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Glycosylations with 2,3-aziridinofuranose derivatives

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ABSTRACT

Two aziridine-containing pentofuranose derivatives were synthesized from D-arabinose and their ability to glycosylate alcohols was explored. The major products are those in which the newly formed glycosidic bond is cis to the aziridine moiety, although in all cases the stereoselectivity is modest. The analogous epoxides have been shown to be more highly stereoselective glycosyl donors. Differences in glycosylation stereoselectivity between the epoxide and aziridine-containing substrates was proposed to arise from steric hindrance between the alcohol acceptor and the nitrogen protecting group in the aziridine substrates.

1. Introduction

Previously, we have reported the use of 2,3-anhydrosugar derivatives (e.g., **1**–**3**, Fig. 1) as donors for the synthesis of glycoside bonds.[1–4] These species are highly stereoselective glycosyl donors, producing the product in which the newly formed bond is cis to the epoxide ring. The products can be further functionalized through regioselective epoxide ring opening to produce glycans containing β-arabinofuranoside,[2] α-arabinofuranoside[5] or α-galactofuranoside[3] moieties. Thioglycosides, such as **1** and **3** are also effective precursors for the stereocontrolled synthesis of 2-deoxy-glycosides.[6,7]

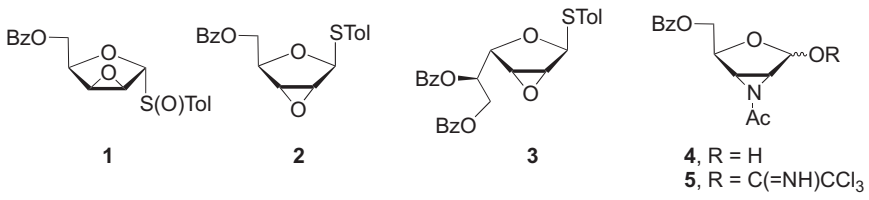

Fig. 1. 2,3-Anhydrosugar glycosyl donors **1**–**3** and related aziridine derivatives **4** and **5**.

In this paper, we report an extension of these investigations and explore the ability of **4** and **5**, analogs of **2** in which the epoxide moiety is replaced with an aziridine, to glycosylate alcohols. To the best of our knowledge, there have been no previous reports on the use of such species as glycosyl donors. If these species are highly stereoselective glycosylating agents, then they may find application in the synthesis of furanose aminosugars through subsequent nucleophilic opening of the aziridine ring.

2. Results and discussion

In developing a route to **4** and **5**, we envisioned an approach (Fig. 2) starting from D-arabinose (**6**) and proceeding through a key azidosugar intermediate (**7**), which possesses a leaving group at C-2. In our earlier studies on 2,3-anhydrosugar donors, we had employed thioglycoside donors, and corresponding sulfoxides derived from them.[1–5] However, based on this work, we expected that use of a thioglycoside (X=SR) in this approach would likely lead to decomposition of **7** via displacement of the C-2 leaving group by neighboring group participation of the sulfur atom, generating oxacarbenium ion **8**.[8] We therefore chose to prepare donors (i.e., **4** and **5**) containing an oxygen at C-1. Should **4** and **5** prove to be highly stereoselective glycosyl donors, an alternate route to targets containing a thioglycoside moiety could be developed.

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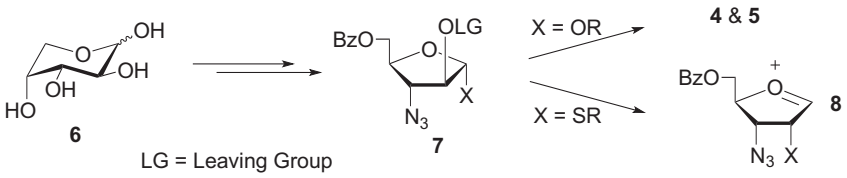
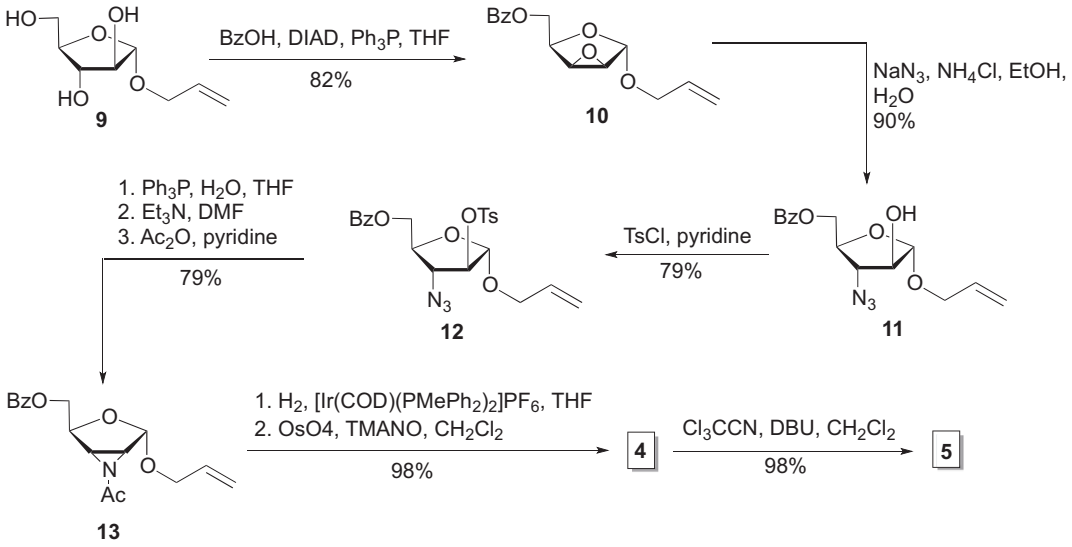


Fig. 2. General strategy to **4** and **5** and predicted decomposition pathway with thioglycosides.

2.1. Synthesis of 4 and 5

The synthesis of **4** (Scheme 1) began with allyl α-D-arabinofuranoside (**9**), which is easily available from D-arabinose (**6**).[9] Reaction of **9** with diisopropyl azodicarboxylate, triphenylphosphine, and benzoic acid provided **10** in 82% yield.[10] The formation of 2,3-epoxide moiety was clear from the chemical shift of signals for C-2 and C-3 in the ^{13}C NMR spectrum, which appeared at 56.3 and 54.1 ppm, respectively. These values are similar to those reported for other 2,3-anhydro-α-D-lyxofuranosides.[11]

The unit cell of the crystal contains two molecules of **13**. The furanose ring in both molecules adopts similar conformations with pseudorational phase angle (P) and puckering amplitude (ϕ_m) values of 266°/28.5° and 277°/20.5°, respectively.[14,15] Interestingly, the relative orientation of the acetyl group differs in the two molecules (Fig. 3b). In one, the acetyl group is positioned away from, and in the other it is oriented under, the furanose ring. These forms appear to represent the two different 'inverted' forms of the nitrogen. It is



Scheme 1. Synthesis of **4** and **5**.

Opening of the epoxide ring in **10** was performed using NaN_3 and NH_4Cl in EtOH and H_2O. The reaction was sluggish and it was necessary to heat the mixture at reflux for 48 h. The product, **11**, was obtained in 90% yield, together with 9% recovered starting material **10**. A peak at 2107 cm^{-1} in the IR spectrum of **11** confirmed the presence of the azido group. The regioselectivity of the reaction was confirmed by the ^{13}C NMR spectrum of **11**. The resonance for C-2 appeared at 80.9 ppm for C-2 and that for C-3, as expected, at lower chemical shift, 67.5 ppm. In addition, the $^3J_{H\text{-}1,H2}$ (1.0 Hz) was consistent with a product possessing the arabinofuranose stereochemistry.[12] The regioselectivity observed in the epoxide opening was expected based on previous work on the nucleophilic opening of 2,3-anhydrofuranosides.[2,13] Reaction of **11** with tosyl chloride in pyridine afforded **12**. Subsequently, the reduction of the azide using the Staudinger reaction, followed by treatment with triethylamine and finally acetylation (Ac_2O, pyridine) produced aziridine **13** in 79% yield. In the ^{13}C NMR spectrum of **13**, the chemical shift of signals for C-2 and C-3 appeared at 42.6 ppm and 40.5 ppm, respectively, an indication of aziridine ring formation. Compound **13** is crystalline and further support for the structure was obtained from an X-ray diffraction study. The structure (Fig. 3a) showed that the aziridine moiety is cis to the allyl group and trans to the benzoyloxymethyl group.[†]

known that aziridine N-acylation reduces the barrier to nitrogen inversion;[16] in **13** it appears that both forms are energetically similar, at least in the solid state. To date, only 23 crystal structures of *N*-acylated aziridines have been deposited in the Cambridge Crystallographic Database[17–37] and in only four of those cases[20,24,27,28] does the until cell contain more than one molecule. In all four of these, the relative position of the acyl group in the different molecules is the same. Thus, **13** appears to be the first *N*-acylated aziridine in which both inverted nitrogen forms are populated in the crystal.

