Design and synthesis of next generation carbohydrate-mimetic cyclitols: towards deactivators of inverting glycosidases and glycosyl transferases

Ofman, T.P.

Chapter 5

Trapping inverting glucosidases with conjugate addition acceptor cyclitols

Introduction

As described in chapter 4, the relatively large enzyme pocket (6 – 12 Å) and the presence of water alongside the substrate glucoside, allows inverting α- and β-glucosidases to employ a Koshland single-displacement mechanism in the hydrolysis of glycosidic linkages (Figure 1).[1–5] During enzyme catalysis, no covalently bound substrate-enzyme adduct is formed,[1–3,6–9] while such a covalent intermediate is crucial for cyclophellitol-based inhibitors during inactivation of retaining α- and β-glucosidases.[10–16] As a result of the one-step hydrolysis mechanism, no effective mechanism-based, covalent and irreversible inhibitors for inverting glucosidases have been developed to date.

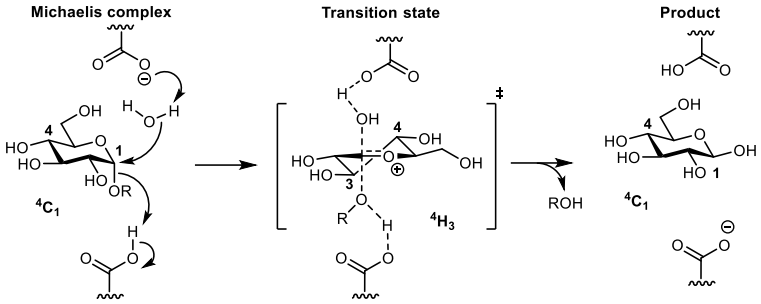


Figure 1. Conformational itinerary of an inverting α-glucosidases *via* a classic Koshland single displacement mechanism.[4]

Stick and Stubbs previously proposed implementing a conjugate addition warhead in their design of a glucosyl transferase inhibitor (Figure 2A, compound **1**).[17] The inhibitor they designed, was equipped with an anomeric vinyl moiety combined with an anomeric leaving group (UDP, in order to mimic the donor substrate of the glucosyl transferase). Unfortunately, due to the intrinsic lability of this compound, induced by the donating effect of the endocyclic oxygen, the synthesis of compound **1** proved troublesome and preparation of allyl phosphate **2** failed due to the elimination of the phosphate, yielding diene **3** instead (Figure 2B).

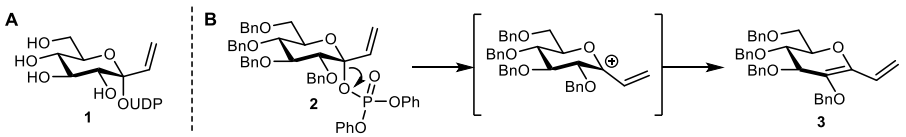


Figure 2. (A) Target compound **1** as proposed by Stick and Stubbs, who envisioned **1** as a putative glucosyl transferase inhibitor and (B) the observed side reaction resulting in compound **3**, troubling preparation of intermediate **2**.[17]

Prompted by Stick and Stubbs' design, a series of inhibitors bearing exotic chemical warheads can be envisioned that target inverting glucosidases. This chapter describes the synthetic endeavors towards this goal. In particular, structures **4** – **9** (Figure 3A), were considered as putative inhibitors targeting inverting glucosidases. Structures **4** – **9** exhibit a conjugate addition warhead, allowing for irreversible conjugate addition on the terminal side of the alkene. By extending the electrophile further from the anomeric center, the proposed inhibitors are envisioned to bridge the relatively large distance (6 – 12 Å) between the carboxylic acid/carboxylate residues in the enzyme active site pocket.[6] This may provoke an irreversible addition reaction with these more distal carboxylate residues to form a stable ester linkage, thereby effectively incapacitating the enzyme (Figure 3B).

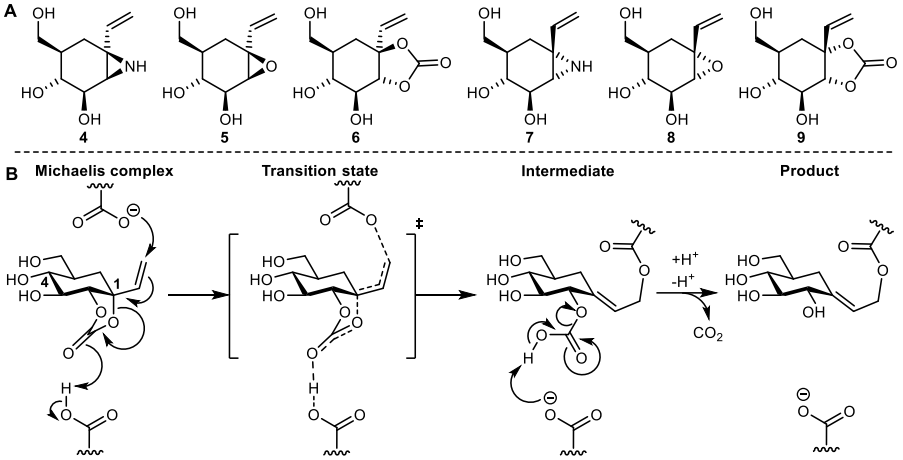


Figure 3. (A) Six proposed inhibitors of inverting α- or β-glucosidases bearing a conjugate addition warhead and (B) proposed mechanism of covalent inhibition of an inverting α-glucosidase by compound **9**.

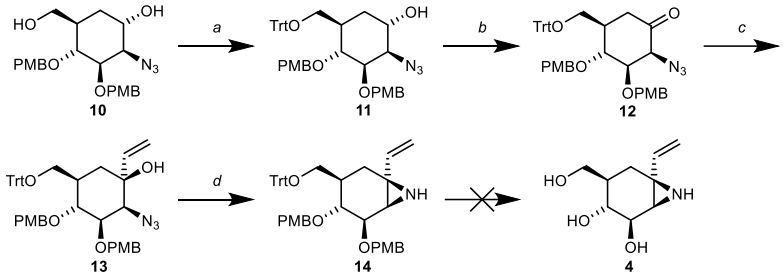
The intrinsic lability of vinylated constructs upon arming of the anomeric center with a leaving group, as in **2**, can likely be circumvented by switching to a carbasugar analogue. Lacking the endocyclic oxygen, the proposed constructs were hypothesized to be more stable and less prone to undesired side reactions when compared to analogues containing this endocyclic oxygen. In addition, previous work has shown the proposed chemical warheads to be suitable conjugate addition acceptors upon treatment with nucleophiles.[18–22] In this chapter, synthesis efforts towards these target molecules are described.

Results and discussion

Synthesis of 1-vinyl-β-aziridine 4. The synthesis scheme started from azido-alcohol **10**, envisioned as a suitably protected construct and a viable starting point towards 1-vinyl-β-aziridine **4** (Scheme 1). The preparation of azido-alcohol **10** is part of the research described in chapter 3. Regioselective protection of the primary hydroxyl as a trityl ether providing alcohol **11** in excellent yield (92%) under standard conditions. Oxidation with Dess-Martin periodinane and $NaHCO_3$ converted the secondary hydroxyl in **11** to ketone **12** in quantitative yield. Upon treatment of compound **12** with vinylmagnesium bromide at low temperature, the ketone was neatly converted into vinyl alcohol **13**, again in near-quantitative yield. The Grignard addition appeared to be very stereoselective as no formation of the C-1 epimer was observed. Proton NMR couplings ($^3J_{H\text{-}H}$ coupling, NOE

interactions), confirmed the assignment of the stereocenters in **13** (see appendix, Figure S1). The observed selectivity can be explained considering the Cornforth and Felkin-Ahn model, stating that addition to the carbonyl occurs following an trajectory *anti* with respect to a polar α-substituent (the azide), resulting only in bottom-side/axial attack.[23,24] With *syn* azido-alcohol **13** in hand, Staudinger cyclisation towards the anticipated 1-vinyl-β-aziridine **14** was investigated.[16,25] To this end, compound **13** was treated with triphenylphosphine in anhydrous acetonitrile at elevated temperature. Gratifyingly, clean conversion towards the desired 1-vinyl-β-aziridine **14** was observed in 45% yield. With the warhead in place, only global deprotection remained. Unfortunately, Birch reduction (Na, NH_3) did not yield target structure **4**. Instead, degradation of the vinyl aziridine was observed.

Scheme 1. Construction of target **4** from azido-alcohol **10**.



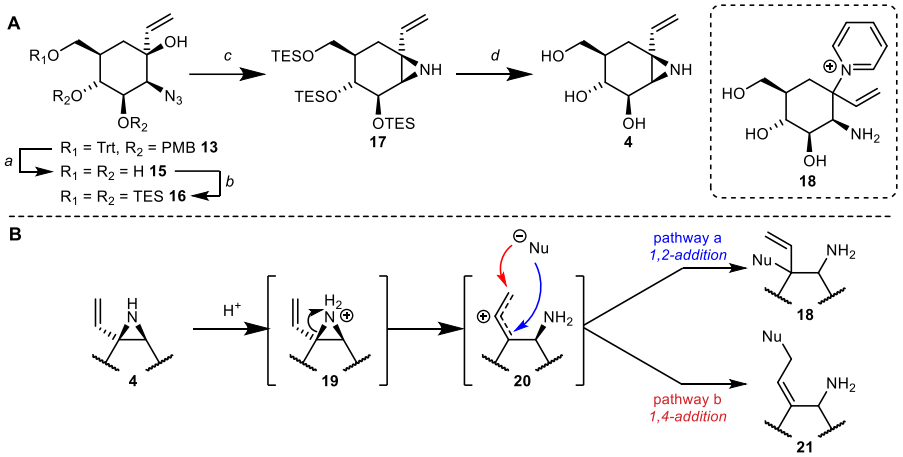
Reagents and conditions: *a*) TrtCl, DMAP, pyridine, DMF, rt, 16 h (92%); *b*) Dess-Martin periodinane, $NaHCO_3$, DCM, rt, 30 min. (quant.); *c*) vinylmagnesium bromide, THF, -78 °C to -30 °C, 2 h (99%); *d*) PPh_3, acetonitrile, 70 °C, 16 h, (45%).

All attempts to deprotect compound **14** under oxidative conditions (DDQ or CAN) proofed futile, again resulting in complete degradation of material.

Prompted by the robustness of the vinyl-aziridine formation aided by a Staudinger cyclisation, it was hypothesized that the problematic global deprotection could be circumvented using an alternative protecting group strategy. To this end, triethylsilyl ether (TES) protecting groups were considered, since it was hypothesized that the TES protecting groups could be removed readily under mild conditions using a fluoride source such as TBAF or $Et_3N{\cdot}HF$. To this end, intermediate **13** was deprotected under acidic conditions (TFA, TES) to yield compound **15** in 77% yield (Scheme 2A). The primary and secondary hydroxyls could be protected selectively under relatively mild conditions (TESCl, pyridine), giving compound **16** in a moderate yield (45%). Next up was the Staudinger cyclisation, which under identical conditions as described above yielded the desired vinyl aziridine **17** in good yield (52%). Global deprotection of compound **17** was first attempted using Olah's reagent (pyridine·HF), which is considered a very mild

fluoride source. However, upon treatment with this mild fluoride source, pyridine adduct **18** was isolated instead. The formation of this side product was rationalized by the slightly acidic nature of the pyridinium ion (Scheme 2B), which facilitates protonation of the relatively basic aziridine **4**. As a result, the aziridine opens, forming a relatively stable tertiary, allylic carbocation **20**.

Scheme 2. Preparation of aziridine **4** (A) and proposed mechanism of observed proton-induced side reaction upon global deprotection of **17** with Olah's reagent (B).



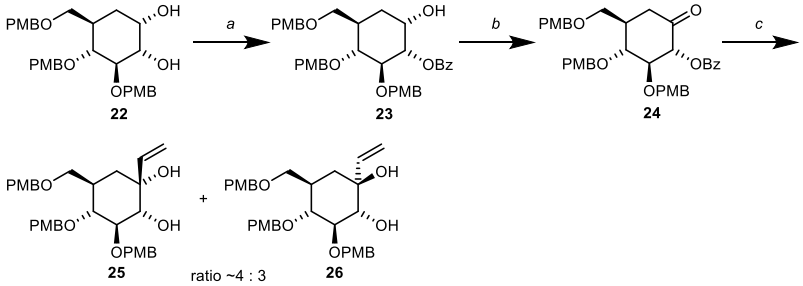
Reagents and conditions: *a*) TFA, TES, DCM, rt, 1 h (77%); *b*) TESCl, pyridine, rt, 16 h (45%); *c*) PPh_3, acetonitrile, 70 °C, 16 h (52%); *d*) TBAF, THF, 0 °C, 2 h, (70%).

A nucleophilic addition by pyridine on the C-1 position then results in the formation of compound **18**. In order to circumvent the acid-catalyzed aziridine opening, attention was shifted to the use of TBAF as an alkaline alternative.[26,27] Indeed, clean conversion was observed upon treatment of compound **17** with TBAF, obtaining target **4** in decent yield (70%). Proton NMR couplings ($^3J_{H\text{-}H}$ coupling), confirmed the correct assignment of the stereocenters in **4** (see appendix, Table S7).

Synthesis of 1-vinyl-β-epoxide 5 and 1-vinyl-β-carbonate 6. After successfully obtaining 1-vinyl-β-aziridine **4**, attention was turned to the preparation of 1-vinyl-β-epoxide **5** and *trans* 5,6-fused 1-vinyl-β-carbonate **6**, incorporating methodologies acquired during the previous synthesis of construct **4**. The synthesis started with the preparation of *syn*- and *anti*-diol **25** and **26**, respectively. *Syn*-diol **22** (Scheme 3), the synthesis of which is described in chapter 3, was regioselectively protected at the 2-OH as a benzoyl ester under mild conditions (BzCl, pyridine, -15 °C), according to literature procedures, to give compound **23** in quantitative yield.[28] Subsequently, oxidation of 1-OH under Dess-Martin oxidation conditions provided ketone **24** in near-quantitative yield (96%).[29,30] Treatment of **24** with excess vinylmagnesium bromide at low temperature (-78 °C) led

to the addition of the vinyl Grignard to the ketone within 15 minutes. Slowly increasing the temperature of the reaction mixture to 0 °C allowed the remaining Grignard reagent to perform an addition to the benzoyl carbonyl, thereby effectively liberating the 2-OH.

