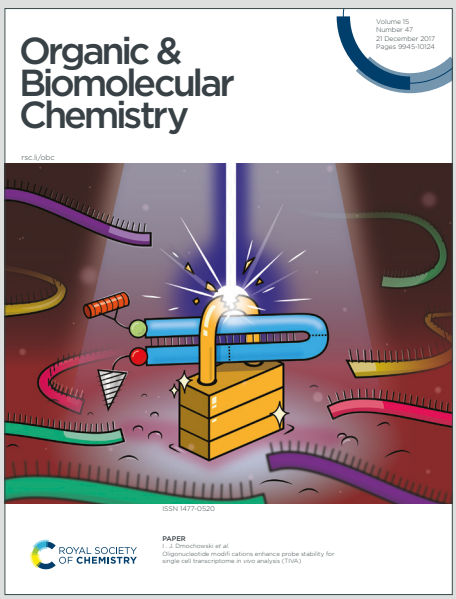
Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: M. Kumar, T. R. Reddy, A. Gurawa and S. Kashyap, *Org. Biomol. Chem.*, 2020, DOI: 10.1039/D0OB01042A.



ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/D0OB01042A

Journal Name

ARTICLE

Copper(II)-Catalyzed Stereoselective 1,2-Addition *vs* Ferrier Glycosylation of "Armed" and "Disarmed" Glycal Donors†

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

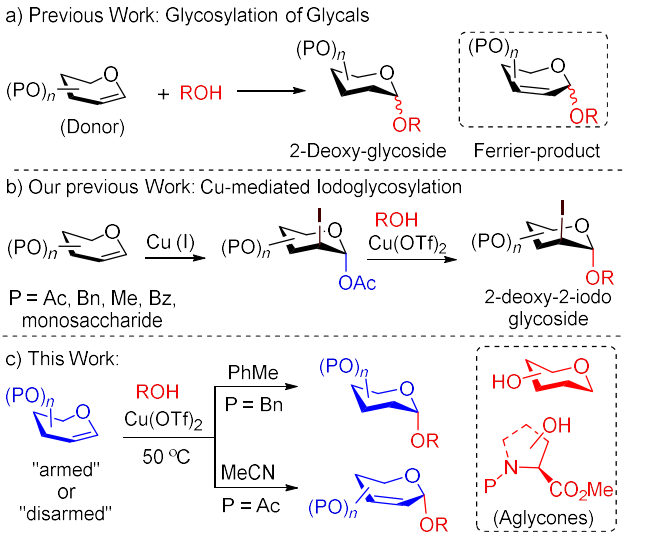
Manoj Kumar,[a] Thurpu Raghavender Reddy,[a] Aakanksha Gurawa[a] and Sudhir Kashyap*[a]

Selective activation of "armed' and ''disarmed'' glycal donor enabling the stereo-controlled glycosylations by employing Cu(II)-catalyst as the promoter has been realized. The distinctive stereochemical outcome in the process is mainly influenced by the presence of diverse protecting groups on the donor and the solvent system employed. The protocol is compatible with a variety of aglycones including carbohydrates, amino-acids, and natural-products to access the deoxy-glycosides and glycoconjugates in high α-anomeric selectivity. Notably, the synthetic practicality of the method is amply verified for the stereoselective assembling of trisaccharides comprising 2-deoxy components. Mechanistic studies involving deuterated experiments validate the *syn*-diastereoselective 1,2-addition of acceptor on the double bond of armed donor.

Introduction

2-Deoxyglycosides constitute a prominent class of carbohydrate chiral skeleton owing to the absence of C-2 hydroxyl substituents[1-3] In addition to the well appreciated role as important structural motif in the synthesis of numerous bioactive molecules, natural products and drug molecules,[2] the 2-deoxysugars are frequently utilized as clinical agents in pharmaceutical studies as well.[3] However, stereo-controlled preparation of 2-deoxyglycosides remains a challenging task due to the absence of a stereo directing linkage or NGP at C-2 position[4] and susceptibility of 2-deoxyglycoside-linkage in acidic conditions to result undesired elimination products.[5] To overcome these obstacles, several indirect strategies involving de novo synthesis,[6] pre-activation of glycosyl donor[7] or installing temporary prosthetic group at the C-2 position have been developed.[8] In parallel, many direct methods including Umpolung approaches for the synthesis of 2-deoxysugar have been evolved utilizing glycosyl halides,[9] glycosyl imidates,[10] thioglycosides,[11] glycosyl phosphate/phosphoroamidite/phosphite/phosphorodithioate,[12] and (2-carboxyl)benzyl glycoside donor.[13]

Besides, suitably functionalized glycals have been widely explored as stable glycosyl donor in nucleophilic addition of aglycones on 1-2 double bond to obtain 2-deoxyglycosides (Scheme 1).[14] However, the lack of C-2 auxiliary group and the presence of stereoelectronically diverse substituent at C-3 position led to direct 1,2-addition or a Ferrier glycosylation involving an allylic coupling of acceptor to enol-ether functionality.[15] The stereochemical outcome in two competing pathways are generally governed by the reactivity of donor and the judicious influence of C-3 electron-donating/withdrawing functional group.[16] The activation of 1,2-double bond in glycals is generally proceeds *via* oxocarbenium ion or allyloxycarbenium intermediates producing kinetically controlled 1,2 addition product and thermodynamically favoured 2,3-unsaturated glycoside respectively. Essentially, the glycosides comprising 2,3-olefinic moiety, also known as "pseudo-glycals" offer further synthetic potential as chiral precursors in numerous complexity-generating chemical transformations.[17]



Scheme 1. Synthesis of 2-deoxyglycosides from glycals and Cu-catalyzed stereoselective glycosylation of "Armed" and "Disarmed" glycal donor

Carbohydrate Chemistry Research Laboratory (CCRL), Department of Chemistry, Malaviya National Institute of Technology (MNIT), Jaipur-302017, INDIA. E-mail: skashyap.chy@mnit.ac.in, skr.kashyap@gmail.com.

Electronic Supplementary Information (ESI) available: [General procedures, characterization data, spectral charts are provided]. See DOI: 10.1039/x0xx00000x

Indeed, these scaffolds constitute several biologically active products, antibiotics, nucleosides, cardiac glycoconjugates, and sugar-based therapeutic targets.[18]

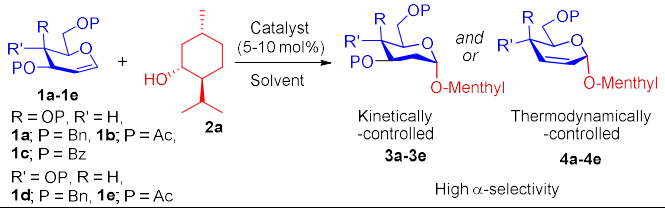
Despite the synthetic difficulties associated with installing selective glycosidic-linkages, development of stereoselective methods for the synthesis of 2-deoxysugars continues to be an interesting and nontrivial goal for carbohydrate researchers. During our endeavour,[19] we previously successfully applied Cu(II)-triflate as a mild Lewis acid catalyst in stereoselective Ferrier glycosylation.[19j] We further demonstrated the versatility and efficiency of Cu-catalysis in regioselective iodoglycosylation of 1,2-glycals comprising both armed and disarmed donors.[19d] Subsequent anomeric activation of 2-iodo-glycosyl acetate employing Cu(II)-catalyst enabling the expeditious synthesis of 2-deoxy-2-iodo glycosides with high anomeric selectivity (Scheme 1). Enamoured of the inherent moisture/air stability and effectiveness in glycosylation,[20] we aimed to investigate the potential of Cu-catalysis in direct activation of armed and disarmed galactal donor. Inspired by these precedents and continuing our research interest in glycochemistry, herein we present the development of stereo-controlled glycosylation employing Cu(II)-triflate as an effective promoter allowing the synthesis of 2-deoxy and 2,3-dideoxyglycosides under additive/ligand-free conditions. The complementary approach is amenable to access structurally defined 2-deoxy-linked trisaccharide by judicious selection of the glycosyl donor and the solvent system.

Results and discussion

To begin our studies, we first examined the activation of per-*O*-benzylated galactal **1a** as an armed donor with menthol (**2a**) as a model acceptor promoted by a catalytic amount of Cu(II)-triflate (5 mol%). As summarized in Table 1, the reaction provided a very poor conversion in acetonitrile at room temperature (entry 1); however a slight improvement was observed when the reaction was performed at 50 °C for 24 h (entry 2). Further changing the solvent to dichloroethane significantly diminished the reaction rate allowing the complete recovery of donor **1a** (entry 3). Subsequently, the use of THF as the solvent gave better conversion to obtain the corresponding 2-deoxy glycoside **3a** in 45% yields (entry 4). To our delight, switching the solvent to toluene resulted selective activation of armed donor **1a** providing 1,2-addition product **3a** in 92% yields without formation of Ferrier rearranged glycoside (entry 5).[21] We further anticipated that the polarity of the solvent and stereo-electronic diverse nature of substituents impart crucial role in the stereochemical outcome and the reactivity of donor substrate. Thus, the glycosylation coupling of readily accessible disarmed donor **1b** with **2a** under aforementioned reaction conditions afforded a mixture of the kinetic 2-deoxy galactoside **3b** (53%, α/β; >80:20) and thermodynamically-controlled 2,3-unsaturated glycoside **4b** (19%, α/β; >99:1) in 78:22 ratio (entry 6). Though, similar results were obtained when the reaction was performed in DCM solvent producing a mixture of 1,2-addition and Ferrier product **3b**:**4b** albeit with a different ratios; 70:30 (entry 7).

Apparently, the thermodynamically-stable glycoside **4b** could be obtained in 90% yields with high α-selectivity (>99:1) by performing the reaction in acetonitrile after 2 h, however competitive kinetic product was not observed (entry 8). The predominant allylic rearrangement attributed by the nature of C-3 acetate as a better leaving group than the ether linkage. In contrast, the substrate with disarmed benzoyl group **1c** failed to undergo 1,2-addition reaction in toluene even after prolonged reaction time (entry 9). Whereas, employing acetonitrile as the solvent led to non-selective activation of **1c** furnishing 2-deoxy **3c** (39%, α/β; >85:15) and rearranged **4c** (10%, α/β; >99:1) in 60:40 ratios (entry 10).

Table 1. Optimization of selective glycosylation of glycal donors in various conditions.[a]



Entry	Donor, Catalyst (mol%)	Solvent	*t* (h), T (°C), Conv.(%)[b]	**3:4**[c]	**3,4** Yields (%)[d] (α-selectivity)[e]
1[f]	**1a**, $Cu(OTf)_2$ (5)	ACN	24, rt, <10	NA	NA
2	**1a**, $Cu(OTf)_2$ (5)	ACN	24, 50, <20	NA	NA
3	**1a**, $Cu(OTf)_2$ (5)	DCE	24, 50, <5	NA	NA
4	**1a**, $Cu(OTf)_2$ (5)	THF	24, 50, 60	100:0	45 (>95)
5	**1a**, $Cu(OTf)_2$ (5)	toluene	0.5, 50, 100	100:0	92 (>95)
6	**1b**, $Cu(OTf)_2$ (5)	toluene	8, 50, 100	78:22	53 (>80), 19 (>99)
7	**1b**, $Cu(OTf)_2$ (5)	DCM	3, 50, 100	70:30	45 (>95), 17 (>99)
8	**1b**, $Cu(OTf)_2$ (5)	ACN	2, 50, 100	0:100	90 (>99)
9	**1c**, $Cu(OTf)_2$ (5)	toluene	24, 50, 0	NR	NR
10	**1c**, $Cu(OTf)_2$ (5)	ACN	3, 50, 100	60:40	39 (>85), 10 (>99)
11[g]	**1d**, $Cu(OTf)_2$ (5)	toluene	12, 50, 100	55:45	34 (>85), 9 (>99)
12	**1e**, $Cu(OTf)_2$ (5)	ACN	1, 50, 100	0:100	88 (>90)
13[h]	**1a,** TMSOTf (10)	toluene	24, 0-rt, 50	NA	NA
14[h,i]	**1a,** TfOH (10)	toluene	0.5, 0-rt, 100	NA	NA complex
15[h]	**1a**, $BF_3{\cdot}OEt_2$ (10)	toluene	24, 0-rt, 50	NA	NA
16[h]	**1b**, TMSOTf (10)	ACN	24, 0-rt, 50	0:100	30 (>99)
17[h]	**1b**, TfOH (10)	ACN	0.5, 0-rt,100	58:42	44 (>82), 16 (>99)

[a]Reaction conditions: Glycal donor **1a-1e** (1.0 equiv.), menthol **2a** (1.2 equiv.), and catalyst (5-10 mol%) in solvent (2 mL), stirred at 50 °C under inert atmosphere (N_2) unless otherwise noted. [b]As observed by thin-layer chromatography. [c]Examined by ^{1}H NMR spectroscopy of crude reaction mixture. [d]The isolated and unoptimized yields. [e]The α/β ratios were determined by ^{1}H NMR analysis. [f]Reaction at rt. [g]Mixture of Ferrier and 2-deoxy benzyl-glucosides, observed by ^{1}H NMR spectrum. [h]Reactions conducted at 0 °C to rt. [i]Inseparable complex mixture of undesired products as a result of decomposition.

