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Stereocontrolled Intramolecular Aziridination of Glycals: Ready Access to Aminoglycosides and Mechanistic Insights from DFT Studies

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Abstract: Stereocontrolled intramolecular aziridination of the glycal-derived sulfamates offers a highly efficient strategy to divergently prepare aminoglycosides. Rhodium-catalyzed nitrogen-atom transfer to C=C bonds formed semistable aziridines, which were subjected to various nucleophiles (C, O, S, and N) to give cyclic sulfamate-containing aminosugar derivatives selectively. The second nucleophilic displacement of sulfonyloxy moieties of [1,2,3]-oxathiazepane-2,2-dioxides allows straightforward access to aminoglycosides with selective α- or β-linkages. This approach is operationally simple, complements existing methods, and is a versatile protocol for the synthesis of polyfunctionalized amino sugars. In addition, the mechanism of the rhodium-catalyzed intramolecular aziridination of glycals and its ring-opening reaction was extensively studied by using DFT calculations.

Keywords: aminoglycosides · aziridine · density functional calculations · oxathiazepane · rhodium · ring-opening reactions

Introduction

Aminoglycosides have attracted growing interest, especially concerning the modification and development of efficient syntheses due to their broad spectrum of applications in the chemistry, medicine, and pharmaceutical fields. Amino sugars play crucial roles for the biological activity of aminoglycoside antibiotics and aminoglycoside-containing natural products.[1,2] 2-Amino sugars are also major structural elements of glycosaminoglycans, such as heparan sulfates and chondroitin sulfates, which are implicated in cell division, neuronal development, angiogenesis, blood coagulation, inflammation, tumor progression, and microbial and viral infection.[3]

To date, the advancement of new methods for selective intramolecular C–N bond formation is elegantly highlighted as a powerful strategy in the asymmetric synthesis of aminoglycosides.[4–7] Among the most currently studied methods are metal-catalyzed intramolecular aziridination and nitrene transfer to C–H bonds. Recently, the groups of Du Bois and Che have independently reported that the formation of aryliodinanes and the insertion of metallonitrenoids into C=C or C–H bonds can be conducted with a one-pot procedure.[8–11] This methodology has been successfully used for the synthesis of natural aminoglycoside frameworks. For example, Rojas showed the use of copper and rhodium catalysts in amidoglycosylation reactions of D-allal-derived carbamates to furnish 2-aminoglycosylated products.[12] However, not many glycal acceptors have been applied in this scaffold so far. We report herein a novel method for nitrogen transfer that allows ready access to natural and unnatural mono-, di-, and tri- aminoglycosides with various amination patterns and stereochemistry.

We envisioned the efficient synthesis of these functionalized aminoglycosides by the flexible installation of a sulfamate ester on the C6 position of a glycal substrate. This offers an exciting approach to α-selective amidoglycosylation through nitrogen atom delivery to a π-bond system on the top face of a glycal scaffold as shown in Equation (1). A regio- and stereospecific ring-opening reaction of the aziridine with nucleophiles would simultaneously achieve the formation of [1,2,3]oxathiazepane-2,2-dioxides with α-linkages. The second nucleophilic replacement of sulfonyloxy

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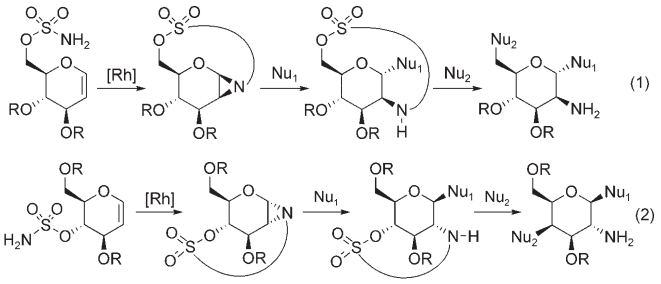
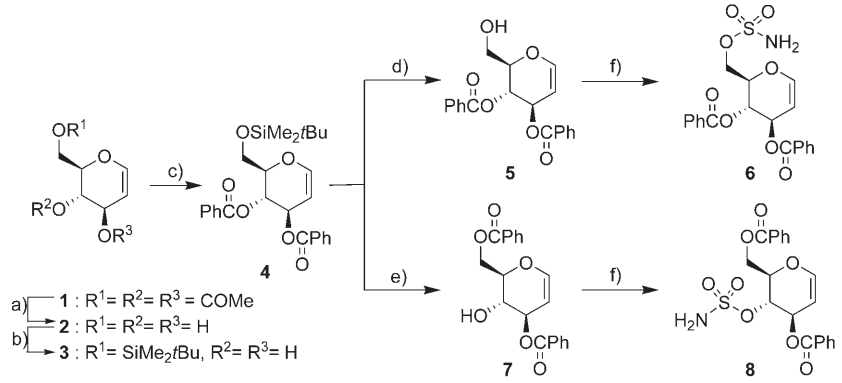
moieties allows ready access to unusual aminoglycosides. In turn, the facial preference on the bottom face of this glycal scaffold could be elaborated by introducing the sulfamate moiety on C4, which gives an opportunity to produce functionalized β-linked 2-amino sugars [Eq. (2)].



Results and Discussion

To evaluate the potential of this hypothesis, we first performed a model study on sulfamate glycals **6** and **8**, which were synthesized from readily available tri-*O*-acetyl-D-glycal in four steps (Scheme 1).[13] Treatment of tri-*O*-acetyl-D-glycal (**1**) with sodium methoxide in dry MeOH provided **2**, which was selectively protected with *tert*-butyldimethylsilyl chloride (TBDMSCl) to give **3**, and benzoyl chloride (BzCl) to give **4**. The TBDMS protecting group in **4** was independently cleaved by a catalytic amount of *p*-toluene sulfonic acid to provide **5**,[14] whereas treatment with tetra-*n*-butylammonium fluoride (TBAF) was used to provide **7** through a rearrangement of a benzoyl group.[15] Conversions of the primary and secondary alcohols **5** and **7** were carried out by using sulfamoyl chloride, which was generated in situ from chlorosulfonyl isocyanate and formic acid, and produced sulfamates **6** and **8** in good yields.[16]



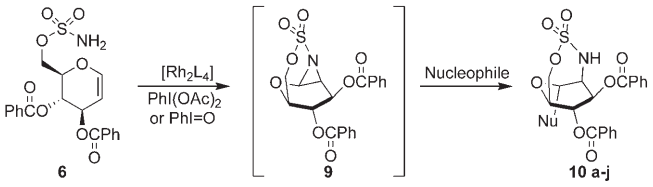
Scheme 1. Preparation of sulfamate-protected glycals. a) NaOMe, MeOH, RT, 2 h, quantitative; b) TBDMSCl, imidazole, DMF, 0 °C to RT, 8 h, 80 %; c) BzCl, DMAP, pyridine, 0 °C to RT, 6 h, 90 %; d) *p*-TSOH, THF/H_2O 10:1, 8 h, 80 %; e) 1 M TBAF, THF, RT, 15 h, 91 %; f) $ClSO_2NCO$, HCO_2H, DMA, 0 °C, 3 h, 83 % from **5**, and 94 % from **7**.

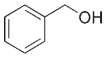
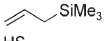
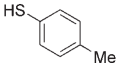
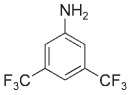
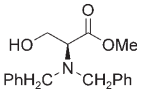
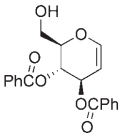
Initially, we had investigated the use of iodosobenzene diacetate ($PhI(OAc)_2$) and catalytic dirhodium(II) carboxylates for the intramolecular aziridination of olefins by starting from sulfamates.[17] Sulfamate glycal **6** was treated with $PhI(OAc)_2$, MgO, and 10 mol % of $[Rh_2(OAc)_4]$ in dichloromethane. The amidoglycosylation reaction proceeded smoothly at room temperature to furnish the glycosyl acetate **10a** in good yield (Table 1, entry 1). Presumably, the aziridine intermediate **9** could not be isolated due to the high reactivity of C1 and the inherent ring strain. The semistable aziridine was simultaneously trapped by an internal acetoxy group in regio- and stereospecific manners. The structure and stereochemistry of the acetate **10a** was determined through NMR spectroscopic experiments (^1H, ^{13}C, DEPT, COSY, HMQC, NOESY).

Alcohols could also be included in the reaction mixture, and this led directly to alkoxylated glycoside derivatives in a single step, but an excess amount of alcohol (up to 20 equiv) was needed to suppress the formation of the glycosyl acetate (Table 1, entries 2–5). The lower yields of coupled products in entries 4 and 5 were most probably due to the attack of a reactive acetoxy species. We then proceeded to investigate the origin of the acetoxy group by replacing the iodosobenzene diacetate with iodosylbenzene (PhIO). Methanol was used as an external nucleophile for this case study. It was found that the glycosyl acetate was not observed on TLC and, moreover, the amount of methanol that was required could be reduced, which implies that the acetoxy group comes from the decomposition of $PhI(OAc)_2$.