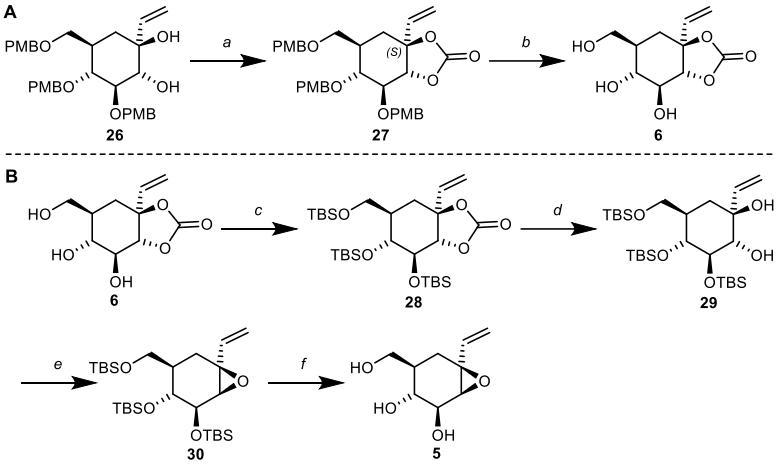
Scheme 3. Construction of *syn*- and *anti*-diol **25** and **26**.



Reagents and conditions: *a*) BzCl, pyridine, -15 °C, 1 h (quant.); *b*) Dess-Martin periodinane, $NaHCO_3$, DCM, rt, 1 h (96%); *c*) vinylmagnesium bromide, THF, -78 °C to 0 °C, 3 h, **25** (40%), **26** (32%).

The *syn*- and *anti*-diol **25** and **26** were obtained as a separable mixture in a 72% overall yield and in an 4:3 ratio, respectively. Proton NMR couplings ($^3J_{H\text{-}H}$ coupling, NOE interactions), confirmed the assignment of the stereocenters in **25** and **26** (see appendix, Figure S2 and S3). Protection of *anti*-diol **26** as the cyclic carbonate proceeded sluggishly and required elevated temperatures to get full consumption of the starting material as a result of the formation of a relatively strained trans 5,6-fused bicycle (Scheme 4). Attention was then turned to the global deprotection of the thus obtained compound **27** in acidic media (TFA, TES). This resulted in complete removal of all PMB ethers and the isolation of target compound **6** in 79% yield (See Figure S4 for the NMR spectra and assignment of the stereocenters in **6**). In addition, carbonate **6** was considered as a suitable intermediate to provide the 1-vinyl-β-epoxide **5**. Therefore, carbonate **6** was protected with silyl ethers (TBSOTf), in line with the methodology used during the preparation of 1-vinyl-β-aziridine **4**, to yield compound **28** in 56% yield. A transesterification attempt on intermediate **28** using NaOMe resulted in degradation of the starting material. However, removal of the carbonate protecting group proceeded smoothly under reductive conditions ($LiBH_4$), setting the stage for preparation of the 1-vinyl-β-epoxide warhead.

Scheme 4. Construction of *trans* 5,6-fused carbonate **6** (A) and 1-vinyl-β-epoxide **5** (B) from *anti*-diol **26**.



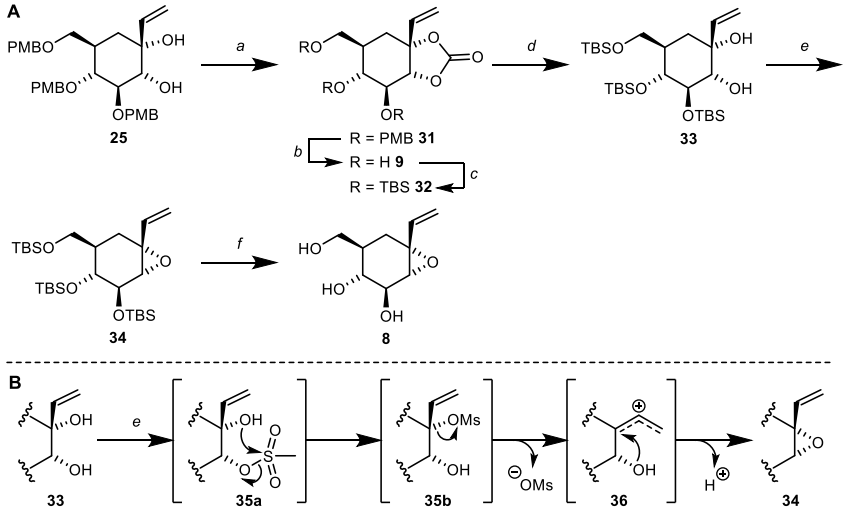
Reagents and conditions: *a*) CDI, DCE, 60 °C, 16 h (56%); *b*) TFA, TES, DCM, rt, 1 h (79%); *c*) TBSOTf, pyridine, DCM, 40 °C, 2 h (56%); *d*) $LiBH_4$, Et_2O, 0 °C to rt, 2 h (64%); *e*) MsCl, Et_3N, DCM, 0 °C, 30 min. (47%); *f*) silica bound TBAF, THF, rt, 2 h (63%).

It was anticipated that, due to the secondary hydroxyl being inherently more reactive than the tertiary hydroxyl, treatment with MsCl would allow for the selective mesylation of the 2-OH. Subsequently, the axial 1-OH is positioned perfectly to perform an intramolecular substitution to form the epoxide. Indeed, under mild conditions (MsCl, Et_3N, 0 °C) rapid formation of the desired epoxide was observed, which was isolated in 47% yield. The use of silica-bound TBAF resulted in clean removal of all protecting groups and in addition allowed for direct concentration and loading on a silica column for purification. This resulted in the isolation of target **5** in good yield (63%).

Synthesis of 1-vinyl-α-epoxide 8 and 1-vinyl-α-carbonate 9. With 1-vinyl-β-epoxide **5** and *trans* 5,6-fused carbonate **6** in hand, attention was then turned to the preparation of 1-vinyl-α-epoxide **8** and *cis* 1,2-fused 1-vinyl-α-carbonate **9** starting from *syn*-diol **25** (Scheme 5A). Following previously optimized methodology, diol **25** was protected as a cyclic carbonate. The reaction proceeded smoother in comparison with that on the corresponding *trans*-diol, as reflected by the lower operation temperature and the higher yield, since the product of this reaction is a less-strained *cis*-fused bicyclic construct. Subsequent removal of all PMB ethers under acidic conditions provided target **9** in excellent yield (91%). Proton NMR couplings ($^3J_{H\text{-}H}$ coupling), confirmed the correct assignment of the stereocenters in **9** (see appendix, Table S8). Compound **9** functioned as an intermediate towards the 1-vinyl-epoxide **8**, and for this, all hydroxyl functionalities were protected as silyl ethers (TBSOTf), followed by reductive cleavage

($LiBH_4$), as described above, of the cyclic carbonate to provide *syn*-diol **33**. Although *syn*-diol **33** bears an equatorially positioned 1-OH, not suited to perform an intramolecular substitution to form the desired epoxide, upon mesylation of *syn*-diol **33**, again, rapid formation of the desired epoxide was observed. It is hypothesized that, based on the inherent higher reactivity of secondary- over tertiary hydroxyls, mesylation occurs on the 2-OH to form intermediate **34** (Scheme 5B). Due to the *syn* orientation to the 1-OH, direct substitution and epoxide formation is considered to be non-viable. Instead, a migration of the mesylate group to the adjacent 1-OH is proposed, forming mesylated tertiary alcohol **35**. Due to the relatively stable carbocation that can form at the C-1 position, expulsion of the mesylate can take place, providing carbocation **36**. The 2-OH can then attack the C-1 cation to form the desired epoxide **34**. Exposure of compound **34** to silica bound TBAF let to removal of all silyl ethers and the isolation of target **8** in good yield (72%).

Scheme 5. Construction of epoxide **8** and *cis* 5,6-fused carbonate **9** from *syn*-diol **25** (A) and proposed mechanism of epoxide formation under mesylating conditions (B).



Reagents and conditions: *a*) CDI, DCM, 40 °C, 16 h (78%); *b*) TFA, TES, DCM, rt, 1 h (91); *c*) TBSOTf, pyridine, DCM, 0 °C to 40 °C, 2 h (77%); *d*) $LiBH_4$, Et_2O, 0 °C, 2 h (71%); *e*) MsCl, Et_3N, DCM, 0 °C, 30 min. (44%); *f*) silica bound TBAF, THF, 0 °C, 4 h (72%).

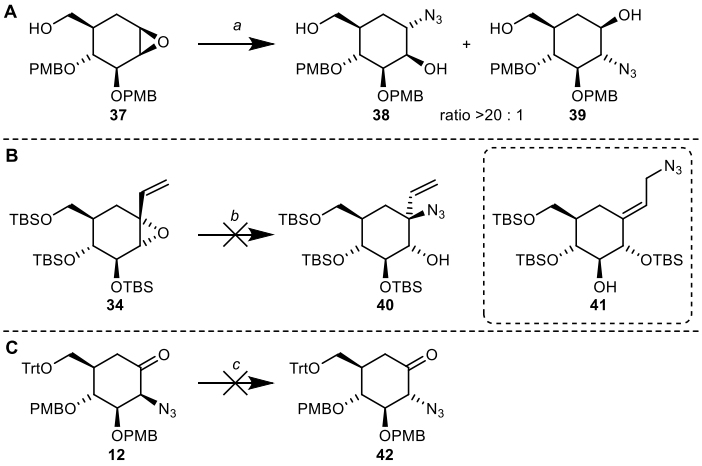
Synthesis of 1-vinyl-α-aziridine 7. Construction of the 1-vinyl-α-aziridine **7** was envisioned to follow identical chemical transformations as those leading to the aforementioned epimer **4**. To this end, β-epoxide **37**, synthesized in chapter 3, was treated with NaN_3 at elevated temperature (Scheme 6A). Unfortunately, opening of the β-epoxide proceeded following the Fürst-Plattner rule, through a favorable chair-like transition state,[31,32] resulting in a >20:1 ratio of the undesired compound **38** and the

desired compound **39**, respectively. Proton NMR couplings ($^3J_{H\text{-}H}$ coupling), confirmed the correct assignment of the stereocenters in **38** (see appendix, Table S9).

In an alternative attempt to synthesize target **7**, opening of the epoxide in compound **30** was envisioned to provide a suitable intermediate towards target **7** (Scheme 6B). For this, compound **34** was considered as an accessible substrate analogue to test the reaction (Scheme 6B). Exposure of **34** to NaN_3 at elevated temperature did not result in consumption of starting material. Turning to tetrabutylammonium azide, a commercially-available alternative known for its high solubility in organic solvents, conversion was observed at elevated temperatures. However, compound **41** was isolated instead in moderate yield (66%), being the product of an 1,4-addition. Although none of the desired azide **40** was obtained, the formation of the 1,4-addition-product can be seen as a proof of concept for these novel conjugate addition warheads.

In a final attempt to find a viable synthetic route towards the 1-vinyl-α-aziridine **7**, compound **12** was considered as a potential substrate to undergo a keto-enol epimerization (Scheme 6C). It was hypothesized that the inherent stability of equatorial substituents over axial ones would function as a driving force in this reaction. To this end, compound **12** was treated with a non-nucleophilic base (Cs_2CO_3) following literature procedures.[33] Although conversion towards the equatorial azide was observed by NMR, purification proved difficult because of degradation of the material in addition to the difficult separation of both C-2 epimers.

Scheme 6. Attempted construction of target **7**. Either following synthetic procedures as for **4** (A), *via* opening of epoxide **34** (B) or base-induced keto-enol C-2 epimerization of **12** (C).



Reagents and conditions: *a*) NaN_3, $LiClO_4$, DMF, 130 °C, 16 h, (72%); *b*) tetrabutylammonium azide, DMF, 100 °C, 2 h (66%); *c*) Cs_2CO_3, MeOH, rt, 16 h.

Conclusion

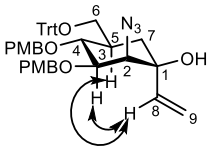
This chapter describes studies on the synthesis of a panel of putative inhibitors designed to inhibit inverting glucosidases. The inhibitors bear an anomeric vinyl functionality paired with bridged electrophiles spanning the C-1 and C-2 position. These bridged electrophiles included an aziridine (**4**), epoxide (**5** and **8**) or cyclic carbonate (**6** and **9**). The vinylogous warheads are envisioned to act as electrophiles, that can span the relatively large enzyme pocket of inverting glycosidases, and trap the catalytic machinery *via* a conjugated 1,4-addition. The use of silyl protecting groups appeared to be crucial during construction of the inhibitors and removal of the silyl protecting groups by TBAF proved imperative, because of its mild and alkaline nature, suppressing degradation and occurrence of side reactions. The synthetic challenges presented during preparation of the 2-deoxy-2-azido carba-glucose backbone, complicated the construction of 1-vinyl-α-aziridine **7**. Construction of a suitable carba-glucose intermediate for the consequent synthesis of 1-vinyl-α-aziridine **7** remains to be an active investigation. Suitably-designed inhibition assays have to show whether this novel class of inhibitors is capable of inhibiting inverting glucosidases.

