Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supplementary Information

Highly stereoselective synthesis of aminoglycosides via rhodium-catalyzed and substrate-controlled aziridination of glycals

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General Experimental Details. All reactions were run under an atmosphere of nitrogen, unless otherwise indicated. Anhydrous solvents were transferred *via* oven-dried syringe. Flasks were flame-dried and cooled under a stream of nitrogen. Solvents and reagents were purified according to the standard procedure prior to use. Evaporation of organic solutions was achieved by rotary evaporation with a water bath temperature below 40 °C. Product purification by flash column chromatography was accomplished using silica gel 60 (0.010-0.063 nm). Technical grade solvents were used for chromatography and distilled prior to use. Infrared spectra were recorded a Bio-RAD FTS 165 FT-IR Spectrometer and reported in cm^{-1}. Samples were prepared in thin film technique. High-resolution mass spectra (ESI/HRMS) were obtained on a Finnigan/MAT LCQ quadrupole ion trap mass spectrometer, coupled with the TSP4000 HPLC system and the Crystal 310 CE system. Accurate masses are reported for the molecular ion $[M+H]^+$ or a suitable fragment ion. NMR spectra were recorded at room temperature on a 300 MHz Bruker ACF 300, 400 MHz Bruker DPX 400 and 500 MHz Bruker AMX 500 NMR spectrometers, respectively. The residual solvent signals were taken as the reference (7.26 ppm for ^1H NMR spectroscopy and 77.0 ppm for ^{13}C NMR spectroscopy). Chemical shifts were reported in delta (δ) units, parts per million (ppm) downfield from trimethylsilane and coupling constants (J) were given in Hz. Following abbreviations classify the multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, br = broad signal. Compound numbers used in the experimental section correspond to those employed in the main paper.

Experimental Procedures and Spectroscopic Data

Typical Procedure for synthesis of sulfamate ester-derived glycal: Formic acid (2 equiv) was added dropwise to a neat chlorosulfonyl isocyanate (2 equiv) at 0 °C with rapid stirring. Vigorous gas evolution was observed during the addition process. The resulting viscous suspension was stirred for 5 mins at 0 °C during which time the mixture solidified. Dry CH_3CN (10 equiv) was added providing a clear solution and the solution was stirred for 1 h at 0 °C then 7 h at room temperature. This solution mixture was cooled to 0 °C, and a solution of glycal (1 equiv) in *N,N*-dimethylacetamide (33 equiv) was added sequentially. The reaction was stirred at 0 °C overnight, and quenched by the successive addition of Et_3N. The mixture was poured into diethyl ether (20 mL) and water (10 mL), the organic phase was collected, and the aqueous layer was extracted with diethyl ether (3 ×). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel to afford the desired sulfamate ester.

Sulfamate ester 1: Yield: 68 %; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.92 (m, 2H), 7.60 (m, 1H), 7.40 (m, 5H), 7.21 (m, 12H), 6.04 (d, J = 10.2 Hz, 1H), 5.85 (d, J = 10.2 Hz, 1H), 5.61 (br d, 1H), 5.27 (d, J = 11.4 Hz, 1H), 4.75 (br s, 2H), 4.03 (m, 1H), 3.50 (d, J = 9.2 Hz, 1H), 3.44 (d, J = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.7, 143.3, 143.0, 133.5, 130.7, 129.7, 128.6, 128.4, 128.0, 127.3, 127.2, 104.6, 77.5, 69.2, 68.2, 65.6, 64.9; IR ($CHCl_3$): $\tilde{\nu}$ = 3381, 3288, 3018, 1718, 1448 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{32}H_{29}NO_7SNa$: 594.1562 [M+Na]$^+$; found: 594.1574.

Sulfamate ester 7: Yield: 77 %; colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.44 (m, 6H), 7.32-7.20 (m, 9H), 6.41 (d, J = 6.2 Hz, 1H), 4.74 (dd, J = 5.7, 3.9 Hz, 1H), 4.65 (t, J = 4.59 Hz, 1H), 4.61 (br s, 2H), 4.32 (br t, 1H), 4.23 (t, J = 3.9 Hz, 1H), 3.62 (dd, J = 11.0, 6.8 Hz, 1H), 3.34 (dd, J = 11.0, 2.6 Hz, 1H), 0.80 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 143.4, 128.7, 127.8, 127.1, 101.5, 86.9, 78.6, 75.3, 64.6, 61.8, 25.7, 17.9, -4.7; IR ($CHCl_3$): $\tilde{\nu}$ = 3429,

3018, 1651, 1450 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{31}H_{39}NO_6SSiNa$: 604.2165 $[M+Na]^+$; found: 604.2154.