Attempts were made to expand the scope of glycosylation to other nucleophiles, such as alkyl, thiol, amine, amino acids, and monosaccharides. Unfortunately, these nucleophiles failed to attack the C1 atom of the aziridine intermediate when catalytic amounts of $[Rh_2(OAc)_4]$ and $PhI(OAc)_2$ were used. Under these conditions, only glycosyl acetate, unreacted nucleophile, and decomposed mixtures were detected. Another choice for the specific aziridination and its ring-opening was inspired by Du Bois.[17c] A rhodium trifluoroacetamide ($[Rh_2(tfacam)_4]$) was able to effectively catalyze the amination of unsaturated sulfamate ester.[18] $[Rh_2(tfacam)_4]$ could prolong the lifetime of the aziridine intermediate, which was able to couple with various nucleophiles.[19] In the presence of PhIO, MgO, and $[Rh_2(tfacam)_4]$, the iminoiodinane intermediate could be generated in situ by reaction of the sulfamate substrate and iodosylbenzene, followed by Rh-catalyzed intramolecular aziridination. A glycal acceptor was injected into the reaction mixture within 15 minutes to trap the semistable aziri-

Table 1. Regio- and stereoselective aziridination of **6** and α-selective glycosylation.



Entry	Nucleophile (NuH)	Product	Yield [%][d]
1[a]	AcO^-	**10a**	82
2[a]	MeOH	**10b**	81
3[a]	EtOH	**10c**	90
4[a]	*i*PrOH	**10d**	70
5[a]		**10e**	71
6[b,c]		**10f** (Nu = allyl)	78
7[b,c]		**10g**	85
8[b]		**10h**	76
9[b]		**10i**	66
10[b]		**10j**	68

[a] Reaction was treated with 10 mol% of $[Rh_2(OAc)_4]$, $PhI(OAc)_2$ (1.5 equiv), MgO (5 equiv), and nucleophile in the presence of 4 Å MS in CH_2Cl_2 at RT. [b] Reaction was treated with 10 mol% of $[Rh_2(tfacam)_4]$, PhI = O (1.5 equiv), MgO (5 equiv) in the presence of 4 Å MS in CH_2Cl_2 at RT for 15 min, and then the nucleophile was added dropwise. [c] Nucleophile and 0.5 equiv of $BF_3{\cdot}OEt_2$ were added at −78 °C and then warmed to RT for 2–3 h. [d] % Isolated yield.

dine; this provided the desired oxathiazepane (Table 1, entries 6–10). In the cases of trimethylallylsilane[20] and *p*-thiocresol[6a] as nucleophiles, the glycosylation step required activation by a Lewis acid, $BF_3{\cdot}OEt_2$. Even though moderate yields of glycosylated products were obtained due to the instability of the aziridine intermediate in reaction mixture, we were successful in the synthesis of the diamino sugar, the disaccharide as well as other functionalized 2-amino sugars in a convenient one-step process.

Notably, the internal nitrogen transfer to the π-system, and the nucleophilic addition of our sulfamate-protected glycal scaffold at C1 is the facially selective version of a previously reported reaction that produces α-selective glycosylated products.[21] A X-ray crystallographic study of a glycosyl methoxide **10b** confirmed the diaxial conformation of oxathiazepane ring and the *trans*-stereochemistry between the *N*-sulfonyloxy moiety and the methoxy group (Figure 1). This observation allowed us to propose that a transient aziridine intermediate **9** exists in the reaction mixture by direct nitrogen delivery on the upper face of the molecule, and this subsequently fosters the nucleophilic attack on the opposite face. This proposed mechanism is further supported by DFT calculations, as detailed in the Computational Studies section.

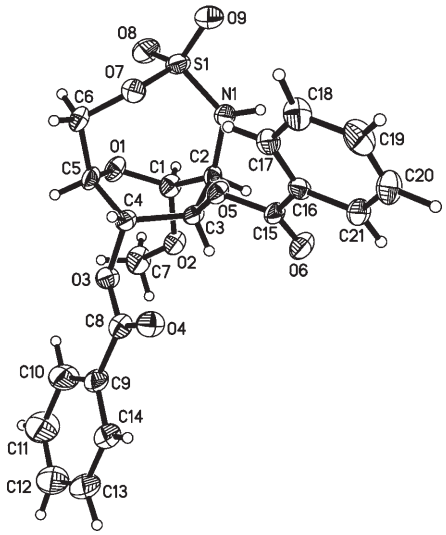
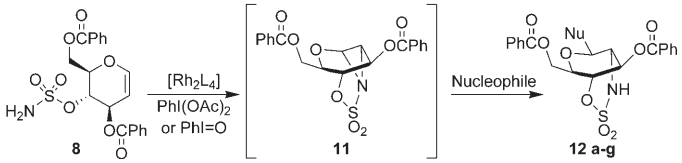


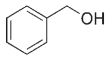
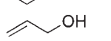
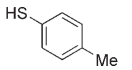
Figure 1. X-ray structure of aminoglycosyl methoxide **10b**.

Likewise, these extraordinary features could be applied to sulfamate glycal **8**. This substrate nicely underwent a nitrogen atom delivery to the C=C bond from the bottom face, and led to β-aminoglycoside derivatives **12a–g**, via specific ring-opening at the positively charged anomeric carbon; this reaction gave moderate-to-excellent yields (Table 2).

Finally, we sought to access unusual amino sugars by a ring-opening reaction at the carbon atom that bears the sul-

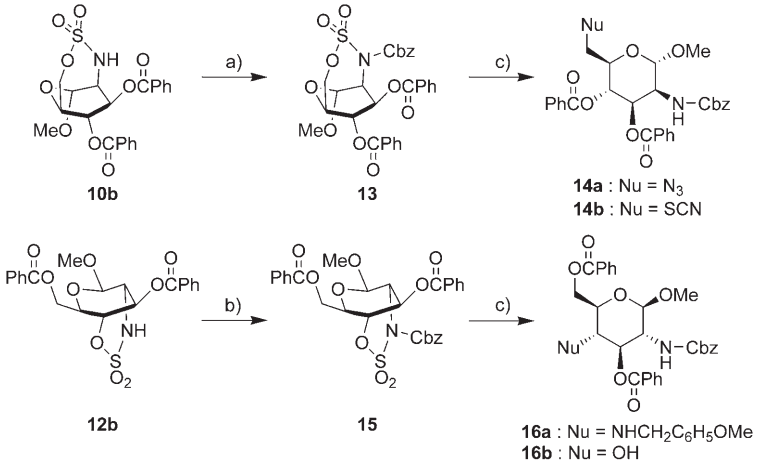
Table 2. Regio- and stereoselective aziridination of **8** and β-selective glycosylation.



Entry	Nucleophile (NuH)	Product	Yield [%][c]
1[a]	AcO^-	**12a**	73
2[a]	MeOH	**12b**	96
3[a]	EtOH	**12c**	87
4[a]	*i*PrOH	**12d**	86
5[a]		**12e**	77
6[a]		**12f**	81
7[b]		**12g**	78

[a] Reaction was treated with $[Rh_2(OAc)_4]$ (10 mol%), $PhI(OAc)_2$ (1.5 equiv), MgO (5 equiv), and nucleophile in the presence of 4 Å MS in CH_2Cl_2 at RT. [b] Reaction was treated with $[Rh_2(tfacam)_4]$ (10 mol%), PhI=O (1.5 equiv), MgO (5 equiv) in the presence of 4 Å MS in CH_2Cl_2 at RT for 30 min, and then *p*-thiocresol as well as 0.5 equiv of $BF_3{\cdot}OEt_2$ were added subsequently at −78 °C, then warmed to RT for 2 h. [c] % Isolated yield.

famate function.[22] The methoxyoxathiazepane **10b** was selected to be a model compound for this reaction study. We had tried to introduce a second nucleophile on the sulfamate moiety without protection of the amino group of oxathiazepane. Unfortunately, none of the desired products were observed when it was treated with *N*-nucleophiles (such as NaN_3, K-phathalimide, and benzylamine) in refluxing DMF. Only starting material and trace amounts of unidentified compounds were detected. This presumably resulted from the reduced electrophilic activity of the eight-membered oxathiazepane. Accordingly, the electron-withdrawing carboxybenzyloxy (Cbz) group was introduced at the nitrogen atom to give **13** (Scheme 2). Treatment of **10b** with benzyl chloroformate (CbzCl) and a catalytic amount of 4-dimethylaminopyridine (DMAP) in Et_3N and THF afforded *N*-Cbz-protected product **13** in excellent yield. This preliminary result suggested that the oxathiazepane **12b** should be derivatized with CbzCl. Under the same conditions as **13**, the *N*-Cbz product **15** was obtained in a low yield (40%), but by changing the base from Et_3N to $NaHCO_3$, we managed to boost the yield to 82% (Scheme 2).



Scheme 2. Ring-opening reaction of *N*-Cbz oxathiazepanes. a) CbzCl, DMAP, Et_3N, THF, 0°C to RT, 92%; b) CbzCl, $NaHCO_3$, THF/H_2O 1:1, 0°C to RT, 82%; c) nucleophiles.

The nucleophilic displacement of a sulfonyloxy moiety of **13** and **15** was subsequently achieved by treating with NaN_3, KSCN, *p*-methoxybenzylamine, and H_2O to give rise to the corresponding coupled products in moderate-to-good yields as summarized in Table 3.

Table 3. Nucleophilic ring-opening reaction of oxathiazepanes **13** and **15**.

Entry	Starting material	Reaction conditions	Yield [%][a]
1	**13**	NaN_3/DMF/120°C	67
2	**13**	KSCN/DMF/150°C	78
3	**15**	$NH_2CH_2C_5H_6OMe$/DMF/70°C	75
4	**15**	H_2O/K_2CO_3/Acetone/RT	80

[a] % Isolated yield.

