glycal **17** as a white crystal (15 mg, 82% yield over two steps). All spectroscopic data for compounds **16** and **17** match with reported data.[4]



18 **19**

Synthesis of glycal 19: Following the general procedure for alkynyl alcohol cycloisomerization, the known substrate **18** (15 mg, 0.10 mmol) underwent reaction using 40 mol % of **3** at 60 °C. Acetylation and chromatographic purification (as described above for glycal **17)** gave the known glycal **19** as a white crystal (15 mg, 82% yield over two steps). All spectroscopic data for compounds **18** and **19** match with reported data.[4]

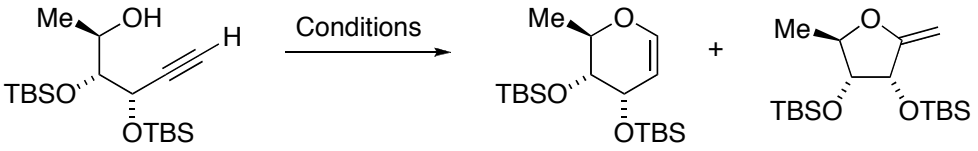
(4) Alcázar, E.; Pletcher, J. M.; McDonald, F. E. *Org. Lett*. **2004**, *6*, 3877.

Comparisons of non-photochemical procedure vs. photochemical procedures

Condition A: The alkynyl alcohol substrate (0.10 mmol) was dissolved in dry THF (1.0 mL) in a conical vial. Et_3N (0.14 mL, 1.0 mmol) and tungsten Fischer carbene **3** (15.3 mg, 0.040 mmol) were added under argon atmosphere. The vial was sealed with a Teflon cap and then stirred for 24 h at 60 ^oC, after which time the reaction mixture was cooled to room temperature and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 20 : 1 with 1% Et_3N) gave pure product.

Condition B: The alkynyl alcohol (0.10 mmol) was dissolved in dry THF (1 mL) with stirring, and $W(CO)_6$ (8.8 mg, 0.025 mmol) and Et_3N (0.14 mL, 1.0 mmol) were added. The flask was fitted with a reflux condenser and then placed into Rayonet Photoreactor under an atmosphere of argon. The reaction mixture was irradiated at 350 nm at 60 ^oC for 6 h, with stirring. Solvent was removed by rotary evaporation, and chromatography (hexanes : EtOAc = 20 : 1 with 1% Et_3N) gave pure product.

Condition C: Condition B, except DABCO (22 mg, 0.20 mmol) was used instead of Et_3N.



20a **21a** **22a**

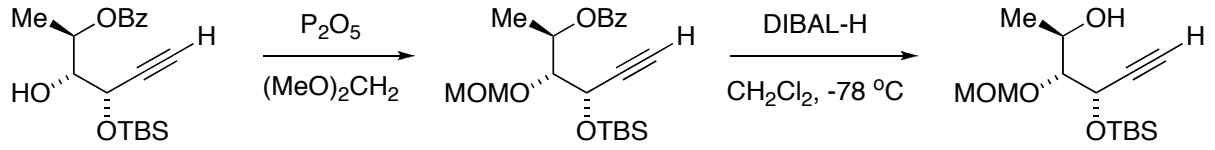
Cycloisomerizations of alkynyl alcohol 20a: Following the general procedure for alkynyl cycloisomerization with the conditions described above, the known alkynyl alcohol **20a** (36 mg, 0.10 mmol) afforded known *endo* glycal **21a**.[2]

Condition A: **21a** (19 mg, 53% yield) and **20a** (11 mg, 30%) was recovered

Condition B: **21a** (33 mg, 92% yield).

All spectroscopic data for compounds **20a** and **21a** match the reported data.[2]

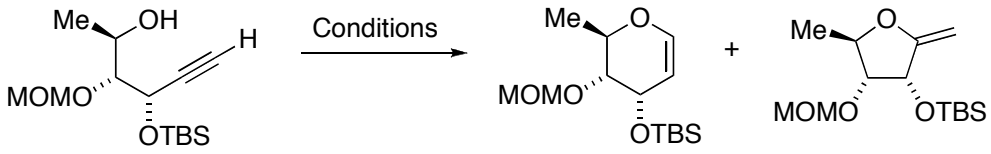
Preparation of alkynyl alcohol 20b



J **K** **20b**

MOM protection: The procedure as described above for alkynyl alcohol **8** was followed with known mono-TBS protected alkynyl alcohol **J**[2] (0.28 g, 0.80 mmol) and P_2O_5 (0.23 g, 1.60 mmol) in DMM (3 mL), and produced MOM-protected product **K** as a colorless oil (0.23 g, 73% yield) after chromatography (hexanes : EtOAc = 15 : 1). $[\alpha]^{23}_D$ = +34.3 (*c* = 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.03 (m, 2H), 7.58-7.54 (m, 1H), 7.46-7.42 (m, 2H), 5.43 (dq, *J* = 4.0, 6.4 Hz, 1H), 4.96 (d, *J* = 6.4 Hz, 1H), 4.81 (d, *J* = 6.8 Hz, 1H), 4.51 (dd, *J* = 2.4, 5.6 Hz, 1H), 3.96 (dd, *J* = 4.0, 5.6 Hz, 1H), 3.43 (s, 3H), 2.46 (d, *J* = 2.4 Hz, 1H), 1.43 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.17 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.81, 133.15, 130.68, 129.83, 128.57, 97.72, 82.83, 81.43, 74.41, 71.20, 64.30, 56.46, 25.91, 18.33, 15.24, -4.26, -5.03; IR (neat) 2954, 2931, 2894, 2858, 2116, 1721, 1274, 839 cm^{-1}; HRMS [M+Na] Calcd. for $C_{21}H_{32}O_5{}^{23}Na_1{}^{28}Si_1$ 415.19112, Found 415.19090.

Alkynyl alcohol 20b: The MOM-protected alkyne **K** (0.23 g, 0.59 mmol) was dissolved in dry CH_2Cl_2 (3 mL), and cooled to -78 °C. DIBAL-H (1.2 mL, 1.2 mmol) was added dropwise at –78 °C, and the reaction mixture was stirred for 1 hr at –78 °C. Cold EtOAc (6 mL) was added to quench the reaction, followed by Rochelle's salt (5 mL). The reaction mixture was stirred until two layers were clearly separated. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 10 :1) gave alkynyl alcohol **20b** as a colorless oil (0.12 g, 71% yield). $[\alpha]^{23}_D$ = +105.8 (*c* = 2.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.82 (d, *J* = 6.4 Hz, 1H), 4.74 (d, *J* = 6.4 Hz, 1H), 4.40 (dd, *J* = 2.4, 6.0 Hz, 1H), 3.98 (dq, *J* = 6.4, 9.6 Hz, 1H), 3.59 (dd, *J* = 4.4, 6.4 Hz, 1H), 3.43 (s, 3H), 2.96 (d, *J* = 8.0 Hz, 1H), 2.44 (d, *J* = 2.4 Hz, 1H), 1.20 (d, *J* = 6.4 Hz, 3H), 0.88 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.59, 86.56, 83.47, 73.97, 67.08, 64.40, 56.41, 25.84, 18.22, 18.14, -4.22, -5.09; IR (neat) 3454 (brs), 3310, 2955, 2931, 2897, 2858, 2115, 1253, 1153, 1104, 1033, 839 cm^{-1}; HRMS Calcd. [M+H] for $C_{14}H_{29}O_4{}^{28}Si_1$ 289.18296, Found 289.18288.



20b **21b** **22b**

Cycloisomerizations of alkynyl alcohol 20b: Following the conditions described for cycloisomerization of **20a**, the alkynyl alcohol substrate **20b** (29 mg, 0.10 mmol) afforded *endo* glycal **21b** and *exo* product **22b**.

Condition A: **21b** (15 mg, 53% yield) and **22b** (10 mg, 35% yield).