Appendix

Structural proofs

Compound 13

Table S1. *^{1}H NMR H-H coupling constants*



H2: overlap with H4
H3: dd, *J* = 9.1 Hz ($H3_{ax}$-$H4_{ax}$), *J* = 3.0 Hz ($H3_{ax}$-$H2_{eq}$)
H4: overlap with H2
H5: ddddd, *J* = 14.0 Hz ($H5_{ax}$-H6), *J* = 8.8 Hz ($H5_{ax}$-$H4_{ax}$), *J* = 8.8 Hz ($H5_{ax}$-$H7_{ax}$), *J* = 2.9 Hz ($H5_{ax}$-$H7_{eq}$), *J* = 2.9 Hz ($H5_{ax}$-H6)
$H7_{ax}$: overlap with $H7_{eq}$
$H7_{eq}$: overlap with $H7_{ax}$

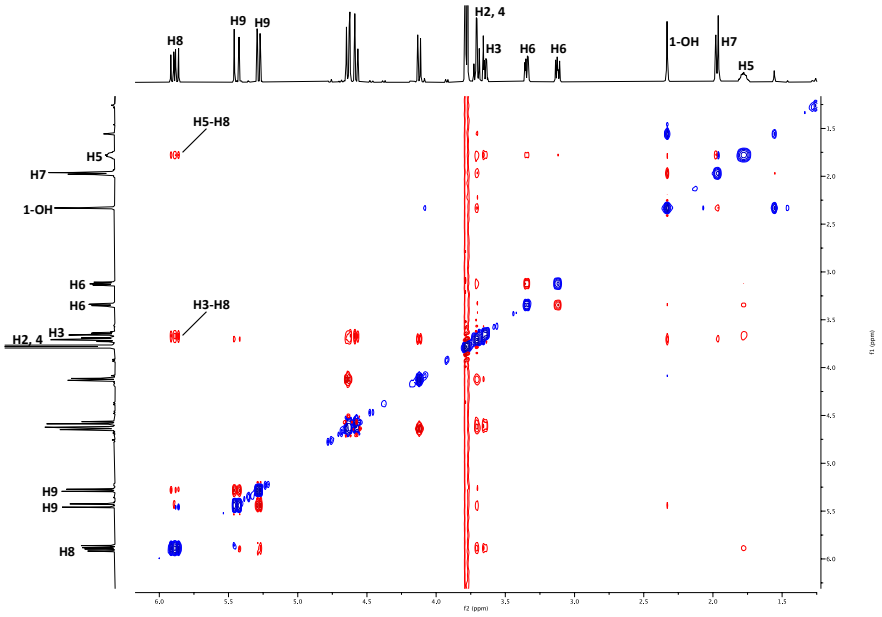
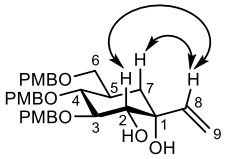


Figure S1. NOESY spectra of compound **13**. The key NOE interactions for **13** can be found between H3-H8 and H5-H8.

Compound 25

Table S2. *^{1}H NMR H-H coupling constants*



H2: d, *J* = 9.1 Hz ($H2_{ax}$-$H3_{ax}$)
H3: dd, *J* = 9.2 Hz ($H3_{ax}$-$H2_{ax}$), *J* = 9.2 Hz ($H3_{ax}$-$H4_{ax}$)
H4: dd, *J* = 9.3 Hz ($H4_{ax}$-$H3_{ax}$), *J* = 10.8 Hz ($H4_{ax}$-$H5_{ax}$)
H5: overlap with 2-OH
$H7_{ax}$: overlap with $H7_{eq}$
$H7_{eq}$: overlap with $H7_{ax}$

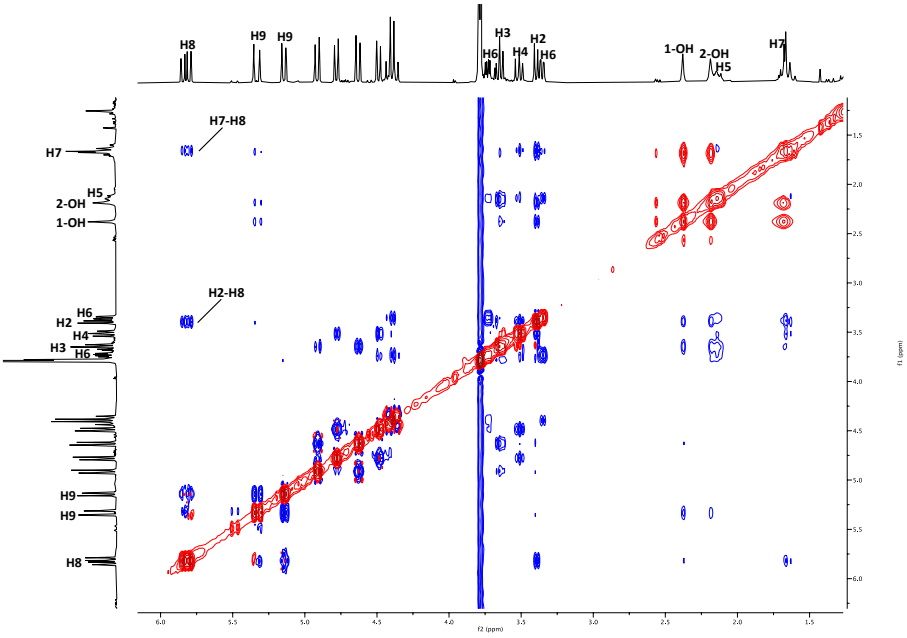
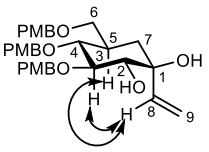


Figure S2. NOESY spectra of compound **25**. The key NOE interactions for **25** can be found between $H2_{ax}$-H8 and $H7_{ax}$-H8.

Compound 26

Table S3. *^{1}H NMR H-H coupling constants*



H2: overlap with H3 and H4
H3: overlap with H2 and H4
H4: overlap with H2 and H3
H5: overlap with $H7_{eq}$
$H7_{ax}$: overlap with H5
$H7_{eq}$: dd, *J* = 2.5 Hz ($H7_{eq}$-$H5_{ax}$), *J* = 11.3 Hz ($H7_{eq}$-$H7_{ax}$)

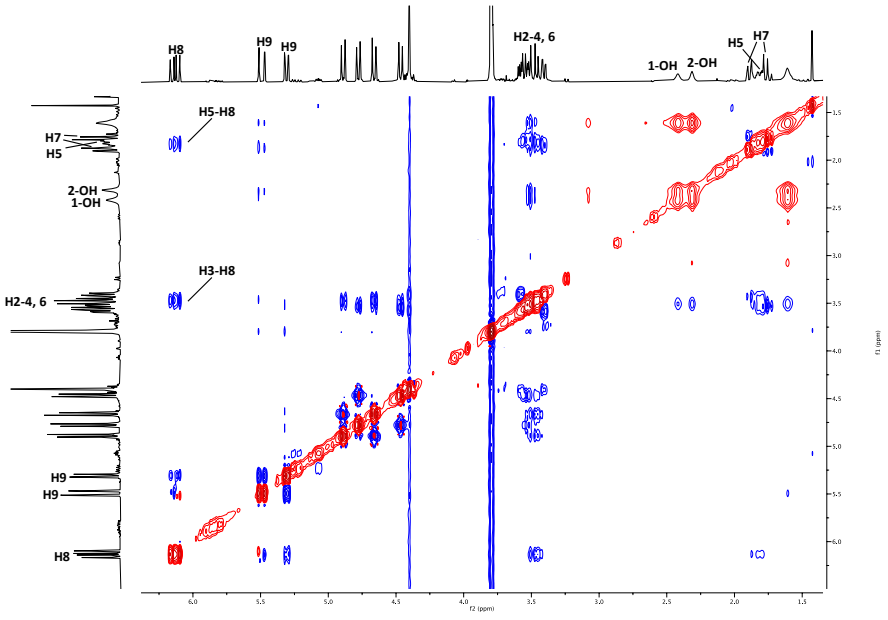
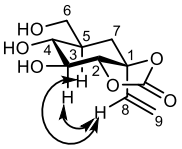


Figure S3. NOESY spectra of compound **26**. The key NOE interactions for **26** can be found between $H3_{ax}$-H8 and $H5_{ax}$-H8.

Compound 6

Table S4. *^{1}H NMR H-H coupling constants*



H2: d, *J* = 11.6 ($H2_{ax}$-$H3_{ax}$)
H3: dd, *J* = 11.6 Hz ($H3_{ax}$-$H2_{ax}$), 7.9 Hz ($H3_{ax}$-$H4_{ax}$)
H4: dd, *J* = 10.0 Hz ($H4_{ax}$-$H5_{ax}$), 7.9 Hz ($H4_{ax}$-$H3_{ax}$)
H5: overlap with $H7_{eq}$
$H7_{ax}$: d, *J* = 7.3 Hz ($H7_{ax}$-$H5_{ax}$), *J* = 10.8 Hz ($H7_{ax}$-$H7_{ax}$)
$H7_{eq}$: overlap with H5

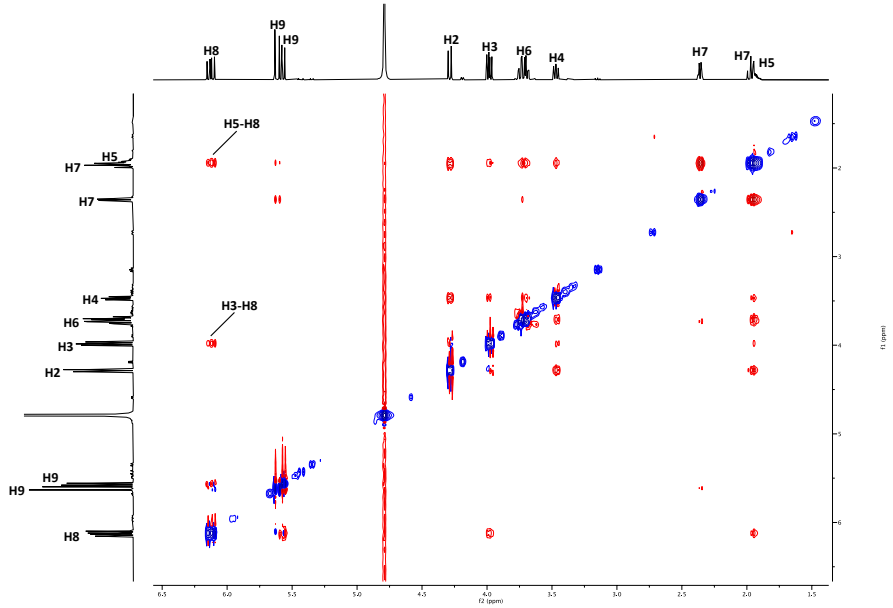
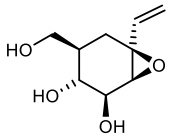


Figure S4. NOESY spectra of compound **6**. The key NOE interactions for **6** can be found between H3-H8 and H5-H8.

Compound 5

Table S5. *^{1}H NMR H-H coupling constants*



H2: d, *J* = 11.1 Hz ($H2_{p\text{-}eq}$-$H3_{p\text{-}ax}$)
H3: overlap with 6-OH
H4: multiplet
H5: multiplet
H7 $_{p\text{-}ax}$**:** dd, *J* = 12.7 Hz ($H7_{p\text{-}ax}$-$H5_{p\text{-}ax}$), *J* = 12.7 Hz ($H7_{p\text{-}ax}$-$H7_{p\text{-}eq}$)
H7 $_{p\text{-}eq}$**:** dd, *J* = 12.1 Hz ($H7_{p\text{-}eq}$-$H7_{p\text{-}ax}$), *J* = 4.4 Hz ($H7_{p\text{-}eq}$-$H5_{p\text{-}ax}$)

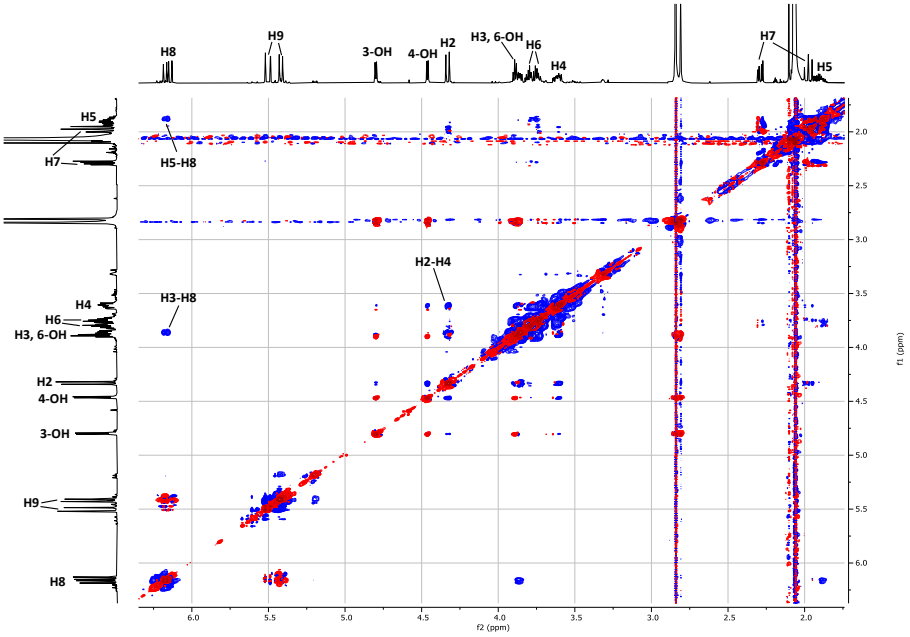
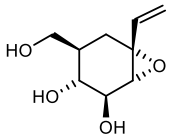


Figure S5. NOESY spectra of compound **5**. The key NOE interactions for **5** can be found between H3-H8 and H5-H8.