Computational studies: To gain a more detailed understanding of the pathways of rhodium-catalyzed intramolecular aziridination and ring-opening, computational studies were carried out by employing density functional theory (DFT) calculations on a simplified model system. As depicted schematically in Figure 2, our proposed mechanism involves three main steps:

I) The Rh–Nitrene complex (Rh–N) was generated by a rhodium-catalyzed elimination of the IPh moiety from iminoiodinane (Sub). Our calculation demonstrated that the Rh catalyst binding to Sub is energetically favorable ($\Delta G = -5.7$ kcal mol^{-1}) and is further stabilized by the departure of the IPh moiety ($\Delta G = -7.3$ kcal mol^{-1}). This complex initially exists in the singlet state and then rapidly relaxes to the even more energetically favorable triplet state.[8a] The triplet state of the Rh–nitrene complex is 9.7 kcal mol^{-1} lower than the singlet state.

II) The formation of the catalyst-bound aziridine (Rh–Azi): we attempted to search for transition states from both Rh–N(S) and Rh–N(T), and only one transition state (TS1) was found on the triplet potential-energy surface. The calculated free energy of TS1 is about 1 kcal mol^{-1} lower than Rh–N(S), hence even if the transition state on the singlet potential-energy surface can be located, our proposed reaction, which starts from triplet Rh–N(T) should still be energetically more favorable. By starting from TS1, we have located an intermediate INT(T) with an established N−C1 bond by using the intrinsic-reaction-coordinate (IRC) method[23] on the triplet potential energy surface. The bond length of N···C1 (2.124 Å) is significantly shorter than that of N···C2 (2.687 Å) in the TS1 structure. Not surprisingly, the N−C1 bond is more likely formed than the N−C2 bond because the C1 atom carries more positive charge due to the neighboring oxygen atom. To form the singlet Rh–Azi, INT(T) needs to undergo an intersystem crossing (ISC), which is enhanced by the heavy atom effect of Rh. Therefore, we carried out geometry optimization on the singlet potential energy surface by using INT(T) as an initial structure, and found that singlet Rh–Azi can be easily derived by following this route. Our DFT computational results agreed with the mechanism that Brandt proposed for the copper-catalyzed aziridination.[24]

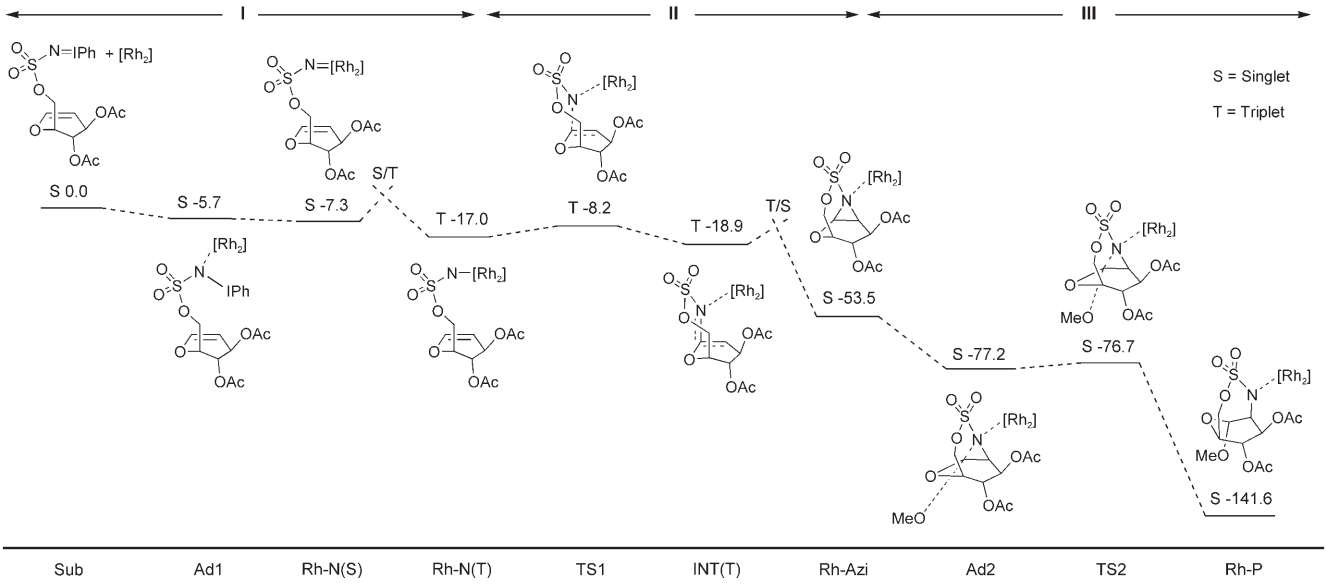


Figure 2. Computed Gibbs free energy profiles of the model system at 298 K, ΔG (kcal mol^{-1}). The substrate (Sub) in our model system was obtained by substituting the phenyl groups in **6** with methyl groups. The catalyst $[Rh_2(OAc)_4]$ was simplified by replacing the methyl groups with hydrogen atoms. Ad1 = the adduct of Sub–$[Rh_2]$; Rh–N = Rh–nitrene; TS1 = the transition state to form N–C1 bond in the triplet state; INT(T) = the intermediate with a N–C in triplet state; Rh–Azi = catalyst-bound aziridine; Ad2 = the adduct of aziridine ring opening by OMe; and TS2 = the transition state to form the catalyst-bound product (Rh-P).

III) Aziridine ring-opening by nucleophile (MeO^-): The transition states of nucleophilic ring-opening by MeO^- have been optimized. The overall process is exothermic. When MeO^- approaches the C1 position, the initial complex Ad2 is formed ($\Delta G = -77.2$ kcal mol^{-1}, and C1···OMe = 2.818 Å), followed by the transition state TS2. The low activation energy of TS2 ($\Delta E =$ 0.5 kcal mol^{-1}) agrees well with the fact that the aziridine intermediate is a transient (semistable) species that could not be isolated in our experiment. This calculated result is also in-line with the regio- and stereochemistry of our product. The nucleophile, MeO^- approaches the positively charged C1 of the Rh–Azi ring system from the bottom face preferably, to form the *trans* product (α-glycosylation product). Furthermore, C1–N bond is partially cleaved (C1–N = 1.654 Å in TS2) even when MeO^- is still 2.592 Å away from C1. The reaction coordinate of TS2 involves the simultaneous breaking of the N–C1 bond, and the formation of glycosidic C1–OMe bond, which also reflects the high activity of Rh–Azi upon the attack of MeO^-.

Conclusion

We have described a new route to aminoglycosides that is based on the intramolecular oxidative aziridination on a glycal scaffold, followed by an efficient ring-opening of aziridine with various nucleophiles (C, O, S, and N). The second nucleophilic replacement of the sulfonyloxy moieties of [1,2,3]oxathiazepane-2,2-dioxides allows ready access to unusual aminoglycosides with selective α- and β-linkages. With the concept described here, the intramolecular nitrogen atom transfer to a C=C bond on the glycal scaffold is highlighted as an attractive alternative to conventional methods of 2-aminoglycoside synthesis. In addition, a variety of glycal acceptors has selectively been coupled at the anomeric position, which results in the high structural and functional group variability of carbohydrate substrates. This series of glycal glycosylations can be applied in the chemical synthesis of highly complex aminosaccharide conjugates.

A DFT computational study was undertaken to better understand the mechanism of rhodium-catalyzed intramolecular aziridination as well as regio- and stereoselective aziridine ring-opening. Our results demonstrate that the nitrene-transfer and aziridination reactions proceed stepwise to form semistable aziridine intermediates, which are regioselectively attacked by nucleophiles at the positively charged anomeric carbons. Significantly, the facial preference, which is controlled by the substrate was found to be the key factor that determines the stereoselectivity.

Application of this new methodology to asymmetric and total synthesis is currently under active investigation in our laboratory.

Experimental Section

General: Unless otherwise noted, all reactions were carried out in oven-dried glassware under an atmosphere of nitrogen, and distilled solvents were transferred by syringe. Solvents and reagents were purified according to standard procedures 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 accom-

plished using silica gel 60 (0.010–0.063 nm). Technical grade solvents were used for chromatography and were distilled prior to use. 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. The residual solvent signals were taken as the reference (7.26 ppm for ^{1}H NMR spectra and 77.0 ppm for ^{13}C NMR spectra). Chemical shift (δ) is reported in ppm, coupling constants (J) are given in Hz. The following abbreviations classify the multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, br = broad signal. Infrared spectra were recorded on a Bio-RAD FTS 165 FT-IR spectrometer and reported in cm^{-1}. Samples were prepared by using the thin film technique. HR-MS (ESI) spectra were recorded on a Finnigan/MAT LCQ quadrupole ion trap mass spectrometer, coupled with the TSP4000 HPLC system and the Crystal 310 CE system. X-ray crystallographic data was collected by using a Bruker X8 Apex diffractometer with $Mo_{K\alpha}$ radiation (graphite monochromator).

General procedure for sulfomylation of 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 min at 0 °C, during which time the mixture solidified. Dry CH_3CN (10 equiv) was added, and the resulting clear solution was stirred for 1 h at 0 °C, then 6 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 dropwise. The reaction was stirred at 0 °C over a 3 h period, 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 (eluent: 30% ethyl acetate in hexane) afforded the desired sulfamate ester.