DOI: 10.1039/D0OB01043A

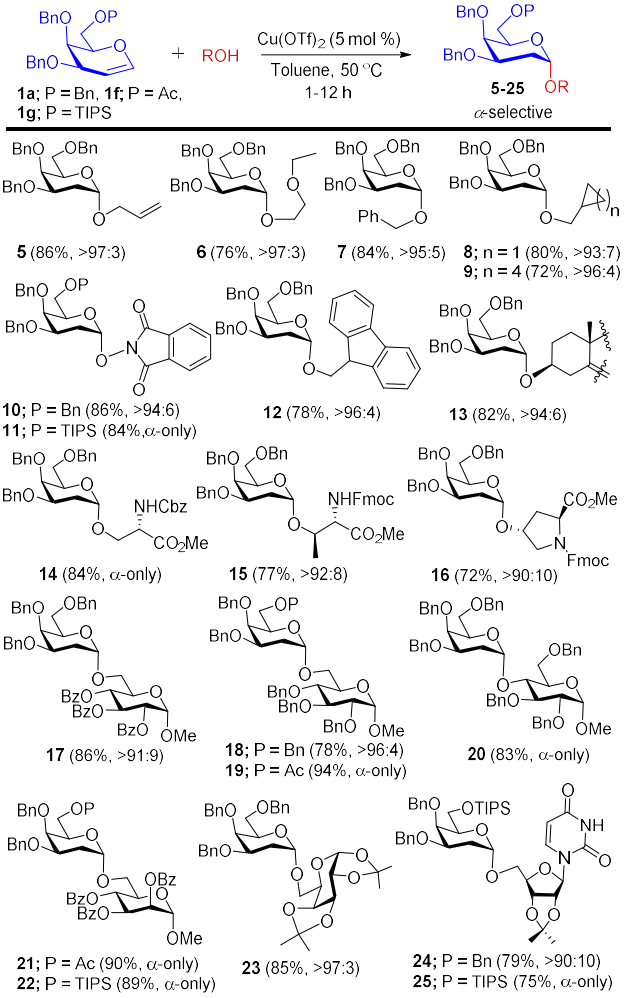
To further probe the selective activation of 1,2-double bond in armed and disarmed glycal donor, benzylated and acetylated glucals (**1d** and **1e**) were subjected to optimal glycosylation reactions. Activation of armed glucal donor **1d** with menthol **2a** in toluene found to be unsatisfactory providing the inconsistent ratios of the corresponding direct 1,2-addition **3d** and Ferrier product **4d** through competitive pathways (entry 11). In addition, we also observed a considerable amount of benzyl-glucosides (2-deoxy/Ferrier), resulting from the facile elimination of C-3 benzyl group and subsequent reacting as competitive nucleophile. Presumably, the disarmed donor **1e** reacted in complete selectivity producing thermodynamically-stable glucoside **4e** (88%, *α/β;* 90:10)[19j] as the sole product (entry 12). Meanwhile, 1,2-addition reaction of **1a** in the presence of various catalysts such as TMSOTf, TfOH, or $BF_3{\cdot}OEt_2$ under optimal conditions found to be sluggish (either very slow or fast) resulting a poor conversion or undesired complex reaction mixture (entries 13-15). Besides, the coupling between **1b** and acceptor **2a** employing TMSOTf as an activator favors the selective Ferrier glycosylation albeit with decreased rate (entry 16). Notably, the use of strong acid TfOH failed to produce selective activation attributing two competitive Ferrier rearrangement and 1,2-addition pathways (entry 17).

Having orthogonal activation model for armed and disarmed glycal donor, we next systematically evaluated the scope of the optimized glycosylation reactions using a range of acceptors. As summarized in Table 2, the kinetic-controlled 1,2-addition of primary and secondary alcohols comprising various functionalities, and diversely protected monosaccharide and amino-acids proceeded smoothly furnishing the corresponding 2-deoxyglycosides **5-25** in good yields (72-94%) with high α-selectivity (up to 100). The Cu(II)-catalyzed 1,2-addition of **1a** with allyl alcohol (**2b**), 2-ethoxyethanol (**2c**), benzyl alcohol (**2d**) performed well to afford 2-deoxyglycosides **5-7** in good yields. Subsequently, the acceptors comprising alicyclic ring system (**2e** and **2f**) underwent stereoselective glycosylation to provide the corresponding glycosides **8** (80%) and **9** (72%), respectively.

Furthermore, *N*-hydroxyphthalimide (**2g**), 9-fluorenemethanol (**2h**) and highly functionalized steroid such as cholesterol (**2i**) were reacted smoothly to obtain the kinetically-favored 2-deoxy-α-glycosides **10-13** in good yields (78-86%). Notably, the *N*-hydroxyl amine derived glycosides constitute a masked *O*-aminoxy-glycosyl, synthetically useful aminoxy functionality at anomeric carbon to access the valuable neoglycoconjugates.[22] Encouragingly, the glycosylation of Cbz-Ser-OMe (**2j**), Fmoc-Thr-OMe (**2k**), and N-Fmoc-protected 4-hydroxy-L-proline (**2l**) were subjected under present conditions to efficiently generate the corresponding amino-acid-conjugated deoxysugars **14-16** in good yields and high α-selectivity. Next, we evaluated the glycosylation of sugar-derived acceptors to access the 2-deoxy-linked disaccharides. Thus, the selective glycosylation of differently protected galactal donors (**1a, 1f** and **1g**) employing glucosyl (**2m-2o**), mannosyl (**2p**), and galactosyl (**2q**) derived acceptors enabling the stereoselective formation of α-(1-6, 1-4)-linked 2-deoxydisaccharides **17-23** in satisfactory yields. Noteworthy, a uridine derived un-protected nucleoside base **2r** was incorporated successfully with excellent selectivity to access the venerable 2-deoxyglycoconjugates **24** and **25** in good yields without formation of thermodynamically favored Ferrier product. These findings further highlight the potential of the protocol in the stereoselective synthesis of 2-deoxyglycoconjugates.

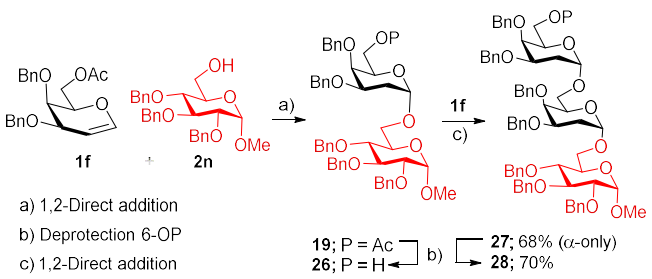
Enthusiastically, we demonstrated the extension of our method in two-step sequential synthesis of oligosaccharide (Scheme 2). Thus, the disaccharide **19** readily synthesized by glycosylation coupling of glycal donor **1f** with **2n** and following sequential deprotection of 6-*O*-ester with NaOMe in MeOH afforded the disaccharide acceptor **26** in 85% yields.[21] Subsequently, 1,2-direct addition of **26** with **1f** employing Cu(II)-catalyzed glycosylation furnished the desired trisaccharide **27** in 68% yields with α-selectivity. The deacetylation reaction was repeated to obtain the corresponding **28** (70%) comprising a free OH group.

Table 2. Scope for the kinetically-controlled glycosylation of armed donor with various aglycones.[a],[b]



[a]Reaction conditions: Glycal Donor **1a, 1f or 1g** (1.0 equiv.), acceptor (1.2 equiv.), and $Cu(OTf)_2$ (5 mol%) in toluene (2 mL), stirred at 50 °C under N_2 atmosphere. [b]Isolated yields after column chromatography as a mixture of α/β, based on relative integration of anomeric protons in ^1H NMR spectrum.

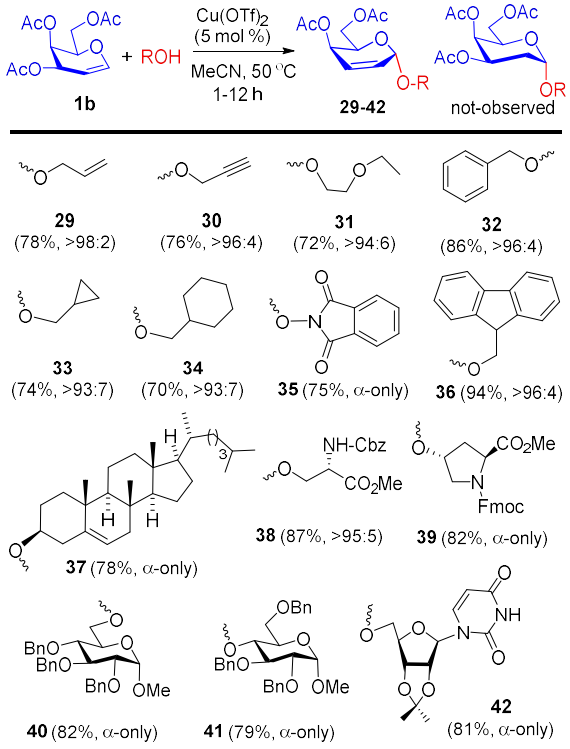
View Article Online DOI: 10.1039/D0OB01043A



Scheme 2. Stereoselective synthesis of the trisaccharide comprising 2-deoxy component in sequential steps. Reaction conditions: (a) 1,2-Addition; glycal **1f** (1.0 equiv.), **2n** (1.2 equiv.), $Cu(OTf)_2$ (5 mol%), toluene (2 mL), 50 °C, 15 h, (b) Deprotection; **19** or **27** (1.0 equiv.), NaOMe (0.1 equiv.), MeOH, rt, 4 h, (c) 1,2-Addition; glycal **1f** (1.0 equiv.), **26** (1.2 equiv.), $Cu(OTf)_2$ (5 mol%), toluene (2 mL), 50 °C, 6 h.

We next investigated the selective glycosylation of disarmed donor **1b** under optimum thermodynamically-controlled conditions. Pleasingly, all the reactions worked well affording the corresponding 2,3-unsaturated galactosides **29-42** in good to excellent yields (70-94%) with α-selectivity (>99:1), results are summarized in Table 3. We accomplished the glycosylation of disarmed donor **1b** with allyl, propargyl, 2-ethoxyethanol, benzyl alcohol, cyclopropyl- and cyclohexylmethanol to obtain the desired products **29-34** in moderate-to-good yields. The Ferrier-type rearrangement of acceptors comprising hydroxyl-amine, fluorenylmethyl and steroidal moieties were performed smoothly affording their corresponding galactosides **35-37** in good yields with excellent selectivites (α/β; up to 100).

Table 3. Scope for the thermodynamically-controlled glycosylation of disarmed donor with various aglycones.[a],[b]

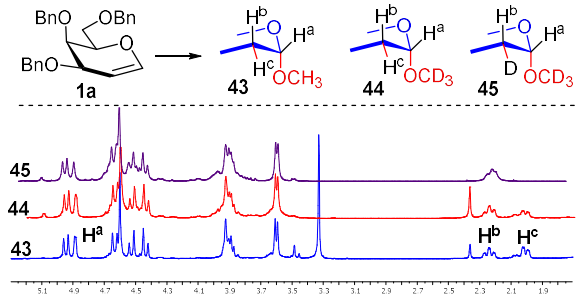


[a]Reaction conditions: Glycal Donor **1b** (1.0 equiv.), acceptor (1.2 equiv.), and $Cu(OTf)_2$ (5 mol%) in acetonitrile (2 mL), stirred at 50 °C under inert atmosphere. [b]The isolated yields as a mixture of α/β anomers, determined by ^1H NMR spectrum.