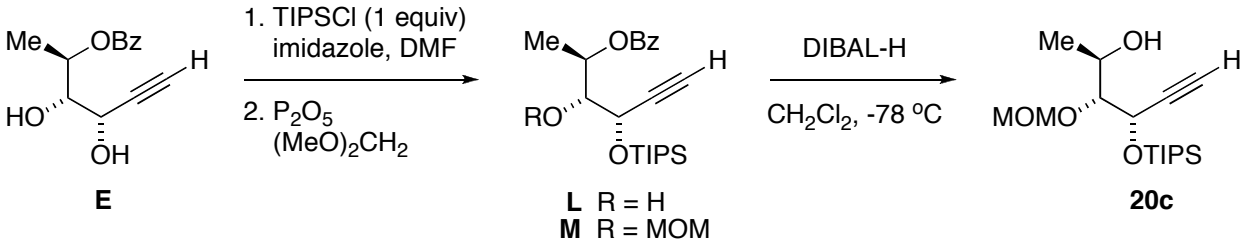
Condition B: **21b** (21 mg, 65% yield) and **22b** (6.6 mg, 20% yield).

Condition C: **21b** (22 mg, 75% yield) and **22b** (4.4 mg, 15% yield).

21b: $[\alpha]^{23}_{D}$ = +297.2 (*c* = 1.48, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, *J* = 6.0 Hz, 1H), 4.81 (d, *J* = 6.4 Hz, 1H), 4.76 (dd, *J* = 6.0 Hz, 1H), 4.61 (d, *J* = 6.4 Hz, 1H), 4.25 (dd, *J* = 3.6, 5.2 Hz, 1H), 4.17 (dq, *J* = 3.6, 6.4 Hz, 1H), 3.51 (dd, *J* = 3.2, 9.2 Hz, 1H 3.40 (s, 3H), 3.34 (d, *J* = 6.4 Hz), 1.28 (d, *J* = 6.4 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.17, 101.98, 94.72, 76.13, 70.01, 61.17, 55.90, 26.08, 18.39, 17.84, -3.75, -4.26; IR (neat) 2953, 2929, 2857, 1642, 1472, 1240, 1149, 1119, 835 cm^{-1}; HRMS Calcd. [M+H] for $C_{14}H_{29}O_4{}^{28}Si_1$ 289.18296, Found 289.18292.

22b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.74 (d, *J* = 7.2 Hz, 1H), 4.68 (d, *J* = 6.4 Hz, 1H), 4.56 (d, *J* = 4.4 Hz, 1H), 4.38 (dq, *J* = 5.2, 6.4 Hz, 1H), 4.33 (dd, *J* = 1.6 Hz, 1H), 4.05 (dd, *J* = 1.2, 1.6 Hz, 1H), 3.71 (dd, *J* = 4.4 Hz, 1H), 3.39 (s, 3H), 1.32 (d, *J* = 6.8 Hz, 3H), 0.92 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); IR (neat) 2917, 2853, 1462, 1052 cm^{-1}; HRMS Calcd. [M+H] for $C_{14}H_{29}O_4{}^{28}Si_1$ 289.18296, Found 289.18285.

Preparation of alkynyl alcohol 20c

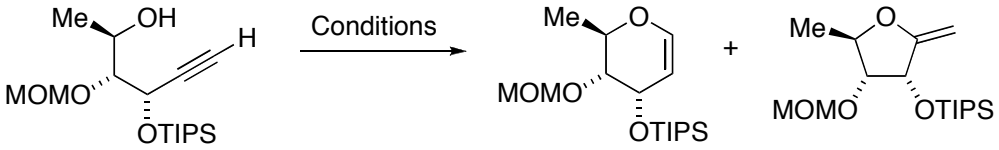


E **L** R = H **M** R = MOM **20c**

Selective TIPS protection of diol: The known diol **E**[2] (1.06 g, 4.53 mmol) was dissolved in dry DMF (5 mL), imidazole (0.616 g, 9.05 mmol) and TIPSCl (1.05 mL, 4.98 mmol) were added, and the reaction mixture was stirred for 1 h at room temperature. The reaction was quenched with water (3 mL) and diluted with ethyl ether (5 mL). The organic layer was separated and the aqueous layer was extracted with ethyl ether (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 15 :1) gave mono-TIPS protected alkynyl alcohol **L** as a colorless oil (1.30 g, 73% yield). $[\alpha]^{23}_D$ = -22.7 (*c* = 1.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-8.00 (m, 2H), 7.57 (dt, *J* = 2.4, 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 5.29 (dq, *J* = 6.4, 7.6 Hz, 1H), 4.72 (dd, *J* = 2.4, 3.6 Hz, 1H), 3.91 (ddd, *J* = 3.6, 7.6 Hz, 1H), 2.67 (d, *J* = 3.6 Hz, 1H), 2.45 (d, *J* = 2.4 Hz, 1H), 1.49 (d, *J* = 6.4 Hz, 3H), 1.22-1.03 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.56, 133.26, 130.53, 129.78, 128.62, 80.98, 76.58, 75.29, 71.66, 64.78, 18.19, 18.17, 17.94, 16.71, 12.36; IR (neat) 3514 (brs), 3308, 2943, 2866, 1720, 1274, 1113, 1067 cm^{-1}; HRMS [M+H] Calcd. for $C_{22}H_{35}O_4{}^{28}Si_1$ 391.22991, Found 392.22853.

MOM protection: The procedure as described above for alkynyl alcohol **8** was followed with TIPS-protected alkynyl alcohol **L** (1.30 g, 3.33 mmol) and P_2O_5 (1.87 g, 6.66 mmol) in dimethoxymethane (5 mL), and gave MOM-protected alkyne **M** as a colorless oil (1.25 g, 87% yield) after chromatography (hexanes : EtOAc = 15 : 1). $[\alpha]^{23}_D$ = +25.7 (*c* = 2.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.03 (m, 2H), 7.56 (dt, *J* = 2.8, 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.41 (dq, *J* = 6.4, 7.2 Hz, 1H), 5.04 (d, *J* = 7.2 Hz, 1H), 4.82 (d, *J* = 7.2 Hz, 1H), 4.69 (dd, *J* = 2.0, 4.4 Hz, 1H), 3.99 (dd, *J* = 4.4, 5.6 Hz, 1H), 3.45 (s, 3H), 2.47 (d, *J* = 2.4 Hz, 1H), 1.46 (d, *J* = 6.4 Hz, 3H), 1.21-1.08 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.70, 133.17, 130.60, 129.83, 128.54, 97.77, 82.49, 81.76, 74.66, 71.17, 64.87, 56.49, 18.23, 18.22, 15.97, 12.44; IR (neat) 2943, 2867, 1721, 1273, 1112, 1036, 712 cm^{-1}; HRMS [M+H] Calcd. for $C_{24}H_{39}O_5{}^{28}Si_1$ 435.25613, Found 435.25507.

Alkynyl alcohol 20c: The tri-*O*-protected alkyne **M** (1.25 g, 2.88 mmol) was dissolved in dry CH_2Cl_2 (10 mL), cooled to -78 ^oC, and DIBAL-H (5.76 mL, 5.76 mmol) was added dropwise at -78 ^oC. The reaction mixture was stirred for 1 h at –78 ^oC after which time cold EtOAc (30 mL) was added to quench the reaction, followed by Rochelle's salt (20 mL). The reaction mixture was stirred until two layers were clearly separated. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography (hexanes : EtOAc = 10 :1) gave alkynyl alcohol **20c** as a colorless oil (0.699 g, 73% yield). $[\alpha]^{23}_D$ = +89.7 (*c* = 0.73, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89 (d, *J* = 6.4 Hz, 1H), 4.76 (d, *J* = 6.4 Hz, 1H), 4.62 (dd, *J* = 2.4, 5.6 Hz, 1H), 4.02 (dq, *J* = 6.4, 12.6 Hz, 1H), 3.62 (t, *J* = 4.8 Hz, 1H), 3.44 (s, 3H), 2.73 (d, *J* = 7.2 Hz, 1H), 2.47 (d, *J* = 2.4 Hz, 1H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.21-1.08 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 98.48, 86.55, 83.38, 74.33, 67.38, 64.91, 56.46, 18.84, 18.25, 12.51; IR (neat) 3436 (brs), 3310, 2943, 2867, 2115, 1463, 1105, 1033 cm^{-1}; HRMS Calcd. for $C_{17}H_{35}O_4{}^{28}Si_1$ 331.22991, Found 331.22895.