Compound 8

Table S6. *^{1}H NMR H-H coupling constants*



H2: d, *J* = 8.0 Hz ($H2_{p\text{-}ax}$-$H3_{p\text{-}ax}$)

H3: ddd, *J* = 9.7 Hz ($H3_{p\text{-}ax}$-$H4_{p\text{-}ax}$), *J* = 8.0 Hz ($H3_{p\text{-}ax}$-$H2_{p\text{-}ax}$), *J* = 4.4 Hz ($H3_{p\text{-}ax}$-3-OH)

H4: ddd, *J* = 10.0 Hz ($H4_{p\text{-}ax}$-$H3_{p\text{-}ax}$), *J* = 10.0 Hz ($H4_{p\text{-}ax}$-$H5_{p\text{-}ax}$), *J* = 3.9 Hz ($H4_{p\text{-}ax}$-4-OH)

H5: overlap with $H7_{ax}$

$H7_{ax}$: overlap with H5

$H7_{eq}$: d, *J* = 11.8 Hz ($H7_{eq}$-$H7_{ax}$)

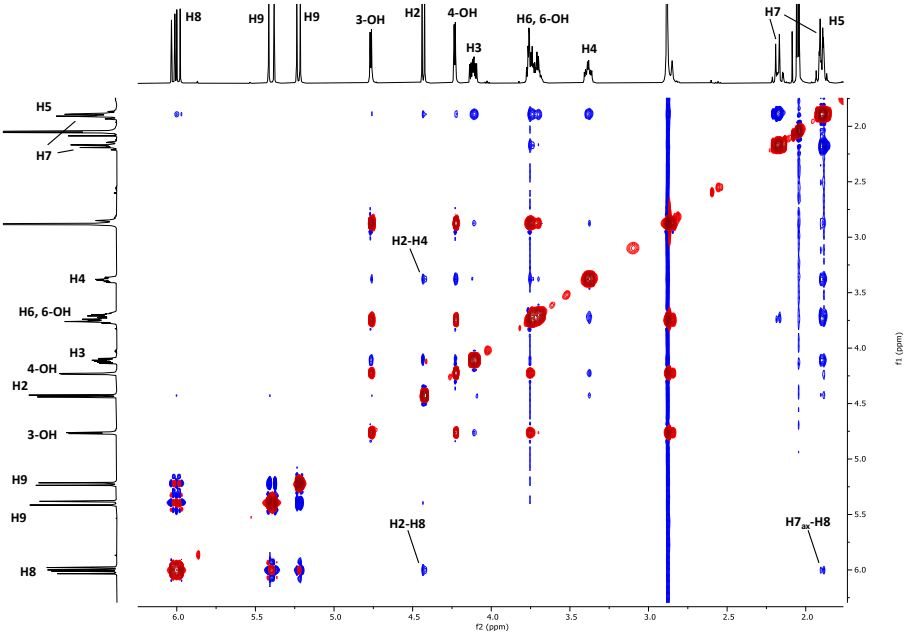
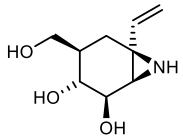


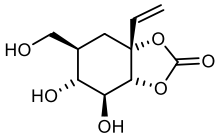
Figure S6. NOESY spectra of compound **8**. The key NOE interactions for **8** can be found between H2-H8 and $H7_{ax}$-H8.

Table S7. Compound **4**, *^{1}H NMR H-H coupling constants*



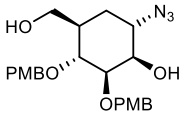
H2: bs
H3: bs
H4: dd, *J* = 11.1 Hz ($H4_{ax}$-$H5_{ax}$), *J* = 8.7 Hz($H4_{ax}$-$H3_{ax}$)
H5: dddd, *J* = 10.0 Hz ($H5_{ax}$-$H4_{ax}$), *J* = 10.0 Hz ($H5_{ax}$-$H7_{ax}$), *J* = 7.5 Hz ($H5_{ax}$-H6), *J* = 4.5 Hz ($H5_{ax}$-$H7_{eq}$)
$H7_{ax}$: dd, *J* = 14.5 Hz ($H7_{ax}$-$H7_{eq}$), *J* = 12.0 Hz ($H7_{ax}$-$H5_{ax}$)
$H7_{eq}$: dd, *J* = 14.6 Hz ($H7_{eq}$-$H7_{ax}$), *J* = 6.1 Hz ($H7_{eq}$-$H5_{ax}$)

Table S8. Compound **9**, *^{1}H NMR H-H coupling constants*



H2: d, *J* = 7.1 Hz ($H2_{ax}$-$H3_{ax}$)
H3: overlap with H6
H4: dd, *J* = 9.6 Hz ($H4_{ax}$-$H3_{ax}$), *J* = 9.6 Hz ($H4_{ax}$-$H5_{ax}$)
H5: overlap with $H7_{ax}$
$H7_{ax}$: overlap with H5
$H7_{eq}$: dd, *J* = 12.2 Hz ($H7_{eq}$-$H7_{ax}$), *J* = 1.3 Hz ($H7_{eq}$-$H5_{ax}$)

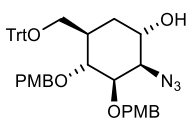
Table S9. Compound **38**, *^{1}H NMR H-H coupling constants*



H1: overlap with H2
H2: overlap with H1
H3: dd, *J* = 8.3 Hz ($H3_{ax}$-$H4_{ax}$), *J* = 3.0 Hz ($H3_{ax}$-$H2_{eq}$)
H4: overlap with H6
H5: multiplet
$H7_{ax}$: ddd, *J* = 14.4 Hz ($H7_{ax}$-$H7_{eq}$), *J* = 11.4 Hz ($H7_{ax}$-$H5_{ax}$), *J* = 3.2 Hz ($H7_{ax}$-$H1_{eq}$)
$H7_{eq}$: ddd, *J* = 14.0 Hz ($H7_{eq}$-$H7_{ax}$), *J* = 4.0 Hz ($H7_{eq}$-$H5_{ax}$), *J* = 4.0 Hz ($H7_{eq}$-$H1_{eq}$)

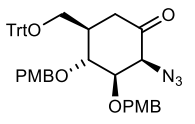
Synthetic procedures.

2-Deoxy-2-azido-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-trityl-carba-α-D-mannose (11).



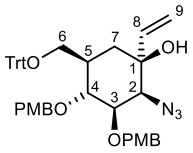
Compound **10** (5.4 g, 12 mmol) was dissolved in DMF (50 mL, 0.25 M) followed by the addition of pyridine (3.0 mL, 37 mmol, 3.0 eq.), DMAP (74 mg, 0.61 mmol, 0.05 eq.) and TrtCl (6.8 g, 24 mmol, 2.0 eq.). The solution was stirred for 16 hours on room temperature upon which TLC confirmed full conversion (R_f 0.3 (EtOAc:pentane, 3:7, v:v)). The reaction mixture was quenched by the addition of sat. aq. $NaHCO_3$ and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (10:90 → 40:60; EtOAc:pentane) yielded the title compound (7.7 g, 11 mmol, 92%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.46 – 7.18 (m, 19H, CH_{arom}), 6.95 – 6.69 (m, 4H, CH_{arom}), 4.62 – 4.54 (m, 3H, C*H*H PMB, C*H*H PMB, CH*H* PMB), 4.22 (d, *J* = 10.4 Hz, 1H, C*H*H PMB), 3.92 (dd, *J* = 4.0 Hz, 1H, H-1), 3.89 (dd, *J* = 8.0, 3.4 Hz, 1H, H-3), 3.79 (d, *J* = 5.8 Hz, 7H, OMe, OMe, H-2), 3.66 (dd, *J* = 8.4 Hz, 1H, H-4), 3.31 (dd, *J* = 8.9, 3.7 Hz, 1H, H-6), 3.21 (dd, *J* = 8.9, 6.4 Hz, 1H, H-6), 2.18 – 2.09 (m, 1H, H-5), 1.94 (ddd, *J* = 13.9, 10.6, 3.1 Hz, 1H, H-7), 1.80 (ddd, *J* = 14.5, 4.6, 4.6 Hz, 1H, H-7); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 159.4, 159.2, 144.2, 130.7, 130.4, 129.7, 129.7, 129.0 ($C_{q\text{-}arom}$), 128.1, 127.9, 127.4, 127.1, 113.9, 113.7 (CH_{arom}), 86.5 (*C*(Ph)$_3$), 80.7 (C-3), 74.1 (C-4), 72.8 (CH_2 PMB), 68.0 (C-1), 64.6 (C-2), 63.3 (C-6), 55.4 (OMe), 37.9 (C-5), 30.8 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{42}H_{43}NaN_3O_6$ 708.30496; Found 708.30438.

2-*Epi*-2-deoxy-2-azido-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-trityl-D-validone (12).



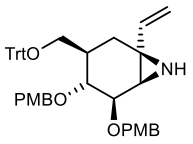
Compound **11** (1.7 g, 2.5 mmol) was dissolved in DCM (12.5 mL, 0.2 M) followed by the addition of $NaHCO_3$ (6.3 g, 75 mmol, 30 eq.) and Dess-Martin periodinane (2.1 g, 5.0 mmol, 2.0 eq.). After stirring the solution for 30 minutes at room temperature, TLC showed full conversion (R_f 0.3 (EtOAc:pentane, 3:7, v:v)). The reaction mixture was quenched by the addition of sat. aq. $Na_2S_2O_3$ and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (10:90 → 20:80; R_f 0.3 (EtOAc:pentane, 3:7, v:v)) yielded the title compound (1.7 g, 2.5 mmol, quant.) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.41 – 6.70 (m, 23H, CH_{arom}), 4.49 (d, *J* = 11.6 Hz, 1H, C*H*H PMB), 4.41 (d, *J* = 11.6 Hz, 1H, CH*H* PMB), 4.37 (d, *J* = 11.1 Hz, 1H, C*H*H PMB), 4.23 (d, *J* = 11.1 Hz, 1H, CH*H* PMB), 4.04 (d, *J* = 3.3 Hz, 1H, H-2), 3.97 (ddd, *J* = 3.3, 3.3, 0.8 Hz, 1H, H-3), 3.83 – 3.79 (m, 6H, OMe, OMe), 3.76 (dd, *J* = 5.5, 3.3 Hz, 1H, H-4), 3.26 – 3.13 (m, 1H, H-6), 2.71 – 2.59 (m, 1H, H-7), 2.27 (q, *J* = 6.2 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 204.1 (C-1), 159.6, 144.0, 129.8, 129.7, 129.6 ($C_{q\text{-}arom}$), 129.2, 128.8, 128.0, 127.2, 114.0, 114.0 (CH_{arom}), 86.9 (*C*(Ph)$_3$), 81.5 (C-3), 75.0 (C-4), 72.6, 72.1 (CH_2 PMB), 65.9 (C-2), 63.5 (C-6), 55.4, 55.4 (OMe), 40.4 (C-5), 38.8 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{42}H_{41}NaN_3O_6$ 706.28931; Found 706.28909.

1-(*S*)-1-Vinyl-1-hydroxyl-2-deoxy-2-azido-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-trityl-carba-D-mannose (13).



Compound **12** (1.4 g, 2.0 mmol) was dissolved in anhydrous THF (8.0 mL, 0.25 M) and cooled to -78 °C. Subsequently, vinyl magnesium bromide (1.0 M solution in THF, 20 mL, 20 mmol, 10 eq.) was added dropwise. The solution was allowed to attain to -30 °C after which TLC confirmed full conversion (R_f 0.2 (pentane:EtOAc, 8:2, v:v)). The reaction mixture was quenched by the addition of sat. aq. $NaHCO_3$ and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (10:90 → 20:80; EtOAc:pentane) yielded the title compound (1.4 g, 2.0 mmol, 99%) as a colorless oil. ^{1}H NMR showed less than 5% of the C-1 epimer to be present. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.46 – 7.16 (m, 17H, CH_{arom}), 6.95 – 6.64 (m, 6H, CH_{arom}), 5.89 (dd, *J* = 17.3, 10.9 Hz, 1H, H-8), 5.44 (dd, *J* = 17.3, 1.0 Hz, 1H, H-9), 5.28 (dd, *J* = 10.9, 1.0 Hz, 1H, H-9), 4.67 – 4.61 (m, 2H, CH_2 PMB), 4.58 (d, *J* = 11.2 Hz, 1H, CH*H* PMB), 4.12 (d, *J* = 10.1 Hz, 1H, C*H*H PMB), 3.78 (m, 6H, OMe, OMe), 3.74 – 3.68 (m, 2H, H-2, H-4), 3.65 (dd, *J* = 9.1, 3.0 Hz, 1H, H-3), 3.35 (dd, *J* = 8.6, 3.0 Hz, 1H, H-6), 3.12 (dd, *J* = 8.6, 5.8 Hz, 1H, H-6), 2.33 (s, 1H, 1-OH), 2.03 – 1.92 (m, 2H, H-7), 1.78 (dddd, *J* = 14.0, 8.8, 2.9, 2.9 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 159.6, 159.2, 144.1 ($C_{q\text{-}arom}$), 138.4 (C-8), 130.6, 130.0, 129.9 ($C_{q\text{-}arom}$), 129.0, 128.9, 127.9, 127.9, 127.9, 127.1 (CH_{arom}), 117.6 (C-9), 114.1, 113.7 (CH_{arom}), 86.4 ($C(Ph)_3$), 82.0 (C-3), 77.3 (C-2/C-4), 74.9 (CH_2 PMB), 72.8, 72.7 (CH_2 PMB, C-1), 69.8 (C-2/C-4), 63.2 (C-6), 55.4 (OMe), 39.1 (C-5), 36.1 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{44}H_{45}NaN_3O_6$ 734.32061; Found 734.32006.

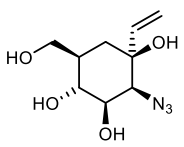
1-(*S*)-1-Vinyl-2-deoxy-1,2-azabicyclo[4.1.0]-3,4,-di-*O*-(4-methoxybenzyl)-6-*O*-trityl-carba-D-mannose (14).