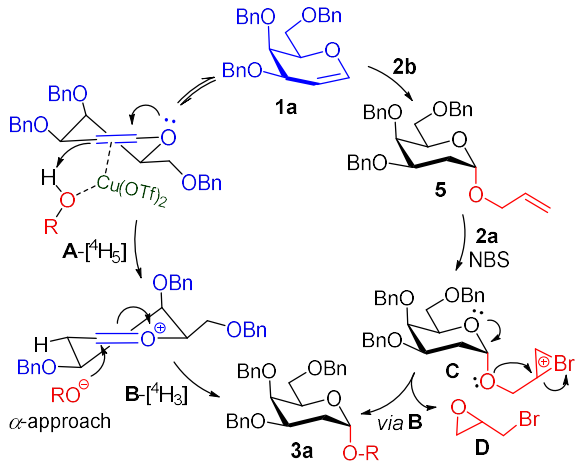
Prominently, amino-acid derived acceptors were auspiciously coupled with donor **1b** employing Ferrier glycosylation to access the corresponding glycoconjugates **38-39** in good yields. Pleasingly, the selective activation of **1b** with primary (6-OH) and secondary (4-OH) glucosyl acceptors were performed successfully to obtain the α-(1-6) **40** and α-(1-4) **41** disaccharides in 82% and 79% yields respectively. Indeed, nucleoside base as glycosyl acceptor favors the formation of thermodynamically-controlled *O*-galactoside **42** as the sole product with 81% yields with exclusive α-anomer. More importantly, the activation of disarmed donor achieved in complete stereoselective manner allowing the expeditious preparation of "pseudo-galactals" derivatives. It is pertinent to mention that the selective glycosylation of **1b** is particularly challenging due to the high reactivity of per-*O*-acetylated galactal towards competing allylic rearrangement and direct 1,2-addition pathways.[16c]

To gain insights into selective glycosylation, we performed 1,2-addition reactions of **1a** with CH_3OH, CD_3OH and CD_3OD as the nucleophilic acceptors, respectively (Scheme 3). The ^1H NMR spectroscopy analyses confirm the formation of corresponding 2-deoxy-α-glycosides **43-45** involving least steric encumbrance pathways. Notably, the glycosylation coupling between **1a** and CD_3OD presumably proceeding through analogous intermediates; **A**-[$^4H_5$] and **B**-[$^4H_3$] ensured the *syn*-diastereoselective addition on C1-C2 double bond to give D_3-methyl-2D-α-galactoside **45**.[14j]

Though a detail mechanism awaits further studies, a plausible rationalization for the kinetic and thermodynamic controlled glycosylation may be proposed (Scheme 4). Initially, the Cu(II)-triflate coordinates with C1-C-2 double bond of the favoured conformation **A**-[$^4H_5$] in armed glycal **1a** and oxygen of the acceptor leading to the polarization of the double bond. Subsequent activation of the enol-ether functionality will facilitate the formation of a half-chair oxocarbenium ion **B** with a preferred [$^4H_3$] configuration. Finally, the nucleophilic addition of activated-acceptor (**RO**$^-$) from the less-hindered axial side of depicted **B**-[$^4H_3$] will unambiguously produce the kinetically favoured α-glycoside **3a**. The predominant α-selectivity certainly attributed to the vinylogous anomeric effect (VAE) and the stereochemistry and stability of the half-chair transient states.[14] Additional experiments were conducted to further substantiate the correlation between rationalized transitions states and distinctive stereochemical outcome.



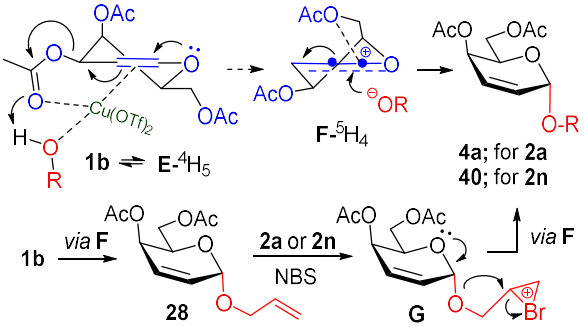
Scheme 3. Glycosylation with acceptors including deuterated methanol to probe the mechanistic hypothesis for *syn*-1,2-addition.



Scheme 4. Mechanistic rationalization for the cu-catalyzed stereoselective glycosylation of "Armed" glycal donor and one-pot sequential anomeric activation.

Accordingly, the coupling of **1a** with **2b** under standard 1,2-addition conditions following one-pot anomeric activation of allyl glycosyl donor **5** with acceptor **2a** using NBS facilitate the formation of bromonium ion **C**.[7d] Subsequent elimination of epibromohydrin **D** following glycosidic linkage with **2a** resulted **3a** with same selectivity albeit with a different yields (62% over 2-steps). Similar results were obtained in the glycosylation coupling of monosaccharide aglycone **2n** affording the corresponding disaccharide **18** in 65% yields. The stereochemical outcome reveals the formation of an identical putative *pseudo*-chair oxocarbenium ion **B**.

The alternative mechanism of allylic rearrangement in disarmed donor could be postulated on the basis of our experimental results and analogy to prior reports.[15] As illustrated in Scheme 5, alongside coordinating with double-bond from sterically favourable α-face in distorted [$^4H_5$] conformation of **1b** and ROH, Cu-catalyst also interacts with pseudo-axial oriented OAc at C-3 position. This significantly induced bond lengthening of C(3)-OAc in Cu-complex **E**-[$^4H_5$] and likely to activate the 3-OAc as leaving group to generate a more-stable allyloxycarbenium ion intermediate **F**-[$^5H_4$]. The delocalization involving ring oxygen and endocyclic double-bond and stereochemical factor (anchimeric assistance of the 6-OAc) associated with the transient state thus directing the approach of acceptor from the α-face to give the thermodynamically-controlled **4a**.



Scheme 5. Proposed hypothesis for the activation of "Disarmed" glycal donor under thermodynamic conditions and one-pot anomeric activation.

In addition, the one-pot sequential Ferrier glycosylation of **1b** following selective anomeric activation of resultant *O*-allyl donor **29** with acceptors **2a** and **2n** by using NBS, facilitating the release of bromonium ion **G** producing unequivocally 2,3-unsaturated glycosides **4a** (68%) and **40** (70%) with equivalent stereoselectivity.[21] These observations infidelity established the role of penultimate transient species and directing influence of the catalyst.

Conclusions

In summary, we have successfully developed a flexible and practical approach for the stereoselective activation of 1,2-double bond in galactal donor employing Cu(II)-catalyst as the promoter to obtain the 2-deoxy and 2,3-unsaturated glycoconjugates. The protocol is highly advantageous and ensured the divergent and stereoselective glycosylation affording kinetic (2-deoxy) or thermodynamic (2,3-dideoxy) product with α-selectivity. The intrinsic reactivity of "armed' and "disarmed" donor with subtle electronic nature of protecting groups led to orthogonal glycosylation processes and largely controlled by the choice of suitable solvent system. The scope of the selective activation methods were substantiated for a wide range of acceptors and tolerated various sensitive functionalities in amino-acids and carbohydrates. Synthetic application of this method is further highlighted in the stereoselective synthesis of 2-deoxy linked oligosaccharides by readily functional group manipulation. Further mechanistic investigations into solvent-dependent glycosylation of armed/disarmed glycosyl donor and potential application to the synthesis of oligosaccharides are in progress.

Experimental

General Synthesis Information: Moisture and air-sensitive reactions were performed in flame-dried round bottom flasks, fitted with rubber septa or glass gas adapters, under a positive pressure of nitrogen. Moisture and air-sensitive liquids or solutions were transferred via nitrogen-flushed syringe. Experiments were monitored by thin layer chromatography (TLC). Melting points were obtained in open capillary tubes using a micro melting point apparatus and were uncorrected. Unless otherwise noted, materials were obtained from commercial suppliers and used without purification. Removal of solvent under reduced pressure refers to distillation with a Büchi rotary evaporator attached to a vacuum pump (~3 mmHg). Products obtained as solids or high boiling oils were dried under vacuum (~1 mmHg). Analytical TLC was performed using Whatman 250-micron aluminum backed UV F254 pre-coated silica gel flexible plates. Subsequent to elution, ultraviolet illumination at 254 nm allowed for visualization of UV active materials. Staining with p-anisaldehyde, basic potassium permanganate solution, or Molisch's reagents allowed for further visualization. Proton and Carbon nuclear magnetic resonance spectra (^1H, ^{13}C NMR) were recorded on Avance 300, 400 or 500 MHz and ECS 400 MHz (JEOL) NMR spectrometers. The proton resonances are annotated as:

chemical shift (δ) relative to tetramethylsilane (δ 0.0) using the residual solvent signal as an internal standard or tetramethylsilane itself: chloroform-d (δ 7.26, singlet), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), coupling constant (*J*, Hz), and number of protons for a given resonance is indicated by nH. The chemical shifts of ^{13}C NMR are reported in ppm relative to the central line of the triplet at δ 77.00 ppm for $CDCl_3$. IR spectra were recorded on a PerkinElmer FT-IR spectrometer and wave numbers of maximum absorption peaks are presented in cm^{-1}. Mass analyses (ESI-MS) and HRMS were performed on Xevo G2-S QTTOF (Waters, USA) Spectrometer.

General experimental procedure for the synthesis of 2-deoxyglycosides:

Menthyl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (3a): A preformed solution of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) and L-Menthol (45 mg, 0.288 mmol, 1.2 equiv.) in toluene (2 mL) was added 5 mol% $Cu(OTf)_2$ and the resulting mixture was stirred at 50 °C temperature under N_2 atmosphere until the completion of starting material, typically for 30 min. (adjudged by TLC). The reaction mixture was diluted with EtOAc (10 mL), quenched with saturated $NaHCO_3$ (5 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, concentrated in vacuo and purified by silica gel column chromatography using hexane-EtOAc as eluent to afford the compound **3a** as a colorless syrup (126 mg, 0.220 mmol, 92% yield, α:β; 95:05). Rf (15% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.31 (m, 7H), 7.31-7.23 (m, 8H), 5.03 (d, *J* = 2.9 Hz, 1H), 4.94 (d, *J* = 11.7 Hz, 1H), 4.67-4.55 (m, 4H), 4.55-4.38 (m, 2H), 4.06 (t, *J* = 6.4 Hz, 1H), 3.93 (m, 1H), 3.64-3.52 (m, 2H), 3.30 (td, *J* = 10.5, 4.2 Hz, 1H), 2.19 (td, *J* = 12.3, 3.4 Hz, 1H), 2.03 (ddd, *J* = 16.7, 14.8, 7.8 Hz, 4H), 1.65-1.54 (m, 3H), 1.22-1.11 (m, 1H), 1.00-0.92 (m, 1H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.88-0.84 (m, 1H), 0.81 (d, *J* = 6.5 Hz, 3H), 0.75 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 138.6, 138.2, 128.4, 128.3, 128.1, 127.6, 127.6, 127.4, 127.4, 127.3, 99.8, 79.9, 74.9, 74.2, 73.4, 73.2, 70.4, 69.8, 69.7, 48.9, 42.9, 34.3, 31.6, 25.7, 23.2, 22.2, 21.1,16.3; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[16d]

General experimental procedure for the synthesis of 2,3-unsaturated glycosides:

Menthyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (4a): A preformed solution of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) and L-Menthol (68 mg, 0.440 mmol, 1.2 equiv.) in acetonitrile (2 mL) was added 5 mol% $Cu(OTf)_2$ and the resulting mixture was stirred at 50 °C temperature under N_2 atmosphere until the completion of starting material, typically for 3 h (adjudged by TLC). The reaction mixture was diluted with EtOAc (10 mL), quenched with saturated $NaHCO_3$ (5 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, concentrated in vacuo and purified by silica gel column chromatography using hexane-EtOAc as eluent to afford the compound **4b** as a pale yellow solid (121 mg, 0.330 mmol, 90% yield; α-only). Mp: 72-74 °C; Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.11 (dd, *J* = 10.0, 5.0 Hz, 1H), 6.05 (dd, *J* = 10.0, 2.8 Hz, 1H), 5.15 (d, *J* = 2.5 Hz, 1H), 5.02 (dd, *J* = 5.1, 2.5 Hz, 1H), 4.42 (ddd, *J* = 7.4, 4.7, 2.6 Hz, 1H), 4.27-4.17 (m, 2H), 3.45 (td, *J* = 10.6, 4.4 Hz, 1H), 2.09 (s, 3H), 2.08 (s, 3H), 1.71-1.59 (m, 3H), 1.52-1.38 (m, 1H), 1.02 (dt, *J* = 13.6, 7.5 Hz, 3H), 0.93 (d, *J* = 3.7 Hz, 3H), 0.91 (d, *J* = 4.2 Hz, 3H), 0.89-0.81 (m, 2H), 0.79 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 170.4, 130.7, 124.7, 95.6, 80.7, 66.6, 63.2, 63.0, 48.9, 43.2, 34.2, 31.7, 25.6, 23.1, 22.4, 21.1, 20.8, 16.1; HRMS (ESI) m/z [M + Na]$^+$ calculated for $[C_{20}H_{32}O_6Na]^+$: 391.2091; found 391.2090.