(2*R*,3*S*,4*R*)-2-Sulfamoyloxymethyl-3,4-dihydro-2*H*-pyran-3,4-diyldibenzoate (6): Yield: 83%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (m, 4H; Ph), 7.56 (m, 2H; Ph), 7.42 (m, 4H; Ph), 6.57 (d, J = 6.1 Hz, 1H; H1), 5.71 (br s, 2H; H3 and H4), 5.14 (br s, 2H; NH_2), 5.10 (d, J = 6.1 Hz, 1H; H2), 4.56 (m, 2H; H5 and CH_2), 4.46 ppm (d, J = 8.2 Hz, 1H; CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.8 (CO), 165.5 (CO), 145.5 (C1), 133.8 (Ph), 133.4 (Ph), 129.9 (Ph), 129.7 (Ph), 129.3 (Ph), 128.7 (Ph), 128.6 (Ph), 128.5 (Ph), 99.2 (C2), 73.6 (C5), 67.6 (C4), 67.5 (CH_2), 67.3 ppm (C3); IR ($CHCl_3$): $\tilde{\nu}$ = 3421, 3288, 3018, 1718, 1649, 1377 cm^{-1}; HR-MS (ESI): *m/z*: calcd for $C_{20}H_{18}NO_8S$: 432.0748 $[M-H]^+$; found: 432.0733.

(2*R*,3*S*,4*R*)-3-Sulfamoyloxy-3,4-dihydro-2*H*-pyran-2-benzoyloxymethyl-4-yl-benzoate (8): Yield: 94%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (m, 4H; Ph), 7.57 (m, 2H; Ph), 7.40 (m, 4H; Ph), 6.56 (d, J = 6.1 Hz, 1H; H1), 5.70 (dd, J = 4.1, 3.6 Hz, 1H; H3), 5.49 (br s, 2H; NH_2), 5.16 (t, J = 5.5 Hz, 1H; H4), 4.98 (dd, J = 6.1, 3.6 Hz, 1H; H2), 4.77 (dd, J = 13.0, 6.9 Hz, 1H; CH_2), 4.59 ppm (m, 2H; H5 and CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.4 (CO), 166.3 (CO), 146.2 (C1), 133.6 (Ph), 133.4 (Ph), 129.8 (Ph), 129.7 (Ph), 129.2 (Ph), 129.1 (Ph), 128.5 (Ph), 128.4 (Ph), 98.0 (C2), 74.3 (C4), 73.7 (C5), 67.4 (C3), 61.5 ppm (CH_2); IR ($CHCl_3$): $\tilde{\nu}$ = 3385, 3275, 3020, 1718, 1647, 1382 cm^{-1}; HR-MS (ESI): *m/z*: calcd for $C_{20}H_{18}NO_8S$: 432.0748 $[M-H]^+$; found: 432.0729.

General procedure for rhodium-catalyzed aziridination with actetoxy as a nucleophile: A mixture of sulfamate ester (1 equiv), $[Rh_2(OAc)_4]$ (10 mol%), $PhI(OAc)_2$ (1.5 equiv), MgO (5 equiv), and 4 Å molecular sieves in dry CH_2Cl_2 (2 mL) was stirred at room temperature. The reaction was monitored by TLC. The suspension 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 (eluent: 30% ethyl acetate in hexane) as eluent to afford the desired oxathiazepane.

9-*O*-Acetyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo[4.2.2]decane-3,3-dioxide (10a): Yield: 82%; white solid; ^{1}H NMR (500 MHz, [D$_6$]acetone): δ = 8.10 (m, 4H; Ph), 7.65 (m, 2H; Ph), 7.53 (m, 4H; Ph), 6.85 (d, J = 1.3 Hz , 1H; H1), 5.87 (dd, J = 5.7, 4.5 Hz, 1H; H3), 5.76 (d, J = 4.5 Hz, 1H; H4), 4.75 (m, 1H; H5), 4.72 (m, 2H; CH_2), 4.23 (dd, J = 5.7, 1.3 Hz, 1H; H2), 2.17 ppm (s, 3H; CH_3); ^{13}C NMR (125 MHz, [D$_6$]acetone): δ = 168.4 (CO), 165.4 (CO), 164.8 (CO), 133.6 (Ph), 133.5 (Ph), 129.8 (Ph), 129.6 (Ph), 129.4 (Ph), 128.6 (Ph), 128.5 (Ph), 90.9 (C1), 77.6 (C5), 75.1 (CH_2), 71.9 (C4), 69.3 (C3), 51.8 (C2), 20.2 ppm (CH_3); IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 1755, 1697 cm^{-1}; HR-MS (ESI): *m/z*: calcd for $C_{22}H_{21}NO_{10}SNa$: 514.0778 $[M+Na]^+$; found: 514.0759.

8-*O*-Acetyl-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-azabicyclo[3.3.1]decane-3,3-dioxide (12a): Yield: 73%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, J = 7.9 Hz, 2H; Ph), 8.01 (d, J = 7.9 Hz, 2H; Ph), 7.65 (t, J = 7.4 Hz, 1H; Ph), 7.58 (t, J = 7.4 Hz, 1H; Ph), 7.51 (t, J = 7.6 Hz, 2H; Ph), 7.44 (t, J = 7.6 Hz, 2H; Ph), 6.50 (s, 1H; H1), 6.09 (br s, 1H; NH), 5.94 (br t, 1H; H3), 5.06 (m, 1H; H4), 5.04 (t, J = 7.3 Hz , 1H; H5), 4.97 (dd, J = 11.0, 7.3 Hz, 1H; CH_2), 4.67 (dd, J = 11.0, 7.3 Hz, 1H; CH_2), 4.07 (m, 1H; H2), 1.81 ppm (s, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7 (CO), 165.9 (CO), 165.3 (CO), 134.4 (Ph), 133.5 (Ph), 129.9 (Ph), 129.7 (Ph), 129.0 (Ph), 128.9 (Ph), 128.5 (Ph), 127.9 (Ph), 91.1 (C1), 75.7 (C4), 72.7 (C5), 63.7 (CH_2), 62.2 (C3), 49.8 (C2), 20.8 ppm (CH_3); IR ($CHCl_3$): $\tilde{\nu}$ = 1710, 1635, 1273 cm^{-1}; HR-MS (ESI): *m/z*: calcd for $C_{22}H_{20}NO_{10}S$: 490.0802 $[M-H]^+$; found: 490.0825.

General procedure for rhodium-catalyzed aziridination with alcohols as nucleophiles: The nucleophile (20 equiv) was added dropwise to a mixture of sulfamate ester (1 equiv), $[Rh_2(OAc)_4]$ (10 mol%), $PhI(OAc)_2$ (1.5 equiv), MgO (5 equiv), and 4 Å molecular sieves in dry CH_2Cl_2 (2 mL). 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 (eluent: 30% ethyl acetate in hexane) to afford the desired oxathiazepane.

9-*O*-Methyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo[4.2.2]decane-3,3-dioxide (10b): Yield: 81%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (m, 4H; Ph), 7.60 (m, 2H; Ph), 7.44 (m, 4H; Ph), 5.84 (dd, J = 5.8, 4.0 Hz, 1H; H3), 5.53 (d, J = 4.0 Hz, 1H; H4), 5.51 (d, J = 1.1 Hz, 1H; H1), 5.18 (br d, J = 3.1 Hz, 1H; NH), 4.72 (dd, J = 12.4, 2.5 Hz, 1H; CH_2), 4.63 (dd, J = 12.4, 2.5 Hz, 1H; CH_2), 4.44 (m, 1H; H5), 4.03 (m, 1H; H2), 3.51 ppm (s, 3H; OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1 (CO), 165.1 (CO), 133.9 (Ph), 133.7 (Ph), 129.98 (Ph), 129.90 (Ph), 128.9 (Ph), 128.7 (Ph), 128.6 (Ph), 96.9 (C1), 76.6 (C5), 75.6 (CH_2), 72.1 (C4), 69.5 (C3), 55.4 (OCH_3), 53.3 ppm (C2); IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 1714, 1697, 1269 cm^{-1}; HR-MS (ESI): *m/z*: calcd for $C_{21}H_{20}NO_9S$: 462.0853 $[M-H]^+$; found: 462.0838.

9-*O*-Ethyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo[4.2.2]decane-3,3-dioxide (10c): Yield: 90%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (m, 4H; Ph), 7.61 (m, 2H; Ph), 7.47 (m, 4H; Ph), 5.88 (dd, J = 6.0, 3.6 Hz, 1H; H3), 5.60 (s, 1H; H1), 5.51 (d, J = 3.6 Hz, 1H; H4), 5.09 (br d, J = 2.9 Hz, 1H; NH), 4.72 (dd, J = 12.4, 2.3 Hz, 1H; CH_2), 4.62 (dd, J = 12.4, 2.3 Hz, 1H; CH_2), 4.43 (m, 1H; H5), 4.03 (m, 1H; H2), 3.91 (dt, J = 16.5, 7.2 Hz, 1H; CH_2CH_3), 3.63 (dt, J = 16.5, 7.2 Hz, 1H; CH_2CH_3), 1.27 ppm (t, J = 7.2 Hz, 3H; CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1 (CO), 165.1 (CO), 133.9 (Ph), 133.7 (Ph), 129.96 (Ph), 129.91 (Ph), 128.9 (Ph), 128.7 (Ph), 128.6 (Ph), 128.5 (Ph), 95.5 (C1), 76.5 (C5), 75.7 (CH_2), 72.2 (C4), 69.5 (C3), 63.8 (CH_2CH_3), 53.5 (C2), 15.1 ppm (CH_2CH_3); IR ($CHCl_3$): $\tilde{\nu}$ = 3020, 1714, 1452, 1274 cm^{-1}; HR-MS (ESI): *m/z*: calcd for $C_{22}H_{23}NO_9SNa$: 500.0986 $[M+Na]^+$; found: 500.0967.