20c **21c** **22c**

Cycloisomerizations of alkynyl alcohol 20c: Following the conditions described for cycloisomerization of **20a**, the alkynyl alcohol substrate **20c** (33 mg, 0.10 mmol) afforded *endo* glycal **21c** and *exo* product **22c**.

Condition A: **21c** (28 mg, 85% yield) and **22c** (3.0 mg, 9% yield).

Condition B: **21c** (29 mg, 88% yield) and **22c** (2.3 mg, 7% yield).

Condition C: **21c** (29 mg, 88% yield) and **22c** (2.0 mg, 6% yield).

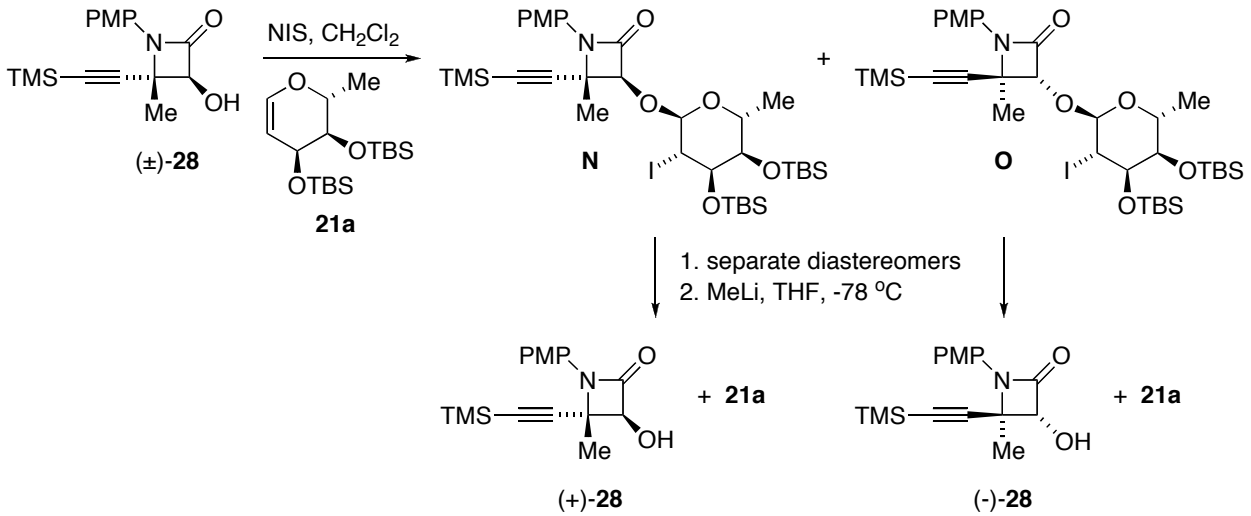
21c: $[\alpha]^{23}_D$ = +279.4 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, *J* = 6.0 Hz, 1H), 4.85 (d, *J* = 6.8 Hz, 1H), 4.83 (dd, *J* = 5.6, 6.0 Hz, 1H), 4.63 (d, *J* = 7.2 Hz, 1H), 4.39 (dd, *J* = 3.6, 5.2 Hz, 1H), 4.23 (dq, *J* = 6.4, 8.8 Hz, 1H), 3.54 (dd, *J* = 3.6, 8.8 Hz, 1H), 3.41 (s, 3H), 1.34 (d, *J* = 6.8 Hz, 3H), 1.07-1.06 (m, 21H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 145.07, 101.97, 94.85, 76.27, 70.19, 61.32, 55.92, 18.37, 17.90, 12.93; IR (neat) 2941, 1641, 1240, 1041, 1005 cm^{-1}; HRMS [M+H] Calcd. for $C_{17}H_{35}O_4{}^{28}Si_1$ 331.22991, Found 331.22919.

22c: $[\alpha]^{23}{}_D$ = -69.8 (*c* = 1.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.77 (d, *J* = 6.8 Hz, 1H), 4.70 (d, *J* = 2.0 Hz, 1H), 4.69 (d, *J* = 6.8 Hz, 1H), 4.40 (dq, *J* = 4.8, 6.8 Hz, 1H), 4.33 (dd, *J* = 1.6 Hz, 1H), 4.13 (dd, *J* = 1.6 Hz, 1H), 3.71 (dd, *J* = 4.4 Hz, 1H), 3.39 (s, 3H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.15-1.07 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.18, 96.26, 83.27, 81.22, 79.03, 71.45, 55.93, 18.98, 18.28, 18.26, 12.78; IR (neat) 2942, 2867, 1463, 1147, 1052, 996 cm^{-1}; HRMS [M+H] Calcd. for $C_{17}H_{35}O_4{}^{28}Si_1$ 331.22991, Found 331.22979.

Synthesis of the altromycin disaccharide 33

Enantiomer resolution of (±)-28



NIS mediated glycosylation: Racemic hydroxyl *beta*-lactam (±)-**28**[3] (2.25 g, 7.42 mmol) and bis-TBS protected glycal **21a** (2.40 g, 6.67 mmol) were dissolved in CH_2Cl_2 (40 mL), and cooled to 0 °C. NIS (1.59 g, 7.05 mmol) was added, and the mixture was slowly warmed to room temperature and stirred overnight at room temperature in the dark. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and quenched with sat. aq. $Na_2S_2O_4$ (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$

and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 30 :1) gave each separable glycosylated *beta*-lactam **N** (2.50 g, 47% yield) as a foam and **O** (2.39 g, 45% yield) as a colorless oil.

Compound N: $[\alpha]^{23}_{D}$ = +114.22 (*c* = 6.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.19 (s, 1H), 4.96 (s, 1H), 4.63 (brs, 1H), 4.29 (d, *J* = 2.4 Hz, 1H), 4.15 (d, *J* = 10.0 Hz, 1H), 4.12 (s, 1H), 3.78 (s, 1H), 1.65 (s, 3H), 1.30 (d, *J* = 6.4 Hz, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.16 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.73, 156.64, 129.85, 119.58, 114.39, 104.17, 102.43, 92.51, 86.57, 74.66, 70.08, 65.15, 57.47, 55.62, 29.27, 26.23, 25.92, 20.52, 18.23, 18.17, 17.98, -0.09, -3.42, -3.59, -4.34, -4.67; IR (neat) 2953, 2932, 2896, 2858, 2253, 2162, 1764, 1513, 1250, 1093, 976, 839 cm^{-1}; HRMS [M+H] Calcd. for $C_{34}H_{59}O_6N_1{}^{127}I_1{}^{28}Si_3$ 788.26895, Found 788.26923.

Compound O: $[\alpha]^{23}_{D}$ = +8.1 (*c* = 2.78, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 9.2 Hz, 2H), 5.27 (s, 1H), 4.84 (s, 1H), 4.38 (d, *J* = 2.4 Hz, 1H), 4.30 (m, 1H), 4.16-4.13 (m, 2H), 3.80 (s, 1H), 1.67 (s, 3H), 1.25 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.88 (s, 9H), 0.17 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.26, 156.78, 129.71, 119.78, 114.47, 104.59, 103.87, 92.52, 89.12, 74.89, 69.96, 65.37, 58.50, 55.68, 29.36, 26.31, 26.10, 20.97, 18.35, 18.32, 17.83, -0.05, -3.35, -3.73, -4.26, -4.56; IR (neat) 2954, 2931, 2896, 2858, 2164, 1761, 1513, 1250, 838 cm^{-1}; HRMS [M+H] Calcd. for $C_{34}H_{59}O_6N_1{}^{127}I_1{}^{28}Si_3$ 788.26895, Found 788.26893.