Prop-2-enyl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (5): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with Allyl alcohol (19 µL, 17 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 4 h, purified by silica gel column chromatography to obtain glycoside **5** as a light yellow solid (98 mg, 0.206 mmol, 86% yield, α/β; 97:03). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.23 (m, 15H), 5.89 (ddd, *J* = 22.4, 10.8, 5.6 Hz, 1H), 5.24 (ddd, *J* = 17.2, 3.3, 1.6 Hz, 1H), 5.17-5.12 (m, 1H), 5.02 (d, *J* = 2.8 Hz, 1H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.69-4.56 (m, 3H), 4.46 (dt, *J* = 14.6, 11.8 Hz, 3H), 4.13 (ddt, *J* = 13.0, 5.1, 1.4 Hz, 1H), 3.98 - 3.90 (m, 3H), 3.64-3.53 (m, 2H), 2.24 (td, *J* = 12.3, 3.7 Hz, 1H), 2.02 (dd, *J* = 12.6, 4.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.5, 138.0, 134.2, 128.3, 128.1, 127.7, 127.6, 127.4, 127.2, 116.9, 97.0, 74.7, 74.2, 73.4, 72.9, 70.4, 69.9, 69.5, 67.8, 31.1; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[16b]

Ethoxyethyl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (6): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with Ethoxy ethanol (28 µL, 26 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 3 h, purified by silica gel column chromatography to obtain glycoside **6** as a yellow oil (93 mg, 0.183 mmol, 76% yield, α/β; 97:03). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.26 (m, 15H), 5.08 (d, *J* = 3.1 Hz, 1H), 4.94 (d, *J* = 11.6 Hz, 1H), 4.63 (ddd, *J* = 29.0, 14.6, 8.9 Hz, 6H), 4.53-4.40 (m, 4H), 4.02-3.92 (m, 3H), 3.69-3.50 (m, 3H), 2.25 (td, *J* = 12.4, 3.7 Hz, 1H), 2.04 (dd, *J* = 12.6, 4.5 Hz, 1H), 0.91-0.83 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 138.5, 138.1, 137.8, 128.4, 128.2, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 127.3, 97.1, 74.8, 74.3, 73.5, 72.9, 70.5, 70.0, 69.5, 68.9, 31.9, 31.1, 22.7, 14.1; HRMS (ESI) m/z [M + Na]$^+$ calculated for $[C_{31}H_{38}O_6Na]^+$: 529.2561; found 529.2560.

***Benzyl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (7)*:** Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with Benzyl alcohol (30 µL, 31 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 4 h, purified by silica gel column chromatography to obtain glycoside **7** as a pale yellow semi solid (106 mg, 0.202 mmol, 84% yield, α/β; 95:05). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.24 (m, 20H), 5.08 (d, *J* = 3.2 Hz, 1H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.70-4.55 (m, 5H), 4.46 (dt, *J* = 14.2, 11.8 Hz, 3H), 4.01-3.92 (m, 2H), 3.66-3.52 (m, 2H), 2.25 (td, *J* = 12.4, 3.7 Hz,

1H), 2.04 (dd, *J* = 12.7, 4.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.4, 138.0, 137.8, 128.3, 128.2, 128.2, 127.9, 127.7, 127.6, 127.6, 127.5, 127.3, 97.0, 74.8, 74.2, 73.4, 72.9, 70.4, 70.0, 69.5, 68.8, 31.1; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14k]

Cyclopropylmethyl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (8): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with cyclopropylmethanol (23 µL 21 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 3 h, purified by silica gel column chromatography to obtain glycoside **8** as a colorless semi solid (93 mg, 0.192 mmol, 80% yield, α/β; 93:07). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (ddd, *J* = 25.3, 14.3, 9.1 Hz, 15H), 5.05 (d, *J* = 2.9 Hz, 1H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.68-4.52 (m, 4H), 4.51-4.39 (m, 2H), 3.95 (dt, *J* = 16.4, 4.4 Hz, 2H), 3.64-3.51 (m, 2H), 3.40 (dd, *J* = 10.7, 7.0 Hz, 1H), 3.27 (dd, *J* = 10.6, 7.0 Hz, 1H), 2.24 (td, *J* = 12.3, 3.7 Hz, 1H), 2.03 (dd, *J* = 12.6, 4.1 Hz, 1H), 1.09-0.98 (m, 1H), 0.55-0.44 (m, 2H), 0.18 (ddd, *J* = 13.2, 9.8, 5.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.5, 138.0, 128.3, 128.3, 128.2, 128.1, 127.7, 127.6, 127.4, 127.2, 97.2, 74.9, 74.2, 73.4, 72.8, 71.9, 70.4, 69.7, 69.6, 31.2, 10.3, 3.3, 2.7; HRMS (ESI) m/z $[M + Na]^+$ calculated for $[C_{31}H_{36}O_5Na]^+$: 511.2455; found 511.2453.

Cyclohexylmethyl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (9): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with cyclohexylmethanol (35 µL, 33 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 9 h, purified by silica gel column chromatography to obtain glycoside **9** as a pale yellow oil (93 mg, 0.175 mmol, 72% yield, α/β; 96:04). Rf (10% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.24 (m, 15H), 4.95-4.90 (m, 2H), 4.66-4.55 (m, 4H), 4.54-4.40 (m, 2H), 3.96-3.87 (m, 2H), 3.58 (qd, *J* = 9.4, 4.9 Hz, 2H), 3.41 (dd, *J* = 9.4, 7.2 Hz, 1H), 3.16 (dd, *J* = 9.4, 6.1 Hz, 1H), 2.26-2.17 (m, 1H), 1.99 (dd, *J* = 13.3, 3.5 Hz, 1H), 1.77-1.62 (m, 4H), 1.60-1.50 (m, 1H), 1.17 (dd, *J* = 22.9, 13.3 Hz, 3H), 0.89 (tdd, *J* = 13.4, 11.2, 5.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 138.5, 138.1, 128.3, 128.3, 128.2, 128.2, 127.7, 127.6, 127.5, 127.3, 97.8, 74.9, 74.2, 73.4, 73.0, 70.4, 69.7, 69.6, 37.8, 31.2, 30.1, 29.9, 26.6, 25.8, 25.7; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[16b]

***Pthalimido-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (10)*:** Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with N-Hydroxyphthalimide (47 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 12 h, purified by silica gel column chromatography to obtain glycoside **10** as a pale yellow semi solid (120 mg, 0.207 mmol, 86% yield, α/β; 94:06). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 3.2 Hz, 2H), 7.71 (d, *J* = 2.8 Hz, 2H), 7.38-7.25 (m, 15H), 5.59 (s, 1H), 4.94 (d, *J* = 11.4 Hz, 1H), 4.80 (t, *J* = 6.4 Hz, 1H), 4.64 (d, *J* = 5.7 Hz, 4H), 4.51 (dd, *J* = 26.5, 11.9 Hz, 2H), 4.10 (d, *J* = 8.6 Hz, 1H), 3.69-3.60 (m, 1H), 3.59-3.50 (m, 1H), 2.41 (d, *J* = 6.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 138.7, 138.3, 138.2, 134.3, 129.0, 128.4, 128.3, 128.2, 128.1, 127.6, 127.5, 127.4, 127.3, 123.5, 103.9, 74.5, 73.6, 73.2, 72.6, 71.7, 70.5, 68.7, 28.8; HRMS (ESI) m/z $[M + NH_4]^+$ calculated for $[C_{35}H_{37}O_7N_2]^+$: 597.2595; found 597.2594.

Pthalimido-3,4-di-O-benzyl-6-O-triisopropylsilyl-2-deoxy-α-D-lyxo-hexapyranoside (11): Glycosylation of 6-OTIPS-2,3-di-*O*-acetyl-D-galactal (100 mg, 0.207 mmol, 1.0 equiv.) with N-Hydroxyphthalimide (40 mg, 0.248 mmol, 1.2 equiv.) at 50 °C for 10 min., purified by silica gel column chromatography to obtain glycoside **11** as a white semi solid (112 mg, 0.173 mmol, 84% yield, α-only). Rf (10% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dt, *J* = 7.6, 3.9 Hz, 2H), 7.75-7.70 (m, 2H), 7.37 (dd, *J* = 9.0, 6.2 Hz, 6H), 7.34-7.22 (m, 4H), 5.60 (s, 1H), 4.96 (d, *J* = 11.3 Hz, 1H), 4.71 (d, *J* = 11.3 Hz, 1H), 4.69-4.61 (m, 2H), 4.60-4.55 (m, 1H), 4.18-4.09 (m, 2H), 3.81 (t, *J* = 8.8 Hz, 1H), 3.72 (dd, *J* = 9.3, 5.8 Hz, 1H), 2.40 (dd, *J* = 9.7, 3.1 Hz, 2H), 1.15-1.01 (m, 21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 139.0, 138.3, 134.3, 129.0, 128.4, 128.2, 128.1, 127.6, 127.4, 127.3, 123.4, 103.7, 74.7, 73.8, 73.6, 72.6, 70.5, 61.6, 28.8, 18.0, 17.9, 11.9, 1.0; HRMS (ESI) m/z $[M + H]^+$ calculated for $[C_{37}H_{48}NO_7Si]^+$: 646.3195; found 646.3194.

9-Fluorenylmethyl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (12): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with 9-Flourenemethanol (9-FM) (56 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 7 h, purified by silica gel column chromatography to obtain glycoside **12** as a pale yellow semi solid (114 mg, 0.187 mmol, 78% yield, α/β; 96:04). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.13 (m, 23H), 5.00 (d, *J* = 3.0 Hz, 1H), 4.86 (d, *J* = 11.6 Hz, 1H), 4.54 (ddd, *J* = 19.2, 15.4, 6.9 Hz, 4H), 4.39 (ddd, *J* = 23.3, 12.9, 7.2 Hz, 4H), 3.94-3.85 (m, 3H), 3.56-3.46 (m, 2H), 2.18 (td, *J* = 12.4, 3.7 Hz, 1H), 1.97 (dd, *J* = 12.6, 4.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.4, 138.0, 137.8, 128.3, 128.2, 128.2, 127.9, 127.7, 127.6, 127.6, 127.5, 127.3, 97.0, 74.8, 74.2, 73.4, 72.9, 70.4, 70.0, 69.5, 68.9, 31.1; HRMS (ESI) m/z $[M + H]^+$ calculated for $[C_{41}H_{41}O_5]^+$: 613.2949; found 613.2942.