Compound **13** (135 mg, 0.2 mmol) was co-evaporated with toluene (3x) and dissolved in anhydrous acetonitrile (2.0 mL, 0.1 M) under N_2 atmosphere. Triphenylphosphine (0.16 g, 0.6 mmol, 3.0 eq.) was added and the solution was stirred for 16 hours at 70 °C. TLC confirmed full conversion and minor hydrolyzed product to be formed (R_f 0.3 (EtOAc:pentane, 3:7, v:v)). The reaction mixture was quenched by the addition of sat. aq. $NaHCO_3$ and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (20:80 → 40:60; EtOAc:pentane) yielded the title compound (60 mg, 90 µmol, 45%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): 7.45 – 7.17 (m, 17H, CH_{arom}), 6.94 – 6.66 (m, 6H, CH_{arom}), 5.54 (dd, *J* = 17.2, 10.5 Hz, 1H, H-8), 5.18 (d, *J* = 17.1 Hz, 1H, H-9), 5.10 (d, *J* = 10.7 Hz, 1H, H-9), 4.73 – 4.60 (m, 3H, C*H*H PMB, C*H*H PMB, CH*H* PMB), 4.24 (d, *J* = 10.3 Hz, 1H, CH*H* PMB), 3.82 – 3.77 (m, 6H, OMe, OMe), 3.77 – 3.72 (m, 1H, H-3), 3.53 (dd, *J* = 11.1, 8.1 Hz, 1H, H-4), 3.38 (dd, *J* = 8.7, 3.1 Hz, 1H, H-6), 3.10 (dd, *J* = 8.6, 6.9 Hz, 1H, H-6), 2.46 (dd, *J* = 14.6, 6.2 Hz, 1H, H-7), 2.39 (d, *J* = 3.3 Hz, 1H, H-2), 1.91 (dd, *J* = 14.6, 11.8 Hz, 1H, H-7), 1.85 – 1.73 (m, 1H, H-5), 1.58 (s, 1H, NH); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 159.3, 159.1, 144.3 ($C_{q\text{-}arom}$), 142.3 (C-

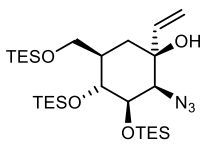
8), 131.0 ($C_{q\text{-}arom}$), 129.7, 129.5, 129.0, 127.9, 127.0, 113.9 (CH_{arom}), 113.7 (C-9), 86.5 ($C(Ph)_3$), 81.3 (C-3), 78.7 (C-4), 74.6, 72.0 (CH_2 PMB), 63.9 (C-6), 55.4 (OMe), 44.1 (C-2), 41.3 (C-5), 40.5 (C-7); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{44}H_{46}NO_5$ 668.33760; Found 668.33713.

1-(*S*)-1-Vinyl-1-hydroxyl-2-deoxy-2-azido-carba-D-mannose (15).



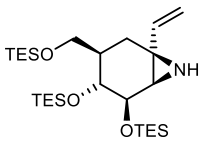
Compound **13** (0.71 g, 1.0 mmol) was dissolved in DCM (20 mL, 0.05 M) followed by the addition of TES (0.64 mL, 4.0 mmol, 4.0 eq.) and TFA (0.77 mL, 10 mmol, 10 eq.). After 1 hour, TLC confirmed full conversion (R_f 0.3 (MeOH:DCM, 1:9, v:v)). The reaction mixture was concentrated under reduced pressure to yield the crude product. Flash column chromatography (5:95 → 20:80; MeOH:DCM) yielded the title compound (0.18 g, 0.77 mmol, 77%) as a white solid. ^{1}H NMR (500 MHz, D_2O, HH-COSY, HSQC): δ 6.08 (dd, *J* = 17.5, 11.0 Hz, 1H, H-8), 5.50 (dd, *J* = 17.5, 0.5 Hz, 1H, H-9), 5.42 (dd, *J* = 11.0, 0.5 Hz, 1H, H-9), 3.91 (dd, *J* = 3.4, 1.8 Hz, 1H, H-2), 3.76 – 3.68 (m, 2H, H-3, H-6), 3.61 (dd, *J* = 11.3, 6.0 Hz, 1H, H-6), 3.50 (dd, *J* = 10.6, 9.6 Hz, 1H, H-4), 1.83 (ddd, *J* = 13.1, 4.2, 1.9 Hz, 1H, H-7), 1.73 (dd, *J* = 13.1, 13.1 Hz, 1H, H-7), 1.60 (dddd, *J* = 12.9, 8.3, 5.3, 2.9 Hz, 1H, H-5); ^{13}C NMR (126 MHz, D_2O, HSQC): δ 138.8 (C-8), 117.5 (C-9), 73.7 (C-1), 72.6 (C-3), 71.6 (C-2), 70.0 (C-4), 62.2 (C-6), 40.0 (C-5), 33.1 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_9H_{15}NaN_3O_4$ 252.09603; Found 252.09548.

1-(*S*)-1-Vinyl-1-hydroxyl-2-deoxy-2-azido-3,4,6-tri-*O*-triethylsilyl-carba-D-mannose (16).



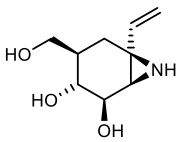
Compound **15** (0.18 g, 0.77 mmol) was dissolved in pyridine (15 mL, 0.05 M) followed by the addition of TESCl (0.78 mL, 4.6 mmol, 6.0 eq.). The solution was stirred for 16 hours on room temperature upon which TLC confirmed full conversion (R_f 0.4 (toluene:pentane, 1:1, v:v)). The reaction mixture was quenched by the addition of sat. aq. $NaHCO_3$ and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (30:70 → 90:10; toluene:pentane) yielded the title compound (200 mg, 0.35 mmol, 45%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.90 (dd, *J* = 17.1, 10.7 Hz, 1H, H-8), 5.52 (dd, *J* = 17.2, 1.4 Hz, 1H, H-9), 5.27 (dd, *J* = 10.7, 1.4 Hz, 1H, H-9), 4.06 (s, 1H, H-4), 3.92 (s, 2H, H-3, H-6), 3.60 (dd, *J* = 10.0, 6.0 Hz, 1H, H-6), 3.55 (s, 1H, H-2), 1.94 (dd, *J* = 14.1, 5.8 Hz, 1H, H-7), 1.77 (s, 1H, H-5), 1.64 (dd, *J* = 14.1, 5.9 Hz, 1H, H-7), 1.04 – 0.91 (m, 27H, $SiCH_2CH_3$), 0.76 – 0.54 (m, 18H, $SiCH_2CH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 140.9 (C-8), 115.7 (C-9), 76.5 (C-3), 70.8 (C-4), 64.3 (C-6), 43.2 (C-5), 36.0 (C-7), 7.3, 7.1, 7.0, 7.0 ($SiCH_2CH_3$), 5.4, 5.1, 4.9, 4.8, 4.6 ($SiCH_2CH_3$); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{27}H_{57}NaN_3O_4Si_3$ 594.35546; Found 594.35491.

1-(*S*)-1-Vinyl-2-deoxy-1,2-azabicyclo[4.1.0]-3,4,6-tri-*O*-triethylsilyl-carba-D-mannose (17).



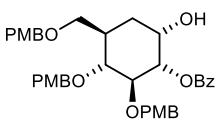
Compound **16** (200 mg, 0.35 mmol) was co-evaporated with toluene (3x) and dissolved in anhydrous acetonitrile (3.5 mL, 0.1 M) under N_2 atmosphere. Triphenylphosphine (0.18 g, 0.7 mmol, 2.0 eq.) was added and the solution was stirred for 16 hours at 70 °C. TLC confirmed full conversion and minor hydrolyzed product to be formed (R_f 0.3 (Et_2O:pentane, 1:9, v:v)). The reaction mixture was quenched by the addition of sat. aq. $NaHCO_3$ and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (50:50 toluene:pentane → 10:90; Et_2O:pentane) yielded the title compound (95 mg, 0.18 mmol, 52%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.53 (dd, *J* = 17.2, 10.6 Hz, 1H, H-8), 5.16 (dd, *J* = 17.2, 0.7 Hz, 1H, H-9), 5.07 (dd, *J* = 10.6, 0.6 Hz, 1H, H-9), 3.86 (s, 1H, H-3), 3.76 (d, *J* = 9.7 Hz, 1H, H-6), 3.51 (dd, *J* = 9.2, 6.9 Hz, 1H, H-4), 3.41 (dd, *J* = 9.7, 7.8 Hz, 1H, H-6), 2.41 – 2.34 (m, 1H, H-7), 2.27 (d, *J* = 3.9 Hz, 1H, H-2), 1.63 – 1.53 (m, 2H, H-5, H-7), 1.06 – 0.89 (m, 27H, $SiCH_2C\mathit{H}_3$), 0.75 – 0.52 (m, 18H, $SiC\mathit{H}_2CH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 142.7 (C-8), 113.4 (C-9), 75.0 (C-3), 73.0 (C-4), 64.5 (C-6), 45.9 (C-2), 43.1 (C-5), 28.5 (C-7), 7.3, 7.2, 7.2, 7.2, 7.0 ($SiCH_2\mathit{C}H_3$), 5.6, 5.5, 5.4, 4.6, 4.6 ($Si\mathit{C}H_2CH_3$); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{58}NO_3Si_3$ 528.37245; Found 528.37190.

1-(*S*)-1-Vinyl-2-deoxy-1,2-azabicyclo[4.1.0]-carba-D-mannose (4).



Compound **17** (26 mg, 50 µmol) was dissolved in anhydrous THF (1.0 mL, 0.05 M). The reaction was cooled on ice and kept under inert atmosphere. TBAF (1.0 M solution in THF, 0.25 mL, 0.25 mmol, 5.0 eq.) was added and stirring continued for 2 hours while the reaction mixture was allowed to attain to room temperature. Upon full conversion (R_f 0.2 (MeOH:DCM, 2:8, v:v)), the mixture was concentrated at 25 °C under reduced pressure yielding the crude product. Flash column chromatography (10:90 → 70:30; acetone:DCM) yielded the title compound (6.5 mg, 35 µmol, 70%) as a colorless oil. ^{1}H NMR (500 MHz, D_2O, HH-COSY, HSQC): δ 5.62 (dd, *J* = 17.3, 10.7 Hz, 1H, H-8), 5.29 (d, *J* = 17.3 Hz, 1H, H-9), 5.18 (d, *J* = 10.7 Hz, 1H, H-9), 3.85 (bs, 1H, H-3), 3.71 (dd, *J* = 11.2, 3.7 Hz, 1H, H-6), 3.54 (dd, *J* = 11.2, 6.5 Hz, 1H, H-6), 3.37 (dd, *J* = 11.1, 8.7 Hz, 1H, H-4), 2.58 (bs, 1H, H-2), 2.41 (dd, *J* = 14.6, 6.1 Hz, 1H, H-7), 1.67 (dddd, *J* = 10.0, 10.0, 7.5, 4.5 Hz, 1H, H-5), 1.59 (dd, *J* = 14.5, 12.0 Hz, 1H, H-7); ^{13}C NMR (126 MHz, D_2O, HSQC): δ 140.8 (C-8), 114.5 (C-9), 72.9 (C-3), 71.4 (C-4), 62.5 (C-6), 45.0 (C-2), 40.8 (C-5), 27.8 (C-7); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_9H_{15}NO_3$ 186.11302; Found 186.11263.

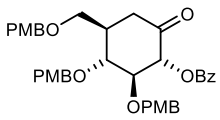
2-*O*-Benzoyl-3,4,6-tri-*O*-(4-methoxybenzyl)-carba-α-D-glucose (23).



Compound **22** (5.4 g, 10 mmol) was dissolved in pyridine (67 mL, 0.15 M) and cooled to -15 °C. BzCl (1.7 mL, 15 mmol, 1.5 eq.) was slowly added followed by stirring the reaction mixture for an hour while keeping the temperature at -15 °C. Upon full conversion (R_f 0.4 (EtOAc:pentane, 1:1, v:v)), the reaction was quenched by the addition of sat. aq. $NaHCO_3$ solution and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined

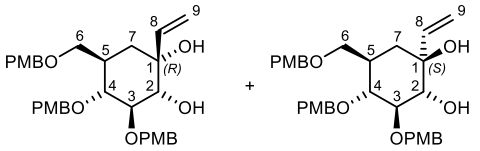
organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (20:80 → 40:60; EtOAc:pentane) yielded the title compound (6.4 g, 10 mmol, quant.) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 8.07 – 6.58 (m, 12H, CH_{arom}), 5.12 (dd, *J* = 10.0, 2.9 Hz, 1H, H-2), 4.79 (d, *J* = 10.5 Hz, 1H, C*H*H PMB), 4.76 (d, *J* = 10.7 Hz, 1H, CH*H* PMB), 4.65 (d, *J* = 10.7 Hz, 1H, C*H*H PMB), 4.46 (d, *J* = 10.5 Hz, 1H, CH*H* PMB), 4.43 (d, *J* = 11.6 Hz, 1H, C*H*H PMB), 4.38 (d, *J* = 11.6 Hz, 1H, CH*H* PMB), 4.25 (dd, *J* = 3.0 Hz, 1H, H-1), 4.07 (dd, *J* = 10.0, 9.1 Hz, 1H, H-3), 3.79 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.70 (s, 4H, OMe, H-6), 3.57 (dd, *J* = 10.9, 9.1 Hz, 1H, H-4), 3.43 (dd, *J* = 9.0, 2.6 Hz, 1H, H-6), 2.23 (dddd, *J* = 14.1, 6.5, 6.5, 3.4 Hz, 1H, H-5), 2.07 (bs, 1H, 1-OH), 1.95 (ddd, *J* = 14.6, 3.8, 3.8 Hz, 1H, H-7), 1.75 (ddd, *J* = 15.0, 13.0, 2.4 Hz, 1H, H-7); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 165.7 (C=O ester), 159.3, 159.2, 159.1, 133.3, 131.0, 130.8 ($C_{q\text{-}arom}$), 130.7, 130.0, 129.8, 129.7, 129.6, 129.3, 128.6, 113.9, 113.9, 113.7 (CH_{arom}), 81.3 (C-3), 80.9 (C-4), 77.5 (C-2), 75.3, 75.0, 72.8 (CH_2 PMB), 69.4 (C-6), 68.0 (C-1), 55.4, 55.4, 55.3 (OMe), 36.9 (C-5), 31.0 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{38}H_{42}NaO_9$ 665.27265; Found 665.27164.