The final step in the synthesis of **4** involved cleavage of the allyl glycoside in **13**. This cleavage was achieved by first rearrangement of the allyl ether to the vinyl ether in the presence of (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate and H_2.[38] Next, treatment with trimethylamine

[†] Crystallographic data (excluding structure factors) for **13** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 917385. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.

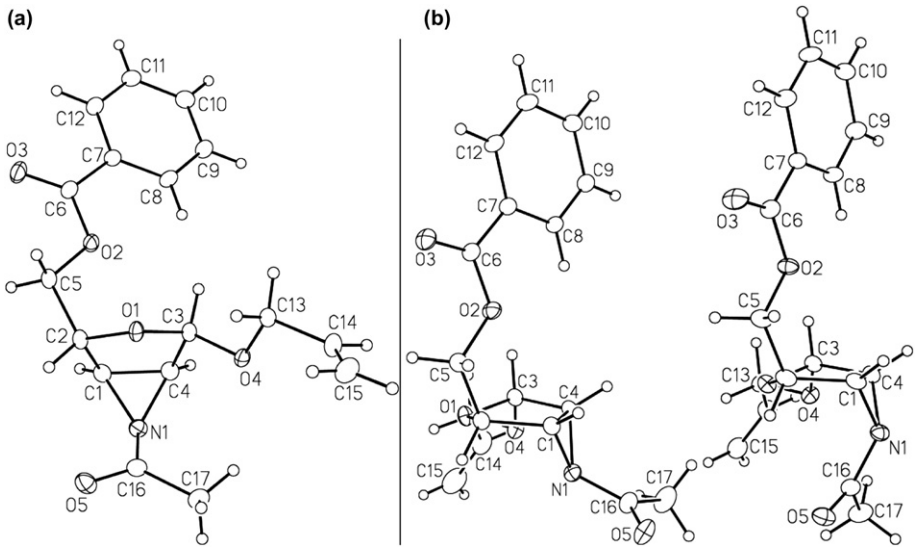


Fig. 3. Crystal structure of **13**. (a) Depicts the orientation of the aziridine ring relative to the allyl and benzoyloxymethyl groups. (b) Shows the different orientations of the acetyl group relative to the furanose ring in the two molecules in the unit cell.

N-oxide and osmium tetroxide[39] resulted in cleavage of the vinyl ether to give the expected hemiacetal (**4**) in 98% yield over the two steps (α/β 1:7). Finally, reaction of **4** with trichloroacetonitrile in the presence of DBU at room temperature produced **5** in excellent yield.[40]

We also explored an alternate route to **4** and **5**, starting from *p*-methoxyphenyl (PMP) glycoside **14**[41] (Scheme 2). As detailed in Scheme S1 (see Supplementary data), **14** could be converted to the expected aziridine **15** using a route analogous to that used to prepare **13**. However, attempted cleavage of the PMP glycoside using with ceric ammonium nitrite (CAN)[42] or 2,3-dichloro-5,6-dicyanobenzoquinone(DDQ)[43] led to decomposition of the molecule and hence this approach was abandoned.

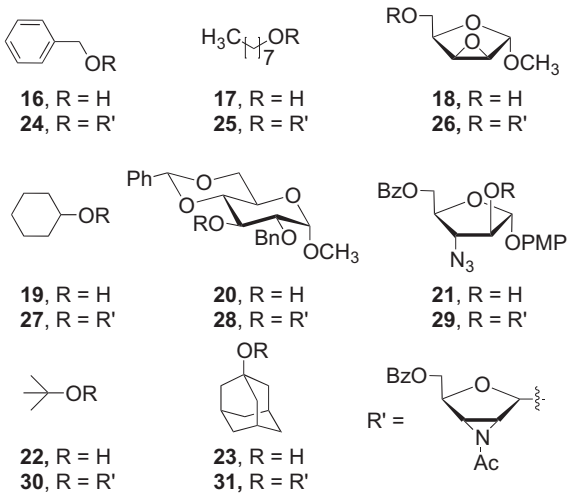
2.2. Method for establishing anomeric stereochemistry in glycoside products

With **4** and **5** in hand, we explored their ability to serve as glycosyl donors. However, before doing that, an unambiguous method for establishing anomeric stereochemistry in the products was needed. Previous studies have reported[11] that the value of the $^1J_{C\text{-}1,H\text{-}1}$ is the only reliable method for determining the stereochemistry at the anomeric center in 2,3-anhydrofuranosides. In these studies, $^1J_{C\text{-}1,H\text{-}1}$ was shown to fall between 163 and 169 Hz when H-1 is trans to the oxirane ring. When H-1 is cis to the epoxide moiety $^1J_{C\text{-}1,H\text{-}1}$ ranged between 174 and 178 Hz.

To determine if this trend was also observed in 2,3-aziridinoglycoisdes, we measured the values of the $^1J_{C\text{-}1,H\text{-}1}$ in **13** and **15**. The X-ray structure for **13** unequivocally established the relative stereochemistry between the aziridine and the anomeric substituent. The similarities in NMR spectra between **13** and **15**, as well as the route by which the compound was synthesized, allowed us to conclude that **15** also has a trans-relationship between the C-1–H-1 bond and the aziridine group. For both **13** and **15**, the $^1J_{C\text{-}1,H\text{-}1}$ value is 169.1 Hz, which is consistent with the trends observed in the corresponding epoxide-functionalized compounds. As described below, in the other glycoside product, where H-1 is cis to the aziridine moiety, the $^1J_{C\text{-}1,H\text{-}1}$ value was ~175 Hz. Thus, it appears that the trends in $^1J_{C\text{-}1,H\text{-}1}$ magnitudes established in the epoxide series also apply for these aziridine-containing compounds.

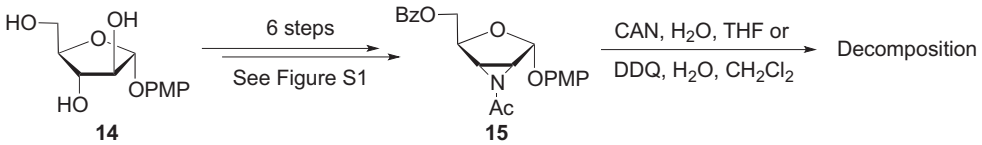
2.3. Stereoselectivity of glycosylation reactions with 4 and 5

To assess the ability of **4** and **5** to act as glycosyl donors, various alcohol acceptors were used (**16**–**23**, Fig. 4). Included were aliphatic primary, secondary, and tertiary alcohols, as well as primary and secondary carbohydrate alcohols.



16, R = H **24**, R = R'
17, R = H **25**, R = R'
18, R = H **26**, R = R'
19, R = H **27**, R = R'
20, R = H **28**, R = R'
21, R = H **29**, R = R'
22, R = H **30**, R = R'
23, R = H **31**, R = R'

Fig. 4. Acceptors studied (**16**–**23**) in glycosylation reactions and possible products (**24**–**31**).



Scheme 2. Attempted synthesis of **4** via PMP glycoside intermediates **14** and **15**.

In situ activation of **4** was performed using the Gin glycosylation protocol.[44] In this reaction, the hemiacetal is activated by the use of trifluoromethanesulfonic anhydride and dimethyl sulfide in the presence of an acid scavenger (2,4,6-tri-*tert*-butyl-pyridine, TTBP). After an appropriate time, a solution of acceptor alcohol is added dropwise and the reaction stirred until complete. Under these conditions we propose that the initially formed oxacarbenium ion pair (**32**, Fig. 5) exists in equilibrium with two glycosyl triflates (**33** and **34**) that react in an S_N2-like fashion with the alcohol when it is added. Previous work on 2,3-anhydrosugar glycosyl triflates suggests that the β-triflate **33** should be more stable than the α-triflate **34**.[45] Hence, if this reaction manifold is operating, the favored product should be the α-glycoside **35**.