9-*O*-Isopropyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo-[4.2.2]decane-3,3-dioxide (10d): Yield: 70%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, J = 7.6 Hz, 4H; Ph), 7.60 (m, 2H; Ph), 7.46 (m, 4H; Ph), 5.91 (dd, J = 5.8, 3.6 Hz, 1H; H3), 5.67 (s, 1H; H1), 5.50 (d, J = 3.6 Hz, 1H; H4), 5.11(br d, J = 3.2 Hz, 1H; NH), 4.71 (dd, J = 12.3, 2.0 Hz, 1H; CH_2), 4.62 (dd, J = 12.3, 2.0 Hz, 1H; CH_2), 4.43 (m, 1H; H5), 4.09 (m, 1H; $CH(CH_3)_2$), 3.98 (m, 1H; H2), 1.25 (d, J = 6.1 Hz, 3H; CH_3), 1.22 ppm (d, J = 6.1 Hz, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2 (CO), 165.1 (CO), 133.9 (Ph), 133.7 (Ph), 129.9 (Ph), 128.9 (Ph), 128.7 (Ph), 128.6 (Ph), 128.5 (Ph), 93.7 (C1), 76.4 (C5), 75.9 (CH_2), 72.3 (C4), 70.0 ($CH(CH_3)_2$), 69.6 (C3), 53.8 (C2), 23.5 (CH_3), 21.5 ppm (CH_3); IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 1718, 1452, 1377, 1276 cm^{-1}; HR-MS (ESI): *m/z*: calcd for $C_{23}H_{25}NO_9SNa$: 514.1142 $[M+Na]^+$; found: 514.1118.

9-*O*-Benzyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo[4.2.2]decane-3,3-dioxide (10e): Yield: 71%; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.08 (d, J=8.0 Hz, 2H; Ph), 7.96 (d, J=8.0 Hz, 2H; Ph), 7.61 (t, J=7.5 Hz, 1H; Ph), 7.56 (t, J=7.5 Hz, 1H; Ph), 7.48 (t, J=7.8 Hz, 2H; Ph), 7.34 (m, 7H; Ph), 5.90 (dd, J=6.3, 3.2 Hz, 1H; H3), 5.67 (d, J=1.6 Hz, 1H; H1), 5.53 (d, J=3.2 Hz, 1H; H4), 5.09 (br d, J=3.8 Hz, 1H; NH), 4.91 (d, J=11.8 Hz, 1H; CH_2Ph), 4.76 (dd, J=12.6, 2.4 Hz, 1H; CH_2), 4.67 (d, J=11.8 Hz, 1H; CH_2Ph), 4.62 (dd, J=12.6, 2.4 Hz, 1H; CH_2), 4.45 (m, 1H; H5), 4.12 ppm (ddd, J=6.3, 3.8, 1.6 Hz, 1H; H2); ^{13}C NMR (125 MHz, $CDCl_3$): δ=166.1 (CO), 165.0 (CO), 136.9 (Ph), 133.9 (Ph), 133.6 (Ph), 129.97 (Ph), 129.95 (Ph), 128.8 (Ph), 128.7 (Ph), 128.6 (Ph), 128.55 (Ph), 128.52 (Ph), 127.9 (Ph), 127.8 (Ph), 95.1 (C1), 76.5 (C5), 75.7 (CH_2), 72.1 (C4), 69.6 (CH_2Ph), 69.4 (C3), 53.2 ppm (C2); IR ($CHCl_3$): $\tilde{\nu}$=3018, 1720, 1452 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{27}H_{25}NO_9SNa$: 562.1142 [M+Na]$^+$; found: 562.1174.

8-*O*-Methyl-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-azabicyclo[3.3.1]decane-3,3-dioxide (12b): Yield: 96%; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.00 (m, 4H; Ph), 7.58 (m, 2H; Ph), 7.45 (m, 4H; Ph), 5.86 (m, 2H; H3 and NH), 5.20 (s, 1H; H1), 5.03 (m, 1H; H4), 4.98 (t, J=7.4 Hz, 1H; H5), 4.88 (dd, J=11.1, 7.4 Hz, 1H; CH_2), 4.73 (dd, J=11.1, 7.4 Hz, 1H; CH_2), 3.99 (m, 1H; H2), 3.48 ppm (s, 3H; OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=165.9 (CO), 165.6 (CO), 134.0 (Ph), 133.4 (Ph), 129.9 (Ph), 129.7 (Ph), 129.2 (Ph), 128.8 (Ph), 128.5 (Ph), 128.3 (Ph), 99.5 (C1), 76.6 (C4), 71.8 (C5), 64.1 (CH_2), 63.0 (C3), 56.6 (OCH_3), 51.3 ppm (C2); IR ($CHCl_3$): $\tilde{\nu}$=1718, 1635, 1274 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{21}H_{20}NO_9S$: 462.0853 [M−H]$^+$; found: 462.0869.

8-*O*-Ethyl-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-azabicyclo[3.3.1]decane-3,3-dioxide (12c): Yield: 87%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.99 (m, 4H; Ph), 7.59 (m, 2H; Ph), 7.45 (m, 4H; Ph), 5.87 (m, 1H; H3), 5.62 (br d, J=4.2 Hz, 1H; NH), 5.26 (s, 1H; H1), 5.04 (m, 1H; H4), 4.96 (t, J=7.4 Hz, 1H; H5), 4.88 (dd, J=11.0, 7.4 Hz, 1H; CH_2), 4.77 (dd, J=11.0, 7.4 Hz, 1H; CH_2), 4.01 (m, 1H; H2), 3.96 (q, J=7.2 Hz, 1H; CH_2CH$_3$), 3.51 (q, J=7.0 Hz, 1H; CH_2CH$_3$), 1.06 ppm (t, J=7.0 Hz, 3H; CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=165.9 (CO), 165.4 (CO), 134.0 (Ph), 133.4 (Ph), 129.9 (Ph), 129.6 (Ph), 129.2 (Ph), 128.7 (Ph), 128.5 (Ph), 128.3 (Ph), 98.1 (C1), 76.7 (C4), 71.8 (C5), 64.7 (CH_2), 64.1 (CH_2), 62.8 (C3), 51.3 (C2), 14.7 ppm (CH$_2$CH_3); IR ($CHCl_3$): $\tilde{\nu}$=3018, 1718, 1273, 1217 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{22}H_{22}NO_9S$: 476.1010 [M−H]$^+$; found: 476.0987.

8-*O*-Isopropyl-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-azabicyclo-[3.3.1]decane-3,3-dioxide (12d): Yield: 86%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.02 (m, 4H; Ph), 7.59 (m, 2H; Ph), 7.45 (m, 4H; Ph), 5.84 (m, 1H; H3), 5.53 (br s, 1H; NH), 5.36 (s, 1H; H1), 5.05 (m, 1H; H4), 4.95 (t, J=7.5 Hz, 1H; H5), 4.84 (m, 2H; CH_2), 4.09 (m, 1H; CH(CH$_3$)$_2$), 3.97 (m, 1H; C2), 1.09 (d, J=6.1 Hz, 3H; CH_3), 1.06 ppm (d, J=6.1 Hz, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=165.9 (CO), 165.4 (CO), 134.0 (Ph), 133.4 (Ph), 129.9 (Ph), 129.6 (Ph), 129.2 (Ph), 128.6 (Ph), 128.5 (Ph), 128.3 (Ph), 95.8 (C1), 76.7 (C4), 71.7 (C5), 70.4 (CH-(CH$_3$)$_2$), 64.2 (CH_2), 62.9 (C3), 51.7 (C2), 22.9 (CH_3), 20.9 ppm (CH_3); IR ($CHCl_3$): $\tilde{\nu}$=2926, 1722, 1645, 1273 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{23}H_{24}NO_9S$: 490.1166 [M−H]$^+$; found: 490.1149.

8-*O*-Benzyl-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-azabicyclo[3.3.1]decane-3,3-dioxide (12e): Yield: 77%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.00 (d, J=8.0 Hz, 2H; Ph), 7.84 (d, J=8.0 Hz, 2H; Ph), 7.55 (m, 2H; Ph), 7.44 (m, 2H; Ph), 7.26 (m, 7H; Ph), 5.89 (m, 1H; H3), 5.45 (br d, J=4.0 Hz, 1H; NH), 5.39 (s, 1H; H1), 5.05 (m, 1H; H4), 4.97 (m, 2H; H5 and CH_2Ph), 4.89 (dd, J=11.1, 7.4 Hz, 1H; CH_2), 4.77 (dd, J=11.1, 7.4 Hz, 1H; CH_2), 4.57 (d, J=11.3 Hz, 1H; CH_2Ph), 4.03 ppm (m, 1H; C2); ^{13}C NMR (100 MHz, $CDCl_3$): δ=166.1 (CO), 166.0 (CO), 136.2 (Ph), 133.8 (Ph), 133.4 (Ph), 130.0 (Ph), 129.9 (Ph), 129.7 (Ph), 129.6 (Ph), 129.5 (Ph), 129.2 (Ph), 128.8 (Ph), 128.6 (Ph), 128.5 (Ph), 128.4 (Ph), 128.1 (Ph), 128.0 (Ph), 97.7 (C1), 76.4 (C4), 72.1 (C5), 71.1 (CH_2Ph), 64.0 (CH_2), 62.5 (C3), 51.4 ppm (C2); IR ($CHCl_3$): $\tilde{\nu}$=2954, 1708, 1635, 1269 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{27}H_{24}NO_9S$: 538.1166 [M−H]$^+$; found: 538.1189.