Sulfamate ester 2a: Yield: 79 %; white solid. ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.06 (d, J = 8.1 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 6.53 (d, J = 6.0 Hz, 1H), 5.62 (t, J = 3.7 Hz, 1H), 5.32 (br s, 2H), 5.19 (t, J = 6.0 Hz, 1H), 4.95 (dd, J = 6.0, 3.7 Hz, 1H), 4.25 (dd, J = 11.0, 5.0 Hz, 1H), 3.98 (dd, J = 11.0, 4.7 Hz, 2H), 0.84 (s, 9H), 0.08 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 166.5, 146.3, 133.5, 129.9, 129.4, 128.5, 97.6, 76.1, 74.6, 67.9, 60.6, 25.7, 18.1, -5.2, -5.4; IR (nujol): $\tilde{\nu}$ = 3373, 1699, 1647, 1463, 1456 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{19}H_{28}NO_7S$: 442.1350 $[M-H]^+$; found: 442.1340.

General procedure for the preparation of oxathiazinane acetates:

A mixture of sulfamate ester (1 equiv), 5 % mol of $Rh_2(OAc)_4$, MgO (1.5 equiv), $PhI(OAc)_2$ (5 equiv), and 4Å molecular sieve was added dry CH_2Cl_2 (3 mL). The suspension was stirred vigorously as stated in the main paper. The reaction mixture was filtered through a pad of Celite. The filter cake was rinsed with CH_2Cl_2 and the combined filtrates were evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired oxathiazinane.

Oxathiazinane acetate 6: Yield: 62 %; white solid; an anomeric mixture (2:1) of acetate product. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.85 (m, 2H), 7.58 (m, 1H), 7.41 (m, 5H), 7.17 (m, 12H), 6.16 (s, 1H), 5.89 (m, 1H), 5.70 (m, 1H), 4.23 (m, 1H), 3.31 (m, 3H), 2.13 (s, 3H); IR ($CHCl_3$): $\tilde{\nu}$ = 2926, 1722, 1448 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{34}H_{30}NO_9S$: 628.1641 $[M-H]^+$; found: 628.1520.

Oxathiazinane acetate 10: Yield: 84 %; white solid. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.47 (d, J = 5.5 Hz, 1H), 7.43 (m, 6H), 7.35-7.27 (m, 9H), 5.93 (d, J = 5.5 Hz, 1H), 5.53 (d, J = 12.6 Hz, 1H), 4.32 (br dt, J = 12.6 Hz, 1H), 3.70 (d, J = 11.5 Hz, 1H), 3.41 (dd, J = 11.5, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 164.6, 142.9, 128.5, 128.1, 127.4, 95.7, 87.3, 80.0, 75.9, 61.2; IR ($CHCl_3$): $\tilde{\nu}$ = 2926, 1707, 1653 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{25}H_{22}NO_5S$: 448.1219 $[M+H]^+$; found: 448.1261.

Oxathiazinane acetate 11a: Yield: 73 %; colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.04 (d, J = 7.2 Hz, 2H), 7.65 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 6.48 (s, 1H), 5.81 (m, 2H), 5.21 (m, 1H), 4.71 (dd, J = 10.2, 6.5 Hz, 1H), 4.08 (t, J = 10.3 Hz, 1H), 4.03 (m, 1H), 3.94 (dd, J = 10.2, 6.5 Hz, 1H), 1.82 (s, 3H), 0.84 (s, 9H), 0.04 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 168.7, 165.2, 134.3, 129.8, 128.7, 128.3, 91.4, 75.5, 74.5, 62.9, 62.2, 50.3, 25.6, 20.9, 18.0, -5.3, -5.6; IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 2954, 2929, 1732, 1388 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{21}H_{31}NO_9SSiNa$: 524.1381 [M+Na]$^+$; found: 524.1401.

General procedure for rhodium-catalyzed aziridination with other nucleophiles:

To a solution of sulfamate ester (1 equiv) in 3 mL of dry CH_2Cl_2 and 4Å molecular sieve were added successively MgO (5 equiv), PhIO (1.5 equiv), and 5 % mol of Rh_2(tfacam)$_4$. Nucleophile was then added, under the conditions noted. The suspension was stirred vigorously at room temperature and monitored by TLC. The reaction mixture was filtered through a pad of Celite. The filter cake was rinsed with CH_2Cl_2 and the combined filtrates were evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (30 % ethyl acetate in hexane) as eluent to afford the desired oxathiazepane.