The results presented in Table 1 can be rationalized based on the pathway shown in Fig. 5. With the less hindered alcohols, modest α-selectivity results, which could be the result of a direct S_N2-like displacement between the acceptor and the β-triflate **33**. The formation of the β-glycoside could arise from the reaction between the α-triflate **34** and the alcohol. Alternatively, the oxacarbenium ion pair **32** could be the immediate precursor to both glycosides, although the β-glycoside **36** would be expected to be favored for steric reasons. The decreasing α-selectivity seen as the steric bulk of the alcohols increases could result from steric hindrance between the acetylated aziridine moiety in **33** and the nucleophile (Fig. 6). This would lead to an increase in product formation through **32** or **34**.

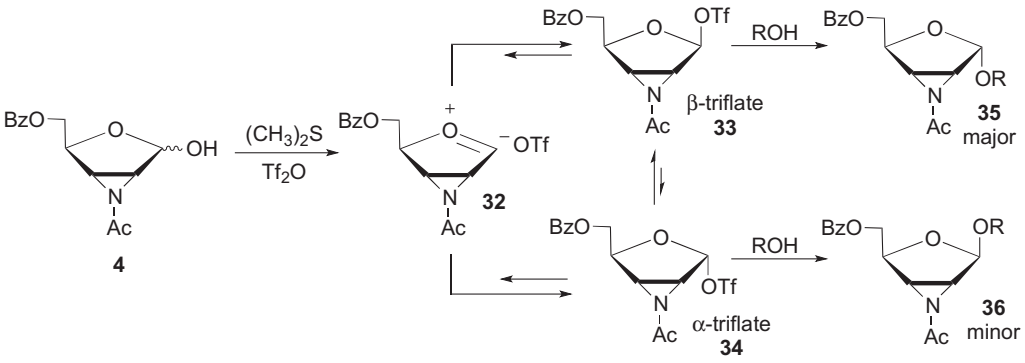


Fig. 5. Plausible mechanistic pathway for glycosylations with **4**.

As illustrated in Table 1, under these conditions, all of the simple alcohols were glycosylated as was the primary carbohydrate alcohol **18**. In contrast, neither of the secondary carbohydrate alcohols (**20** or **21**) led to a product. In these cases, unreacted donor was observed. For those reactions in which a product was formed, the yields were generally good; however, the α/β stereoselectivities were modest. The best results were obtained with benzyl alcohol (**16**), which gave the product in a 2.6:1 α/β ratio. With the more sterically encumbered tertiary alcohols **22** and **23**, the selectivities were lower (~1.5:1 α/β). In general, the glycosylation selectivity decreased as the size of the acceptor alcohol increased. In all cases, the anomeric stereochemistry was determined by measurement of the $^1J_{C\text{-}1,H\text{-}1}$ values of the purified products. For all of the α-glycosides, this value ranged from 167.4 to 169.1 Hz and for all of the β-glycosides this value was between 174.5 Hz and 177.2 Hz.

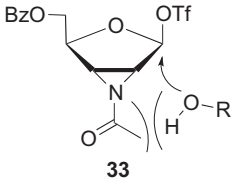


Fig. 6. Proposed negative steric interactions between the aziridine moiety in **33** and alcohols.

We next explored the glycosylation of the trichloroacetimidate **5**. These reactions involved the addition of **5** to a solution of the alcohol in dichloromethane, followed by the dropwise addition of TMSOTf. We also explored the effect of diethyl ether on the selectivity of the glycosylation for some acceptors. Overall, the trends observed in reactions with **4** are also observed with **5** (Table 2).

Table 1
Glycosylation of alcohols **16**–**23** with **4**[a]

Entry	Acceptor	Product	Yield (%)	α/β ratio[b]
1	**16**	**24**	81	2.6:1
2	**17**	**25**	74	1.8:1
3	**18**	**26**	85	2.4:1
4	**19**	**27**	78	1.7:1
5	**20**	**28**	—	—
6	**21**	**29**	—	—
7	**22**	**30**	78	1.6:1
8	**23**	**31**	76	1.3:1

[a] Conditions: see Method A in experimental.
[b] Ratio determined by the integration of the H-1 signal of the glycosides in the ^1H NMR spectrum of the crude products.

Table 2
Glycosylation of alcohols **16**–**23** with **5**[a]

Entry	Solvent	Acceptor	Product	Yield (%)	α/β ratio[b]
1	CH_2Cl_2	**16**	**24**	67	2.2:1
2	CH_2Cl_2	**17**	**25**	72	2.8:1
3	CH_2Cl_2	**18**	**26**	72	4.8:1
4	CH_2Cl_2	**19**	**27**	62	2.8:1
5	CH_2Cl_2	**20**	**28**	—	—
6	CH_2Cl_2	**21**	**29**	—	—
7	CH_2Cl_2	**22**	**30**	71	1.2:1
8	CH_2Cl_2	**23**	**31**	70	1.6:1
9	9:1 CH_2Cl_2–Et_2O	**16**	**24**	68	4.0:1
10	9:1 CH_2Cl_2–Et_2O	**17**	**25**	69	3.6:1
11	9:1 CH_2Cl_2–Et_2O	**22**	**30**	75	1.8:1

[a] Conditions: see Methods B or C in experimental.
[b] Ratio determined by the integration of the H-1 signal of the glycosides in the ^1H NMR spectrum of the crude products.

The glycosylations are modestly α-selective, and, as the steric hindrance on the alcohol increases, the selectivity decreases. When comparing the two donors, the use of the imidate donor generally gives better α-selectivity than the hemiacetal. Finally, when a small amount of ether is added to the reactions involving **5**, the α-selectivity increases further for some alcohols (Table 2, compare entries 1 and 9, entries 2 and 10, and entries 7 and 11).

We propose that the mechanism of the reaction involves a pathway as shown in Fig. 7.[40] Activation of **5** by TMSOTf would lead to **37**, which can proceed down one of two pathways. Direct S_N2-like displacement on **37** by the alcohol will lead directly to the α-glycoside **35**. On the other hand, **37** can also dissociate into an oxacarbenium ion pair **38**, which can react with alcohols to generate a mixture of α and β glycosides **39**. The modest increase in α-selectivity with some alcohols in the presence of diethyl ether[46] can be rationalized by the formation of adduct **40** (from **38**), which would lead to the increase amount of attack cis to the aziridine. Similar to what was proposed for the reactions involving hemiacetal **4**, we speculate that as the steric hindrance on the alcohol increases, direct S_N2 attack on intermediates, such as **37** and **39** become disfavored and that the reaction proceeds through species, such as **38**. This pathway is anticipated to be less α-selective.

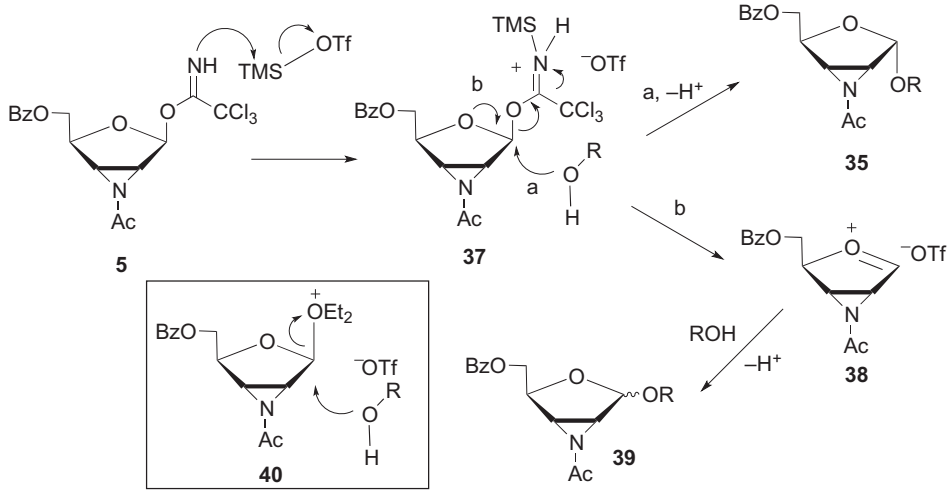


Fig. 7. Plausible mechanistic pathway for glycosylations with **5**.

3. Conclusion

In summary, we describe here the synthesis of two aziridine-containing glycosyl donors, hemiacetal **4** and trichloroacetimidate **5**. The former is obtained in nine steps from D-arabinose and the latter in one additional step. When the ability of these compounds to glycosylate alcohols was studied, the major products were those in which the newly formed glycosidic bond was cis to the aziridine moiety. Trichloroacetimidate **5** provides the products with marginally better stereoselectivity than **4**, and the addition of ether to the reaction mixture modestly enhances this selectivity in some cases.