8-*O*-Allyl-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-azabicyclo[3.3.1]decane-3,3-dioxide (12f): Yield: 81%; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.01 (m, 4H; Ph), 7.58 (m, 2H; Ph), 7.36 (m, 4H; Ph), 5.88 (m, 1H; H3), 5.75 (ABX system, J_{AX}=17.0, J_{BX}=10.5, J_{AB}=5.4 Hz, 1H; CH_2CH=CH$_2$), 5.55 (br d, J=4.6 Hz, 1H; NH), 5.32 (s, 1H; H1), 5.05–5.17 (m, 3H; CH$_2$CH=CH_2 and H4), 4.97 (t, J=7.4 Hz, 1H; H5), 4.88 (dd, J=11.5, 7.4 Hz, 1H; CH_2), 4.80 (dd, J=12.4, 5.4 Hz, 1H; CH_2CH=CH$_2$), 4.75 (dd, J=11.5, 7.4 Hz, 1H; CH_2), 4.38 (dd, J=12.4, 5.4 Hz, 1H; CH_2CH=CH$_2$), 4.03 ppm (m, 1H; H2); ^{13}C NMR (100 MHz, $CDCl_3$): δ=165.8 (CO), 165.4 (CO), 134.0 (Ph), 133.5 (Ph), 132.8 (CH$_2$CH=CH$_2$), 130.0 (Ph), 129.6 (Ph), 129.2 (Ph), 128.7 (Ph), 128.5 (Ph), 128.2 (Ph), 118.2 (CH$_2$CH=CH_2), 97.5 (C1), 76.5 (C4), 71.9 (C5), 69.6 (CH_2CH=CH$_2$), 64.0 (CH_2), 62.7 (C3), 51.3 ppm (C2); IR ($CHCl_3$): $\tilde{\nu}$=3018, 1722, 1627, 1274 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{23}H_{22}NO_9S$: 488.1010 [M−H]$^+$; found: 488.1003.

General procedure for rhodium-catalyzed aziridination with alkyl, thiol, amine, amino acid, and glycal as nucleophiles: A mixture of sulfamate ester (1 equiv), [Rh_2(tfacam)$_4$] (10 mol%),[25] PhIO (1.5 equiv),[26] MgO (5 equiv), and 4 Å molecular sieves in dry CH_2Cl_2 (2 mL) was stirred at room temperature for 15 min, then the nucleophile (1.5 equiv) was added dropwise. The suspension was stirred vigorously at room temperature and monitored by TLC. The resulting 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 chromatography on silica gel (eluent: 30% ethyl acetate in hexane) to afford the oxathiazepane.

9-Allyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo[4.2.2]decane-3,3-dioxide (10f): Yield: 78%; white solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.89 (d, J=7.3 Hz, 2H; Ph), 7.82 (d, J=7.3 Hz, 2H; Ph), 7.46 (m, 2H; Ph), 7.32 (m, 2H; Ph), 7.27 (m, 2H; Ph), 6.09 (t, J=10.0 Hz, 1H; H3), 5.79 (ABX system, J_{AX}=17.1 Hz, J_{BX}=10.1, J_{AB}=7.0 Hz, 1H; CH_2CH=CH$_2$), 5.66 (d, J=9.0 Hz, 1H; H4), 5.17 (dd, J=10.1, 1.4 Hz, 1H; CH$_2$CH=CH_2), 5.12 (dd, J=10.1, 1.4 Hz, 1H; CH$_2$CH=CH_2), 4.62 (dd, J=12.6, 4.4 Hz, 1H; CH_2), 4.56 (dd, J=12.6, 4.4 Hz, 1H; CH_2), 4.49 (m, 1H; H5), 4.23 (br s, 1H; NH), 3.74 (m, 1H; H1 and H2), 2.48 (dd, J=14.4, 7.0 Hz, 1H; CH_2CH=CH$_2$), 2.41 ppm (dd, J=14.4, 7.0 Hz, 1H; CH_2CH=CH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=166.4 (CO), 166.0 (CO), 133.9 (Ph), 133.68 (CH$_2$CH=CH$_2$), 133.63 (Ph), 129.8 (Ph), 129.6 (Ph), 128.55 (Ph), 128.52 (Ph), 128.4 (Ph), 128.3 (Ph), 118.9 (CH$_2$CH=CH_2), 75.8 (C4), 73.1 (C5), 72.4 (CH_2), 69.4 (C3), 68.7 (C1), 57.0 (C2), 37.7 ppm (CH_2CH=CH$_2$); IR ($CHCl_3$): $\tilde{\nu}$=2956, 1714, 1600, 1367, 1278 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{23}H_{23}NO_8S$: 473.1144 [M]$^+$; found: 473.0993.

9-*p*-Tolylthio-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo-[4.2.2]decane-3,3-dioxide (10g): Yield: 85%; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.06 (m, 4H; Ph), 7.59 (m, 2H; Ph), 7.51 (d, J=8.0 Hz, 2H; Ph), 7.47 (m, 4H; Ph), 7.18 (d, J=8.0 Hz, 2H; Ph), 6.27 (s, 1H; H1), 5.99 (t, J=5.5 Hz, 1H; H3), 5.68 (d, J=5.5 Hz, 1H; H4), 5.08 (br d, J=2.9 Hz, 1H; NH), 4.77 (dd, J=13.0, 3.5 Hz, 1H; CH_2), 4.71 (dd, J=13.0, 1.5 Hz, 1H; CH_2), 4.51 (m, 1H; H5), 4.27 (br t, J=3.8 Hz, 1H; H2), 2.36 ppm (s, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=166.3 (CO), 165.0 (CO), 139.2 (Ph), 134.1 (Ph), 134.0 (Ph), 133.8 (Ph), 130.2 (Ph), 130.0 (Ph), 128.7 (Ph), 128.6 (Ph), 128.5 (Ph), 127.7 (Ph), 81.5 (C1), 78.4 (C5), 75.4 (CH_2), 71.9 (C4), 70.4 (C3), 54.5 (C2), 21.2 ppm (CH_3); IR ($CHCl_3$): $\tilde{\nu}$=3018, 1722, 1273 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{27}H_{25}NO_8S_2Na$: 578.0914 [M+Na]$^+$; found: 578.0939.

9-*N*-(3,5-Bis(trifluoromethyl)phenyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo[4.2.2]decane-3,3-dioxide (10h): Yield: 76%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.07 (d, J=7.4 Hz, 2H; Ph), 8.00 (d, J=7.4 Hz, 2H; Ph), 4.10 (m, 1H; H2), 7.60 (m, 2H; Ph), 7.45 (m, 4H; Ph), 7.35 (s, 1H; Ph), 7.21 (s, 2H; Ph), 6.46 (d, J=9.0 Hz, 1H; H1), 5.85 (dd, J=6.6, 4.2 Hz, 1H; H3), 5.79 (d, J=6.6 Hz, 1H; H4), 5.29 (br s, 1H; NH), 5.13 (br d, J=9.0 Hz, 1H; NHPh), 4.89 (dd, J=13.3, 1.5 Hz, 1H; CH_2), 4.80 (dd, J=13.3, 1.5 Hz, 1H; CH_2), 4.52 (m, 1H; H5), 4.10 ppm (m, 1H; H2); ^{13}C NMR (100 MHz, $CDCl_3$): δ=166.1 (CO), 165.7 (CO), 145.3 (Ph), 134.3 (Ph), 134.0 (Ph), 132.6 (Ph), 130.0 (Ph), 129.8 (Ph), 128.8 (Ph), 128.6 (Ph), 128.4 (Ph), 128.0 (Ph), 114.0 (CF_3), 113.4 (CF_3), 78.7 (C1), 77.6 (C5), 75.2 (CH_2), 71.8 (C4), 70.5 (C3), 55.1 ppm (C2); IR ($CHCl_3$): $\tilde{\nu}$=3018, 1720, 1624, 1473, 1388, 1278 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{28}H_{23}F_6N_2O_8S$: 661.1079 [M+H]$^+$; found: 661.1029.

9-*N*-[Methyl-*N*-(dibenzyl)-L-serinate-3-yl]-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo[4.2.2]decane-3,3-dioxide (10i): Yield: 66%; colorless

oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09 (m, 2H; Ph), 7.89 (m, 2H; Ph), 7.61 (m, 1H; Ph), 7.55 (m, 1H; Ph), 7.48 (m, 2H; Ph), 7.38 (m, 6H; Ph), 7.30 (m, 4H; Ph), 7.21 (m, 2H; Ph), 5.80 (dd, J = 5.6, 4.3 Hz, 1H; H3), 5.61 (d, J = 1.2 Hz, 1H; H1), 5.50 (d, J = 4.3 Hz, 1H; H4), 5.08 (brs, 1H; NH), 4.69 (dd, J = 12.1, 2.6 Hz, 1H; CH_2OSO_2), 4.62 (dd, J = 12.1, 2.6 Hz, 1H; CH_2OSO_2), 4.39 (m, 1H; H5), 4.18 (dd, J = 10.3, 6.3 Hz, 1H; CH_2O), 3.99 (dd, J = 5.6, 1.2 Hz, 1H; H2), 3.94 (d, J = 13.9 Hz, 1H; CH_2Ph), 3.85 (dd, J = 10.3, 6.3 Hz, 1H; CH_2O), 3.75 (m, 1H; CHN), 3.74 (s, 3H; OCH_3), 3.70 ppm (d, J = 13.9 Hz, 1H; CH_2Ph); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.2 (CO), 166.1 (CO), 164.9 (CO), 139.2 (Ph), 133.9 (Ph), 133.6 (Ph), 129.9 (Ph), 129.8 (Ph), 128.77 (Ph), 128.73 (Ph), 128.6 (Ph), 128.5 (Ph), 128.3 (Ph), 127.1 (Ph), 95.9 (C1), 76.8 (C5), 75.7 (CH_2OSO_2), 72.0 (C4), 69.4 (C3), 66.3 (CH_2O), 61.0 (OCH_3), 55.2 (CH_2Ph), 53.3 (C2), 51.4 ppm (CHN); IR ($CHCl_3$): $\tilde{\nu}$ = 2926, 1724, 1452, 1261 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{38}H_{39}N_2O_{11}S$: 731.2269 $[M+H]^+$; found: 731.2286.