8-*O*-Allyl-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-aza-bicyclo[3.3.1]decane-3,3-dioxide (11c): Yield: 85 %; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.01 (m, 4H), 7.58 (m, 2H), 7.36 (m, 4H), 5.88 (m, 1H), 5.75 (ABX system, J_{AX} = 17.0, J_{BX} = 10.5, J_{AB} = 5.4 Hz, 1H), 5.55 (br d, J = 4.6 Hz, 1H), 5.32 (s, 1H), 5.17-5.05 (m, 3H), 4.97 (t, J = 7.4 Hz, 1H), 4.88 (dd, J = 11.5, 7.4 Hz, 1H), 4.75 (dd, J = 11.5, 7.4 Hz, 1H), 4.38 (dd, J = 12.4, 5.4 Hz, 1H), 4.08 (dd, J = 12.4, 5.4 Hz, 1H), 4.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.8, 165.4, 134.0, 133.5, 132.8, 130.0, 129.6, 129.2, 128.7, 128.5, 128.2, 118.2, 97.5, 76.5, 71.9, 69.6, 64.0, 62.7, 51.3; IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 1722, 1627, 1274 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{23}H_{22}NO_9S$: 488.1010 [M-H]$^+$; found: 488.1003.

8-*O*-Propargyl-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-aza-bicyclo[3.3.1]decane-3,3-dioxide (11d): Yield: 80 %; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.01 (m, 4H), 7.59 (m, 2H), 7.44 (m, 4H), 5.89 (m, 1H), 5.85 (br d, J = 4.5 Hz, 1H),

5.50 (s, 1H), 5.05 (m, 1H), 4.99 (t, J = 7.1 Hz, 1H), 4.88 (dd, J = 11.1, 7.5 Hz, 1H), 4.71 (dd, J = 11.1, 7.5 Hz, 1H), 4.39 (m, 2H), 4.00 (m, 1H), 2.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 165.8, 165.5, 134.1, 133.5), 130.0, 129.7, 129.1, 128.7, 128.5, 128.2, 96.4, 78.1, 76.4, 75.4, 72.0, 64.0, 62.6, 55.5, 51.3; IR ($CHCl_3$): $\tilde{\nu}$ = 2304, 2121, 1718, 1637 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{23}H_{21}NO_9SNa$: 510.0835 [M+Na]$^+$; found: 510.0883.

8-*O*-Ethyloxyallyloxy-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-aza-bicyclo[3.3.1]decane-3,3-dioxide (11e): Yield: 90 %; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm): 8.02 (m, 4H), 7.59 (m, 2H), 7.46 (m, 4H), 5.85 (br t, J = 3.2 Hz, 1H), 5.69 (ABX system, J_{AX} = 17.2, J_{BX} = 10.4, J_{AB} = 5.4 Hz, 1H), 5.37 (br d, J = 4.6 Hz, 1H), 5.31 (s, 1H), 5.12 (d, J = 17.2 Hz, 1H), 5.07 (d, J = 10.4 Hz, 1H), 5.04 (m, 1H), 4.96 (t, J = 7.3 Hz, 1H), 4.91 (dd, J = 11.1, 7.4 Hz, 1H), 4.78 (dd, J = 11.1, 7.4 Hz, 1H), 4.07 (m, 1H), 4.04 (m, 1H), 3.76 (m, 2H), 3.66 (m, 1H), 3.45 (m, 1H), 3.40 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm): 165.8, 165.3, 134.3, 133.9, 133.4, 129.9, 129.6, 129.2, 128.7, 128.4, 128.3, 117.1, 98.5, 76.6, 72.0, 68.7, 68.4, 64.1, 62.8, 51.1; IR ($CHCl_3$): $\tilde{\nu}$ = 3053, 1718, 1637 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{25}H_{27}NO_{10}SNa$: 556.1253 [M+Na]$^+$; found: 556.1225.

8-Benzylthio-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-aza-bicyclo[3.3.1]decane-3,3-dioxide (11g): Yield: 86 %; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm): 8.04 (m, 4H), 7.93 (s, 1H), 7.64 (m, 1H), 7.58 (m, 1H), 7.48 (m, 5H), 7.40 (m, 2H), 7.30 (m, 2H), 5.70 (m, 1 H), 5.61 (m, 1H), 5.15 (br s, 1H), 5.03 (d, J = 5.6 Hz, 1H), 4.91 (dd, J = 12.6, 1.7 Hz, 1H), 4.57 (dd, J = 5.6, 1.8 Hz, 1H), 4.44 (dd, J = 12.6, 1.7 Hz, 1H), 3.97 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm): 165.8, 165.0, 158.7, 134.3, 133.4, 129.9, 129.8, 129.2, 129.1, 128.8, 128.5, 127.7, 77.9, 66.7, 64.1, 61.3, 61.2, 36.0; IR ($CHCl_3$): $\tilde{\nu}$ = 3055, 1728, 1637, 1421 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{27}H_{25}NO_8S_2Na$: 578.0919 [M+Na]$^+$; found: 578.0912.