Enantiomerically pure hydroxyl beta lactam (+)-28: The glycosylated *beta*-lactam **N** (2.50 g, 3.17 mmol) was dissolved in dry THF (50 mL), and cooled to -78 ^{o}C. MeLi (2.18 mL, 1.6 M in Et_2O) was added dropwise at -78 ^{o}C. The reaction mixure was stirred for 10 min at -78 ^{o}C and quenched with aq. sat. NH_4Cl (10 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 30 :1 to 10 : 1) gave each separable bis-TBS protected glycal **21a** (1.05 g, 92% yield) as a colorless oil, and enantiomerically pure hydroxyl beta lactam (+)-**28** (0.83 g, 87%) as a white solid. MP = 116 ^{o}C; $[\alpha]^{23}_{D}$ =

+193.5 (*c* = 1.2, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 9.2 Hz, 2H), 6.82 (d, *J* = 9.2 Hz, 2H), 5.04 (s, 1H), 3.78 (s, 3H), 1.73 (s, 3H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.68, 156.93, 129.42, 119.94, 114.37, 104.06, 92.53, 83.37, 59.04, 55.56, 19.96, -0.09; IR (KBr) 3368 (brs), 2168, 1756, 1032, 941; HRMS [M+H] Calcd. for $C_{16}H_{22}O_3{}^{28}Si_1$ 304.13640, Found 304.13562.

(-)-28: The procedure as described above for preparation of (+)-**28** was followed with compound **O** (2.39 g, 3.03 mmol) and MeLi (2.18 mL, 1.6 M in Et_2O) in THF (50 mL), affording each separable bis-TBS protected glycal **21a** (1.05 g, 96%) as a colorless oil and (-)-**28** (0.85 g, 92%) as a white solid.

Crystal structure of (+)-28: The absolute stereochemistry of hydroxyl *beta*-lactam (+)-**28** was confirmed by single crystal X-ray analysis on crystals grown at room temperature from a mixed solution of hexanes and ethyl acetate; absolute structure parameter 0.08(3). The thermal ellipsoid diagram for (+)-**28** is shown below:

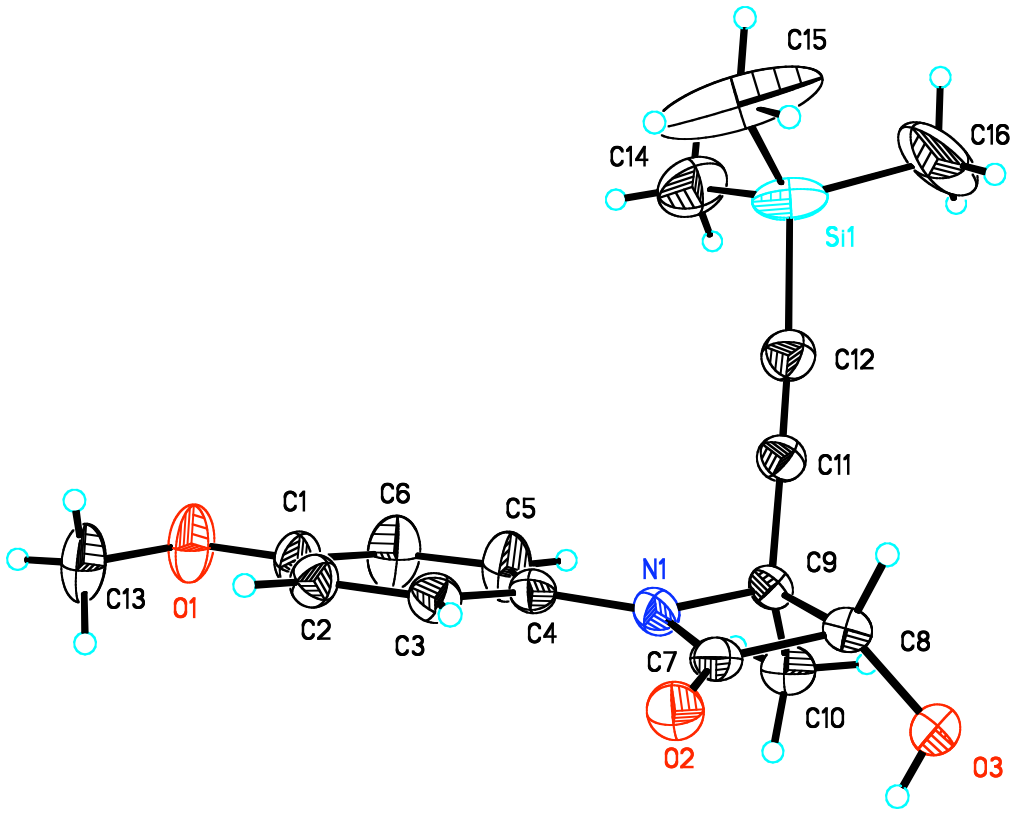


Table 1. Crystal data and structure refinement for (+)-**28**.

Identification code	**28**	
Empirical formula	C_{16} H_{21} N O_3 Si	
Formula weight	303.43	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.6408(8) Å	α = 90°.
	b = 6.0649(5) Å	β = 101.346(4)°.
	c = 13.6002(10) Å	γ = 90°.
Volume	860.54(11) $Å^3$	
Z	2	
Density (calculated)	1.171 Mg/m^3	
Absorption coefficient	1.280 mm^{-1}	
F(000)	324	
Crystal size	0.40 x 0.13 x 0.06 mm^3	
Theta range for data collection	3.31 to 65.71°.	
Index ranges	-8<=h<=12, -6<=k<=6, -16<=l<=15	
Reflections collected	6072	
Independent reflections	2403 [R(int) = 0.0200]	
Completeness to theta = 65.71°	94.2 %	
Max. and min. transmission	0.9272 and 0.6285	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2403 / 1 / 196	
Goodness-of-fit on F^2	1.016	
Final R indices [I>2sigma(I)]	R1 = 0.0279, wR2 = 0.0716	
R indices (all data)	R1 = 0.0293, wR2 = 0.0729	
Absolute structure parameter	0.08(3)	
Largest diff. peak and hole	0.142 and -0.168 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (+)-**28**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	5502(2)	7544(3)	1477(1)	34(1)
C(2)	4509(2)	8835(3)	963(1)	31(1)
C(3)	3249(2)	8357(3)	1027(1)	30(1)
C(4)	2967(2)	6597(3)	1602(1)	28(1)
C(5)	3968(2)	5346(4)	2129(2)	45(1)
C(6)	5218(2)	5802(4)	2056(2)	48(1)
C(7)	529(2)	6735(3)	1114(1)	28(1)
C(8)	-216(2)	5464(3)	1785(1)	29(1)
C(9)	1143(2)	4575(3)	2334(1)	28(1)
C(10)	1336(2)	2131(4)	2175(1)	36(1)
C(11)	1537(2)	5257(3)	3389(1)	31(1)
C(12)	1866(2)	5846(4)	4242(2)	39(1)
C(13)	7079(2)	9459(4)	785(2)	51(1)
C(14)	4095(2)	5972(5)	5974(2)	64(1)
C(15)	2338(5)	9966(6)	5432(3)	158(3)
C(16)	1368(3)	5873(8)	6331(2)	100(2)
N(1)	1684(1)	6074(3)	1646(1)	29(1)
O(1)	6774(1)	7846(3)	1464(1)	50(1)
O(2)	236(1)	7902(2)	371(1)	33(1)
O(3)	-1143(1)	3965(2)	1341(1)	37(1)
Si(1)	2425(1)	6909(1)	5522(1)	48(1)

Table 3. Bond lengths [Å] and angles [°] for (+)-**28**.