These results suggest that these species behave analogously to the epoxide-containing (2,3-anhydrosugar) donors we have previously investigated. However, the stereoselectivities with the aziridine substrates are lower. We attribute this to the need for a protecting group on the aziridine nitrogen. The steric bulk of this group could hinder the approach of the nucleophile into an electrophilic intermediate (e.g., **33**, Fig. 6) from the face cis to the aziridine moiety. In the epoxide series, a protecting group is not necessary. Further refinement of this reaction through the use of other donor types (e.g., thioglycosides, sulfoxides), or other nitrogen protecting groups could enhance the α-selectivity. In addition, modification of the nitrogen protecting group, for example, by replacement with a carbamate, could also be anticipated to influence the stereochemical outcome of the reaction via altering the electronic character of the nitrogen.[16] However, the selectivities observed here, and the limitation that secondary carbohydrate alcohols cannot be glycosylated by these species, suggest these donors have limited future application in the synthesis of complex glycans.

4. Experimental section

4.1. General methods

Starting materials and reagents used in reactions were purchased from commercial sources, Sigma–Aldrich and Fluka, and were used without further purification, unless stated otherwise. Solvents used in reactions were purified by passage through columns of alumina and copper under argon pressure. Unless noted differently, all reactions were carried out under a positive pressure of argon/nitrogen and were monitored by TLC on silica gel G-25 UV_{254} (0.25 mm, E. Merck). Spots were detected under UV light or by charring with 10% H_2SO_4 in ethanol or charring with a solution of anisaldehyde in ethanol, acetic acid, and H_2SO_4. Solvents were evaporated under reduced pressure and below 60 °C (bath), and organic solutions of crude products were dried over anhydrous Na_2SO_4. Column chromatography was performed on Silica Gel 60 (40–60 μM) and the ratio between silica gel and crude product ranged from 100 to 50:1 (w/w). Optical rotations were measured at 21±2 °C at the sodium D line (589 nm) on a Perkin–Elmer polarimeter and are in units of deg mL/(dm g). ^{1}H NMR spectra were recorded at 400 or 500 MHz and ^{13}C NMR spectra at 100 or 125 MHz. ^{1}H chemical shifts were referenced to TMS (0.0, $CDCl_3$) or internal CD_3OD (3.31, CD_3OD). ^{13}C chemical shifts were referenced to $CDCl_3$ (77.00, $CDCl_3$) or CD_3OD (49.15, CD_3OD). Peaks assignments were made by 2D NMR (gCOSY, gHSQC, and gHMBC) experiments. IR spectra were obtained as film (by application of a solution of the compound in $CHCl_3$ to an NaCl plate followed by evaporation of the solvent). Electrospray mass spectra were recorded on samples suspended in mixtures of THF and CH_3OH with added NaCl. All acceptors were either commercially available or prepared as previously reported.[6] Product yields from glycosylation reactions are shown in Tables 1 and 2. Crystallographic data (excluding structure factors) for **13** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 917385. Copies of the data can be obtained, free of

charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.

4.2. *N*-Acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-D-ribofuranose (4)

A solution of $[Ir(COD)(PMePh_2)_2]PF_6$ (0.12 g, 0.14 mmol) in THF (24 mL) was stirred under a hydrogen atmosphere for 20 min at room temperature. The catalyst immediately lost its pink color and started to dissolve. The clear solution was injected carefully into a solution of **13** (1.4 g, 4.41 mmol) dissolved in THF (46.4 mL) and the reaction mixture was stirred overnight at room temperature under an argon atmosphere. Concentration of the mixture resulted in a colorless oil, which was dissolved in dichloromethane (58 mL). Trimethylamine *N*-oxide dehydrate (0.75 g, 6.7 mmol) and osmium tetroxide (11.8 mg) were added to the solution and the reaction mixture was stirred for another 12 h at room temperature. The reaction solution was then concentrated and purified by column chromatography (hexanes–EtOAc 1:1) to afford **4** (1.2 g, 98%) as a colorless oil and as a mixture of isomers (α/β-1.0:7.0), R_f 0.21 (1:1, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.11–8.08 (m, 2.38H, Ar), 7.63–7.58 (m, 1.27H, Ar), 7.51–7.46 (m, 2.42H, Ar), 5.52 (d, 0.15H, *J*=1.0 Hz, H-1α), 5.51 (s, 1H, H-1β), 4.58–4.48 (m, 2.64H), 4.44–4.35 (m, 1.24H), 4.34–4.30 (m, 0.34H), 3.44 (d, 1H, *J*=4.0 Hz), 3.41 (dd, 0.17H, *J*=1.0, 4.0 Hz), 3.38–3.34 (m, 1H), 2.21 (s, 0.42H, acetate CH_3α), 2.10 (s, 3H, acetate CH_3β); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 180.8 (C=O), 179.7 (C=O), 166.3 (C=O), 166.0 (C=O), 133.5 (Ar–C), 133.4 (Ar–C), 129.7 (Ar–C), 129.6 (Ar–C), 129.4 (Ar–C), 128.6 (Ar–C), 128.6 (Ar–C), 128.5 (Ar–C), 97.9 (C-1α), 95.3 (C-1β), 74.9 (C-4β), 74.7 (C-4α), 65.3 (C-5β), 65.0 (C-5α), 43.6 (C-2β), 41.5 (C-2α), 40.9 (C-2α), 40.8 (C-2β), 23.9 (CH_3), 23.6 (CH_3). HRMS (ESI) calcd for (M+Na) $C_{14}H_{15}NO_5$+Na: 300.0847, found 300.0845.

4.3. *N*-Acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranosyl trichloroacetimidate (5)

To a stirring solution of **1** (0.5 g, 1.8 mmol) and trichloroacetonitrile (1.26 mL, 12.6 mmol) in dichloromethane (18.0 mL) cooled to 0 °C was added a solution of DBU (13.48 μL, 0.09 mmol) in dichloromethane (0.6 mL) over a period of 5 min. The reaction mixture then warmed to room temperature over 10 min and was stirred for 2 h at room temperature. The solution then concentrated at room temperature under reduced pressure, and the residue was purified by silica gel flash chromatography (6:4, hexanes–EtOAc with 0.5% Et_3N, R_f 0.28) to give trichloroacetimidate **2** (0.74 g, 98%) as an amorphous white solid; $[\alpha]_D$ −25.1 (*c* 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.68 (s, 1H), 8.08–8.06 (m, 2H, Ar), 7.63–8.59 (m, 1H, Ar), 7.50–7.46 (m, 2H, Ar), 6.56 (s, 1H, H-1), 4.73 (dd, 1H, *J*=6.0, 7.0 Hz, H-4), 4.53 (dd, 1H, *J*=7.0, 12.5 Hz, H-5), 4.49 (dd, 1H, *J*=6.0, 11.5 Hz, H-5), 3.65 (d, 1H, *J*=4.0 Hz, H-2), 3.61 (dd, 1H, *J*=4.0 Hz, H-3), 2.22 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 176.4 (C=O), 163.5 (C=O), 158.2 (*C*=NH), 130.8 (Ar), 127.2 (Ar), 126.8 (Ar), 125.9 (Ar), 95.9 (C-1), 89.0 (CCl_3), 74.9 (C-4), 62.8 (C-5), 40.5 (C-2), 39.2 (C-3), 22.1 (CH_3); $J_{C\text{-}1,H\text{-}1}$=183.1 Hz. HRMS (ESI) calcd for (M+Na) $C_{16}H_{15}Cl_3N_2O_5$+Na: 442.9943, found 442.9943.