Cholesteryl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (13): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with Cholesterol (111 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 5 min., purified by silica gel column chromatography to obtain glycoside **13** as a white solid (158 mg, 0.196 mmol, 82% yield, α/β; 94:06). Rf (10% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.25 (m, 15H), 5.26 (d, *J* = 4.4 Hz, 1H), 5.14 (d, *J* = 3.1 Hz, 1H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.67-4.55 (m, 3H), 4.47 (dd, *J* = 30.7, 11.7 Hz, 2H), 4.02-3.96 (m, 1H), 3.94 (d, *J* = 2.4 Hz, 1H), 3.65-3.54 (m, 2H), 3.50-3.40 (m, 1H), 2.28 (d, *J* = 8.0 Hz, 2H), 2.22 (dd, *J* = 11.6, 3.6 Hz, 1H), 2.05-1.78 (m, 6H), 1.60 (s, 3H), 1.55-1.29 (m, 14H), 1.10 (ddd, *J* = 23.4, 16.6, 6.4 Hz, 5H), 0.99 (s, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.86 (dd, *J* = 6.6, 1.8 Hz, 6H), 0.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 138.9, 138.6, 138.1, 128.4, 128.4, 128.2, 127.7, 127.6, 127.5, 127.3, 121.6, 95.6, 76.1, 75.0, 74.3, 73.4, 73.1, 70.5, 69.8, 69.6, 56.7, 56.1, 50.1, 42.3, 40.0, 39.7, 39.5, 37.1, 36.7, 36.2, 35.8, 31.9, 31.8, 31.7, 28.2, 28.0, 27.8, 24.3, 23.8, 22.8, 22.6, 21.0, 19.4, 18.7, 11.8; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14k]

O-(3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-N-(benzyloxycarbonyl)-L-serinemethyl ester (14): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with Cbz-Ser-OMe (63 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 15 min., purified by silica gel column chromatography to obtain glycoside **14** as a pale yellow semi solid (134 mg, 0.201 mmol, 84% yield, α-only). Rf (30% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.24 (m, 20H), 5.84 (d, *J* = 8.8 Hz, 1H), 5.14-5.04 (m, 2H), 4.91 (dd, *J* = 10.8, 7.4 Hz, 2H), 4.58 (dd, *J* = 11.3, 3.5 Hz, 3H), 4.52 (dd, *J* = 9.2, 4.1 Hz, 1H), 4.42 (dd, *J* = 40.8, 12.0 Hz, 2H), 3.96 (dd, *J* = 10.7, 3.5 Hz, 1H), 3.90-3.79 (m, 4H), 3.73 (s, 3H), 3.58-3.48 (m, 2H), 2.19 (td, *J* = 12.4, 3.7 Hz, 1H), 1.92 (dd, *J* = 12.7, 4.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 170.4, 170.3, 155.9, 136.1, 129.8, 128.5, 128.2, 128.1, 125.4, 94.6, 69.2, 67.2, 67.1, 62.7, 62.5, 54.4, 52.6, 20.8, 20.6; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[7c]

O-(3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-N-(Fluorenylmethyloxycarbonyl)-L-threoninemethyl ester (15): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with Fmoc-Thr-OMe(106 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 3 h, purified by silica gel column chromatography to obtain glycoside **15** as a colorless viscous oil (142mg, 0.184 mmol, 77% yield, α/β; 92.08). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.4 Hz, 2H), 7.63 (dd, *J* = 6.8, 5.0 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 3H), 7.36-7.29 (m, 16H), 5.43 (d, *J* = 9.7 Hz, 1H), 4.93 (dd, *J* = 7.4, 4.1 Hz, 2H), 4.65-4.58 (m, 4H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.45-4.40 (m, 3H), 4.38-4.34 (m, 1H), 4.27 (t, *J* = 7.0 Hz, 1H), 3.94 (d, *J* = 6.7 Hz, 2H), 3.86 (ddd, *J* = 12.2, 4.3, 2.1 Hz, 1H), 3.73 (s, 3H), 3.56 (dd, *J* = 6.3, 4.0 Hz, 2H), 2.22-2.12 (m, 1H), 1.86 (dd, *J* = 12.6, 4.4 Hz, 1H), 1.25 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 156.1, 143.8, 143.7, 141.3, 138.7, 138.2, 137.9, 128.4, 128.3, 128.2, 128.2, 127.7, 127.6, 127.6, 127.5, 127.4, 127.0, 125.0, 120.0, 99.3, 75.1, 74.2, 73.5, 72.7, 70.3, 69.4, 67.1, 58.7, 52.4, 47.1, 31.2, 24.6, 18.5;HRMS (ESI) m/z $[M + H]^+$ calculated for $[C_{47}H_{50}NO_9]^+$: 772.3480; found 772.3482.

O-(3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-N-(Fluorenylmethyloxycarbonyl)-L-Proline methyl ester (16): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with Fmoc-Hyp-OMe (105 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 15 min., purified by silica gel column chromatography to obtain glycoside **16** as a white semi solid (135 mg, 0.172 mmol, 72% yield, α/β; 90:10). Rf (40% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.5 Hz, 2H), 7.61-7.51 (m, 2H), 7.38 (t, *J* = 7.5 Hz, 3H), 7.35-7.27 (m, 16H), 5.04 (dd, *J* = 11.8, 3.1 Hz, 1H), 4.93 (dd, *J* = 11.6, 3.3 Hz, 1H), 4.63-4.56 (m, 3H), 4.52-4.44 (m, 2H), 4.44-4.38 (m, 3H), 4.38-4.29 (m, 2H), 4.26 (t, *J* = 7.0 Hz, 1H), 3.90 (s, 1H), 3.88-3.85 (m, 1H), 3.70 (s, 1H), 3.69-3.62 (m, 2H), 3.60 (s, 1H), 3.55 (dt, *J* = 12.2, 5.9 Hz, 3H), 2.45-2.34 (m, 1H), 2.31-2.21 (m, 1H), 2.12 (ddd, *J* = 13.0, 9.5, 6.2 Hz, 1H), 1.96 (dd, *J* = 10.9, 6.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 172.8, 154.7, 154.4, 144.0, 143.8, 143.7, 143.5, 141.2, 141.1, 141.0, 138.6, 138.5, 138.3, 138.2, 137.9, 137.8, 128.3, 128.3, 128.3, 128.1, 128.0, 127.6, 127.6, 127.5, 127.4, 127.4, 127.4, 127.4, 127.4, 127.2, 127.1, 127.0, 126.9, 126.9, 126.8, 124.9, 124.9, 124.8, 124.7, 119.9, 119.8, 97.2, 97.1, 74.5, 74.4, 74.2, 74.1, 73.6, 73.4, 73.3, 72.8, 72.8, 70.5, 70.4, 70.3, 69.7, 69.6, 67.5, 67.3, 58.1, 57.7, 52.3, 52.2, 51.8, 51.3, 47.1, 47.0, 37.5, 36.4, 31.1, 30.9; HRMS (ESI) m/z $[M + Na]^+$ calculated for $[C_{48}H_{49}NO_9Na]^+$: 806.3300; found 806.3302.

Methyl 2,3,4-tri-O-benzoyl-6-O-(3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-α-D-glucopyranoside (17): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with 6-Hydroxy-2,3,4-tri-*O*-benzoyl-α-methoxy glucopyranoside (146 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 15 min., purified by silica gel column chromatography to obtain glycoside **17** as a white solid (190 mg, 0.206 mmol, 86% yield, α/β; 91:09). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz,) δ 7.99 (d, *J* = 7.1 Hz, 2H), 7.92 (d, *J* = 7.1 Hz, 2H), 7.87 (d, *J* = 7.1 Hz, 2H), 7.54-7.16 (m, 24H), 6.12 (t, *J* = 9.9 Hz, 1H), 5.64 (t, *J* = 9.9 Hz, 1H), 5.28 (dd, *J* = 10.2, 3.6 Hz, 1H), 5.20 (d, *J* = 3.6 Hz, 1H), 5.00 (d, *J* = 3.0 Hz, 1H), 4.89 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 12.3 Hz, 4H), 4.27 (dd, *J* = 32.7, 12.0 Hz, 2H), 4.21-4.16 (m, 1H), 3.95 (ddd, *J* = 12.0, 4.4, 2.3 Hz, 1H), 3.87 (s, 1H), 3.83 (dd, *J* = 10.8, 5.5 Hz, 2H), 3.58 (dd, *J* = 11.1, 3.0 Hz, 1H), 3.50-3.42 (m, 1H), 3.39 (s, 3H), 2.18 (td, *J* = 12.4, 3.6 Hz, 1H), 1.98 (dd, *J* = 12.7, 4.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 165.3, 138.9, 138.6, 138.2, 133.3, 133.2, 133.0, 129.9, 129.8, 129.7, 129.3, 129.1, 129.0, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 127.5, 127.5, 127.4, 98.1, 96.9, 74.4, 74.2, 73.1, 72.9, 72.0, 70.7, 70.4, 69.8, 69.4, 69.3, 68.1, 65.7, 55.4, 30.9; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[7c]

Methyl 2,3,4-tri-O-benzyl-6-O-(3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-α-D-glucopyranoside (18): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with 6-Hydroxy-2,3,4-tri-*O*-benzyl-α-methoxy glucopyranoside (133 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 20 min., purified by silica gel column chromatography to obtain glycoside **18** as a colorless oil (165mg, 0.187 mmol, 78% yield, α/β; 96:04). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.21 (m, 30H), 5.02 (d, *J* = 2.8 Hz, 1H), 4.98 (d, *J* = 10.7 Hz, 1H), 4.91 (d, *J* = 11.6 Hz, 1H), 4.84 (d, *J* = 10.9 Hz, 1H), 4.79 (dd, *J* = 11.6, 2.9 Hz, 2H), 4.68 (d, *J* = 12.2 Hz, 1H), 4.59 (dd, *J* = 7.6, 4.0 Hz, 2H), 4.57-4.54 (m, 2H), 4.52 (d, *J* = 10.9 Hz, 1H), 4.37 (dd, *J* = 29.9, 11.8 Hz, 2H), 3.98 (t, *J* = 9.2 Hz, 1H), 3.88 (d, *J* = 6.2 Hz, 3H), 3.81 (dd, *J* = 11.4, 4.6 Hz, 1H), 3.71 (dd, *J* = 9.4, 3.8 Hz, 1H), 3.59 (dd, *J* = 15.4, 9.1 Hz, 1H), 3.54-3.43 (m, 4H), 3.31 (s, 3H), 2.20 (td, *J* = 12.5, 3.5 Hz, 1H), 2.01 (dd, *J* = 12.6, 4.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.7, 138.3, 138.2, 138.1, 138.0, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, 127.5, 127.4, 98.3, 97.8, 82.1, 79.9, 77.8, 75.8, 75.0, 74.3, 74.2, 73.3, 72.8, 70.2, 70.0, 69.8, 69.3, 66.0, 55.0, 31.0 the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[7c,14k]

Methyl 2,3,4-tri-O-benzyl-6-O-(6-O-Acetyl-3,4-di-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-α-D-glucopyranoside (19): Glycosylation of 6-OAc-3,4-di-*O*-benzyl-D-galactal (100 mg, 0.271 mmol, 1.0 equiv.) 6-Hydroxy-2,3,4-tri-*O*-benzyl-α-methoxy glucopyranoside (151 mg, 0.326 mmol, 1.2 equiv.) at 50 °C for 15 h, purified by silica gel column chromatography to

obtain glycoside **19** as a white solid (212 mg, 0.254 mmol, 94% yield, α-only). Mp: 86-87 ^{o}C; Rf (30% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 - 7.19 (m, 25H), 5.03 (d, J = 2.5 Hz, 1H), 4.96 (dd, J = 21.4, 11.2 Hz, 2H), 4.87 (d, J = 11.0 Hz, 1H), 4.79 (d, J = 11.3 Hz, 2H), 4.69 (d, J = 12.2 Hz, 1H), 4.64 (d, J = 4.6 Hz, 1H), 4.62-4.55 (m, 3H), 4.48 (d, J = 11.1 Hz, 1H), 4.08 (dd, J = 11.2, 7.2 Hz, 1H), 4.04-3.96 (m, 2H), 3.88-3.81 (m, 1H), 3.80-3.70 (m, 4H), 3.60 (d, J = 10.4 Hz, 1H), 3.51 (dd, J = 9.6, 3.5 Hz, 1H), 3.43 (t, J = 9.3 Hz, 1H), 3.31 (s, 3H), 2.20 (td, J = 12.4, 3.4 Hz, 1H), 2.10-1.95 (m, 1H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 138.6, 138.3, 138.1, 138.0, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 127.6, 127.4, 127.3, 98.0, 97.7, 82.0, 79.9, 77.9, 75.8, 74.9, 74.1, 73.9, 73.2, 72.4, 70.2, 69.6, 69.0, 65.9, 64.0, 54.9, 30.6, 20.7; HRMS (ESI) m/z $[M + H]^+$ calculated for $[C_{50}H_{57}O_{11}]^+$: 833.3895; found 833.3894.