C(1)-O(1)	1.369(2)	C(5)-C(4)-N(1)	120.36(17)
C(1)-C(6)	1.386(3)	C(3)-C(4)-N(1)	120.85(16)
C(1)-C(2)	1.388(3)	C(6)-C(5)-C(4)	120.37(19)
C(2)-C(3)	1.391(2)	C(5)-C(6)-C(1)	120.97(19)
C(3)-C(4)	1.391(3)	O(2)-C(7)-N(1)	131.87(16)
C(4)-C(5)	1.388(3)	O(2)-C(7)-C(8)	134.99(16)
C(4)-N(1)	1.413(2)	N(1)-C(7)-C(8)	93.14(14)
C(5)-C(6)	1.381(3)	O(3)-C(8)-C(7)	118.49(14)
C(7)-O(2)	1.223(2)	O(3)-C(8)-C(9)	119.07(16)
C(7)-N(1)	1.358(2)	C(7)-C(8)-C(9)	85.47(13)
C(7)-C(8)	1.530(3)	C(11)-C(9)-N(1)	111.54(15)
C(8)-O(3)	1.389(2)	C(11)-C(9)-C(10)	113.15(16)
C(8)-C(9)	1.585(2)	N(1)-C(9)-C(10)	115.01(14)
C(9)-C(11)	1.473(3)	C(11)-C(9)-C(8)	114.98(15)
C(9)-N(1)	1.500(2)	N(1)-C(9)-C(8)	85.79(13)
C(9)-C(10)	1.518(3)	C(10)-C(9)-C(8)	113.67(15)
C(11)-C(12)	1.198(3)	C(12)-C(11)-C(9)	178.9(2)
C(12)-Si(1)	1.842(2)	C(11)-C(12)-Si(1)	176.16(19)
C(13)-O(1)	1.425(3)	C(7)-N(1)-C(4)	133.78(15)
C(14)-Si(1)	1.852(3)	C(7)-N(1)-C(9)	95.29(13)
C(15)-Si(1)	1.860(4)	C(4)-N(1)-C(9)	130.92(15)
C(16)-Si(1)	1.832(3)	C(1)-O(1)-C(13)	116.84(15)
		C(16)-Si(1)-C(12)	108.99(13)
O(1)-C(1)-C(6)	115.82(17)	C(16)-Si(1)-C(14)	110.98(14)
O(1)-C(1)-C(2)	125.08(17)	C(12)-Si(1)-C(14)	108.46(11)
C(6)-C(1)-C(2)	119.10(17)	C(16)-Si(1)-C(15)	110.7(2)
C(1)-C(2)-C(3)	119.91(18)	C(12)-Si(1)-C(15)	106.50(14)
C(2)-C(3)-C(4)	120.84(17)	C(14)-Si(1)-C(15)	111.09(18)
C(5)-C(4)-C(3)	118.78(16)		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (+)-**28**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	27(1)	41(1)	34(1)	6(1)	2(1)	-4(1)
C(2)	33(1)	29(1)	31(1)	4(1)	5(1)	-3(1)
C(3)	30(1)	33(1)	27(1)	1(1)	3(1)	3(1)
C(4)	28(1)	35(1)	21(1)	-1(1)	3(1)	-2(1)
C(5)	35(1)	56(2)	41(1)	25(1)	1(1)	-3(1)
C(6)	29(1)	59(2)	53(1)	27(1)	-3(1)	4(1)
C(7)	30(1)	29(1)	23(1)	-4(1)	3(1)	0(1)
C(8)	30(1)	33(1)	25(1)	-5(1)	7(1)	-3(1)
C(9)	31(1)	33(1)	21(1)	0(1)	8(1)	-5(1)
C(10)	40(1)	34(1)	33(1)	0(1)	6(1)	1(1)
C(11)	35(1)	34(1)	24(1)	1(1)	6(1)	-3(1)
C(12)	42(1)	41(1)	32(1)	0(1)	6(1)	-6(1)
C(13)	30(1)	58(2)	65(1)	20(1)	12(1)	-6(1)
C(14)	55(1)	71(2)	57(2)	-8(1)	-8(1)	-4(1)
C(15)	248(6)	46(2)	120(3)	-25(2)	-115(4)	27(3)
C(16)	78(2)	192(5)	34(1)	-23(2)	19(1)	14(2)
N(1)	30(1)	35(1)	22(1)	2(1)	6(1)	-2(1)
O(1)	25(1)	61(1)	62(1)	25(1)	5(1)	-2(1)
O(2)	32(1)	37(1)	29(1)	5(1)	3(1)	2(1)
O(3)	33(1)	45(1)	33(1)	-6(1)	7(1)	-10(1)
Si(1)	64(1)	44(1)	30(1)	-11(1)	-9(1)	5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10 ^{3}) for (+)-**28**.

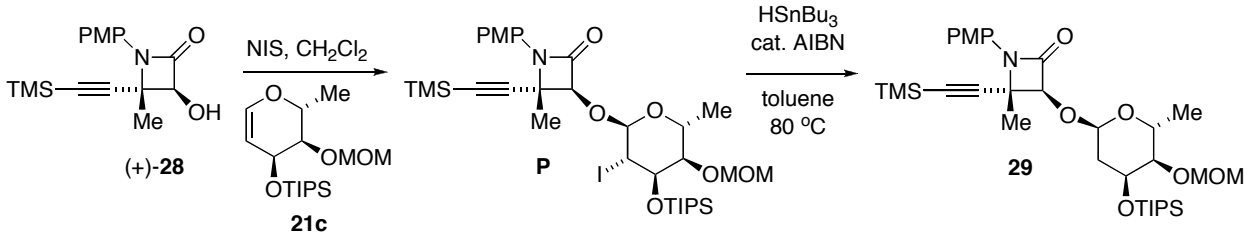
	x	y	z	U(eq)
H(2)	4686	10019	577	37
H(3)	2587	9225	680	36
H(5)	3797	4193	2534	54
H(6)	5879	4928	2400	58
H(8)	-569	6479	2222	35
H(10A)	2210	1743	2445	54
H(10B)	1144	1809	1470	54
H(10C)	777	1296	2507	54
H(13A)	6601	9163	123	76
H(13B)	7979	9402	781	76
H(13C)	6861	10898	994	76
H(14A)	4138	4399	5907	95
H(14B)	4368	6371	6666	95
H(14C)	4646	6659	5583	95
H(15A)	2935	10484	5038	237
H(15B)	2548	10593	6092	237
H(15C)	1486	10401	5118	237
H(16A)	495	6228	6039	150
H(16B)	1596	6547	6980	150
H(16C)	1460	4303	6397	150
H(3A)	-921	3396	855	55

Table 6. Hydrogen bonds for (+)-**28** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(3)-H(3A)...O(2)#1	0.82	1.97	2.7663(17)	163.6

Symmetry transformations used to generate equivalent atoms:
#1 -x,y-1/2,-z

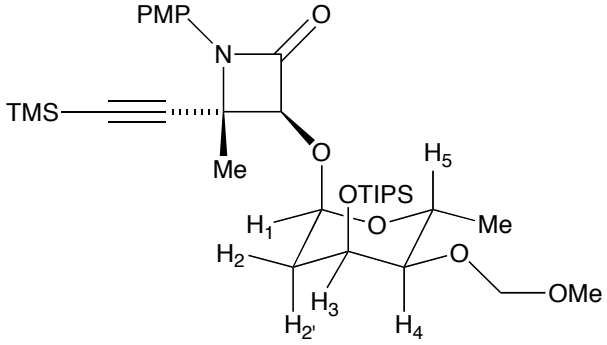
Preparation of glycosylated *beta*-lactam 29