4.4. Allyl 2,3-anhydro-5-*O*-benzoyl-α-D-lyxofuranoside (10)

To a solution of **9**[9] (3.10 g, 16.30 mmol) in THF (180 mL), triphenylphosphine (10.73 g, 40.76 mmol) and benzoic acid (3.0 g, 24.46 mmol) were added. The resulting mixture was then cooled to 0 °C and diisopropyl azodicarboxylate (3.86 mL, 19.5 mmol) was added dropwise over a period of 10 min. The reaction mixture was allowed to stir at room temperature for 2 h under an argon atmosphere. The solution was subsequently concentrated under reduced pressure to yield a crude oil from, which most of the triphenylphosphine oxide precipitated upon trituration with cold diethyl ether. The triphenylphosphine oxide was filtered off and the filtrate was concentrated. The resulting residue was purified by chromatography (hexanes–EtOAc, 7:1) to obtain compound **10** (3.7 g, 82%) as a white crystalline solid. R_f 0.62 (hexanes–EtOAc, 4:1); $[\alpha]_D$ +41.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ_H) 8.12–8.03 (m, 2H, Ar), 7.62–7.52 (m, 1H, Ar), 7.51–7.40 (m, 2H, Ar), 5.99–5.83 (m, 1H, C*H*=CH_2), 5.31 (ddd, 1H, *J*=1.6, 3.2, 17.1 Hz, CH=C*H*$_2$), 5.22 (ddd, 1H, *J*=1.6, 2.8, 10.3 Hz, CH=C*H*$_2$), 5.15 (s, 1H, H-1), 4.55 (dd, 1H, *J*=6.0, 11.5 Hz, H-5), 4.50 (dd, 1H, *J*=6.0, 11.5 Hz, H-5), 4.36 (dd, 1H, *J*=5.6, 6.0 Hz, H-4), 4.27 (dddd, 1H, *J*=1.2, 1.2, 5.2, 12.8 Hz, OC*H*$_2$CH=CH_2), 4.06 (dddd, 1H, *J*=1.2, 1.2, 6.0, 12.8 Hz, OC*H*$_2$CH=CH_2), 3.83 (dd, 1H, *J*=0.8, 2.8 Hz, H-2), 3.73 (d, 1H, *J*=2.8 Hz, H-3); ^{13}C NMR (125.3 MHz, $CDCl_3$, δ_C) 166.2 (C=O), 133.7 (*C*H=CH_2), 133.1 (Ar–C), 129.7 (Ar–C), 129.7 (Ar–C), 128.3 (Ar–C), 117.7 (CH=*C*H$_2$), 100.5 (C-1), 74.0 (C-4), 69.0 (O*C*H$_2$CH=CH_2), 62.8 (C-5), 56.3 (C-2), 54.1 (C-3). HRMS (ESI) calcd for (M+Na) $C_{15}H_{16}O_5$+Na: 299.1563, found 299.1560.

4.5. Allyl 3-azido-5-*O*-benzoyl-3-deoxy-α-D-arabinofuranoside (11)

To a solution of compound **10** (2.6 g, 9.49 mmol) in EtOH–H_2O (9:1, 95 mL) were added NaN_3 (3.67 g, 56.5 mmol) and NH_4Cl (5.03 g, 94.1 mmol). The reaction mixture was heated at reflux for 48 h, cooled to room temperature, and extracted with EtOAc (2×50 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The product was purified by column chromatography (5:1, hexanes–EtOAc) to yield **11** (2.57 g, 85%, 9% starting material **10** was also recovered) as a colorless syrup: R_f 0.25 (5:1, hexanes–EtOAc); $[\alpha]_D$ +100.6 (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.12–8.03 (m, 2H, Ar), 7.62–7.52 (m, 1H, Ar), 7.51–7.40 (m, 2H, Ar), 5.94–5.86 (m, 1H, C*H*=CH_2), 5.31 (ddd, 1H, *J*=1.6, 3.2, 17.1 Hz, CH=C*H*$_2$), 5.22 (ddd, 1H, *J*=1.6, 2.8, 10.3 Hz, CH=C*H*$_2$), 5.05 (d, 1H, *J*=1.5 Hz, H-1), 4.58 (dd, 1H, *J*=4.0, 12.0 Hz, H-5), 4.50 (dd, 1H, *J*=4.5, 12.0 Hz, H-5), 4.35–4.20 (m, 3H, H-4, 2× OC*H*$_2$CH=CH_2), 4.05 (ddd, 1H, *J*=1.0, 6.0, 13.0 Hz, H-2), 3.80 (dd, 1H, *J*=3.5, 7.0 Hz, H-3), 3.12 (br, 1H); ^{13}C NMR (125.3 MHz, $CDCl_3$, δ_C) 166.4 (C=O), 133.6 (*C*H=CH_2), 133.4 (Ar–C), 129.8 (Ar–C), 129.7 (Ar–C), 128.5 (Ar–C), 117.7 (CH=*C*H$_2$), 106.8 (C-1), 80.9 (C-2), 79.1 (C-4), 68.5 (OCH_2CH=CH_2), 67.5 (C-3), 63.8 (C-5); IR (film) 3467.2 (br), 3061.9, 2956.1, 2107.2 (N=N=N), 1723.5 (C=O), 1275.4 (C–O). HRMS (ESI) calcd for (M+Na) $C_{15}H_{17}N_3O_5$+Na: 342.1066, found 342.1056.

4.6. Allyl 3-azido-5-*O*-benzoyl-3-deoxy-2-*O*-*p*-toluenesulfonyl-α-D-arabinofuranoside (12)

A solution of compound **11** (2.4 g, 7.51 mmol) dissolved in dichloromethane (28 mL) and pyridine (4.5 mL) was treated at 0 °C with *p*-toluenesulfonyl chloride (5.3 g, 27.8 mmol), and the reaction mixture was stirred for 50 h at room temperature under argon. The reaction mixture was quenched by the addition of a small piece of ice and then diluted with dichloromethane (22 mL). The organic layer was washed with a satd aq $NaHCO_3$ solution and then water. The crude solution was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (7:1, *n*-hexanes–EtOAc) to yield **12** (2.81 g, 79%) as an oil. R_f 0.35 (7:1, hexanes–EtOAc); $[\alpha]_D$ +86.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.10–8.04 (m, 2H, Ar), 7.82–7.77 (m, 2H, Ar), 7.61–7.56 (m, 1H, Ar), 7.49–7.40 (m, 2H, Ar),7.35 (d, 2H, *J*=8.0 Hz, Ar), 5.57–5.55 (m, 1H, C*H*=CH_2), 5.25 (ddd, 1H, *J*=1.5, 3.5, 17.0 Hz, CH=C*H*$_2$), 5.18 (ddd, 1H, *J*=1.0, 2.5, 11.5 Hz, CH=C*H*$_2$), 5.08 (s, 1H, H-1), 4.78 (d, 1H, *J*=2.5 Hz, H-2), 4.55 (dd, 1H, *J*=4.0, 12.0 Hz, H-5), 4.46 (dd, 1H, *J*=4.0, 12.0 Hz, H-5), 4.18

(ddd, 1H, J=4.0, 4.0,7.0 Hz, H-4), 4.12 (dddd, 1H, J=1.5, 1.5, 5.0, 13.0 Hz, OCH_2CH=CH_2), 3.96 (dd, 1H, J=3.0, 6.5 Hz, H-3), 3.94 (dddd, 1H, J=1.5, 1.5, 6.5, 13.0 Hz, OCH_2CH=CH_2), 2.94 (s, 3H, CH_3); ^{13}C NMR (125.3 MHz, $CDCl_3$, δ_C) 166.1 (C=O), 145.7 (Ar), 133.4 (*C*H=CH_2), 133.1, 132.6, 130.2, 129.8, 129.3, 128.5, 128.1, 118.0 (CH=*C*H_2), 104.1 (C-1), 87.4 (C-2), 79.3 (C-4), 68.2 (O*C*H_2CH=CH_2), 65.9 (C-3), 62.9 (C-5), 21.7 (CH_3); IR (film) 3060.9, 2946.7, 2111.0 (N=N=N), 1724.1 (C=O), 1273.0 (C–O). HRMS (ESI) calcd for (M+Na) $C_{22}H_{23}N_3O_7S$+Na: 496.1153, found 496.1151.