9-*O*-[3,4-Di-*O*-benzoyl-1,2-dideoxy-D-glcopyranosyl]-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azabicyclo[4.2.2]decane-3,3-dioxide (10j): Yield: 68%; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.03 (m, 9H; Ph), 7.61 (m, 1H; Ph), 7.49 (m, 6H; Ph), 7.35 (m, 4H; Ph), 6.51 (d, J = 6.2 Hz, 1H; H1′), 5.86 (dd, J = 5.9, 3.9 Hz, 1H; H3), 5.76 (dd, J = 6.7, 5.7 Hz, 1H; H4′), 5.63 (m, 2H; H1 and H3′), 5.49 (d, J = 3.9 Hz, 1H; H4), 5.06 (dd, J = 6.2, 3.4 Hz, 1H; H2′), 4.98 (d, J = 3.6 Hz, 1H; NH), 4.66 (dd, J = 12.4, 2.5 Hz, 1H; CH_2OSO_2), 4.61 (dd, J = 12.4, 2.5 Hz, 1H; CH_2OSO_2), 4.56 (ABq, J = 11.2, 5.7 Hz, 1H; H5′), 4.49 (m, 1H; H5), 4.13 (dd, J = 11.2, 5.7 Hz, 1H; CH_2O), 4.06 (dd, J = 11.2, 5.7 Hz, 1H; CH_2O), 3.97 ppm (m, 1H; H2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2 (CO), 165.8 (CO), 164.9 (CO), 164.8 (CO), 145.9 (C1′), 133.9 (Ph), 133.5 (Ph), 133.39 (Ph), 133.30 (Ph), 129.95 (Ph), 129.87 (Ph), 129.83 (Ph), 129.7 (Ph), 129.6 (Ph), 129.2 (Ph), 128.97 (Ph), 128.7 (Ph), 128.6 (Ph), 128.5 (Ph), 128.48 (Ph), 128.45 (Ph), 98.8 (C2′), 96.4 (C1), 76.7 (C5), 75.7 (CH_2OSO_2), 74.5 (C5′), 72.1 (C4), 69.3 (C3), 68.0 (C4′), 67.7 (C3′), 66.3 (CH_2O), 53.1 ppm (C2); IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 1720, 1647, 1602, 1273 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{40}H_{35}NO_{14}SNa$: 808.1676 $[M+Na]^+$; found: 808.1468.

8-*p*-Tolylthio-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-azabicyclo-[3.3.1]decane-3,3-dioxide (12g): Yield: 78%; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (m, 2H; Ph), 8.00 (m, 2H; Ph), 7.67 (m, 1H; Ph), 7.54 (m, 3H; Ph), 7.42 (m, 4H; Ph), 7.14 (d, J = 7.9 Hz, 2H; Ph), 5.79 (m, 1H; H3), 5.58 (brs, 1H; NH), 5.37 (m, 1H; H5), 5.26 (m, 1H; H4), 5.12 (m, 1H; H2), 4.94 (m, 1H; H1), 4.86 (dd, J = 12.2, 3.7 Hz, 1H; CH_2), 4.25 (dd, J = 12.2, 3.7 Hz, 1H; CH_2), 2.33 ppm (s, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.8 (CO), 164.8 (CO), 134.35 (Ph), 133.4 (Ph), 133.0 (Ph), 130.3 (Ph), 130.1 (Ph), 129.7 (Ph), 128.8 (Ph), 128.5 (Ph), 123.6 (Ph), 80.1 (C4), 66.7 (C1), 66.6 (C2 and C5), 62.7 (C3), 61.1 (CH_2), 21.1 ppm (CH_3); IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 2929, 1718, 1649, 1388, 1269 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{27}H_{25}NO_8S_2Na$: 578.0914 $[M+Na]^+$; found: 578.0891.

9-*O*-Methyl-7,8-di-*O*-benzoyl-4,10-dioxa-3-thia-2-azidobicyclo-[4.2.2]decane-3,3-dioxide (13): CbzCl (0.3 mL, 2.11 mmol) and a catalytic amount of DMAP (30 mg, 0.25 mmol) were subsequently added to a mixture solution of oxathiazepane **10b** (110 mg, 0.23 mmol) in THF (1 mL) and Et_3N (0.7 mL, 5.02 mmol) at 0°C. The reaction was stirred at room temperature for 2.5 h and then quenched with saturated aqueous NH_4Cl. The mixture was extracted with EtOAc (2×). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by chromatography on silica gel (eluent: 50% ethyl acetate in hexane) to yield **13** (130 mg, 92%) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, J = 7.4 Hz, 2H; Ph), 7.88 (d, J = 7.4 Hz, 2H), 7.47 (m, 4H; Ph), 7.30 (m, 7H; Ph), 5.73 (dd, J = 10.1, 4.2 Hz, 1H; H3), 5.54 (t, J = 10.1 Hz, 1H; H4), 5.00 (s, 2H; CH_2), 4.85 (brs, 1H; H1), 4.72 (dd, J = 8.8, 4.3 Hz, 1H; H2), 4.21 (m, 1H; H5), 3.72 (dd, J = 12.1, 6.0 Hz, 1H; CH_2), 3.66 (dd, J = 12.1, 6.0 Hz, 1H; CH_2), 3.50 ppm (s, 3H; OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.5 (CO), 165.4 (CO), 155.8 (CO), 136.0 (Ph), 133.6 (Ph), 133.0 (Ph), 129.8 (Ph), 129.7 (Ph), 129.3 (Ph), 128.7 (Ph), 128.59 (Ph), 128.51 (Ph), 128.29 (Ph), 128.22 (Ph), 100.4 (C1), 70.0 (C5), 69.7 (C4), 67.7 (C3), 67.1 (CH_2), 55.5 (OCH_3), 52.3 (C2), 43.8 ppm (CH_2); IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 1726, 1512, 1274 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{29}H_{26}NO_{11}S$: 596.1221 $[M-H]^+$ found: 596.1226.

8-*O*-Methyl-9,10-di-*O*-benzoyl-5,7-dioxa-3-thia-2-azidobicyclo-[3.3.1]decane-3,3-dioxide (15): Aqueous $NaHCO_3$ (100 mg in 1 mL of water) and CbzCl (350 μL, 2.46 mmol) were sequentially added to a solution of oxathiazepane **12b** (116 mg, 0.24 mmol) in THF (1 mL) with vigorous stirring at 0°C. The reaction mixture was kept at this temperature for 1 h and then warmed up to room temperature overnight. The mixture was extracted with EtOAc (3×). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by chromatography on silica gel (eluent: 50% ethyl acetate in hexane) to yield **15** (120 mg, 82%) as white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15 (d, J = 7.7 Hz, 2H; Ph), 8.05 (d, J = 7.7 Hz, 2H; Ph), 7.57 (m, 2H; Ph), 7.34 (m, 4H; Ph), 7.31 (m, 5H; Ph), 5.71 (d, J = 3.2 Hz, 1H; H3), 5.10 (ABq, J = 16.0, 12.2 Hz, 2H; CH_2), 4.59 (dd, J = 11.3, 6.5 Hz, 1H; CH_2), 4.49 (d, J = 7.9 Hz, 1H; H1), 4.38 (dd, J = 11.3, 6.5 Hz, 1H; CH_2), 4.12 (m, 1H; H4), 4.12 (m, 1H; H4), 4.08 (t, J = 6.4 Hz, 1H; H5), 3.71 (m, 1H; H2), 3.55 ppm (s, 3H; OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.2 (CO), 166.1 (CO), 157.4 (CO), 135.8 (Ph), 133.4 (Ph), 133.2 (Ph), 130.0 (Ph), 129.7 (Ph), 129.5 (Ph), 129.3 (Ph), 128.6 (Ph), 128.5 (Ph), 128.4 (Ph), 128.3 (Ph), 128.2 (Ph), 101.8 (C1), 71.5 (C5), 71.4 (C4), 69.5 (C3), 67.4 (CH_2), 62.4 (CH_2), 57.1 (OCH_3), 56.1 ppm (C2); IR (Nujol): $\tilde{\nu}$ = 1720, 1714, 1273 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{29}H_{26}NO_{11}S$: 596.1221 $[M-H]^+$; found: 596.1221.