NIS mediated glycosylation: The hydroxyl *beta*-lactam (+)-**28** (0.411 g, 1.36 mmol) and glycal **21c** (0.407 g, 1.23 mmol) were dissolved in CH_2Cl_2 (8 mL), and cooled to 0 °C. NIS (0.291 g, 1.29 mmol) was added at 0 °C. The mixture was slowly warmed to room temperature and then stirred overnight in the dark. The resulting solution was diluted with CH_2Cl_2 (5 mL) and quenched with sat. aq. $Na_2S_2O_4$ (10 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 15 :1) gave iodoglycal *beta*-lactam **P** as a colorless oil (0.766 g, 82% yield). $[\alpha]^{23}_D$ = +132.9 (*c* = 3.45, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 9.2 Hz, 2H), 6.87 (d, *J* = 9.2 Hz, 2H), 5.23 (s, 1H), 4.97 (s, 1H), 4.71 (d, *J* = 6.4 Hz, 1H), 4.68 (dq, *J* = 6.4, 9.6 Hz, 1H), 4.59 (d, *J* = 7.2 Hz, 1H), 4.40 (t, *J* = 2.4 Hz, 1H), 4.36 (d, *J* = 2.4 Hz, 1H), 4.04 (dd, *J* = 2.0, 9.6 Hz, 1H), 3.79 (s, 3H), 3.42 (s, 3H), 1.64 (s, 3H), 1.38 (d, *J* = 6.4 Hz, 3H), 1.06 (s, 21H), 0.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.18, 156.67, 129.87, 119.63, 114.43, 104.15, 102.47,

95.56, 92.58, 86.67, 74.16, 72.55, 64.10, 57.52, 56.36, 55.66, 29.33, 20.54, 18.22, 18.13, 17.86, 12.76, -0.09; IR (neat) 2942, 2252, 2162, 2057, 1950, 1871, 1760, 1513, 1373, 1247, 844 cm^{-1}; HRMS [M+H] Calcd. for $C_{33}H_{55}O_7N_1{}^{127}I_1{}^{28}Si_2$ 760.25564, Found 760.25794.

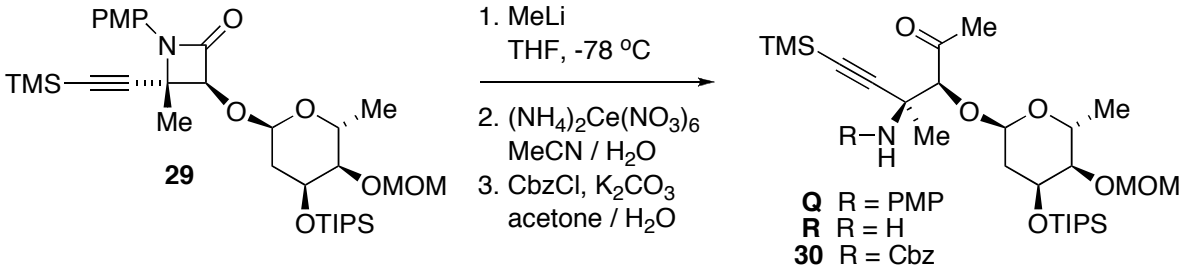
Deiodination: Compound **P** (0.550g, 0.754 mmol) was dissolved in toluene (25 mL), and $HSnBu_3$ (1.00 mL, 3.77 mmol) and AIBN (12.4 mg, 0.075 mmol) were added. Air was removed through vacuum-argon exchange (3 times). The reaction mixture was heated to 80 ^oC and stirred for 5 h. The reaction mixture was cooled to room temperature, and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 40 : 1, gradient to 30 : 1 and to 20 : 1) gave compound **29** as a colorless oil (0.416 g, 88% yield). $[\alpha]^{23}{}_D$ = +114.3 (*c* = 1.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 9.2 Hz, 2H), 6.87 (d, *J* = 9.2 Hz, 2H), 5.02 (s, 1H), 4.93 (dd, *J* = 2.4, 4.8 Hz, 1H), 4.76 (d, *J* = 7.2 Hz, 1H), 4.59 (d, *J* = 7.2 Hz, 1H), 4.55 (dq, *J* = 6.4, 8.4 Hz, 1H), 4.26 (ddd, *J* = 2.8, 2.8 4.8 Hz, 1H), 3.79 (s, 3H), 3.40 (s, 3H), 3.37 (dd, *J* = 2.8, 8.4 Hz, 1H), 2.19 (ddd, *J* = 2.4, 4.8, 14.4 Hz, 1H), 1.92 (ddd, *J* = 2.8, 4.8, 14.4 Hz, 1H), 1.63 (s, 3H), 1.34 (d, *J* = 6.4 Hz, 3H), 1.06 (s, 21H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.30, 156.56, 130.10, 119.60, 114.40, 104.62, 97.70, 95.28, 92.14, 86.97, 78.40, 65.76, 64.66, 57.53, 56.05, 55.68, 36.69, 20.54, 18.32, 18.27, 12.76, -0.05; IR (neat) 2941, 2866, 2162, 1763, 1512, 1248 cm^{-1}; HRMS Calcd. [M+H] for $C_{33}H_{56}O_7N_1{}^{28}Si_2$ 634.35899, Found 634.35891.



Coupling constants for **29** were consistent with the axial glycoside as shown:

$J_{1,2}$ = 4.8 Hz, diequatorial HCCH
$J_{1,2'}$ = 2.4 Hz, equatorial, axial HCCH
$J_{2,3}$ = 4.8 Hz, diequatorial HCCH
$J_{2',3}$ = 2.8 Hz, axial, equatorial HCCH
$J_{3,4}$ = 2.8 Hz, equatorial, axial HCCH
$J_{4,5}$ = 8.4 Hz, diaxial HCCH

Preparation of alkynyl ketone 30



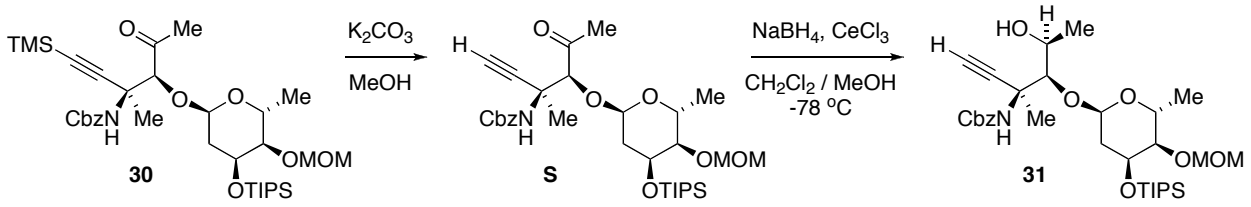
MeLi addition: *Beta*-lactam compound **29** (0.416 g, 0.733 mmol) was dissolved in dry THF (10 mL) and cooled to -78 °C. MeLi (0.687 mL, 1.10 mmol, 1.6 M in Et_2O) was added dropwise at -78 °C. The reaction mixture was stirred for 30 min at -78 °C and quenched with aq. sat. $NaHCO_3$ (5 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 10 :1) gave ketone **Q** as a colorless oil (0.425 g, 90% yield). $[\alpha]^{23}_D$ = +80.5 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, *J* = 9.2 Hz, 2H), 6.76 (d, *J* = 9.2 Hz, 2H), 4.94 (dd, *J* = 4.0 Hz, 1H), 4.78 (d, *J* = 6.8 Hz, 1H), 4.62 (d, *J* = 6.8 Hz, 1H), 4.24-4.17 (m, 2H), 4.00 (s, 1H), 3.99 (d, *J* = 4.0 Hz, 1H), 3.76 (s, 3H), 3.39 (s, 3H), 3.38 (dd, *J* = 2.8, 6.0 Hz, 1H), 2.35 (s, 3H), 2.27 (ddd, *J* = 4.0, 6.4, 14.0 Hz, 1H), 1.94 (ddd, *J* = 4.0, 14.4 Hz, 1H), 1.42 (s, 3H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.10 (s, 21H), 0.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.60, 154.83, 138.33, 122.63, 114.11, 107.10, 99.91, 95.90, 90.53, 87.80, 78.19, 66.61, 65.99, 56.42, 55.98, 55.72, 36.65, 29.17, 24.27, 18.39, 18.34, 17.74, 12.72, -0.04; IR (neat) 2942, 2867, 2166, 1712, 1510, 1248, 1035, 842 cm^{-1}; HRMS Calcd. [M+H] for $C_{34}H_{60}O_7N_1{}^{28}Si_2$ 650.39029, Found 650.38986.