8-Azido-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-aza-bicyclo[3.3.1]decane-3,3-dioxide (11i): Yield: 76 %; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.04 (m, 4H), 7.60 (m, 2H), 7.46 (m, 4H), 5.93 (m, 1H), 5.73 (m, 1H), 5.37 (br d, J = 4.5 Hz, 1H), 5.18 (t, J = 7.28 Hz, 1H), 5.05 (m, 1H, H3), 4.87 (dd, J = 11.3, 7.3 Hz, 1H), 4.69 (dd, J = 11.3, 7.3 Hz, 1H), 3.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm):

165.9, 165.3, 134.3, 133.5, 130.0, 129.7, 128.9, 128.5, 86.1, 76.3, 72.0, 63.9, 63.3, 51.6; IR ($CHCl_3$): $\tilde{\nu}$ = 3053, 2125, 1722, 1637 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{20}H_{18}N_4O_8SNa$: 497.0743 $[M+Na]^+$; found: 497.0662.

9-*O*-Allyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-aza-bicyclo[4.2.2]decane-3,3-dioxide (12c): Yield: 94 %; white solid; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.07 (m, 4H), 7.60 (m, 2H), 7.46 (m, 4H), 5.95 (ABX system, J_{AX} = 16.1, J_{BX} = 10.6, J_{AB} = 5.5 Hz, 1H), 5.87 (dd, *J* = 6.1, 3.6 Hz, 1H), 5.63 (br s, 1H), 5.53 (d, *J* = 3.6 Hz, 1H), 5.35 (d, *J* = 16.1 Hz, 1H), 5.24 (d, *J* = 10.6 Hz, 1H), 5.12 (br d, *J* = 2.1 Hz, 1H), 4.73 (d, *J* = 12.5 Hz, 1H), 4.61 (dd, *J* = 12.5, 2.3 Hz, 1H), 4.43 (m, 1H), 4.36 (dd, *J* = 12.8, 5.1 Hz, 1H), 4.14 (dd, *J* = 12.8, 5.1 Hz, 1H), 4.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 166.0, 165.0, 133.9, 133.7, 133.5, 129.9, 128.9, 128.7, 128.6, 128.5, 117.7, 95.1, 76.5, 75.6, 72.0, 69.4, 68.6, 53.3; IR ($CHCl_3$): $\tilde{\nu}$ = 3053, 1720, 1602, 1452 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{23}H_{23}NO_9S$: 489.1088 $[M]^+$; found: 489.1095.

9-*O*-Propargyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-aza-bicyclo[4.2.2]decane-3,3-dioxide (12d): Yield: 89 %; white solid; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.08 (m, 4H), 7.61 (m, 2H), 7.47 (m, 4H), 5.84 (dd, *J* = 6.3, 3.2 Hz, 1H), 5.78 (br s, 1H), 5.53 (d, *J* = 3.2 Hz, 1H), 5.08 (br d, *J* = 3.6 Hz, 1H), 4.76 (d, *J* = 12.6 Hz, 1H), 4.63 (dd, *J* = 12.6, 2.4 Hz, 1H), 4.44 (m, 3H), 4.40 (m, 1H), 4.09 (m, 1H), 2.46 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 166.0, 165.0, 133.9, 133.7, 129.9, 128.8, 128.7, 128.5, 94.3, 78.4, 76.6, 75.5, 75.2, 72.0, 69.1, 54.6, 52.9; IR ($CHCl_3$): $\tilde{\nu}$ = 2304, 2150, 1637 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{23}H_{21}NO_9SNa$: 510.0835 $[M+Na]^+$; found: 510.0844.