4.7. Allyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-α-D-ribofuranoside (13)

To a solution of azide **12** (2.2 g, 4.6 mmol) in THF (5.2 mL), water (0.41 mL) and triphenylphosphine (3.02 g, 11.5 mmol) were added. The resulting mixture was stirred for 20 h at room temperature. The solution then dried over Na_2SO_4 and concentrated under high vacuum resulting in a colorless crude oil. Without further purification, DMF (24 mL) and triethylamine (0.83 mL) were added to the crude product at room temperature. The reaction mixture was stirred at 100 °C for 20 h and then cooled to room temperature. Pyridine (27 mL) and acetic anhydride (4.6 mL) were then added to the mixture cooled at 0 °C. After stirring for 4 h at room temperature, the mixture was extracted with EtOAc (3×30 mL). The organic phases were combined, washed with a satd aq $NaHCO_3$ solution and then water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (7:1, hexanes–EtOAc) to yield **13** (2.81 g, 79%) as a white solid: R_f 0.35 (2:1, hexanes–EtOAc); $[\alpha]_D$ −59.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.01–8.04 (m, 2H, Ar), 7.60–7.56 (m, 1H, Ar), 7.47–7.41 (m, 2H, Ar), 5.95–5.86 (m, 1H, C*H*=CH_2), 5.65 (d, 1H, J=1.5 Hz, H-1), 5.3 (ddd, 1H, J=1.5, 3.5, 17.0 Hz, CH=CH_2), 5.19 (ddd, 1H, J=1.0, 2.5, 10.5 Hz, CH=CH_2), 4.71 (dd, 1H, J=4.0, 4.0 Hz, H-4), 4.5 (dd, 1H, J=4.0, 12.0 Hz, H-5), 4.38 (dd, 1H, J=4.0, 12.0 Hz, H-5), 4.32 (dddd, 1H, J=1.5, 1.5, 5.0, 13.0 Hz, OCH_2CH=CH_2), 4.15 (dddd, 1H, J=1.5, 1.5, 6.5, 13.0 Hz, OCH_2CH=CH_2), 3.4 (dd, 1H, J=1.5, 4.5 Hz, H-2), 3.3 (d, 1H, J=4.0 Hz, H-3), 3.22 (s, 3H, *C*H_3); ^{13}C NMR (125.3 MHz, $CDCl_3$, δ_C) 180.8 (C=O), 166.1 (C=O), 133.6 (Ar–C), 133.4 (*C*H=CH_2), 129.6 (Ar–C), 129.5 (Ar–C), 128.6 (Ar–C), 117.6 (CH=CH_2), 101.5 (C-1), 74.9 (C-4), 70.9 (OCH_2CH=CH_2), 65.2 (C-5), 42.6 (C-2), 40.5 (C-3), 24.0 (*C*H_3); $J_{C\text{-}1,H\text{-}1}$=169.1 Hz. HRMS (ESI) calcd for (M+Na) $C_{17}H_{19}NO_5$+Na: 340.1160, found 340.1145.

4.8. General procedures for glycosylation reactions

*4.8.1. Method A: glycosylation with **4** using $(CH_3)_2S$ and Tf_2O.*[44] To a stirring solution of *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-D-ribofuranose (**4**, 35 mg, 0.13 mmol), 2,4,6-tri-*tert*-butylpyridine (140.3 mg, 0.56 mmol), and dimethyl sulfide (18.64 μL, 0.3 mmol) in dichloromethane (1.8 mL) was added trifluoromethanesulfonic acid anhydride (31.85 μL, 0.19 mmol, 1.5 equiv) at −45 °C under an argon atmosphere. The resulting solution was stirred for 1 h at this temperature, followed by 15 min at 0 °C and finally another 15 min at room temperature. A solution of an alcohol (**20** to **27**, 0.19 mmol, 1.5 equiv) in dichloromethane (0.44 mL) was then added dropwise. The reaction mixture then stirred for 12 h at room temperature, and diluted with dichloromethane (20 mL). The diluted solution was washed with a satd aq $NaHCO_3$ and water. The organic layer was dried, filtered, and concentrated. The crude residue was purified by chromatography to afford the products shown in Table 2.

*4.8.2. Method B: glycosylation with imidate **5** using TMSOTf in dichloromethane.*[40] To a stirring solution of an alcohol (**16** to **23**, 0.1 mmol, 0.8 equiv) in dichloromethane (1.0 mL) at −25 °C containing 4 Å molecular sieves (10 mg) was added a solution of trichloroacetimidate **5** (50 mg, 0.12 mmol) dissolved in dichloromethane (1.0 mL). A solution of TMSOTf (0.05 equiv) in dichloromethane (0.16 mL) was added dropwise to the reaction mixture over a period of 5 min. The resulting mixture was stirred at this temperature for 15 min, then another 15 min at −20 °C, and finally warmed slowly to −5 °C over 1 h. After quenching the acid by the addition of Et_3N, the reaction mixture was diluted with dichloromethane (3 mL) and filtered through Celite. The filtrate was concentrated under reduced pressure to give a crude residue that was purified by column chromatography to afford products shown in Table 2.

*4.8.3. Method C: glycosylation with imidate **5** using TMSOTf in dichloromethane and 10% diethyl ether.*[40] The donor **5** (50 mg, 0.12 mmol) was dissolved in dichloromethane (1.0 mL) and then added to a solution of alcohol (**16**, **17** or **22**) dissolved in dichloromethane (1.0 mL) and diethyl ether (0.1 mL) containing 4 Å molecular sieves (10 mg, stirred already for 10 min) at −25 °C. At this temperature, a solution of TMSOTf (0.05 equiv) in dichloromethane (0.16 mL) was added dropwise over 5 min. The resulting mixture was stirred for 15 min followed by another 15 min at −20 °C, and at last warmed slowly to −5 °C over 1 h. The reaction mixture then quenched by the addition of Et_3N (0.56 μL), diluted with dichloromethane (3 mL), and filtered through Celite. The filtrate was concentrated to give a crude residue that was purified by column chromatography to afford the products shown in Table 2 (Results and discussion section).

4.9. Benzyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-α-D-ribofuranoside (24α)

The compound was isolated after chromatography (hexanes–EtOAc, 3:1) as a colorless oil. R_f 0.26 (hexanes–EtOAc, 2:1); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.07–8.03 (m, 2H, Ar), 7.62–7.58 (m, 1H, Ar), 7.46–7.42 (m, 2H, Ar), 7.26–7.22 (m, 5H, Ar), 5.39 (d, 1H, J=1.5 Hz, H-1), 4.87 (d, 1H, J=12.0 Hz, PhCH_2), 4.76 (dd, 1H, J=4.0, 4.0 Hz, H-4), 4.59 (d, 1H, J=12.0 Hz, PhCH_2), 4.52 (dd, 1H, J=4.0, 12.0 Hz, H-5), 4.39 (dd, 1H, J=4.0, 12.0 Hz, H-5), 3.78 (dd, 1H, J=1.0, 3.5 Hz, H-2), 3.78 (d, 1H, J=4.0 Hz, H-3), 2.15 (s, 3H, acetate CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 180.7 (C=O), 166.0 (C=O), 136.9 (Ar–C), 133.4 (Ar–C), 129.5 (Ar–C), 129.4 (Ar–C), 128.5 (Ar–C), 128.4 (Ar–C), 128.0 (Ar–C), 127.9 (Ar–C), 101.1 (C-1), 74.7 (C-4), 71.6 (OCH_2), 65.2 (C-5), 42.5 (C-2), 40.4 (C-3), 24.1 (*C*H_3); $J_{C\text{-}1,H\text{-}1}$=168.3 Hz. HRMS (ESI) calcd for (M+Na) $C_{21}H_{11}NO_5$+Na: 390.1316, found 390.1314.

4.10. Benzyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranoside (24β)

The compound was isolated after chromatography (hexanes–EtOAc, 3:1) as a colorless oil. R_f 0.28 (hexanes–EtOAc, 2:1); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.10–8.05 (m, 2H, Ar), 7.61–7.54 (m, 1H, Ar), 7.49–7.40 (m, 2H, Ar), 7.38–7.31 (m, 5H), 5.29 (s, 1H, H-1), 4.78 (d, 1H, J=11.5 Hz, PhCH_2), 4.63 (dd, 1H, J=6.5, 6.5 Hz, H-4), 4.56 (d, 1H, J=11.5 Hz, PhCH_2), 4.51 (dd, 1H, J=6.0, 11.5 Hz, H-5), 4.48 (dd, 1H, J=6.5, 11.5 Hz, H-5), 3.46 (d, 1H, J=3.5 Hz, H-2), 3.42 (d, 1H, J=4.0 Hz, H-3), 2.16 (s, 3H, acetate CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 179.2 (C=O), 166.1 (C=O), 136.7 (Ar–C), 133.2 (Ar–C), 129.7 (Ar–C), 129.6 (Ar–C), 128.5 (Ar–C), 128.4 (Ar–C), 128.2 (Ar–C), 128.0 (Ar–C), 100.2 (C-1), 75.0 (C-4), 70.2 (OCH_2), 64.8 (C-5), 42.8 (C-2), 40.7 (C-3), 23.7 (*C*H_3); $J_{C\text{-}1,H\text{-}1}$=175.1 Hz. HRMS (ESI) calcd for (M+Na) $C_{21}H_{11}NO_5$+Na: 390.1316, found 390.1314.