2-*O*-Benzoyl-3,4,6-tri-*O*-(4-methoxybenzyl)-D-validone (24).



Compound **23** (6.4 g, 10 mmol) was dissolved in DCM (100 mL, 0.1 M). $NaHCO_3$ (25 g, 300 mmol, 30 eq.) and Dess-Martin periodinane (8.5 g, 20 mmol, 2.0 eq.) were added respectively. After stirring for 1 hour, TLC showed full conversion (R_f 0.4 (EtOAc:pentane, 3:7, v:v)) and the reaction was quenched by the addition of sat. aq. $Na_2S_2O_3$ solution and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (20:80 → 30:70; EtOAc:pentane) yielded the title compound (6.1 g, 9.6 mmol, 96%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.63 – 6.64 (m, 12H, CH_{arom}), 5.55 (dd, *J* = 10.4, 1.1 Hz, 1H, H-2), 4.86 (d, *J* = 10.4 Hz, 1H, CH*H* PMB), 4.77 (s, 2H, CH_2 PMB), 4.52 (d, *J* = 10.4 Hz, 1H, C*H*H PMB), 4.43 (d, *J* = 11.6 Hz, 1H, CH*H* PMB), 4.39 (d, *J* = 11.6 Hz, 1H, C*H*H PMB), 4.00 (dd, *J* = 10.7, 9.1 Hz, 1H, H-4), 3.87 (dd, *J* = 10.3, 9.1 Hz, 1H, H-3), 3.81 – 3.74 (m, 7H, H-6, OMe, OMe), 3.72 (s, 3H, OMe), 3.38 (dd, *J* = 9.0, 2.6 Hz, 1H, H-6), 2.77 (ddd, *J* = 14.1, 14.1, 1.2 Hz, 1H, H-7), 2.48 (dd, *J* = 14.3, 4.2 Hz, 1H, H-7), 1.91 (dddd, *J* = 10.4, 10.4, 2.7, 2.7 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 200.8 (C-1), 165.5 (C=O ester), 159.4, 159.4, 159.4, 133.4, 130.4, 130.1 ($C_{q\text{-}arom}$), 130.0, 129.8, 129.7, 129.5, 129.4, 128.5, 113.9, 113.9 (CH_{arom}), 83.8 (C-3), 80.0 (C-2), 79.5 (C-4), 75.3, 75.3, 72.9 (CH_2 PMB), 68.2 (C-6), 55.4, 55.4, 55.3 (OMe), 39.9 (C-7), 39.3 (C-5); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{38}H_{40}NaO_9$ 663.25700; Found 663.25652.

1-(*R*)-1-Vinyl-1-hydroxyl-3,4,6-tri-*O*-(4-methoxybenzyl)-carba-D-glucose (25) and 1-(*S*)-1-vinyl-1-hydroxyl-3,4,6-tri-*O*-(4-methoxybenzyl)-carba-D-glucose (26).

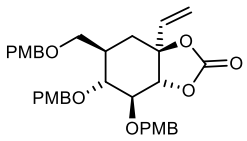


Compound **24** (6.1 g, 9.6 mmol) was dissolved in THF (96 mL, 0.1 M) and cooled to -78 °C. Vinyl magnesium bromide (1.0 M solution in THF, 72 mL, 72 mmol, 7.5 eq.) was added slowly. The reaction mixture was slowly allowed to attain to 0 °C and kept at this temperature for 3 hours. Upon full conversion was observed (R_f 0.2 and 0.1 for compound **25** and **26**, respectively (EtOAc:pentane, 7:3, v:v)), the reaction was quenched by the addition of sat. aq. $NaHCO_3$ solution and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (30:70 → 50:50; EtOAc:pentane) yielded the title compounds as a separable mixture of *syn*- and *anti*-diols **25** and **26** in a ratio of 56:44 respectively. Yielding **25** (2.2 g, 3.8 mmol, 40%) and **26** (1.7 g, 3.1 mmol, 32%) both as a colorless oil.

Data of the major stereoisomer **25** (*syn*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.33 – 7.11 (m, 6H, CH_{arom}), 6.92 – 6.79 (m, 6H, CH_{arom}), 5.82 (dd, *J* = 17.2, 10.7 Hz, 1H, H-8), 5.33 (dd, *J* = 17.2, 1.3 Hz, 1H, H-9), 5.14 (dd, *J* = 10.7, 1.2 Hz, 1H, H-9), 4.91 (d, *J* = 11.3 Hz, 1H, C*H*H PMB), 4.78 (d, *J* = 10.4 Hz, 1H, CH*H* PMB), 4.63 (d, *J* = 11.3 Hz, 1H, C*H*H PMB), 4.49 (d, *J* = 10.4 Hz, 1H, CH*H* PMB), 4.42 (d, *J* = 11.5 Hz, 1H, C*H*H PMB), 4.37 (d, *J* = 11.6 Hz, 1H, CH*H* PMB), 3.80 – 3.77 (m, 9H, OMe, OMe, OMe), 3.73 (dd, *J* = 9.0, 4.0 Hz, 1H, H-6), 3.65 (dd, *J* = 9.2, 9.2 Hz, 1H, H-3), 3.51 (dd, *J* = 10.8, 9.3 Hz, 1H, H-4), 3.40 (d, *J* = 9.1 Hz, 1H, H-2), 3.35 (dd, *J* = 9.1, 2.5 Hz, 1H, H-6), 2.38 (s, 1H, 1-OH), 2.22 – 2.11 (m, 2H, 2-OH, H-5), 1.71 – 1.61 (m, 2H, H-7); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 159.5, 159.3, 159.3 ($C_{q\text{-}arom}$), 143.0 (C-8), 131.0, 130.9, 130.6 ($C_{q\text{-}arom}$), 129.7, 129.7, 129.5, 129.4, 129.3 , 114.3, 113.9, 113.9 (CH_{arom}), 113.8 (C-9), 84.2 (C-3), 80.7 (C-4), 76.1 (C-2), 75.0 (CH_2 PMB), 74.7 (CH_2 PMB), 74.3 (C-1), 72.9 (CH_2 PMB), 69.3 (C-6), 55.4, 55.4, 55.4 (OMe), 38.2 (C-5), 36.1 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{40}NaO_8$ 587.26209; Found 587.26166.

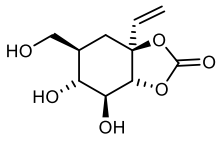
Data of the major stereoisomer **26** (*anti*): ^{1}H NMR (400 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.34 – 6.73 (m, 12H, CH_{arom}), 6.13 (dd, *J* = 17.3, 10.9 Hz, 1H, H-8), 5.49 (dd, *J* = 17.3, 1.3 Hz, 1H, H-9), 5.31 (dd, *J* = 10.9, 1.4 Hz, 1H, H-9), 4.89 (d, *J* = 10.9 Hz, 1H, C*H*H PMB), 4.78 (d, *J* = 10.3 Hz, 1H, CH*H* PMB), 4.66 (d, *J* = 10.9 Hz, 1H, C*H*H PMB), 4.47 (d, *J* = 10.4 Hz, 1H, CH*H* PMB), 4.40 (m, 2H, CH_2 PMB), 3.84 – 3.75 (m, 9H, OMe, OMe, OMe), 3.63 – 3.35 (m, 5H, H-2, H-3, H-4, H-6), 2.42 (bs, 1H, 1-OH), 2.31 (bs, 1H, 2-OH), 1.89 (dd, *J* = 11.3, 2.5 Hz, 1H, H-7), 1.86 – 1.72 (m, 2H, H-5, H-7); ^{13}C NMR (101 MHz, $CDCl_3$, HSQC): δ 159.4, 159.3 ($C_{q\text{-}arom}$), 138.2 (C-8), 130.8, 130.7, 130.5 ($C_{q\text{-}arom}$), 129.7, 129.7, 129.6, 129.5, 129.4 (CH_{arom}), 116.8 (C-9), 114.2, 114.0, 113.9, 113.9 (CH_{arom}), 84.6, 81.2, 79.1 (C-2, C-3, C-4), 75.1, 74.9 (CH_2 PMB), 74.5 (C-1), 72.9 (CH_2 PMB), 69.5 (C-6), 55.4, 55.4 (OMe), 39.1 (C-5), 37.4 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{40}NaO_8$ 587.26209; Found 587.26182.

1-(*S*)-1-Vinyl-1,2-*trans*-*O*-carbonate-3,4,6-tri-*O*-(4-methoxybenzyl)-carba-D-glucose (27).



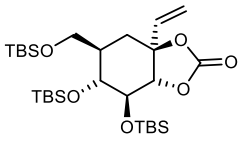
Compound **26** (1.7 g, 3.1 mmol) was dissolved in DCE (61 mL, 0.05 M) followed by the addition of CDI (3.0 g, 18 mmol, 6.0 eq.). The reaction was stirred at 60 °C for 16 hours upon which TLC confirmed full conversion (R_f 0.8 (EtOAc:pentane, 1:1, v:v)). The mixture was allowed to attain to room temperature and subsequently quenched by the addition of sat. aq. $NaHCO_3$ solution and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (20:80 → 30:70; EtOAc:pentane) yielded the title compound (1.0 g, 1.7 mmol, 56%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.36 – 6.76 (m, 12H, CH_{arom}), 5.98 (dd, *J* = 17.1, 11.1 Hz, 1H, H-8), 5.63 (d, *J* = 17.1 Hz, 1H, H-9), 5.47 (d, *J* = 11.0 Hz, 1H, H-9), 4.81 (m, 2H, CH_2 PMB), 4.57 (d, *J* = 10.8 Hz, 1H, C*H*H PMB), 4.42 – 4.34 (m, 2H, CH_2 PMB), 4.31 (d, *J* = 11.6 Hz, 1H, C*H*H PMB), 4.11 (dd, *J* = 11.3, 0.7 Hz, 1H, H-2), 3.96 (dd, *J* = 11.3, 7.5 Hz, 1H, H-3), 3.84 – 3.75 (m, 9H, OMe, OMe, OMe), 3.65 (dd, *J* = 10.3, 7.5 Hz, 1H, H-4), 3.55 (dd, *J* = 9.1, 4.2 Hz, 1H, H-6), 3.35 (dd, *J* = 9.1, 2.6 Hz, 1H, H-6), 2.20 – 2.06 (m, 2H, H-7), 2.03 – 1.92 (m, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 159.6, 159.5, 159.4 ($C_{q\text{-}arom}$), 155.1 (C=O), 131.4 (C-8), 130.3, 130.1, 130.0 ($C_{q\text{-}arom}$), 129.9, 129.8, 129.6 (CH_{arom}), 120.6 (C-9), 114.0, 113.9, 113.9 (CH_{arom}), 86.7 (C-2), 84.7 (C-1), 80.0 (C-4), 79.0 (C-3), 75.6, 73.1, 72.9 (CH_2 PMB), 68.7 (C-6), 55.4, 55.4 (OMe), 41.1 (C-5), 33.1 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{34}H_{38}NaO_9$ 613.24135; Found 613.24099.

1-(*S*)-1-Vinyl-1,2-*trans*-*O*-carbonate-carba-D-glucose (6).



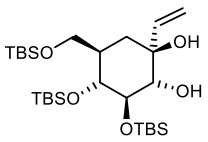
Compound **27** (1.0 g, 1.7 mmol) was dissolved in DCM (34 mL, 0.05 M) followed by the addition of TES (1.6 mL, 10 mmol, 6.0 eq.) and TFA (1.3 mL, 17 mmol, 10 eq.). After 1 hour, TLC confirmed full conversion (R_f 0.3 (MeOH:DCM, 1:9, v:v)). The reaction mixture was concentrated under reduced pressure to yield the crude product. Flash column chromatography (5:95 → 20:80; MeOH:DCM) yielded the title compound (0.31 g, 1.3 mmol, 79%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.13 (dd, *J* = 17.2, 11.1 Hz, 1H, H-8), 5.62 (d, *J* = 17.2 Hz, 1H, H-9), 5.57 (dd, *J* = 11.1, 0.7 Hz, 1H, H-9), 4.29 (d, *J* = 11.6, 1H, H-2), 3.98 (dd, *J* = 11.6, 7.9 Hz, 1H, H-3), 3.75 (dd, *J* = 11.4, 3.0 Hz, 1H, H-6), 3.69 (dd, *J* = 11.4, 5.1 Hz, 1H, H-6), 3.47 (dd, *J* = 10.0, 7.9 Hz, 1H, H-4), 2.39 – 2.36 (d, *J* = 7.3, 10.8 Hz, 1H) H-7), 2.02 – 1.89 (m, 2H, H-5, H-7); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 159.5 (C=O), 133.4 (C-8), 123.3 (C-9), 88.5 (C-1), 88.2 (C-2), 76.6 (C-4), 73.2 (C-3), 64.3 (C-6), 45.1 (C-5), 34.0 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{10}H_{14}NaO_6$ 253.06881; Found 253.06835.

1-(*S*)-1-Vinyl-1,2-*trans*-*O*-carbonate-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-carba-D-glucose (28).