Removal of PMP: The ketone **Q** (0.425g, 0.660 mmol) was dissolved in a mixture of CH_3CN (12 mL) and water (6 mL), and cooled to 0 °C. Ceric ammonium nitrate (0.724 g, 1.32 mmol) dissolved in water (6 mL) was added dropwise at 0 °C, and the reaction

mixture was slowly warmed to room temperature and stirred for 1 h. The resulting solution was quenched with aq. sat. $NaHCO_3$ (20 mL) and then stirred for 1 h at room temperature. The solution was filtered through Celite using EtOAc as eluent and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 10 mL), the combined organic layer was dried over $MgSO_4$, and solvents were removed by rotary evaporation, to afford crude amine **R** which was used in the next step without further purification.

Cbz protection: The procedure as described above for (±)-**4,** (±)-**6, 8** and **14** was followed with crude amine **R,** K_2CO_3 (9.1 mg, 0.066 mmol) and CbzCl (0.14 mL, 0.99 mmol) in acetone (6 mL) and water (6 mL), to provide ketone **30** as a colorless oil (0.29 g, 65 % over 2 steps) after chromatography (hexanes : EtOAc = 5 : 1). $[\alpha]^{23}_{D}$ = +87.8 (*c* = 3.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 5H), 5.67 (s, 1H), 5.07 (s, 2H), 4.81 (dd, *J* = 3.2, 5.2 Hz, 1H), 4.74 (d, *J* = 6.8 Hz, 1H), 4.58 (d, *J* = 6.8 Hz, 1H), 4.12 (ddd, *J* = 3.2, 6.0 Hz, 1H), 4.11 - 4.07 (m, 2H), 3.37 (s, 3H), 3.31 (dd, *J* = 2.8, 8.0 Hz, 1H), 2.35 (s, 3H), 2.16 (ddd, *J* = 2.8, 5.6, 14.0 Hz, 1H), 1.85 (ddd, *J* = 3.6, 5.2, 14.0 Hz, 1H), 1.65 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.06 (s, 21H), 0.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.41, 154.58, 136.71, 128.60, 128.32, 128.16, 109.96, 99.91, 95.60, 88.94, 86.10, 78.11, 66.62, 65.79, 65.70, 55.97, 52.80, 36.54, 30.24, 24.29, 18.29, 18.23, 17.70, 12.63, -0.03; IR (neat) 2943, 2867, 2173, 1726, 1504, 1248, 1036, 843 cm^{-1}; HRMS [M+Na] Calcd. for $C_{35}H_{59}O_8N_1{}^{23}Na_1{}^{28}Si_2$ 700.36715, Found 700.36652.

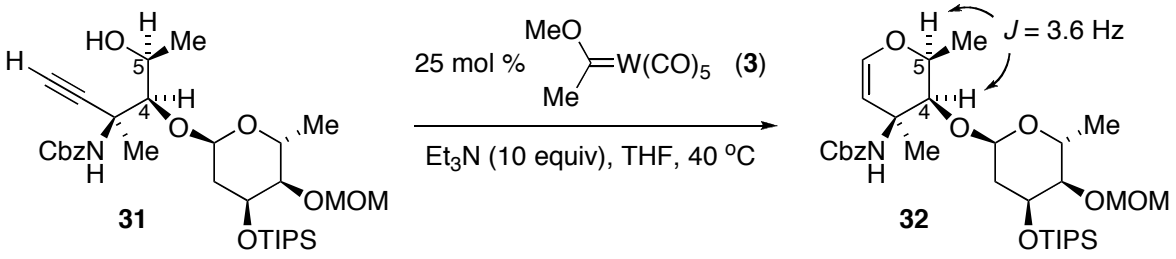
Preparation of alkynyl alcohol 31



Desilylation: The alkynylsilane compound **30** (0.15 g, 0.22 mmol) was dissolved in MeOH (8 mL), K_2CO_3 (6.0 mg, 0.044 mmol) was added, and the reaction mixture was stirred overnight at room temperature. The reaction was quenched with aq. sat. NH_4Cl (5 mL) and diluted with CH_2Cl_2 (10 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 10 :1) gave terminal alkyne **S** as a colorless oil (0.13 g, 95% yield). $[\alpha]^{23}_D$ = +86.5 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 5.75 (s, 1H), 5.16-5.03 (m, 2H), 4.85 (dd, *J* = 3.2, 5.2 Hz, 1H), 4.75 (d, *J* = 7.2 Hz, 1H) , 4.58 (d, *J* = 7.2 Hz, 1H), 4.17 (ddd, *J* = 3.2, 6.0 Hz, 1H), 4.14-4.07 (m, 2H), 3.37 (s, 3H), 3.20 (dd, *J* = 3.5, 8.0 Hz, 1H), 2.44 (s, 1H), 2.36 (s, 3H), 2.18 (ddd, *J* = 3.6, 6.0, 14.4 Hz, 1H), 1.88 (ddd, *J* = 3.6, 4.8, 14.4 Hz, 1H), 1.66 (s, 3H), 1.13 (d, *J* = 6.4 Hz, 3H), 1.05 (s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.07, 154.76, 136.54, 128.63, 128.43, 128.24, 100.09, 95.61, 85.70, 83.39, 78.03, 72.68, 66.77, 65.86, 65.73, 56.00, 52.19, 36.49, 30.50, 24.15, 18.38, 18.29, 18.22, 17.79, 12.63; IR (neat) 2943, 2867, 2173, 1726, 1504, 1248, 1036, 843 cm^{-1}; HRMS [M+Na] Calcd. for $C_{32}H_{51}O_8N_1{}^{23}Na_1{}^{28}Si_1$ 628.32762, Found 628.32721.

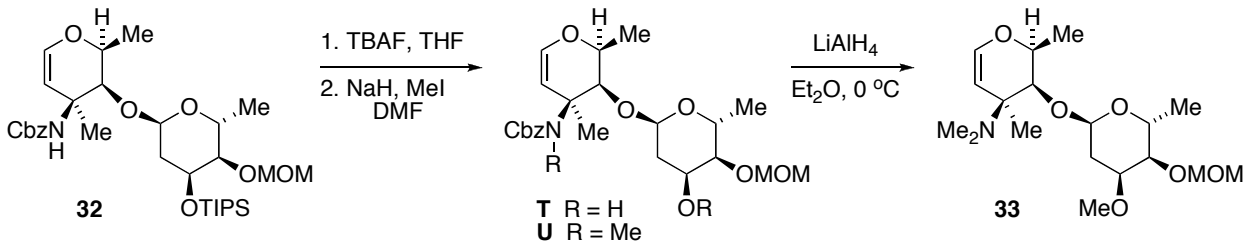
Diastereoselective reduction of ketone: Ketone **S** (0.13 g, 0.21 mmol) was dissolved in a mixture of CH_2Cl_2 (4 mL) and MeOH (2 mL), and $CeCl_3 \cdot 7H_2O$ (0.16 g, 0.42 mmol) was added. The reaction mixture was stirred for 20 min at room temperature and then cooled to –78 ^oC. $NaBH_4$ (8.0 mg, 0.21 mmol) was added to the reaction mixture and then stirred for 1 h at –78 ^oC. An additional portion of $NaBH_4$ (8.0 mg, 0.21 mmol) was added and then stirred for 1 hr at –78 ^oC. The reaction mixture was quenched with aq. sat. $NaHCO_3$ (4 mL) and then diluted with CH_2Cl_2 (5 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent was removed by rotary evaporation. Chromatography (hexanes : EtOAc = 10 :1) gave alkynyl alcohol **31** as a colorless oil (0.11 g, 89 % yield). $[\alpha]^{23}_D$ = +93.2 (*c* = 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 6.12 (s, 1H), 5.13-5.01 (m, 3H), 4.79 (d, *J* = 6.8 Hz, 1H), 4.60 (d, *J* = 7.2 Hz, 1H), 4.26 (ddd, *J* = 6.8, 14.0 Hz, 1H), 4.23-4.12 (m, 2H), 3.66 (d, *J* = 1.2 Hz, 1H), 3.40 (s, 3H), 3.38 (dd, *J* = 3.6, 7.6 Hz, 1H), 2.84 (d, *J* = 10.4 Hz, 1H), 2.37 (s, 1H), 2.23 (ddd, *J* = 3.6, 6.0, 14.0 Hz, 1H), 1.94 (ddd, *J* = 3.6, 7.6, 14.0 Hz, 1H), 1.64 (s, 3H), 1.28 (d, *J* = 6.4 Hz, 3H), 1.26 (d, *J* = 6.4 Hz, 3H), 1.06 (s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.09, 136.69, 128.61, 128.35, 128.20, 99.25, 95.70, 84.87, 77.75, 71.52, 66.63, 66.21, 65.99, 65.95, 56.13, 55.10, 36.78, 23.73, 22.85, 18.31, 18.19, 17.82, 12.69; IR (neat) 2943, 1726, 1514, 1249, 1035 cm^{-1}; HRMS [M+Na] Calcd. for $C_{32}H_{53}O_8N_1{}^{23}Na_1{}^{28}Si_1$ 630.34327, Found 630.34292.