4.11. *n*-Octyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-α-D-ribofuranoside (25α)

The compound was isolated after chromatography (4:1, hexanes–EtOAc) as a colorless oil: R_f 0.40 (3:1, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.09–8.01 (m, 2H, Ar), 7.65–7.52 (m, 1H, Ar), 7.51–7.40 (m, 2H, Ar), 5.34 (d, 1H, J=1.5 Hz, H-1), 4.76 (dd, 1H, J=4.0, 4.0 Hz, H-4), 4.53 (dd, 1H, J=4.0, 12.0 Hz, H-5), 4.40 (dd, 1H, J=4.0, 12.0 Hz, H-5), 3.81 (ddd, 1H, J=6.5, 7.0, 9.5 Hz, octyl OC*H*$_2$), 3.53 (ddd, 1H, J=6.5, 7.0, 9.0 Hz, octyl OC*H*$_2$), 3.42 (dd, 1H, J=1.5, 4.5 Hz, H-2), 3.31 (d, 1H, J=4.0 Hz, H-3), 2.23 (s, 3H, acetate CH_3), 1.71–1.58 (m, 4H, octyl CH_2), 1.42–1.18 (m, 8H, octyl CH_2), 0.95 (t, 3H, J=6.8 Hz, octyl CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 180.8 (C=O), 166.1 (C=O), 133.4 (Ar–C), 129.6 (Ar–C), 129.5 (Ar–C), 128.6 (Ar–C), 102.5 (C-1), 74.3 (C-4), 70.8 (octyl OC*H*$_2$), 65.3 (C-5), 42.6 (C-2), 40.3 (C-3), 31.8 (octyl-*C*H$_2$), 29.7 (octyl-*C*H$_2$), 29.6 (octyl-*C*H$_2$), 29.5 (octyl-*C*H$_2$), 25.9 (octyl-*C*H$_2$), 24.1 (acetate-*C*H$_3$), 14.1 (octyl-*C*H$_3$); $J_{C\text{-}1,H\text{-}1}$=169.0 Hz. HRMS (ESI) calcd for (M+Na) $C_{22}H_{31}NO_5$+Na: 412.2099, found 412.2093.

4.12. *n*-Octyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranoside (25β)

The compound was isolated after chromatography (4:1, hexanes–EtOAc) as a colorless oil: R_f 0.43 (3:1, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.12–8.03 (m, 2H, Ar), 7.62–7.55 (m, 1H, Ar), 7.51–7.46 (m, 2H, Ar), 5.17 (s, 1H, H-1), 4.60 (dd, 1H, J=6.0, 6.5 Hz, H-4), 4.45 (d, 2H, J=6.5 Hz, H-5), 3.75 (ddd, 1H, J=6.5, 7.0, 9.5 Hz, octyl OC*H*$_2$), 3.47 (ddd, 1H, J=6.5, 7.0, 9.0 Hz, octyl OC*H*$_2$), 3.43 (d, 1H, J=3.5 Hz, H-2), 3.36 (d, 1H, J=3.5 Hz, H-3), 2.18 (s, 3H, acetate CH_3), 1.64–1.50 (m, 4H, octyl CH_2), 1.20–1.14 (m, 8H, octyl CH_2), 0.91 (t, 3H, J=7.0 Hz, octyl CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 179.2 (C=O), 166.1 (C=O), 133.2 (Ar–C), 129.7 (Ar–C), 129.6 (Ar–C), 128.4 (Ar–C), 100.9 (C-1), 74.6 (C-4), 68.9 (octyl-OC*H*$_2$), 64.9 (C-5), 42.6 (C-2), 40.7 (C-3), 31.8 (octyl-*C*H$_2$), 29.7 (octyl-*C*H$_2$), 29.5 (octyl-*C*H$_2$), 29.3 (octyl-*C*H$_2$), 26.1 (octyl-*C*H$_2$), 23.7 (acetate-*C*H$_3$), 14.1 (octyl-*C*H$_3$); $J_{C\text{-}1,H\text{-}1}$=177.0 Hz. HRMS (ESI) calcd for (M+Na) $C_{22}H_{31}NO_5$+Na: 412.2099, found 412.2093.

4.13. Methyl 5-*O*-(*N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-α-D-ribofuranosyl)-2,3-anhydro-α-D-lyxofuranoside (26α)

The compound was isolated after chromatography (3:1, hexanes–EtOAc) as white solid: R_f 0.19 (3:2, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.09–8.01 (m, 2H, Ar), 7.65–7.52 (m, 1H, Ar), 7.51–7.40 (m, 2H, Ar), 5.43 (d, 1H, J=1.5 Hz, H-1′), 4.93 (s, 1H, H-1), 4.76 (dd, 1H, J=4.0, 4.0 Hz, H-4′), 4.55 (dd, 1H, J=3.5, 12.0 Hz, H-5′), 4.42 (dd, 1H, J=4.0, 12.0 Hz, H-5′), 4.25 (dd, 1H, J=5.5, 10.0 Hz, H-5), 3.96 (dd, 1H, J=5.0, 10.0 Hz, H-5), 3.82–3.76 (m, 2H, H-3, H-4), 3.65 (d, 1H, J=3.5 Hz, H-2), 3.48 (dd, 1H, J=1.5, 4.0 Hz, H-2′), 3.41 (s, 3H,OCH_3), 3.34 (d, 1H, J=4.0 Hz, H-3′), 2.06 (s, 3H, acetate CH_3);[13] C NMR (125.7 MHz, $CDCl_3$, δ_C) 180.6 (C=O), 166.1 (C=O), 133.4 (Ar–C), 129.4 (Ar–C), 128.5 (Ar–C), 102.7 (azi-C-1), 102.1 (epo-C-1), 74.9 (C-4′), 74.5 (C-4), 67.3 (C-5), 64.8 (C-5′), 56.3 (C-2), 55.5 (C-3), 42.5 (C-2′), 40.5 (C-2′), 24.0 (OCH_3); $J_{C\text{-}1,H\text{-}1}$=169.1 Hz. HRMS (ESI) calcd for (M+Na) $C_{20}H_{23}NO_8$+Na: 428.1321, found 428.1316.

4.14. Methyl 5-*O*-(*N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranosyl)-2,3-anhydro-β-D-lyxofuranoside (26β)

The compound was isolated after chromatography (3:1, hexanes–EtOAc) as white solid: R_f 0.22 (3:2, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.06–8.04 (m, 2H, Ar), 7.66–7.63 (m, 1H, Ar), 7.52–7.48 (m, 2H, Ar), 5.24 (s, 1H, H-1′), 4.97 (s, 1H, H-1), 4.61 (dd, 1H, J=6.0, 7.0 Hz, H-4′), 4.48 (dd, 2H, J=7.0, 7.0 Hz, H-5′), 4.19 (dd, 1H, J=6.0, 10.0 Hz, H-5), 3.96 (dd, 1H, J=5.5, 10.0 Hz, H-5), 3.63–3.74 (m, 3H, H-2′, H-2, H-4), 3.43–3.47 (m, 2H, H-3′, H-3), 3.41 (s, 3H,OCH_3), 2.15 (s, 3H, acetate CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 179.2 (C=O), 166.1 (C=O), 133.3 (Ar–C), 129.7 (Ar–C), 128.4 (Ar–C), 102.4 (azi-C-1), 101.4 (epo-C-1), 75.1 (C-4′), 75.0 (C-4), 67.4 (C-5), 64.8 (C-5′), 56.0 (C-2), 55.6 (C-3), 42.7 (C-2′), 40.6 (C-3′), 23.7 (OCH_3); $J_{C\text{-}1,H\text{-}1}$=177.2 Hz. HRMS (ESI) calcd for (M+Na) $C_{20}H_{23}NO_8$+Na: 428.1321, found 428.1316.

4.15. Cyclohexyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-α-D-ribofuranoside (27α)

The compound was isolated after chromatography (hexanes–EtOAc, 4:1) as a colorless oil. R_f 0.32 (hexanes–EtOAc, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.12–8.03 (m, 2H, Ar), 7.62–7.55 (m, 1H, Ar), 7.51–7.46 (m, 2H, Ar), 5.46 (d, 1H, J=1.0 Hz, H-1), 4.76 (dd, 1H, J=4.0, 4.5 Hz, H-4), 4.53 (dd, 1H, J=4.0, 12.0 Hz, H-5), 4.40 (dd, 1H, J=4.5, 12.0 Hz, H-5), 3.57–3.64 (m, 1H, cyclohexyl CH), 3.38 (dd, 1H, J=1.0, 4.0 Hz, H-2), 3.26 (d, 1H, J=4.0 Hz, H-3), 2.18 (s, 3H, acetate CH_3), 1.98–1.18 (m, 10H, cyclohexyl CH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 180.8 (C=O), 166.1 (C=O), 133.4 (Ar–C), 129.6 (2Ar–C), 128.6 (2Ar–C), 100.7 (C-1), 78.2 (cyclohexyl-*C*H), 73.9 (C-4), 65.3 (C-5), 42.9 (C-2), 39.8 (C-3), 33.1 (cyclohexyl *C*H$_2$), 32.0 (cyclohexyl *C*H$_2$), 29.7 (cyclohexyl *C*H$_2$), 29.6 (cyclohexyl *C*H$_2$), 24.2 (OCH_3), 24.1 (cyclohexyl *C*H$_2$); $J_{C\text{-}1,H\text{-}1}$=168.2 Hz. HRMS (ESI) calcd for (M+Na) $C_{20}H_{25}NO_5$+Na: 382.1629, found 382.1623.