9-*O*-Ethyloxyallyloxy-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-aza-bicyclo[4.2.2]decane-3,3-dioxide (12e): Yield: 95 %; white solid; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.07 (m, 4H), 7.60 (m, 2H), 7.46 (m, 4H), 5.89 (m, 2H), 5.67 (br s, 1H), 5.52 (d, *J* = 3.8 Hz, 1H), 5.29 (d, *J* = 17.2 Hz, 1H), 5.19 (d, *J* = 10.4 Hz, 1H), 5.13 (br d, *J* = 3.6 Hz, 1H), 4.72 (d, *J* = 12.5 Hz, 1H), 4.63 (dd, *J* = 12.5, 2.5 Hz, 1H), 4.44 (m, 1H), 4.10 (m, 1H), 4.02 (m, 2H), 3.97 (m, 1H), 3.79 (m, 1H), 3.65 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 166.1, 165.0, 134.5, 133.9, 133.7, 129.9, 128.9, 128.7, 128.6, 128.5, 117.2, 96.1, 76.7, 75.6, 72.2, 69.3, 68.9, 67.4, 53.3; IR

($CHCl_3$): $\tilde{\nu}$ = 3055, 1718, 1653 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{25}H_{27}NO_{10}SNa$: 556.1253 $[M+Na]^+$; found: 556.1262.

9-*O*-Ethylthio-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-aza-bicyclo[4.2.2]decane-3,3-dioxide (12f): Yield: 84 %; white solid; ^1H NMR (500 MHz, $CDCl_3$): δ (ppm): 8.06 (m, 4H), 7.59 (m, 2H), 7.45 (m, 4H), 6.23 (s, 1H), 5.94 (dd, *J* = 6.1, 4.1 Hz, 1H), 5.68 (d, *J* = 4.1 Hz, 1H), 5.18 (br d, *J* = 2.3 Hz, 1H), 4.80 (dd, *J* = 13.1, 3.8 Hz, 1H), 4.71 (dd, *J* = 13.1, 1.3 Hz, 1H), 4.47 (m, 1H), 4.16 (m, 1H), 2.88 (dt, *J* = 12.8, 7.4 Hz, 1H), 2.80 (dt, *J* = 12.8, 7.4 Hz, 1H), 1.37 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 166.3, 165.1, 134.0, 133.8, 130.0, 128.7, 128.5, 78.0, 77.2, 75.4, 72.0, 71.0, 55.3, 25.7, 14.7; IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 1722, 1627 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{22}H_{23}NO_8S_2Na$: 516.0763 $[M+Na]^+$; found: 516.0765.

9-*O*-Benzylthio-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-aza-bicyclo[4.2.2]decane-3,3-dioxide (12g): Yield: 83 %; white solid; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.03 (m, 4H), 7.59 (m, 2H), 7.45 (m, 4H), 7.33 (m, 5H), 6.07 (s, 1H), 5.94 (dd, *J* = 5.9, 4.8 Hz, 1H), 5.67 (d, *J* = 4.8 Hz, 1H), 5.05 (br d, *J* = 2.7 Hz, 1H), 4.79 (dd, *J* = 13.0, 3.6 Hz, 1H), 4.69 (dd, *J* = 13.0, 1.4 Hz, 1H), 4.47 (m, 1H), 4.04 (m, 1H), 4.03 (d, *J* = 13.2 Hz, 1H), 3.94 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 166.3, 165.0, 136.9, 134.0, 133.8, 130.0, 129.9, 129.0, 128.7, 128.6, 128.4, 127.5, 78.0, 76.8, 75.4, 72.0, 70.8, 54.7, 35.5; IR ($CHCl_3$): $\tilde{\nu}$ = 3055, 1718, 1653, 1421 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{27}H_{25}NO_8S_2Na$: 578.0919 $[M+Na]^+$; found: 578.0898.

9-(2-Methoxyphenylthio)-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-aza-bicyclo[4.2.2]decane-3,3-dioxide (12h): Yield: 78 %; colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm): 8.08 (m, 4H), 7.58 (m, 2H), 7.46 (m, 5H), 7.35 (m, 1H), 6.96 (m, 2H), 6.48 (s, 1H), 6.12 (dd, *J* = 5.7, 3.2 Hz, 1H), 5.67 (d, *J* = 5.7 Hz, 1H), 5.09 (br d, *J* = 2.8 Hz, 1H), 4.74 (m, 2H), 4.50 (m, 1H), 4.28 (m, 1H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm): 166.2, 164.9, 159.1, 135.2, 133.9, 133.7, 130.6, 130.0, 129.9, 128.7, 128.5, 121.3, 119.2, 111.3, 79.2, 78.3, 75.3, 72.0, 70.1, 55.9, 54.8; IR ($CHCl_3$): $\tilde{\nu}$ = 3053, 1718, 1637, 1452 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{27}H_{25}NO_9S_2Na$: 594.0868 $[M+Na]^+$; found: 594.0874.