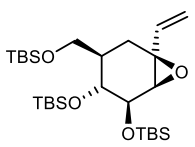
Compound **6** (0.83 g, 2.3 mmol) was dissolved in DCM (23 mL, 0.1 M). The mixture was cooled on ice followed by the addition of pyridine (3.7 mL, 46 mmol, 20 eq.) and TBSOTf (2.1 mL, 9.2 mmol, 4.0 eq.). The reaction mixture was heated to 40 °C and stirred for 2 hours upon which TLC confirmed full conversion (R_f 0.7 (Et_2O:pentane, 1:1, v:v)). Subsequent quenching by addition of sat. aq. $NaHCO_3$ solution and dilution with water followed. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (2:98 → 8:92; Et_2O:pentane) yielded the title compound (0.74 g, 1.3 mmol, 56%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.05 (dd, *J* = 17.2, 11.0 Hz, 1H, H-8), 5.61 (d, *J* = 17.2 Hz, 1H, H-9), 5.50 (d, *J* = 11.0 Hz, 1H, H-9), 3.94 (dd, *J* = 11.3, 6.6 Hz, 1H, H-3), 3.88 (d, *J* = 11.3 Hz, 1H, H-2), 3.64 (dd, *J* = 4.1, 1.5 Hz, 2H, H-6), 3.58 (dd, *J* = 8.9, 6.6 Hz, 1H, H-4), 2.20 (dd, *J* = 11.7, 4.4 Hz, 1H, H-7), 1.96 – 1.80 (m, 2H, H-5, H-7), 0.97 – 0.85 (m, 27H, $C(CH_3)_3$), 0.19 – 0.02 (m, 18H, $SiCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 154.9 (C=O), 131.9 (C-8), 120.2 (C-9), 86.5 (C-2), 84.4 (C-1), 76.6 (C-4), 73.5 (C-3), 62.9 (C-6), 44.7 (C-5), 33.2 (C-7), 26.5, 26.3, 26.1 ($C(CH_3)_3$), 18.6, 18.4, 18.3 ($C(CH_3)_3$), -2.2, -2.4, -3.5, -4.0, -5.1, -5.4 ($SiCH_3$); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{28}H_{56}NaO_6Si_3$ 595.32824; Found 595.32778.

1-(*S*)-1-Vinyl-1-hydroxyl-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-carba-D-glucose (29).



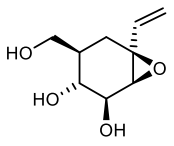
Compound **28** (85 mg, 0.15 mmol) was dissolved in anhydrous Et_2O (5.0 mL, 0.05 M) and cooled on ice. Subsequently, $LiBH_4$ (2.0 M solution in THF, 0.38 mL, 0.75 mmol, 5.0 eq.) was added and stirring continued for another 2 hours while attaining to room temperature. Upon full conversion (R_f 0.5 (Et_2O:pentane, 1:9, v:v)), The mixture was quenched by the addition of sat. aq. $NaHCO_3$ solution and diluted with water. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (10:90 → 20:80; Et_2O:pentane) yielded the title compound (53 mg, 96 µmol, 64%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 6.12 (ddd, *J* = 17.3, 10.8, 1.0 Hz, 1H, H-8), 5.39 (dd, *J* = 17.3, 2.0 Hz, 1H, H-9), 5.15 (dd, *J* = 10.8, 2.0 Hz, 1H, H-9), 4.23 (d, *J* = 2.8 Hz, 1H, H-2), 4.13 (d, *J* = 1.1 Hz, 1H, 1-OH), 4.12 – 4.01 (m, 3H, H-4, H-6, 2-OH), 3.64 (dd, *J* = 10.2, 5.0 Hz, 1H, H-6), 3.45 (ddd, *J* = 9.8, 3.1, 1.4, Hz, 1H, H-3), 2.23 (dd, *J* = 14.9, 7.1 Hz, 1H, H-7), 2.08 (ddd, *J* = 12.3, 8.6, 4.2 Hz, 1H, H-5), 1.52 (d, *J* = 14.9 Hz, 1H, H-7), 0.96 – 0.84 (m, 27H, $C(CH_3)_3$), 0.21 – 0.09 (m, 12H, $SiCH_3$), 0.07 – -0.04 (m, 6H, $SiCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 143.3 (C-8), 113.3 (C-9), 74.9 (C-3), 73.9 (C-4), 73.9 (C-1), 71.2 (C-2), 65.6 (C-6), 43.9 (C-5), 29.9 (C-7), 26.1, 25.8 ($C(CH_3)_3$), 18.4, 18.1, 17.9 ($C(CH_3)_3$), -4.7, -4.8, -5.2 ($SiCH_3$); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{27}H_{58}NaO_5Si_3$ 569.34897; Found 569.34834.

1-(*S*)-1-Vinyl-1,2-anhydro-3,4,6-tri-*O-tert*-butyldimethylsilyl-carba-D-mannose (30).



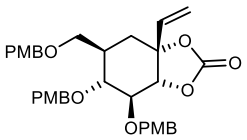
Compound **29** (55 mg, 0.1 mmol) was dissolved in DCM (2.0 mL, 0.05 M) and the mixture was cooled on ice. Subsequently, Et_3N (0.14 mL, 1.0 mmol, 10 eq.) and MsCl (16 µL, 0.2 mmol, 2.0 eq.) were added respectively. After stirring for 30 minutes, full conversion was observed (R_f 0.5 (toluene:pentane, 2:8, v:v)), the reaction was quenched by the addition of sat. aq. $NaHCO_3$ solution and diluted with water. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (20:80 → 50:50; toluene:pentane) yielded the title compound (25 mg, 47 µmol, 47%) as a colorless oil.
^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.98 (dd, *J* = 17.1, 10.9 Hz, 1H, H-8), 5.46 (dd, *J* = 17.0, 0.7 Hz, 1H, H-9), 5.41 (ddd, *J* = 10.9, 0.7, 0.7 Hz, 1H, H-9), 4.32 (dd, *J* = 11.0, 0.6 Hz, 1H, H-2), 3.90 (dd, *J* = 10.9, 7.3 Hz, 1H, H-3), 3.72 (dd, *J* = 9.8, 3.4 Hz, 1H, H-6), 3.63 – 3.51 (m, 2H, H-4, H-6), 2.32 (dd, *J* = 12.4, 4.2 Hz, 1H, H-7), 1.88 (dd, *J* = 12.6, 12.6 Hz, 1H, H-7), 1.83 – 1.75 (m, 1H, H-5), 0.96 – 0.80 (m, 27H, $C(CH_3)_3$), 0.15 – -0.04 (m, 18H, $SiCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 133.8 (C-8), 119.5 (C-9), 90.2 (C-1), 84.4 (C-2), 77.0 (C-4), 73.7 (C-3), 63.6 (C-6), 44.2 (C-5), 33.6 (C-7), 26.5, 26.3, 26.1 ($C(CH_3)_3$), 18.7, 18.4, 18.3($C(CH_3)_3$), -2.0, -2.1, -3.4, -3.7, -5.1, -5.3 ($SiCH_3$); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{27}H_{56}NaO_4Si_3$ 551.33841; Found 551.33786.

1-(*S*)-1-Vinyl-1,2-anhydro-carba-D-mannose (5).



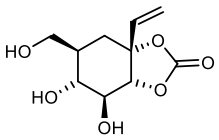
Compound **30** (31 mg, 59 µmol) was dissolved in anhydrous THF (2.4 mL, 0.025 M). The reaction was cooled on ice and kept under inert atmosphere. TBAF on silica gel (loading F^- ~1.5 mmol/g, 0.39 g, 0.59 mmol, 10 eq.) was added and stirring continued for 6 hours while the reaction mixture was allowed to attain to room temperature. Upon full conversion was observed (R_f 0.4 (acetone:DCM, 1:1, v:v)), the mixture was concentrated at 25 °C under reduced pressure yielding the crude product. Flash column chromatography (10:90 → 40:60; acetone:DCM) yielded the title compound (6.9 mg, 37 µmol, 63%) as a colorless oil. ^{1}H NMR (500 MHz, Acetone-d6, HH-COSY, HSQC): δ 6.16 (dd, *J* = 16.9, 10.9 Hz, 1H, H-8), 5.50 (dd, *J* = 16.9, 1.0 Hz, 1H, H-9), 5.42 (dd, *J* = 10.9, 0.9 Hz, 1H, H-9), 4.80 (d, *J* = 4.7 Hz, 1H, 3-OH), 4.46 (d, *J* = 5.0 Hz, 1H, 4-OH), 4.33 (d, *J* = 11.1 Hz, 1H, H-2), 3.91 – 3.84 (m, 2H, H-3, 6-OH), 3.83 – 3.78 (m, 1H, H-6), 3.75 (ddd, *J* = 10.5, 5.6, 5.6 Hz, 1H, H-6), 3.65 – 3.58 (m, 1H, H-4), 2.29 (dd, *J* = 12.1, 4.4 Hz, 1H, H-7), 1.98 (dd, *J* = 12.7, 12.7 Hz, 1H, H-7), 1.95 – 1.85 (m, 1H, H-5); ^{13}C NMR (126 MHz, Acetone-d6, HSQC): δ 135.5 (C-8), 119.1 (C-9), 91.5 (C-1), 85.4 (C-2), 76.9 (C-4), 72.5 (C-3), 63.9 (C-6), 43.3 (C-5), 34.3 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_9H_{14}NaO_4$ 209.07898; Found 209.07843.

1-(*R*)-1-Vinyl-1,2-*O*-carbonate-3,4,6-tri-*O*-(4-methoxybenzyl)-carba-D-glucose (31).



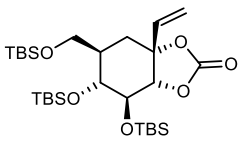
Compound **25** (2.2 g, 3.8 mmol) was dissolved in DCM (77 mL, 0.05 M) followed by the addition of CDI (1.9 g, 11.5 mmol, 3.0 eq.). The reaction was stirred at 40 °C for 16 hours upon which TLC confirmed full conversion (R_f 0.8 (EtOAc:pentane, 1:1, v:v)). The mixture was allowed to attain to room temperature and subsequently quenched by the addition of sat. aq. $NaHCO_3$ solution and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (20:80 → 30:70; EtOAc:pentane) yielded the title compound (1.8 g, 3.0 mmol, 78%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.33 – 6.76 (m, 12H, CH_{arom}), 5.81 (dd, *J* = 17.2, 10.8 Hz, 1H, H-8), 5.46 (d, *J* = 17.2 Hz, 1H, H-9), 5.28 (d, *J* = 10.8 Hz, 1H, H-9), 4.69 – 4.55 (m, 3H, CH*H* PMB, C*H*H PMB, CH*H* PMB), 4.47 – 4.33 (m, 4H, C*H*H PMB, CH*H* PMB, C*H*H PMB, H-2), 3.87 – 3.74 (m, 9H, OMe, OMe, OMe), 3.72 (dd, *J* = 7.1, 5.3 Hz, 1H, H-3), 3.61 (dd, *J* = 9.1, 4.4 Hz, 1H, H-6), 3.51 (dd, *J* = 8.9, 7.0 Hz, 1H, H-4), 3.36 (dd, *J* = 9.2, 3.5 Hz, 1H, H-6), 2.10 (dd, *J* = 15.3, 3.7 Hz, 1H, H-7), 2.01 (dddd, *J* = 8.8, 8.8, 4.2, 4.2 Hz, 1H, H-5), 1.87 (dd, *J* = 15.3, 12.8 Hz, 1H, H-7); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 159.5, 159.3 ($C_{q\text{-}arom}$), 154.1 (C=O), 137.6 (C-9), 130.4, 130.3, 129.7 ($C_{q\text{-}arom}$), 129.7, 129.6, 129.4, 129.4 (CH_{arom}), 116.1 (C-8), 114.0, 113.9, 113.9 (CH_{arom}), 84.5 (C-1), 83.5 (C-2), 81.5 (C-3), 76.4 (C-4), 73.6, 73.4, 72.9 (CH_2 PMB), 69.5 (C-6), 55.4, 55.4 (OMe), 36.4 (C-5), 32.5 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{34}H_{38}NaO_9$ 613.24135; Found 613.24105.

1-(*R*)-1-Vinyl-1,2-*O*-carbonate-carba-D-glucose (9).



Compound **31** (0.3 g, 0.51 mmol) was dissolved in DCM (20 mL, 0.025 M) followed by the addition of TES (0.49 mL, 3.1 mmol, 6.0 eq.) and TFA (0.39 mL, 5.1 mmol, 10 eq.). After 1 hour, TLC confirmed full conversion (R_f 0.3 (MeOH:DCM, 1:9, v:v)). The reaction mixture was concentrated under reduced pressure to yield the crude product. Flash column chromatography (5:95 → 10:90; MeOH:DCM) yielded the title compound (107 mg, 0.46 mmol, 91%) as a colorless oil. ^{1}H NMR (300 MHz, D_2O, HH-COSY, HSQC): δ 5.96 (ddd, *J* = 17.2, 10.9, 1.0 Hz, 1H, H-8), 5.44 (dd, *J* = 17.2, 1.0 Hz, 1H, H-9), 5.36 (dd, *J* = 10.9, 1.0 Hz, 1H, H-9), 4.60 (d, *J* = 7.1 Hz, 1H, H-2), 3.80 – 3.63 (m, 3H, H-3, H-6), 3.46 (dd, *J* = 9.6 Hz, 1H, H-4), 2.27 (dd, *J* = 12.2, 1.0 Hz, 1H, H-7), 1.89 – 1.75 (m, 2H, H-5, H-7); ^{13}C NMR (75 MHz, $CDCl_3$, HSQC): δ 156.5 (C=O), 136.7 (C-8), 116.2 (C-9), 86.6 (C-1), 85.1 (C-2), 76.2 (C-3), 70.1 (C-4), 61.4 (C-6), 38.3 (C-5), 31.8 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{10}H_{14}NaO_6$ 253.06881; Found 253.06822.

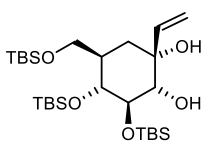
1-(*R*)-1-Vinyl-1,2-*O*-carbonate-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-carba-D-glucose (32).