Methyl-6-azido-2-benzyloxycarbonylamino-3,4-di-*O*-benzoyl-2,6-dideoxy-D-glucopyranoside (14a): NaN_3 (6 mg, 9.2×10^{-2} mmol) was added to a solution of *N*-Cbz oxathiazepane **13** (28 mg, 4.7×10^{-2} mmol) in dry DMF (0.3 mL) in the presence of 4 Å molecular sieves. After heating at 120°C for 5 h, the reaction mixture was cooled to room temperature. NaH_2PO_4 (2 mL, 1 M) was added and the mixture was stirred for an hour. The mixture was filtered and the filtrate was washed with water (3×), dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel (eluent: 50% ethyl acetate in hexane) to yield **14a** (18 mg, 67%) as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, J = 7.4 Hz, 2H; Ph), 7.87 (d, J = 7.4 Hz, 2H; Ph), 7.49 (m, 3H; Ph), 7.35 (m, 8H; Ph), 5.71 (dd, J = 10.6, 4.1 Hz, 1H; H3), 5.47 (t, J = 10.6 Hz, 1H; H4), 5.20 (brd, J = 8.2 Hz, 1H; NH), 5.01 (m, 2H; CH_2), 4.84 (m, 1H; H1), 4.60 (m, 1H; H2), 4.13 (m, 1H; H5), 3.51 (s, 3H; CH_3), 3.48 ppm (m, 2H; CH_2N_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5 (CO), 165.3 (CO), 155.8 (CO), 133.6 (Ph), 133.0 (Ph), 129.8 (Ph), 129.7 (Ph), 128.6 (Ph), 128.5 (Ph), 128.4 (Ph), 128.28 (Ph), 128.20 (Ph), 100.3 (C1), 69.8 (C5), 69.5 (C3), 67.4 (CH_2), 67.1 (C4), 55.5 (OCH_3), 52.3 (CH_2N_3), 51.2 ppm (C2); IR ($CHCl_3$): ν = 2102, 1724, 1672, 1273 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{29}H_{28}N_4O_8Na$: 583.1804 $[M+Na]^+$; found: 583.1822.

Methyl-6-thiocyanato-2-benzyloxycarbonylamino-3,4-di-*O*-benzoyl-2,6-dideoxy-D-glucopyranoside (14b): Potassium thiocyanate (23 mg, 0.23 mmol) was added to a solution of *N*-Cbz oxathiazepane **13** (28 mg, 4.7×10^{-2} mmol) in dry DMF (0.5 mL) in the presence of 4 Å molecular sieves. The mixture was stirred at 150°C for 12 h under a nitrogen atmosphere. After cooling the reaction to room temperature, 1 M NaH_2PO_4 (2 mL) was added and the mixture was stirred for another hour. The mixture was filtered and the filtrate was washed with water (3×), dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel (eluent 50% ethyl acetate in hexane) to yield **14b** (21 mg, 78%) as a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.98 (m, 2H; Ph), 7.89 (d, J = 7.4 Hz, 2H; Ph), 7.57 (t, J = 7.4 Hz, 2H; Ph), 7.50 (t, J = 7.4 Hz, 1H; Ph), 7.42 (t, J = 7.8 Hz, 2H; Ph), 7.34 (m, 7H; Ph), 5.78 (dd, J = 10.0, 4.1 Hz, 1H; H3), 5.43 (t, J = 10.0 Hz, 1H; H4), 5.22 (d, J = 9.1 Hz, 1H; NH), 5.05 (m, 2H; CH_2), 4.90 (m, 1H; H1), 4.63 (dd, J = 9.1, 4.1 Hz, 1H; H2), 4.29 (t, J = 7.9 Hz, 1H; H5), 3.57 (s, 3H; CH_3), 3.29 (dd, J = 13.9, 2.6 Hz, 1H; CH_2SCN), 3.15 ppm (dd, J = 13.9, 8.4 Hz, 1H; CH_2SCN); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.9 (CO), 165.3 (CO), 155.7 (CO), 135.9 (Ph), 133.9 (Ph), 133.1 (Ph), 129.9 (Ph), 129.7 (Ph), 129.2 (Ph), 128.6 (Ph), 128.3 (Ph), 128.2 (Ph), 111.9 (CN), 100.5 (C1), 69.5 (C3), 69.2 (C4), 68.9 (C5), 67.2 (CH_2), 55.8 (OCH_3), 52.3 (C2), 35.9 ppm (CH_2SCN); IR ($CHCl_3$): $\tilde{\nu}$ = 3018, 1780, 1703, 1386, 1215 cm^{-1}; HR-MS (ESI): m/z: calcd for $C_{30}H_{28}N_2O_8SNa$: 599.1459 $[M+Na]^+$; found: 599.1445.

Methyl-*N*-4-methoxybenzylamino-2-benzyloxycarbonylamino-3,6-di-*O*-benzoyl-2,4-dideoxy-D-glucopyranoside (16a): A solution of compound **15** (11 mg, 2.4×10^{-2} mmol) in dry DMF (0.5 mL) was treated with *p*-methoxybenzylamine (15 μL, 11.4×10^{-2} mmol) under a nitrogen atmosphere. The reaction mixture was heated at 70 °C for 30 h and then cooled to room temperature. The solvent was removed under reduced pressure, then EtOAc (10 mL) was added to the residue, and the solution was washed with water (3×). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification by chromatography on silica gel (eluent: 30% ethyl acetate in hexane) gave **16a** (9 mg, 75%) as colorless viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.02$ (d, $J=7.6$ Hz, 2H; Ph), 7.77 (d, $J=8.0$ Hz, 2H; Ph), 7.56 (m, 1H; Ph), 7.39 (m, 6H; Ph), 7.27 (m, 2H; Ph), 7.18 (m, 4H; Ph), 6.88 (d, $J=8.0$ Hz, 2H; Ph), 5.30 (m, 1H; H1), 5.03 (m, 3H; CH_2 and NH), 4.59 (m, 5H; H3, CH_2 and CH_2N), 4.23 (m, 1H; H4), 4.15 (m, 1H; H2), 3.98 (m, 1H; H5), 3.80 (s, 3H; OCH_3), 3.54 (s, 3H; OCH_3), 2.50 ppm (brs, 1H; NH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=166.4$ (CO), 166.1 (CO), 159.1 (CO), 136.2 (Ph), 134.4 (Ph), 133.5 (Ph), 133.3 (Ph), 131.5 (Ph), 130.2 (Ph), 129.9 (Ph), 129.7 (Ph), 129.5 (Ph), 129.3 (Ph), 129.1 (Ph), 128.59 (Ph), 128.52 (Ph), 128.4 (Ph), 128.3 (Ph), 127.9 (Ph), 127.7 (Ph), 126.9 (Ph), 114.2 (Ph), 73.2 (C5), 72.1 (C1), 66.8 (C4 and CH_2), 62.7 (C3 and CH_2), 56.9 (OCH_3), 55.3 (OCH_3), 52.4 (C2), 43.6 ppm (CH_2); IR (Nujol): $\tilde{\nu}=$ 1720, 1689, 1635 cm^{-1}; HR-MS (ESI): *m/z*: calcd for $C_{37}H_{39}N_2O_9$: 655.2650 $[M+H]^+$; found: 655.2634.

Methyl-2-benzyloxycarbonylamino-3,6-di-*O*-benzoyl-2-deoxy-D-glucopyranoside (16b): A solution of compound **15** (7 mg, 1.2×10^{-2} mmol) in acetone (0.3 mL) and water (0.3 mL) was treated with K_2CO_3 (4 mg, 2.9×10^{-2} mmol). The reaction mixture was stirred at room temperature for 14 h and then quenched with 1 M NaH_2PO_4 (0.5 mL). The organic phase was separated and the aqueous phase was extracted with EtOAc (2×). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification by chromatography on silica gel (eluent: 50% ethyl acetate in hexane) gave **16b** (5 mg, 80%) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.04$ (m, 4H; Ph), 7.58 (m, 2H; Ph), 7.44 (m, 4H; Ph), 7.20 (m, 5H; Ph), 5.32 (m, 1H; H1), 5.03 (q, $J=$ 12.4 Hz, 2H; CH_2), 4.86 (brs, 1H; NH), 4.62 (m, 3H; H3 and CH_2), 4.23 (m, 1H; H4), 4.13 (q, $J=7.4$ Hz, 1H; H2), 3.98 (t, $J=6.2$ Hz, 1H; H5), 3.54 (s, 3H; OCH_3), 2.51 ppm (brs, 1H; OH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=166.4$ (CO), 166.0 (CO), 156.1 (CO), 136.2 (Ph), 133.5 (Ph), 133.3 (Ph), 129.9 (Ph), 129.7 (Ph), 129.5 (Ph), 129.1 (Ph), 128.5 (Ph), 128.4 (Ph), 128.3 (Ph), 127.9 (Ph), 127.7 (Ph), 73.3 (C5), 72.1 (C1), 66.8 (C4 and CH_2), 62.7 (C3 and CH_2), 56.9 (OCH_3), 52.4 ppm (C2); IR (Nujol): $\nu=3294$, 1722, 1685 cm^{-1}; HR-MS (ESI): *m/z*: calcd for $C_{29}H_{29}NO_9Na$: 558.1735 $[M+Na]^+$; found: 558.1760.

Computational studies: DFT calculations were carried out with the Gaussian 03 package.[27] The energy profiles of the reaction were computed at the B3LYP level.[28] Effective core potentials (ECPs) with double-ξ valence basis (LANL2DZ)[29] were used to describe the heavy atoms (Rh and I) and the standard 6-31+G(d) basis set was used for all other atoms (C, O, H, S, and N). Analytical second derivatives (normal modes) were also calculated for zero-point energy correction and estimation of the Gibbs free energy at room temperature.

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