9-Azido-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-aza-bicyclo[4.2.2]decane-3,3-dioxide (12i): Yield: 80 %; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.06 (m, 4H), 7.60 (m, 2H), 7.46 (m, 4H), 6.23 (s, 1H), 5.80 (dd, J = 5.2, 4.5 Hz, 1H), 5.60 (d, J = 4.5 Hz, 1H), 5.27 (br s, 1H), 4.76 (d, J = 12.8 Hz, 1H), 4.69 (dd, J = 12.8, 2.8 Hz, 1H), 4.58 (m, 1H), 3.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 166.0, 165.0, 134.1, 133.9, 130.0, 129.9, 128.7, 128.6, 128.3, 84.6, 78.0, 75.2, 71.7, 68.8, 52.6; IR ($CHCl_3$): $\tilde{\nu}$ = 3055, 2119, 1722, 1635 cm^{-1}; HRMS (ESI): *m/z*: calcd for $C_{20}H_{19}N_4O_8S$: 475.0918 $[M+H]^+$; found: 475.0899.

Optimization Condition of Rhodium-catalyzed Aziridination

Aiming at a reliably regio- and stereoselective glycosylation of sulfamate ester-derived glycal, we extensively investigated the utilization of iodosobenzene diacetate, [$PhI(OAc)_2$], alone or in the presence of base such as Al_2O_3, Cs_2CO_3, and MgO for the rhodium-catalyzed aziridination of glycal. Inspection of entries 1-4 in Table 1 revealed that the addition of base had influence on this reaction overcome. The reaction could proceed smoothly, fast, and high yield of glycosyl acetate **12** (Nu = OAc) when MgO was used. On the other hand, Al_2O_3, Cs_2CO_3, and no additives gave only low yield and sluggish reaction. Subsequent examination of reactions between **3**, MgO, and $PhI(OAc)_2$ in the presence of $Rh_2(OAc)_4$ under elevated temperatures and different solvents was performed. The $Rh_2(OAc)_4$-catalyzed aminoglycosylation of **3** would best carry out in dichloromethane at room temperature.

Table 1 Intramolecular aziridination of sulfamate glycal **3** with $PhI(OAc)_2$ catalyzed by $Rh_2(OAc)_4$ in various additives, temperatures, and solvents [a]

Entry	Additive	Solvent	Temperature (°C)	Time (h)	% Yield [b]
1	-	CH_2Cl_2	RT	36	67
2	Al_2O_3	CH_2Cl_2	RT	27	27
3	Cs_2CO_3	CH_2Cl_2	RT	24	34
4	MgO	CH_2Cl_2	RT	5	82
5	MgO	CH_2Cl_2	40 °C	3.5	71
6	MgO	CH_2Cl_2	60 °C	2	56
7	MgO	Toluene	RT	18	14 (21) [c]
8	MgO	CH_3CN	RT	18	22 (55) [c]
9	MgO	Et_2O	RT	18	No reaction

[a] Sulfamate glycal **3** (69 mmol) was treated with $Rh_2(OAc)_4$ (5 mol%), $PhI(OAc)_2$ (1.5 equiv), additive (5 equiv), and solvent (3 mL) in the presence of 4Å molecular sieve. [b] Isolated Yield. [c] Yield in parentheses denotes conversion.

Preliminary efforts to couple the glycal substrates with an exogeneous nucleophile were encountered with limitation of $PhI(OAc)_2$. Due to the in situ generation of a reactive acetate residue from $PhI(OAc)_2$, an excess amount of nucleophile was needed to suppress the attack of AcO^- (entries 1-2, Table 2). Consequently, the use of either PhIO or $[Rh_2(tfacam)_4]$ was examined (entries 3-6, Table 2). Not only the lower equivalents of nucleophile could be applied, but also the higher yield as well as the shorter reaction time could be achieved.

Table 2 Optimized condition for aminoglycosylation of **2** and **3** [a]

Entry	Substrate	Catalyst	Oxidant	MeOH (equiv)	Time (h)	% Yield [b]
1	**2**	$Rh_2(OAc)_4$	$PhI(OAc)_2$	20	2	91
2	**3**	$Rh_2(OAc)_4$	$PhI(OAc)_2$	20	3.5	96
3	**2**	$Rh_2(OAc)_4$	PhIO	2	0.5	75
4	**3**	$Rh_2(OAc)_4$	PhIO	2	1	78
5	**2**	$Rh_2(tfacam)_4$	PhIO	2	1	82
6	**3**	$Rh_2(tfacam)_4$	PhIO	2	2	93

[a] Unless otherwise noted, the reaction was carried out at room temperature by using substrate (69 mmol), 5 mol% of rhodium catalyst, hypervalent iodine (1.5 equiv), MgO (5 equiv), and CH_2Cl_2 (3 mL) in the presence of 4 Å MS.
[b] Isolated Yield.