Synthesis of disaccharide glycal 32 via alkynyl alcohol cycloisomerization



Disaccharide glycal 32: Following the general procedure for alkynyl alcohol cycloisomerization, substrate **31** (0.114 g, 0.188 mmol) afforded disaccharide glycal **32** as a colorless oil (95 mg, 83 % yield). At this stage, the relative stereochemistry between C4 and C5, set in the previous ketone reduction step to provide **31**, could be determined, based on the relatively small coupling constant of 3.6 Hz. $[\alpha]^{23}_{D}$ = +78.7 (*c* = 3.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 5H), 6.18 (d, *J* = 6.4 Hz, 1H), 5.35 (s, 1H), 5.08-5.01 (m, 3H), 4.88 (dd, *J* = 3.2, 5.2 Hz, 1H), 4.76 (d, *J* = 7.2 Hz, 1H), 4.59 (d, *J* = 7.2 Hz, 1H), 4.31-4.21 (m, 2H), 4.15 (ddd, *J* = 3.2, 5.2 Hz, 1H), 3.71 (d, *J* = 3.6 Hz, 1H), 3.39 (s, 3H), 3.34 (dd, *J* = 2.4, 3.6 Hz, 1H), 2.14 (ddd, *J* = 3.2, 5.6, 14.0 Hz, 1H), 1.83 (ddd, *J* = 3.6, 14.0 Hz, 1H), 1.48 (s, 3H), 1.38 (d, *J* = 6.8 Hz, 1H), 1.23 (d, *J* = 6.8 Hz, 1H), 1.04 (s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.14, 141.69, 136.91, 128.63, 128.28, 128.15, 104.14, 99.81, 95.67, 80.44, 78.23, 71.67, 66.37, 65.95, 65.38, 56.02, 51.24, 36.84, 27.03, 18.32, 18.22, 15.20, 2.65; IR (neat) 2940, 2867, 1726, 1495, 1035 cm^{-1}; HRMS [M+Na] Calcd. for $C_{32}H_{53}O_8N_1{}^{23}Na_1{}^{28}Si_1$ 630.34327, Found 630.34292.

Synthesis of disaccharide glycal 33



Desilylation: Silyl ether **32** (60 mg, 0.099 mmol) was dissolved in dry THF (3 mL), and TBAF (0.2 mL, 1M in THF, 0.2 mmol) was added. The reaction mixture was stirred for 30 min at room temperature. The reaction was diluted with EtOAc (2 mL) and quenched with water (3 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 5 mL) and washed with brine. The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. The crude material **T** was used for the next step without further purification.

***N,O*-Dimethylation:** The crude amino alcohol **T** was dissolved in dry DMF (3 mL), and cooled to 0 °C. Sodium hydride (16 mg, 0.40 mmol) was added, and the mixture was slowly warmed to room temperature and stirred for 20 min. Iodomethane (31 μL, 0.50 mmol) was added to the reaction mixture and then stirred for 1 h at room temperature. The reaction mixture was carefully quenched with water (1 mL) and then diluted with EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layer was dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 5 : 1) gave *N*- and *O*-methylated product **U** as a colorless oil (42 mg, 85 % over 2 steps). $[\alpha]^{23}_{D}$ = +6.4 (*c* = 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.18 (m, 5H), 6.19 (d, *J* = 6.4 Hz, 1H), 5.09 (d, *J* = 12.0 Hz, 1H), 4.89 (d, *J* = 12.4 Hz, 1H), 4.63 (d, *J* = 6.8 Hz, 1H), 4.62 (dd, *J* = 2.4, 6.4 Hz, 1H), 4.56 (dd, *J* = 3.6, 4.4 Hz, 1H), 4.54 (d, *J* = 6.8 Hz, 1H), 4.18 (ddd, *J* =

2.8, 14.0 Hz, 1H), 4.03 (brs, 1H), 3.98 (d, *J* = 2.4 Hz, 1H), 3.39 (brs, 1H), 3.27 (s, 3H), 3.22 (dd, *J* = 3.2, 7.6 Hz, 1H), 3.20 (s, 3H), 2.93 (s, (3H), 1.89 (d, *J* = 12.0 Hz, 1H), 1.53 (s, 3H), 1.40-1.29 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 1H), 1.06 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.96, 128.22, 128.42, 127.98, 104.78, 97.45, 95.53, 77.84, 77.31, 73.34, 71.78, 66.70, 65.23, 58.81, 55.91, 55.38, 31.10, 17.61; IR (neat) 2932, 1964, 1345, 1105, 1040 cm^{-1}; HRMS [M+Na] Calcd. for $C_{25}H_{37}O_8N_1{}^{23}Na_1$ 502.24114, Found 502.24075.

$LiAlH_4$ reduction: Compound **U** obtained above (42 mg, 0.084 mmol) was dissolved in dry Et_2O (3 mL) and cooled to 0 ^oC. $LiAlH_4$ (0.25 mL, 1 M solution in Et_2O) was added dropwise at 0 ^oC. The reaction mixture was slowly warmed to room temperature and stirred for 5 h. The reaction mixture was diluted with Et_2O (2 mL), quenched with water (0.05 mL) and 3 M NaOH (0.1 mL), and then stirred for additional 1 h. The solution was then dried over $MgSO_4$ and solvent removed by rotary evaporation. Chromatography (hexanes : EtOAc = 5 : 1, gradient to 2 : 1 and to 1 : 1) gave the disaccharide glycal **33** as a yellowish oil (28 mg, 94 % yield). $[\alpha]^{23}_D$ = +83.6 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 (d, *J* = 6.4 Hz, 1H), 5.23 (dd, *J* = 1.6, 4.8 Hz, 1H), 4.78 (d, *J* = 6.8 Hz, 1H), 4.68-4.66 (m, 2H), 4.30 (dq, *J* = 6.6, 8.8 Hz, 1H), 4.16 (dq, *J* = 2.4, 6.4 Hz, 1H), 3.72 (dd, *J* = 2.8, 7.2 Hz, 1H), 3.58 (dd, *J* = 2.4 Hz, 1H), 3.41 (s, 3H), 3.40 (s, 3H), 3.34 (dd, *J* = 2.8, 8.8 Hz, 1H), 2.37 (ddd, *J* = 2.0, 4.4, 14.8 Hz, 1H), 2.30 (s, 6H), 1.70 (ddd, *J* = 2.8, 4.8, 14.8 Hz, 1H), 1.41 (d, *J* = 6.0 Hz, 3H), 1.22 (d, *J* = 6.8 Hz, 1H), 1.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.73, 104.57, 97.30, 95.75, 78.86, 78.60, 73.56, 73.24, 64.22, 56.21, 55.73, 40.62, 31.13, 22.97, 18.14, 17.27; IR (neat) 2929, 1111, 1042, 985 cm^{-1}; [M+H] Calcd. for $C_{18}H_{34}O_6N_1$ 360.23806, Found 360.23788.