Methyl 2,3,6-tri-O-benzyl-4-O-(3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-α-D-glucopyranoside (20): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with 4-Hydroxy-2,3,6-tri-*O*-benzyl-α-methoxy glucopyranoside (133 mg, 0.288 mmol, 1.2 equiv.) at 50 ^{o}C for 15 min., purified by silica gel column chromatography to obtain glycoside **20** as a colorless oil (175 mg, 0.199 mmol, 83% yield, α-only). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.13 (m, 30H), 5.40 (d, J = 3.2 Hz, 1H), 4.92 (d, J = 10.9 Hz, 1H), 4.80 (d, J = 11.7 Hz, 1H), 4.66 (d, J = 12.1 Hz, 1H), 4.60-4.53 (m, 2H), 4.51 (dd, J = 7.8, 3.9 Hz, 3H), 4.45 (dd, J = 11.6, 9.7 Hz, 3H), 4.34-4.20 (m, 3H), 3.80 (ddd, J = 20.0, 19.0, 9.3 Hz, 4H), 3.66-3.50 (m, 3H), 3.41 (ddd, J = 10.5, 7.8, 3.7 Hz, 3H), 3.31 (s, 3H), 2.06 (td, J = 12.5, 3.9 Hz, 1H), 1.80 (dd, J = 12.4, 4.2 Hz, 1H);^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.7, 138.4, 138.3, 138.0, 137.9, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 127.3, 99.6, 97.7, 93.3, 82.0, 79.9, 75.8, 75.5, 74.4, 74.3, 74.2, 73.5, 73.4, 73.2, 73.0, 72.9, 72.6, 70.6, 70.4, 70.3, 70.3, 69.8, 69.5, 69.2, 55.2, 31.9, 31.6, 30.8; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[7c]

Methyl 2,3,4-tri-O-benzoyl-6-O-(3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-α-D-mannopyranoside (21): Glycosylation of 6-OAc-3,4-di-*O*-benzyl-D-galactal (100 mg, 0.271 mmol, 1.0 equiv.) with 6-hydroxy-2,3,4-tri-*O*-benzoyl-α-methoxy mannopyranoside (165 mg, 0.326 mmol, 1.2 equiv.) at 50 ^{o}C for 7 h, purified by silica gel column chromatography to obtain glycoside **21** as a white solid (213 mg, 0.243 mmol, 90% yield; α-only). Mp: 59-61 °C; Rf (30% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.1 Hz, 2H), 7.94 (d, J = 7.3 Hz, 2H), 7.83 (d, J = 7.3 Hz, 2H), 7.51 (t, J = 7.4 Hz, 2H), 7.43 (t, J = 8.0 Hz, 3H), 7.40-7.34 (m, 6H), 7.34-7.23 (m, 8H), 6.01 (t, J = 10.0 Hz, 1H), 5.85 (dd, J = 10.1, 3.2 Hz, 1H), 5.66 (dd, J = 3.0, 1.8 Hz, 1H), 5.07 (d, J = 2.8 Hz, 1H), 4.98-4.89 (m, 2H), 4.61 (d, J = 11.6 Hz, 1H), 4.59-4.51 (m, 2H), 4.22 (d, J = 9.9 Hz, 1H), 4.02 (dt, J = 13.7, 6.9 Hz, 2H), 3.93 (dd, J = 11.2, 4.6 Hz, 1H), 3.86 (dt, J = 12.2, 6.0 Hz, 2H), 3.80 (s, 1H), 3.64 (dd, J = 11.0, 2.6 Hz, 1H), 3.47 (s, 3H), 2.23 (td, J = 12.4, 3.5 Hz, 1H), 2.05 (dd, J = 12.5, 4.4 Hz, 1H), 1.69 (s, 3H); ^{13}C NMR (101 MHz,$CDCl_3$) δ 170.4, 165.5, 165.4, 165.3, 138.3, 138.3, 133.5, 133.4, 133.1, 129.7, 129.6, 129.6, 129.3, 129.1, 129.1, 128.5, 128.4, 128.3, 128.2, 127.6, 127.5, 127.2, 98.5, 97.8, 74.8, 73.9, 72.5, 70.4, 70.4, 70.2, 69.2, 68.9, 67.1, 65.7, 64.3, 55.3, 30.7, 20.4; HRMS (ESI) m/z $[M + NH_4]^+$ calculated for $[C_{50}H_{54}NO_{14}]^+$: 892.3539; found 892.3540.

Methyl 2,3,4-tri-O-benzoyl-6-O-(6-O-triisopropylsilyl-3,4-di-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-α-D-mannopyranoside (22): Glycosylation of 6-OTIPS-3, 4-di-*O*-benzyl-D-galatal (100 mg, 0.207 mmol, 1.0 equiv.) with 6-hydroxy-2,3,4-tri-*O*-benzoyl-α-methoxy mannopyranoside (126 mg, 0.248 mmol, 1.2 equiv.) at 50 ^{o}C for 2 h, purified by silica gel column chromatography to obtain glycoside **22** as a white semi solid (182 mg, 0.184 mmol, 89% yield, α-only). Rf (10% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz,$CDCl_3$) δ 8.09 (d, J = 7.3 Hz, 2H), 7.96 (d, J = 7.4 Hz, 2H), 7.82 (d, J = 7.4 Hz, 2H), 7.55 (d, J = 7.2 Hz, 1H), 7.52-7.41 (m, 3H), 7.40-7.24 (m, 15H), 5.87 (dd, J = 13.2, 6.4 Hz, 2H), 5.67-5.62 (m, 1H), 5.02 (d, J = 2.8 Hz, 1H), 4.91 (dd, J = 6.4, 5.1 Hz, 2H), 4.65 (d, J = 11.5 Hz, 1H), 4.46 (s, 2H), 4.23-4.11 (m, 1H), 3.94-3.83 (m, 3H), 3.71 (dd, J = 13.2, 5.2 Hz, 3H), 3.64 (d, J = 3.2 Hz, 1H), 3.43 (s, 3H), 2.22-2.13 (m, 1H), 1.93 (d, J = 4.3 Hz, 1H), 1.60 (s, 3H), 0.96 (d, J = 3.5 Hz, 18H); ^{13}C NMR (101 MHz,$CDCl_3$) δ 165.4, 165.4, 165.4, 138.9, 138.5, 133.4, 133.2, 133.0, 129.8, 129.7, 129.6, 129.3, 129.2, 129.1, 128.5, 128.3, 128.3, 128.2, 128.1, 127.4, 127.3, 127.2, 98.3, 97.7, 74.5, 74.3, 72.8, 71.7, 70.4, 70.1, 70.1, 69.3, 67.6, 66.2, 62.5, 55.1, 30.9, 17.9, 17.9, 11.7; HRMS (ESI) m/z $[M + NH_4]^+$ calculated for $[C_{57}H_{72}NO_{13}Si]^+$: 1006.4767; found 1006.4766.

1,2,3,4-di-O-isopropylidene-6-O-(3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-α-D-galactopyranoside (23): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with 6-hydroxy-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranoside (75 mg, 0.288 mmol, 1.2 equiv.) at 50 ^{o}C for 15 min., purified by silica gel column chromatography to obtain glycoside **23** as a white solid (138 mg, 0.240 mmol, 85% yield, α/β; 96:04). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.22 (m, 15H), 5.52 (d, J = 5.0 Hz, 1H), 5.03 (d, J = 2.9 Hz, 1H), 4.92 (d, J = 11.6 Hz, 1H), 4.65-4.54 (m, 4H), 4.45 (dd, J = 28.0, 11.8 Hz, 2H), 4.30 (dd, J = 5.0, 2.4 Hz, 1H), 4.21 (dd, J = 7.9, 1.5 Hz, 1H), 3.95 (d, J = 6.5 Hz, 4H), 3.75 (dd, J = 10.7, 6.8 Hz, 1H), 3.70-3.57 (m, 2H), 3.54 (dd, J = 9.1, 5.7 Hz, 1H), 2.22 (td, J = 12.3, 3.3 Hz, 1H), 2.03 (dd, J = 12.6, 4.2 Hz, 1H), 1.51 (s, 3H), 1.42 (s, 3H), 1.32 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.5, 138.0, 128.3, 128.2, 128.1, 127.8, 127.6, 127.4, 127.3, 109.2, 108.5, 97.5, 96.3, 74.6, 74.3, 73.3, 72.8, 71.0, 70.6, 70.5, 70.3, 69.7, 69.1, 65.8, 65.5, 31.0, 26.1, 25.9, 24.9, 24.5; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[7c,14k]

5-O-(3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)(1→5')-2'-3'-O-isopropylidene uridine (24): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with 2,3-*O*-isopropylidene uridine (82 mg, 0.288 mmol, 1.2 equiv.) at 50 ^{o}C for 3 h, purified by silica gel column chromatography to obtain glycoside **24** as a colorless semi solid (133 mg, 0.189 mmol, 79% yield, α/β ; 90:10). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.39-7.25 (m, 15H), 5.81 (d, J = 2.6 Hz, 1H), 5.65 (dd, J =

8.1, 1.9 Hz, 1H), 4.99 (d, *J* = 3.1 Hz, 1H), 4.92 (d, *J* = 11.6 Hz, 1H), 4.64-4.59 (m, 2H), 4.58-4.52 (m, 3H), 4.52-4.39 (m, 3H), 4.37 (dd, *J* = 6.6, 3.2 Hz, 1H), 3.91 (s, 1H,), 3.83-3.76 (m, 3H), 3.61 (dd, *J* = 11.2, 3.0 Hz, 1H), 3.56 (dd, *J* = 6.3, 1.8 Hz, 2H), 2.26 (td, *J* = 12.6, 3.6 Hz, 1H), 1.83 (dd, *J* = 12.8, 4.4 Hz, 1H), 1.57 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 149.9, 140.7, 138.5, 137.9, 137.7, 128.4, 128.3, 128.2, 128.2, 127.8, 127.7, 127.7, 127.7, 127.5, 127.5, 127.4, 114.2, 101.9, 97.9, 92.9, 85.2, 84.9, 80.8, 74.2, 73.6, 73.5, 72.2, 70.4, 70.1, 69.4, 67.1, 30.8, 29.6, 29.6, 27.1, 25.2; HRMS (ESI) m/z $[M + Na]^+$ calculated for $[C_{39}H_{44}N_2O_{10}Na]^+$: 723.2888; found 723.2887.

5-O-(6-O-triisopropylsilyl-3,4-di-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)(1→5')-2'-3'-O-isopropylidene uridine (25): Glycosylation of 6-OTIPS-3, 4-di-*O*-benzyl-D-galatal(100 mg, 0.207 mmol, 1.0 equiv.) with 2,3-*O*-isopropylidene uridine (70 mg, 0.248 mmol, 1.2 equiv.) at 50 ^{o}C for 4 h, purified by silica gel column chromatography to obtain glycoside **25** as a white semi solid (119 mg, 0.155 mmol, 75% yield, α-only). Rf (40% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (d, *J* = 23.0 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.31 (ddd, *J* = 20.7, 11.6, 8.1 Hz, 10H), 5.86 (d, *J* = 2.6 Hz, 1H), 5.68 (d, *J* = 8.1 Hz, 1H), 4.98 (d, *J* = 3.0 Hz, 1H), 4.94 (d, *J* = 11.6 Hz, 1H), 4.68 (d, *J* = 11.6 Hz, 1H), 4.61 (dd, *J* = 6.1, 2.7 Hz, 1H), 4.55 (d, *J* = 6.3 Hz, 3H), 4.38 (d, *J* = 2.7 Hz, 1H), 3.94 (s, 1H), 3.76 (ddd, *J* = 20.1, 10.8, 4.2 Hz, 3H), 3.60 (dd, *J* = 7.4, 4.2 Hz, 2H), 2.27 (td, *J* = 12.6, 3.6 Hz, 1H), 1.83 (dd, *J* = 12.1, 4.0 Hz, 2H), 1.58 (s, 3H), 1.33 (s, 3H), 1.05 (dd, *J* = 10.1, 4.6 Hz, 21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 149.9, 140.4, 138.6, 137.9, 128.5, 128.2, 127.7, 127.5, 127.5, 114.1, 101.9, 97.8, 92.8, 85.1, 80.9, 74.2, 73.7, 72.7, 72.1, 70.1, 66.8, 62.9, 30.9, 27.2, 25.3, 17.9, 11.8; HRMS (ESI) m/z $[M + H]^+$ calculated for $[C_{41}H_{59}N_2O_{10}Si]^+$: 767.3933; found 767.3932.