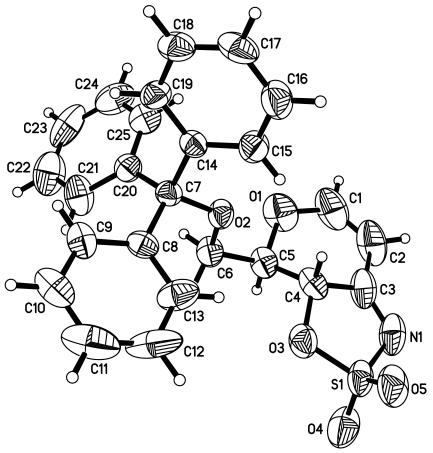

Figure 1. X-ray structure of Compound **10**. The possibility chosen for the ellipsoids in the ORTEP plot is 50%

The structure and absolute stereochemistry of compound **10** was identified as ethanol solvate. The asymmetric unit has one molecule of compound **10** in a general position and half of two molecules of ethanol [C26-C27-O6] lying about a twofold axis (Table 3).

Table 3 Crystal data and structure refinement for compound **10**

Identification code	Compound **10**	
Empirical formula	C26 H24 N O5.50 S	
Formula weight	470.52	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 28.5943(12) Å	$\alpha = 90^{\circ}$.
	b = 9.1264(4) Å	$\beta = 90.748(2)^{\circ}$.
	c = 9.5011(4) Å	$\gamma = 90^{\circ}$.
Volume	2479.22(18) $Å^3$	
Z	4	
Density (calculated)	1.261 Mg/m^3	
Absorption coefficient	0.168 mm^{-1}	

F(000)	988
Crystal size	0.28 x 0.24 x 0.20 mm^3
Theta range for data collection	2.14 to 27.15°.
Index ranges	-36<=h<=36, -11<=k<=11, -12<=l<=12
Reflections collected	14828
Independent reflections	5416 [R(int) = 0.0459]
Completeness to theta = 27.15°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9671 and 0.9543
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5416 / 15 / 316
Goodness-of-fit on F^2	1.103
Final R indices [I>2sigma(I)]	R1 = 0.0700, wR2 = 0.2025
R indices (all data)	R1 = 0.0814, wR2 = 0.2216
Absolute structure parameter	0.02(12)
Largest diff. peak and hole	0.779 and -0.321 e. $Å^{-3}$

Computational Details for Mechanistic Studies

All DFT calculations were carried out using B3LYP functional. Effective core potentials (ECP) with double-zeta valence basis (LANL2DZ)[1,2] were used for rhodium, whereas, LANL2DZ basis augmented with an additional p and d polarization function, with exponents, 0.00308 and 0.29400, respectively, were used for iodine.[3] The standard 6-31G(d) basis set was used for H, C, N, O and S. This combination of basis sets is denoted as BSI. The gas phase calculations for the complexes involved in the azridination reaction for sulfamate glycal **2**, including their optimizations, were carried out using BSI. For complexes of diradical nature, the unrestricted DFT calculations with keyword, "guess=mix" in Gaussian 03 package[4] were used with the initial orbital guess in triplet state. In case of singlet diradical calculations, we found the $<S^2>$ values after annihilation to be less than 0.1, indicating negligible spin contamination.

Solvent effect plays an important role in such reactions. We therefore use the polarizable continuum model (PCM) to study these effects.[5] BSIII basis was used for all calculations with solvent effect. In BSIII we replace the 6-31G(d) basis for H, C, N, O and S, by 6-311+G(d, p). Solvent effect using BSIII on glycal aziridination reaction for **1**, **2** and **3** optimized using BSI basis were also studied. Since, re-optimizations using BSIII are expensive, only single point calculations were performed for structures optimized at lower basis for the above cases. Calculations including solvent effect were done for dicholoromethane (DCM) with a dielectric constant of 8.93, at 298K.

We confirmed all stationary structures to be a true minimum or saddle point by the harmonic frequency calculations. The transition states found were further confirmed by the intrinsic reaction coordinate (IRC) calculations,[6] where they have shown to connect the relevant reactants to their products.

For convenience we have labelled each of the complexes along the reaction pathway, followed by the series number in parenthesis. The series number has been given based on the position of the *–OSO$_2$N* group on the carbon skeleton of the sugar ring. $(HCOO)_4Rh_2$ (**[Rh$_2$]**) was used to be a model of the rhodium catalyst used in the experiments. All protecting groups on sugar rings were replaced by the acetyl group [$CH_3C(O)$] for calculations.