Compound **9** (107 mg, 0.46 mmol) was dissolved in DCM (9.2 mL, 0.05 M) and cooled on ice. Subsequently, pyridine (1.5 mL, 18 mmol, 40 eq.) and TBSOTf (1.1 mL, 4.6 mmol, 10 eq.) were added slowly. The reaction mixture was heated to 40 °C and stirred for 2 hours upon which TLC confirmed full conversion (R_f 0.5 (toluene:pentane, 1:1, v:v)). Subsequent quenching by addition of sat. aq. $NaHCO_3$ solution and dilution with water

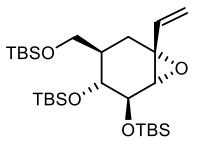
followed. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (40:60 → 60:40; toluene:pentane) yielded the title compound (202 mg, 0.35 mmol, 77%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.87 (dd, *J* = 17.2, 10.9 Hz, 1H, H-8), 5.44 (dd, *J* = 17.2, 0.5 Hz, 1H, H-9), 5.25 (dd, *J* = 10.9, 0.6 Hz, 1H, H-9), 4.26 (dd, *J* = 2.5, 1.6 Hz, 1H, H-2), 3.96 (dd, *J* = 2.5, 2.5 Hz, 1H, H-3), 3.73 (ddd, *J* = 3.5, 2.5, 1.6 Hz, 1H, H-4), 3.61 (dd, *J* = 9.7, 5.5 Hz, 1H, H-6), 3.54 (dd, *J* = 9.7, 6.6 Hz, 1H, H-6), 2.05 – 1.95 (m, 2H, H-5, H-7), 1.83 – 1.73 (m, 1H, H-7), 0.94 – 0.84 (m, 27H, $C(CH_3)_3$), 0.16 – 0.01 (m, 18H, $SiCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 154.1 (C=O), 139.4 (C-8), 115.2 (C-9), 82.9 (C-1), 80.5 (C-2), 71.3 (C-3), 70.2 (C-4), 66.0 (C-6), 40.6 (C-5), 30.4 (C-7), 26.1, 25.8, 25.8 ($C(CH_3)_3$), 18.6, 18.1, 18.0 ($C(CH_3)_3$), -4.3, -4.5, -4.7, -4.8, -5.2 ($SiCH_3$); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{28}H_{56}NaO_6Si_3$ 595.32824; Found 595.32769.

1-(*R*)-1-Vinyl-1-hydroxyl-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-carba-D-glucose (33).



Compound **32** (143 mg, 0.25 mmol) was dissolved in anhydrous Et_2O (12.5 mL, 0.02M) and cooled on ice. Subsequently, LiBH4 (2.0 M solution in THF, 0.15 mL, 0.3 mmol, 1.2 eq.) was added and stirring continued for another 15 minutes while keeping on ice. Upon full conversion was observed (R_f 0.5 (EtOAc:pentane, 1:1, v:v)) The mixture was quenched by the addition of sat. aq. $NaHCO_3$ solution and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (10:90 → 20:80; Et_2O:pentane) yielded the title compound (97 mg, 0.18 mmol, 71%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.91 (dd, *J* = 17.2, 10.8 Hz, 1H, H-8), 5.38 (dd, *J* = 17.2, 1.4 Hz, 1H, H-9), 5.14 (dd, *J* = 10.8, 1.4 Hz, 1H, H-9), 3.90 (ddd, *J* = 5.6, 4.8, 0.6 Hz, 1H, H-3), 3.76 (dd, *J* = 5.5, 5.5 Hz, 1H, H-4), 3.68 (dd, *J* = 9.7, 6.6 Hz, 1H, H-6), 3.57 (dd, *J* = 9.7, 6.1 Hz, 1H, H-6), 3.46 (s, 1H, 1-OH), 3.40 (dd, *J* = 6.2, 4.9 Hz, 1H, H-2), 2.81 (d, *J* = 6.2 Hz, 1H, 2-OH), 2.05 (ddd, *J* = 10.7, 5.5, 5.5 Hz, 1H, H-5), 1.87 (dd, *J* = 14.3, 5.8 Hz, 1H, H-7), 1.47 (dd, *J* = 14.3, 10.0 Hz, 1H, H-7), 0.99 – 0.82 (m, 27H, $C(CH_3)_3$), 0.20 – -0.00 (m, 18H, $SiCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 143.0 (C-8), 113.6 (C-9), 77.6 (C-2), 76.9 (C-3), 73.1 (C-1), 72.7 (C-4), 64.7 (C-6), 42.2 (C-5), 34.0 (C-7), 26.2, 26.2, 26.1 ($C(CH_3)_3$), 18.5, 18.4, 18.2 ($C(CH_3)_3$), -3.4, -3.5, -4.0, -4.1, -5.2, -5.2 ($SiCH_3$); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{27}H_{58}NaO_5Si_3$ 569.34897; Found 569.34840.

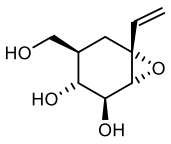
1-(*R*)-1-Vinyl-1,2-anhydro-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-carba-D-glucose (34).



Compound **33** (27 mg, 50 µmol) was dissolved in DCM (5.0 mL, 0.01 M) and the mixture was cooled on ice. Subsequently, Et_3N (0.14 mL, 1.0 mmol, 20 eq.) and MsCl (50 µL, 0.50 mmol, 10 eq.) were added respectively. After stirring for 30 minutes, full conversion was observed (R_f 0.5 (toluene:pentane, 2:8, v:v)). The reaction was quenched by the addition of sat. aq. $NaHCO_3$ solution and diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with H_2O, sat. aq. $NaHCO_3$ and brine

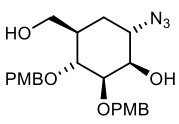
respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (10:90 → 20:80; toluene:pentane) yielded the title compound (12 mg, 22 µmol, 44%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.82 (dd, *J* = 17.1, 10.6 Hz, 1H, H-8), 5.44 (d, *J* = 17.0 Hz, 1H, H-9), 5.21 (d, *J* = 10.7 Hz, 1H, H-9), 4.23 (d, *J* = 5.2 Hz, 1H, H-2), 4.19 (dd, *J* = 5.1, 5.1 Hz, 1H, H-3), 3.73 (dd, *J* = 10.0, 3.6 Hz, 1H, H-6), 3.64 – 3.53 (m, 2H, H-4, H-6), 2.24 (dp, *J* = 9.0, 2.8 Hz, 1H, H-5), 2.14 (dd, *J* = 15.2, 3.3 Hz, 1H, H-7), 1.83 (dd, *J* = 15.2, 12.3 Hz, 1H, H-7), 0.95 – 0.85 (m, 27H, $C(CH_3)_3$), 0.18 – 0.02 (m, 18H, $SiCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 139.6 (C-8), 115.3 (C-9), 90.8 (C-1), 87.9 (C-2), 77.0 (C-3), 73.1 (C-4), 63.5 (C-6), 39.7 (C-5), 33.0 (C-7), 26.3, 26.1, 26.1 ($C(CH_3)_3$), 18.4, 18.4, 18.2 ($C(CH_3)_3$), -3.1, -3.3, -3.6, -4.0, -5.2, -5.2 ($SiCH_3$); HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{27}H_{57}O_4Si_3$ 529.35646; Found 529.35602.

1-(*R*)-1-Vinyl-1,2-anhydro-carba-D-glucose (8).



Compound **34** (24 mg, 44 µmol) was dissolved in anhydrous THF (1.8 mL, 0.025 M). The reaction was cooled on ice and kept under inert atmosphere. TBAF on silica gel (loading F^- ~1.5 mmol/g, 147 mg, 0.22 mmol, 5.0 eq.) was added and stirring continued for 4 hours while the reaction mixture was allowed to attain to room temperature. Upon full conversion was observed (R_f 0.3 (acetone:DCM, 1:1, v:v)), the mixture was concentrated at 25 °C under reduced pressure yielding the crude product. Flash column chromatography (20:80 → 50:50; acetone:DCM) yielded the title compound (5.9 mg, 32 µmol, 72%) as a colorless oil. ^{1}H NMR (500 MHz, acetone-d6, HH-COSY, HSQC, NOESY): δ 6.01 (dd, *J* = 17.0, 10.7 Hz, 1H, H-8), 5.40 (dd, *J* = 17.0, 0.7 Hz, 1H, H-9), 5.23 (dd, *J* = 10.7, 0.7 Hz, 1H, H-9), 4.77 (d, *J* = 4.3 Hz, 1H, 3-OH), 4.43 (dd, *J* = 8.0, 0.6 Hz, 1H, H-2), 4.23 (d, *J* = 4.0 Hz, 1H, 4-OH), 4.12 (ddd, *J* = 9.7, 8.0, 4.4 Hz, 1H, H-3), 3.81 – 3.66 (m, 3H, H-6, 6-OH), 3.38 (ddd, *J* = 10.0, 10.0, 3.9 Hz, 1H, H-4), 2.18 (d, *J* = 11.8 Hz, 1H, H-7), 1.92 – 1.88 (m, 2H, H-5, H-7); ^{13}C NMR (126 MHz, acetone-d6, HSQC): δ 140.4 (C-8), 115.5 (C-9), 93.2 (C-1), 89.1 (C-2), 78.8 (C-3), 73.7 (C-4), 63.1 (C-6), 39.7 (C-5), 34.0 (C-7); HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_9H_{14}NaO_4$ 209.07898; Found 209.07835.

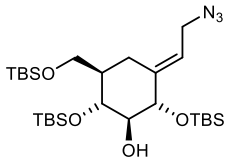
1-Deoxy-1-azido-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-trityl-carba-α-D-mannose (38).



Compound **37** (0.58 g, 1.5 mmol) was dissolved in DMF (14 mL, 0.1 M) followed by the addition of $LiClO_4$ (0.8 g, 7.5 mmol, 5.0 eq.) and NaN_3 (488 mg, 7.5 mmol, 15 eq.). The reaction mixture was heated to 130 °C and stirring continued for 16 hours. Upon full conversion was observed (R_f 0.3 (EtOAc:pentane, 3:7 v:v)), the mixture was diluted with water. The aqueous layer was extracted with EtOAc (3x) followed by washing the combined organic layers with sat. aq. $NaHCO_3$ and brine respectively. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (40:60 → 50:50; EtOAc:pentane) yielded the title compound (0.22 g, 0.5 mmol, 72%). ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 7.34 – 7.18 (m, 4H, CH_{arom}), 6.97 – 6.74 (m, 4H, CH_{arom}), 4.79 (d, *J* = 10.9 Hz, 1H, C*H*H PMB), 4.65 (d, *J* = 11.1 Hz, 1H, C*H*H PMB), 4.59 (d, *J* = 11.1 Hz, 1H, CH*H* PMB), 4.55 (d, *J* = 10.9 Hz, 1H, CH*H* PMB), 3.94 – 3.87 (m, 2H, H-1, H-2), 3.81 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.72 (dd, *J* = 8.3, 3.0 Hz, 1H, H-3), 3.65 – 3.58 (m, 3H, H-4, H-6), 2.58 (d, *J* = 2.3 Hz, 1H, 2-OH), 2.04 (dd, *J* = 6.9, 4.5 Hz, 1H,

6-OH), 1.96 – 1.88 (m, 1H, H-5), 1.83 (ddd, *J* = 14.4, 11.4, 3.2 Hz, 1H, H-7), 1.67 (ddd, *J* = 14.0, 4.0, 4.0 Hz, 1H, H-7); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 159.7, 159.5, 130.4 ($C_{q\text{-}arom}$), 129.9 (CH_{arom}), 129.9 ($C_{q\text{-}arom}$), 129.8, 114.2, 114.1 (CH_{arom}), 81.3 (C-3), 78.3 (C-4), 74.3 (CH_2 PMB), 72.7 (CH_2 PMB), 69.7 (C-2), 64.9 (C-6), 60.0 (C-1), 55.4 (OMe), 39.2 (C-5), 26.5 (C-7); HRMS (ESI) m/z: [M+Na$^+$] calcd for $C_{23}H_{29}N_3O_6Na$ 466.19541, found 466.1949.

1-(2-Azidoethylidene)-2,4,6-tri-*O*-*tert*-butyldimethylsilyl-carba-D-glucose (41).



Compound **34** (25 mg, 46 µmol) was dissolved in DMF (1.0 mL, 0.05 M) followed by the addition of tetrabutylammonium azide (0.13 g, 0.46 mmol, 10 eq.). The reaction mixture was heated to 100 °C and stirring continued for 2 hours. Upon full conversion was observed (R_f 0.5 (toluene:pentane, 3:7 v:v)), the mixture was diluted with water. The aqueous layer was extracted with Et_2O (3x) followed by washing the combined organic layers with brine. Subsequently, the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield the crude product. Flash column chromatography (2:98 → 7:93; Et_2O:pentane) yielded the title compound (18 mg, 30 µmol, 66%). ^{1}H NMR (500 MHz, $CDCl_3$, HH-COSY, HSQC): δ 5.69 (dd, *J* = 7.7, 7.7, 1.6, 1.6 Hz, 1H, H-8), 3.87 – 3.76 (m, 3H, H-2, H-9), 3.73 (dd, *J* = 9.8, 3.0 Hz, 1H, H-6), 3.63 (dd, *J* = 9.9, 6.0 Hz, 1H, H-6), 3.51 (dd, *J* = 10.1, 8.5 Hz, 1H, H-4), 3.16 (ddd, *J* = 8.8, 8.8, 2.2 Hz, 1H, H-3), 2.61 (dd, *J* = 13.9, 3.9 Hz, 1H, H-7), 2.25 (d, *J* = 2.2 Hz, 1H, 3-OH), 1.68 (dd, *J* = 13.5 Hz, 1H, H-7), 1.45 (ddd, *J* = 13.0, 6.4, 6.4, 3.5, 3.5 Hz, 1H, H-5), 0.99 – 0.85 (m, 27H, $C(CH_3)_3$), 0.17 – 0.04 (m, 18H, $SiCH_3$); ^{13}C NMR (126 MHz, $CDCl_3$, HSQC): δ 143.9 (C-1), 113.9 (C-8), 81.2 (C-3), 76.4 (C-2), 73.7 (C-4), 63.5 (C-6), 47.3 (C-9), 46.4 (C-5), 27.3 (C-7), 26.2, 26.1 ($C(CH_3)_3$), 18.6, 18.5, 18.4 ($C(CH_3)_3$), -3.5, -4.4, -4.6, -4.6, -5.1, -5.3 ($SiCH_3$); HRMS (ESI) m/z: [M+Na]$^+$ Calcd for $C_{27}H_{57}N_3NaO_4Si_3$ 594.35546; Found 594.35491.

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