4.16. Cyclohexyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranoside (27β)

The compound was isolated after chromatography (hexanes–EtOAc, 4:1) as a colorless oil. R_f 0.37 (hexanes–EtOAc, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.12–8.03 (m, 2H), 7.62–7.55 (m, 1H), 7.51–7.46 (m, 2H), 5.33 (s, 1H, H-1), 4.40–4.60 (m, 3H, H-4, H-5), 3.70–3.64 (m, 1H), 3.44 (d, 1H, J=3.5 Hz, H-2), 3.33 (d, 1H, J=4.0 Hz, H-3), 2.08 (s, 3H, acetate CH_3), 1.98–1.17 (m, 10H, cyclohexyl CH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 179.3 (C=O), 166.1 (C=O), 133.2 (Ar–C), 129.7 (Ar–C), 129.6 (Ar–C), 128.4 (Ar–C), 99.1 (C-1), 78.2 (cyclohexyl-*C*H), 74.3 (C-4), 65.0 (C-5), 42.7 (C-2), 41.0 (C-3), 33.2 (cyclohexyl *C*H$_2$), 32.1 (cyclohexyl *C*H$_2$), 29.6 (cyclohexyl *C*H$_2$), 29.4 (cyclohexyl *C*H$_2$), 24.1 (acetate *C*H$_3$), 24.1 (cyclohexyl *C*H$_2$); $J_{C\text{-}1,H\text{-}1}$=175.1 Hz. HRMS (ESI) calcd for (M+Na) $C_{20}H_{25}NO_5$+Na: 382.1629, found 382.1623.

4.17. *tert*-Butyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-α-D-ribofuranoside (30α)

The compound was isolated after chromatography (3:1, hexanes–EtOAc) as a colorless oil: R_f 0.26 (2:1, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.06–8.03 (m, 2H, Ar), 7.61–7.58 (m, 1H, Ar), 7.53–7.47 (m, 2H, Ar), 5.52 (d, 1H, J=1.0 Hz, H-1), 4.74 (dd, 1H, J=4.5, 4.5 Hz, H-4), 4.55 (dd, 1H, J=4.5, 12.0 Hz, H-5), 4.40 (dd, 1H, J=4.5, 12.0 Hz, H-5), 3.29 (dd, 1H, J=1.5, 4.0 Hz, H-2), 3.23 (d, 1H, J=4.0 Hz, H-3), 2.24 (s, 3H, acetate CH_3), 1.23 (s, 9H, *tert*-butyl CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 181.0 (C=O), 166.1 (C=O), 133.4 (Ar–C), 129.6 (Ar–C), 129.6 (Ar–C), 128.5 (Ar–C), 96.8 (C-1), 75.8 (O*C*(CH_3)$_3$), 73.8 (C-4), 65.1 (C-5), 43.3 (C-2), 39.3 (C-3), 29.7 (C(*C*H$_3$)$_3$), 28.4 (C(*C*H$_3$)$_3$), 24.2 (acetate *C*H$_3$); $J_{C\text{-}1,H\text{-}1}$=168.6 Hz. HRMS (ESI) calcd for (M+Na) $C_{18}H_{23}NO_5$+Na: 356.1473, found 356.1468.

4.18. *tert*-Butyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranoside (30β)

The compound was isolated after chromatography (3:1, hexanes–EtOAc) as a colorless oil: R_f 0.31 (2:1, hexanes–EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.07–8.02 (m, 2H, Ar), 7.60–7.58 (m, 1H, Ar), 7.53–7.47 (m, 2H, Ar), 5.47 (s, 1H, H-1), 4.55–4.44 (m, 3H, H-4, 2H-5), 3.45 (d, 1H, J=4.0 Hz, H-2), 3.24 (d, 1H, J=4.0 Hz, H-3), 2.15 (s, 3H, acetate CH_3), 1.28 (s, 9H, *tert*-butyl CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 181.0 (C=O), 166.1 (C=O), 133.2 (Ar–C), 129.8 (Ar–C), 129.7 (Ar–C), 128.4 (Ar–C), 95.5 (C-1), 75.8 ($OC(CH_3)_3$), 74.3 (C-4), 65.1 (C-5), 43.1 (C-2), 41.4 (C-3), 29.7 ($C(CH_3)_3$), 28.8 ($C(CH_3)_3$), 23.7 (acetate CH_3); $J_{C\text{-}1,H\text{-}1}$=174.5 Hz. HRMS (ESI) calcd for (M+Na) $C_{18}H_{23}NO_5$+Na: 356.1473, found 356.1468.

4.19. 1-Adamantyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-α-D-ribofuranoside (31α)

The compound was isolated after chromatography (hexanes–EtOAc, 3:1) as a colorless oil. R_f 0.22 (hexanes–EtOAc, 2:1); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.12–8.03 (m, 2H, Ar), 7.62–7.52 (m, 1H, Ar), 7.51–7.40 (m, 2H, Ar), 5.64 (d, 1H, J=1.5 Hz, H-1), 4.74 (dd, 1H, J=4.5, 4.5 Hz, H-4), 4.55 (dd, 1H, J=4.5, 12.0 Hz, H-5), 4.39 (dd, 1H, J=4.5, 12.0 Hz, H-5), 3.28 (dd, 1H, J=1.5, 4.0 Hz, H-2), 3.22 (d, 1H, J=4.0 Hz, H-3), 2.18 (br s, 3H), 1.90–1.75 (m, 6H, adamantyl CH_2), 1.55–1.65 (m, 6H, adamantyl CH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 181.0 (C=O), 166.1 (C=O), 133.3 (Ar–C), 129.7 (Ar–C), 129.6 (Ar–C), 128.5 (Ar–C), 95.2 (C-1), 75.0 (C-4), 73.7 (adamantyl *C*O), 65.1 (C-5), 43.4 (C-2), 42.2 (adamantyl *C*H), 39.4 (C-3), 36.2 (adamantyl *C*H), 30.6 (adamantyl *C*H), 24.3 (CH_3); $J_{C\text{-}1,H\text{-}1}$=167.4 Hz. HRMS (ESI) calcd for (M+Na) $C_{24}H_{29}NO_5$+Na: 434.1942, found 434.1936.

4.20. 1-Adamantyl *N*-acetyl-2,3-aziridino-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranoside (31β)

The compound was isolated after chromatography (hexanes–EtOAc, 3:1) as a colorless oil. R_f 0.24 (hexanes–EtOAc, 2:1); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.12–8.03 (m, 2H, Ar), 7.62–7.52 (m, 1H, Ar), 7.51–7.40 (m, 2H, Ar), 5.60 (s, 1H, H-1), 4.56–4.45 (m, 3H, H-4, H-5), 3.45 (d, 1H, J=3.5 Hz, H-2), 3.25 (d, 1H, J=3.5 Hz, H-3), 2.14 (br s, 3H), 1.90–1.76 (m, 6H, adamantyl CH_2), 1.58–1.68 (m, 6H, adamantyl CH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$, δ_C) 179.4 (C=O), 166.1 (C=O), 133.2 (Ar–C), 129.9 (Ar–C), 129.7 (2 Ar–C), 128.4 (2 Ar–C), 94.0 (C-1), 75.2 (C-4), 74.2 (adamantyl *C*O), 65.1 (C-5), 43.0 (C-2), 42.8 (adamantyl *C*H), 41.4 (C-3), 36.1 (adamantyl *C*H), 30.6 (adamantyl *C*H), 23.7 (acetate *C*H$_3$); $J_{C\text{-}1,H\text{-}1}$=176.9 Hz. HRMS (ESI) calcd for (M+Na) $C_{24}H_{29}NO_5$+Na: 434.1942, found 434.1936.

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Supplementary data

These data include additional experimental details on the attempted preparation of **4** from **13** and ^{1}H and ^{13}C NMR spectral data for all new compounds. Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.tet.2013.03.074.

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