Selected Bond Distances

The variations in selected bond lengths of the complexes involved in aziridination reaction as computed from DFT/B3LYP calculations are tabulated in Table 4. These variations in bond length in addition to chemical intuition supplement in understanding the reaction mechanism based on the relative energies of the complexes involved in the reaction pathway.

Table 4 Selected bond distances (Å) for complexes involved in the aziridination

Complex[a]	**Bond Length** (Å)	
	N-C1	N-C2
17 (**1**)	2.038	2.547
17 (**2**)	2.035	2.611
17 (**3**)	2.124	2.687
18 (**1**)	1.508	2.448
18 (**2**)	1.497	2.509
18 (**3**)	1.504	2.485

[a] The number in parenthesis was given based on the position of the *–OSO_2N* group on the sugar ring.

Transition States

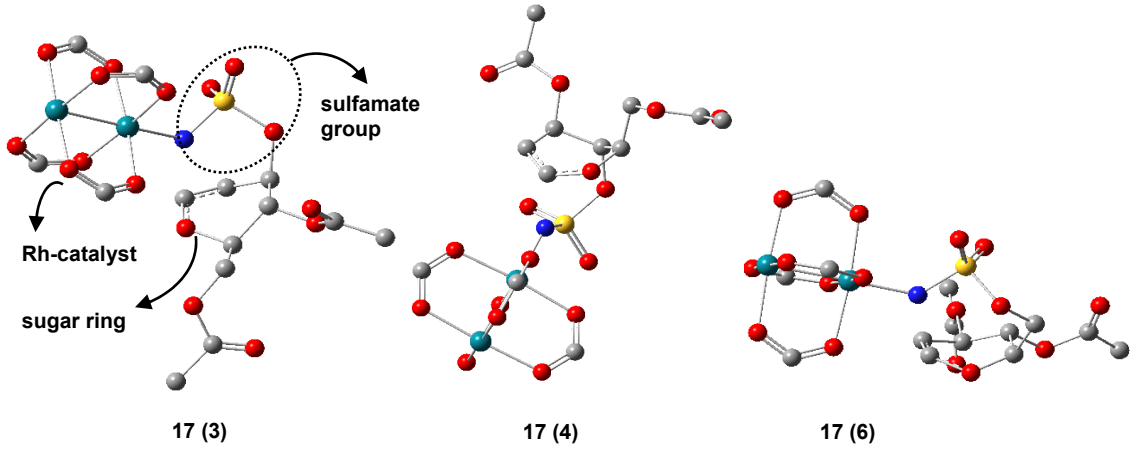

Figure 1. Transition state **17** in the aziridination step for sulfamate glycals **1**, **2**, and **3**

A new six-membered ring was formed in **17** (**3**) as seen in Figure 1. The atoms C1, C2 and C3 now belong to the new ring as well as the sugar ring. This framework makes an aziridine ring more rigid. It thus becomes difficult to adjust the relative position of C3. The attack of N to C1 forced C3 to move upward causing a twist in the sugar ring. This leads to a lot of strain in the sugar ring. There is also a large repulsion between the sulfamate group and sugar ring owing to the shortest distance of 2.599Å in **17** (**3**)**,** which is much shorter than that in **17** (**4**) and **17** (**6**). An added repulsion between the *–CH_2OAc* group at the equatorial C5 position and the bulky catalyst cannot be ignored either. In **17** (**6**), a new seven-membered ring is formed with the *N–C1* bond length of 2.124Å. In this case, the atoms C1, C2 and O, lead to the rigidity in both rings. **17** (**6**) has less activation energy as compared to **17** (**3**), this can be attributed to the relaxation in the structure due to the presence of a longer chain at C6. Thus it requires less conformational changes in the sugar ring due to increase in the distance between the sulfamate ester group and the sugar ring. The shortest distance of 3.216 Å is noted between the S atom and the sugar ring in **17** (**6**). In comparison to **17** (**3**) and **17** (**6**), the ring structure in **17** (**4**) is more flexible as the C4 atom is not directly connected to the rigid atoms C1 and C2. Thus, the sugar ring in **17** (**4**) has a clear boat conformation. The sulfamate side chain can thus easily elongate to facilitate the anchoring of N atom to C1 in the sugar ring without significant conformational changes in the skeletal framework. Thus **17** (**4**) has the

least structural strain among the three series, which in turn is reflected in its lowest barrier for N delivery.

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