Methyl 2,3,4-tri-O-benzyl-6-O-(3,4-di-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-α-D-glucopyranoside (26): A preformed solution of Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(6-*O*-acetyl-2-deoxy-3,4-di-*O*-benzyl-α-D-lyxohexapyranosyl)-α-D-glucopyranoside **19** (100 mg, 0.120 mmol, 1.0 equiv.) in MeOH (5 mL) was treated with NaOMe (8 mg, 0.144 mmol, 0.1 equiv.) at room temperature under nitrogen atmosphere. The reaction was stirred until the completion of starting material, typically for 4 h (adjudged by TLC). The reaction mixture was diluted with DCM (10 mL), quenched with saturated $NaHCO_3$ (5 mL) and extracted with DCM (3 × 30 mL). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, concentrated in vacuo and purified by silica gel column chromatography using hexane and EtOAc as eluent to afford the compound **26** as colorless oil (80 mg, 0.102 mmol, 85% yield). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.22 (m, 25H), 5.05 (d, *J* = 2.8 Hz, 1H), 5.03-4.95 (m, 2), 4.94-4.86 (m, 2H), 4.80 (d, *J* = 11.3 Hz, 2H), 4.69 (d, *J* = 12.1 Hz, 1H), 4.67-4.55 (m, 4H), 4.47 (d, *J* = 11.3 Hz, 1H), 3.99 (t, *J* = 9.2 Hz, 1H), 3.88-3.81 (m, 1H), 3.80-3.71 (m, 3H), 3.63 (dd, *J* = 11.1, 6.2 Hz, 1H), 3.60-3.50 (m, 3H), 3.43 (dt, *J* = 14.0, 7.0 Hz, 2H), 3.32 (s, 3H), 2.20 (td, *J* = 12.4, 3.5 Hz, 1H), 2.04 (dd, *J* = 12.6, 4.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6, 138.3, 138.2, 138.0, 128.4, 128.4, 127.9, 127.8, 127.8, 127.6, 127.4, 127.3, 98.1, 97.8, 82.0, 79.9, 77.8, 75.7, 74.7, 74.2, 73.9, 73.2, 73.1, 70.8, 70.2, 69.6, 65.9, 62.8, 55.0, 30.6; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14m]

Methyl 2,3,4-tri-O-benzyl (6-O-acetyl-3,4-di-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-(1→6)-(3,4-di-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-(1→6)-α-D-glucopyranoside (27): Glycosylation of 6-OAc-3,4-di-*O*-benzyl-D-galactal (100 mg, 0.271 mmol, 1.0 equiv.) was treated with Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(3,4-di-*O*-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-α-D-glucopyranoside **26** (271 mg, 0.326 mmol, 1.2 equiv.) at 50 ^{o}C for 6 h, purified by silica gel column chromatography to obtain glycoside **27** as a white semi solid (213 mg, 0.184 mmol, 68% yield, α-only). Rf (30% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.33 (dt, *J* = 9.1, 5.0 Hz, 35H), 5.00 (d, *J* = 2.7 Hz, 1H), 4.98 (d, *J* = 10.8 Hz, 1H), 4.93 (d, *J* = 4.1 Hz, 1H), 4.90 (d, *J* = 4.1 Hz, 1H), 4.83 (d, *J* = 11.0 Hz, 1H), 4.79 (d, *J* = 6.7 Hz, 1H), 4.77 (d, *J* = 5.3 Hz, 1H), 4.67 (dd, *J* = 7.2, 4.9 Hz, 2H), 4.60 (dt, *J* = 6.4, 3.0 Hz, 6H), 4.48 (s, 2H), 4.06 (dd, *J* = 6.2, 3.5 Hz, 1H), 3.97 (t, *J* = 9.3 Hz, 1H), 3.86 (d, *J* = 9.4 Hz, 1H), 3.76-3.66 (m, 7H), 3.55-3.49 (m, 3H), 3.32 (d, *J* = 5.5 Hz, 3H), 2.15 (dd, *J* = 12.3, 3.5 Hz, 1H), 2.06 (dd, *J* = 20.8, 8.5 Hz, 4H), 1.93 (t, *J* = 3.3 Hz, 1H), 1.90 (d, *J* = 2.9 Hz, 3H), 1.77 (d, *J* = 3.9 Hz, 1H); ^{13}C NMR (101 MHz,$CDCl_3$) δ 170.6, 138.6, 138.6, 138.4, 138.4, 138.3, 138.3, 138.1, 113.9, 98.2, 97.9, 97.3, 82.0, 79.9, 77.7, 75.8, 74.8, 74.7, 74.4, 74.0, 73.9, 73.3, 72.7, 72.4, 70.4, 70.3, 69.8, 69.7, 68.7, 66.4, 65.8, 63.9, 55.1, 30.8, 30.7, 20.7;HRMS (ESI) m/z $[M + H]^+$ calculated for $[C_{70}H_{79}O_{15}]^+$: 1159.5413; found 1159.5413.

Methyl 2,3,4-tri-O-benzyl (3,4-di-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-(1→6)-(3,4-di-O-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-(1→6)-α-D-glucopyranoside (28): A preformed solution of Methyl (6-*O*-acetyl-3,4-di-*O*-benzyl-2deoxy-α-D-lyxo-hexapyranosyl)-(1→*6)*-(3,4-di-*O*-benzyl-2-deoxy-α-D-lyxo-hexapyranosyl)-(1→*6)*-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **27** (100 mg, 0.086 mmol, 1.0 equiv.) in MeOH (5 mL) was treated with NaOMe (5 mg, 0.103 mmol, 0.1 equiv.) at room temperature under nitrogen atmosphere for 4 h, purified by silica gel column chromatography to obtain glycoside **28** as a white solid (67 mg, 0.060 mmol, 70% yield). Rf (40% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 35H), 5.00 (d, *J* = 2.5 Hz, 1H), 4.97 (d, *J* = 10.7 Hz, 1H), 4.93 (d, *J* = 2.4 Hz, 1H), 4.91 (d, *J* = 2.2 Hz, 1H), 4.83 (d, *J* = 11.0 Hz, 1H), 4.79 (d, *J* = 8.7 Hz, 1H), 4.76 (d, *J* = 7.2 Hz, 1H), 4.69-4.63 (m, 3H), 4.63-4.57 (m, 6H), 4.52 (d, *J* = 12.4 Hz, 2H), 3.97 (t, *J*= 9.2 Hz, 1H), 3.86 (d, *J* = 9.7 Hz, 1H), 3.72 (dd, *J* = 18.8, 7.6 Hz, 6H), 3.58-3.49 (m, 5H), 3.43 (dd, *J* = 11.4, 7.0 Hz, 2H), 3.38-3.34 (m, 1H), 3.31 (s, 3H), 2.22-2.15 (m, 1H), 2.08 (dd, *J* = 12.6, 3.6 Hz, 1H), 2.02 (dd, *J* = 12.2, 3.9 Hz, 1H), 1.76 (dd, *J* = 12.6, 4.1 Hz, 1H); ^{13}C NMR (101 MHz,$CDCl_3$) δ 138.7, 138.4, 138.2, 128.6, 128.5, 128.5, 128.4, 128.1, 128.0, 128.0, 127.8, 127.7, 127.6, 127.5, 127.3, 98.5, 98.0, 82.2, 80.0, 78.0, 75.9, 74.9, 74.5, 74.1, 74.0, 73.4, 73.1, 72.5, 71.0, 70.5, 70.4, 69.8, 69.6, 66.6, 66.3, 63.1, 55.2, 31.0; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14m]

Prop-2-enyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (29): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with Allyl alcohol (30 µL, 25 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 3 h, purified by silica gel column chromatography to obtain glycoside **29** as a pale yellow semi solid (67 mg, 0.249 mmol, 78% yield, *α:β*; 98:02). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 6.13 (dd, *J* = 10.0, 5.3 Hz, 1H), 6.05 (dd, *J* = 10.0, 2.9 Hz, 1H), 5.95 (ddd, *J* = 22.5, 11.0, 5.7 Hz, 1H), 5.31 (d, *J* = 17.1 Hz, 1H), 5.22 (d, *J* = 10.2 Hz, 1H), 5.13 (d, *J* = 2.7 Hz, 1H), 5.03 (dd, *J* = 5.3, 2.4 Hz, 1H), 4.40-4.35 (m, 1H), 4.30-4.22 (m, 3H), 4.09 (dd, *J* = 12.7, 6.4 Hz, 1H), 2.09 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 170.6, 170.3, 133.9, 130.5, 125.3, 117.7, 93.0, 68.9, 66.7, 62.8, 20.8, 20.7; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[16b,16f]

2'-Propyn-1'-yl-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (3): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with Propargyl alcohol (25 µL, 24 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 1 h, purified by silica gel column chromatography to obtain glycoside **30** as a yellow oil (75 mg, 0.278 mmol, 76% yield, *α:β*; 96:04). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 6.16 (dd, *J* = 10.0, 5.5 Hz, 1H), 6.05 (dd, *J* = 10.0, 2.9 Hz, 1H), 5.30 (d, *J* = 2.5 Hz, 1H), 5.04 (dd, *J* = 5.3, 2.2 Hz, 1H), 4.33 (t, *J* = 5.6 Hz, 3H), 4.24 (d, *J* = 6.1 Hz, 2H), 2.48 (d, *J* = 2.2 Hz, 1H), 2.09 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 170.5, 170.3, 130.0, 125.7, 92.0, 78.8, 74.8, 67.0, 62.6, 62.5, 54.5, 20.7, 20.7; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14k,16f]

Ethoxyethyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (31): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with Ethoxy ethanol (42 µL, 39 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 3 h, purified by silica gel column chromatography to obtain glycoside **31** as a light yellow semi solid (76 mg, 0.264 mmol, 72% yield, *α:β*; 94:06). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 6.04 (dd, *J* = 10.1, 4.9 Hz, 1H), 6.00 (dd, *J* = 10.0, 2.7 Hz, 1H), 5.06 (d, *J* = 2.6 Hz, 1H), 4.96 (dd, *J* = 4.9, 2.5 Hz, 1H), 4.34-4.28 (m, 1H), 4.20-4.10 (m, 2H), 3.83 (dt, *J* = 10.7, 4.3 Hz, 1H), 3.64 (dt, *J* = 10.7, 5.2 Hz, 1H), 3.57-3.53 (m, 1H), 3.46 (dd, *J* = 7.0 Hz, 1H), 2.01 (s, 3H), 2.00 (s, 3H), 1.14 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 170.5, 170.3, 130.5, 125.1, 94.0, 69.6, 67.4, 66.6, 66.5, 62.7, 62.7, 20.7, 20.7, 15.1; HRMS (ESI) m/z $[M + H]^+$ calculated for $[C_{14}H_{23}O_6]^+$: 303.1438; found 303.1437.

Benzyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (32): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with Benzyl alcohol (45 µL, 47 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 1 h, purified by silica gel column chromatography to obtain glycoside **32** as a light yellow viscous oil (101 mg, 0.315 mmol, 86% yield, *α:β*; 96:04). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.39-7.28 (m, 5H), 6.13 (dd, *J* = 10.1, 5.1 Hz, 1H), 6.05 (dd, *J* = 10.0, 2.9 Hz, 1H), 5.17 (d, *J* = 2.8 Hz, 1H), 5.04 (dd, *J* = 5.4, 2.5 Hz, 1H), 4.82 (d, *J* = 11.5 Hz, 1H), 4.59 (d, *J* = 11.5 Hz, 1H), 4.43 (ddd, *J* = 7.6, 5.3, 2.5 Hz, 1H), 4.30 - 4.18 (m, 2H), 2.09 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 170.6, 170.4, 137.3, 130.5, 128.5, 128.2, 127.9, 125.3, 92.8, 69.8, 66.9, 62.8, 20.8, 20.8; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14k,16b,16f]

Cyclopropylmethyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (33): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with cyclopropylmethanol (35 µL, 31 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 4 h, purified by silica gel column chromatography to obtain glycoside **33** as a pale yellow oil (77 mg, 0.271 mmol, 74% yield, *α:β*; 93:07). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 6.12 (dd, *J* = 10.3, 5.1 Hz, 1H), 6.06 (dd, *J* = 10.0, 2.8 Hz, 1H), 5.13 (d, *J* = 2.8 Hz, 1H), 5.03 (dd, *J* = 5.2, 2.5 Hz, 1H), 4.40 (td, *J* = 6.3, 2.5 Hz, 1H), 4.27-4.16 (m, 2H), 3.53 (dd, *J* = 10.3, 7.4 Hz, 1H), 3.44 (dd, *J* = 10.4, 6.9 Hz, 1H), 2.09 (s, 3H), 2.07 (s, 3H), 1.15-1.07 (m, 1H), 0.63-0.53 (m, 2H), 0.29 - 0.21 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 170.5, 170.3, 130.7, 125.1, 93.2, 73.0, 66.6, 62.9, 62.8, 20.8, 20.7, 10.4, 3.3, 2.9; HRMS (ESI) m/z $[M + Na]^+$ calculated for $[C_{14}H_{20}O_6Na]^+$: 307.1152; found 307.1154.

Cyclohexylmethyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (34): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with cyclohexylmethanol (54 µL, 50 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 1 h, purified by silica gel column chromatography to obtain glycoside **34** as a light yellow solid (84 mg, 0.256 mmol, 70% yield, *α:β*; 95:05). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 6.11 (dd, *J* = 10.1, 5.2 Hz, 1H), 6.04 (dd, *J* = 10.0, 2.9 Hz, 1H), 5.05-4.99 (m, 2H), 4.35 (ddd, *J* = 7.5, 5.1, 2.5 Hz, 1H), 4.28-4.18 (m, 2H), 3.60 (dd, *J* = 9.2, 7.0 Hz, 1H), 3.31 (dd, *J* = 9.2, 6.2 Hz, 1H), 2.09 (s, 6H), 1.81-1.65 (m, 5H), 1.60 (ddd, *J* = 14.4, 7.5, 3.7 Hz, 1H), 1.32-1.13 (m, 3H), 0.95 (dd, *J* = 23.8, 12.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 170.6, 170.4, 130.7, 125.0, 93.8, 74.1, 66.7, 62.9, 62.9, 37.9, 30.2, 30.0, 26.5, 25.8, 25.7, 20.8, 20.8; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[16b]

Pthalimido-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (35): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with N-Hydroxy phthalimide (71 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 20 min., purified by silica gel column chromatography to obtain glycoside **35** as a white solid (104 mg, 0.278 mmol, 75% yield, *α*-only). Mp: 147-149 °C; Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.5, 3.1 Hz, 2H), 6.33 (dd, *J* = 10.0, 4.9 Hz, 1H), 6.22 (dd, *J* = 10.1, 3.0 Hz, 1H), 5.64 (d, *J* = 2.9 Hz, 1H), 5.12 (dd, *J* = 5.5, 2.7 Hz, 1H), 4.87 (td, *J* = 6.4, 2.7 Hz, 1H), 4.28 (dd, *J* = 11.3, 6.1 Hz, 1H), 4.05 (dd, *J* = 11.3, 6.7 Hz, 1H), 2.02 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 170.6, 170.2, 163.5, 134.5, 128.9, 128.8, 126.1, 123.5, 98.4, 68.2, 61.9, 61.9, 20.8, 20.7; HRMS (ESI) m/z $[M + Na]^+$ calculated for $[C_{18}H_{17}NO_8Na]^+$: 398.0846; found 398.0845.

9-Fluorenylmethyl-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (36): Ferrier glycosylation of 3,4,6-tri-*O*-

acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with 9-Fluorenemethanol(9-FM) (86 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 25 min., purified by silica gel column chromatography to obtain glycoside **36** as a light yellow solid (141 mg, 0.344 mmol, 94% yield, $\alpha:\beta$; 96:04). Mp: 57-58 °C; Rf (30% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.79-7.74 (m, 2H), 7.61 (t, *J* = 7.9 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.32 (q, *J* = 7.8 Hz, 2H), 6.18 (dd, *J* = 10.1, 5.2 Hz, 1H), 6.12 (dd, *J* = 10.0, 2.7 Hz, 1H), 5.15 (d, *J* = 2.6 Hz, 1H), 5.06 (dd, *J* = 5.2, 2.4 Hz, 1H), 4.41-4.35 (m, 1H), 4.25-4.18 (m, 1H), 4.17-4.08 (m, 2H), 4.06 (t, *J* = 5.5 Hz, 1H), 3.76 (dd, *J* = 9.0, 7.7 Hz, 1H), 2.08 (s, 3H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 170.4, 144.7, 144.5, 144.3, 141.5, 141.2, 141.1, 130.5, 127.6, 127.5, 127.1, 127.0, 126.9, 125.3, 125.1, 125.1, 124.7, 120.1, 119.9, 94.3, 71.1, 67.1, 65.1, 62.9, 50.3, 47.8, 20.8, 20.5; HRMS (ESI) m/z [M + Na]$^+$ calculated for $[C_{24}H_{24}O_6Na]^+$: 431.1465; found 431.1464.

Cholesteryl-4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranoside (37): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with Cholesterol (170 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 2 h, purified by silica gel column chromatography to obtain glycoside **37** as a white solid (163 mg, 0.286 mmol, 78% yield, α-only). Mp: 109-111 °C; Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.11 (dd, *J* = 10.0, 5.3 Hz, 1H), 6.02 (dd, *J* = 10.0, 3.0 Hz, 1H), 5.36 (d, *J* = 5.1 Hz, 1H), 5.22 (d, *J* = 2.8 Hz, 1H), 5.02 (dd, *J* = 5.3, 2.5 Hz, 1H), 4.46-4.38 (m, 1H), 4.28-4.16 (m, 2H), 3.58 (ddd, *J* = 15.8, 11.2, 4.6 Hz, 1H), 2.42 (dd, *J* = 12.5, 4.2 Hz, 1H), 2.33 (t, *J* = 11.2 Hz, 1H), 2.08 (s, 3H), 2.07 (s, 3H), 1.93-1.77 (m, 3H), 1.70-1.37 (m, 10H), 1.40-1.28 (m, 4H), 1.22-1.02 (m, 9H), 1.00 (s, 3H), 0.91 (t, *J* = 6.3 Hz, 3H), 0.86 (dd, *J* = 6.6, 1.7 Hz, 6H), 0.68 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 170.4, 140.8, 131.1, 125.0, 121.8, 92.4, 77.9, 66.7, 63.0, 56.7, 56.1, 50.1, 42.3, 40.3, 39.7, 39.5, 37.1, 36.6, 36.2, 35.7, 31.9, 31.8, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.0, 20.8, 19.3, 18.7, 11.8; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14k]

O-(4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-N-(benzyloxycarbonyl)-L-serine methyl ester (38): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with Cbz-Ser-OMe (96 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 15 min., purified by silica gel column chromatography to obtain glycoside **38** as a light yellow semi solid (137 mg, 0.319 mmol, 87% yield, $\alpha:\beta$; 95:05). Rf (60% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.31 (m, 5H), 6.11 (dd, *J* = 10.0, 5.5 Hz, 1H), 5.94 (dd, *J* = 10.0, 3.0 Hz, 1H), 5.84 (d, *J* = 8.7 Hz, 1H), 5.17-5.09 (m, 2H), 5.02 (d, *J* = 2.8 Hz, 1H), 4.99 (dd, *J* = 5.5, 2.3 Hz, 1H), 4.57 (dt, *J* = 8.5, 3.0 Hz, 1H), 4.30-4.25 (m, 1H), 4.24-4.15 (m, 2H), 4.03 (ddd, *J* = 23.6, 10.5, 3.2 Hz, 2H), 3.77 (s, 3H), 2.08 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 170.4, 170.3, 155.9, 136.1, 129.8, 128.5, 128.2, 128.1, 125.4, 94.6, 69.2, 67.2, 67.1, 62.7, 62.5, 54.4, 52.6, 20.7, 20.6; HRMS (ESI) m/z [M + Na]$^+$ calculated for $[C_{22}H_{27}NO_{10}Na]^+$: 488.1527; found 488.1526.

O-(4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-N-(Fluorenylmethyloxycarbonyl)-L-Proline methyl ester (39): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with Fmoc-Hyp-OMe (161 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 5 min., purified by silica gel column chromatography to obtain glycoside **39** as a light yellow semi solid (174 mg, 0.300 mmol, 82% yield, α-only). Rf (60% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.5, 3.8 Hz, 2H), 7.62-7.52 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.30 (dd, *J* = 9.8, 4.9 Hz, 2H), 6.15 (td, *J* = 9.5, 5.6 Hz, 1H), 5.99 (dt, *J* = 10.1, 2.7 Hz, 1H), 5.15 (d, *J* = 2.8 Hz, 1H), 5.03 (dd, *J* = 5.5, 2.4 Hz, 1H), 4.54-4.43 (m, 3H), 4.43-4.37 (m, 1H), 4.34 (ddd, *J* = 7.4, 6.0, 2.3 Hz, 2H), 4.23 (d, *J* = 6.1 Hz, 2H), 3.79 (dd, *J* = 11.5, 5.2 Hz, 1H), 3.76 (s, 2H), 3.72 (t, *J* = 3.4 Hz, 1H), 3.65 (s, 1H), 2.55 (qd, *J* = 8.0, 3.9 Hz, 1H), 2.28-2.20 (m, 1H), 2.10 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 172.8, 170.6, 170.5, 170.2, 154.7, 154.4, 144.0, 143.9, 143.7, 143.5, 141.2, 130.1, 130.0, 127.6, 127.0, 125.4, 125.3, 125.0, 125.0, 124.9, 124.8, 119.9, 94.0, 93.7, 76.6, 75.2, 67.6, 67.5, 67.2, 67.1, 63.1, 63.0, 62.6, 62.6, 58.0, 57.6, 52.4, 52.3, 52.2, 51.8, 47.2, 47.1, 37.8, 36.7, 20.8, 20.6, 20.6; HRMS (ESI) m/z [M + H]$^+$ calculated for $[C_{31}H_{34}NO_{10}]^+$: 580.2177; found 580.2178.

Methyl 2,3,4-tri-O-benzyl-6-O-(4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)- α-D-glucopyranoside (4): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with 6-Hydroxy-2,3,4-tri-*O*-Benzyl-α-methoxy glucopyranoside (204 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 10 min., purified by silica gel column chromatography to obtain glycoside **40** as a pale yellow semi solid (203 mg, 0.300 mmol, 82% yield, α-only). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (m, 15H), 6.10 (dd, *J* = 10.1, 5.1 Hz, 1H), 6.04 (dd, *J* = 10.0, 2.8 Hz, 1H), 5.15 (d, *J* = 2.7 Hz, 1H), 4.99 (dd, *J* = 5.2, 2.5 Hz, 1H), 4.99-4.89 (m, 2H), 4.83-4.77 (m, 2H), 4.70-4.58 (m, 3H), 4.32-4.26 (m, 1H), 4.19 (dd, *J* = 11.3, 5.6 Hz, 1H), 4.11 (dd, *J* = 11.3, 7.3 Hz, 1H), 3.98 (dt, *J* = 10.9, 6.8 Hz, 2H), 3.80-3.70 (m, 2H), 3.59-3.49 (m, 2H), 3.37 (s, 3H), 2.07 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 170.4, 138.6, 138.2, 138.1, 130.5, 128.4, 128.4, 128.1, 127.9, 127.9, 127.7, 127.6, 127.5, 124.9, 98.0, 94.2, 82.0, 79.9, 77.7, 75.8, 74.9, 73.3, 69.9, 66.8, 66.7, 62.6, 62.6, 55.2, 20.8, 20.6; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14k,16f]

Methyl 2,3,6-tri-O-benzyl-4-O-(4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-α-D-glucopyranoside (41): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with 4-Hydroxy-2,3,6-tri-*O*-benzyl-α-methoxy glucopyranoside (204 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 20 min., purified by silica gel column chromatography to obtain glycoside **41** as a light yellow semi solid (196 mg, 0.289 mmol, 79% yield, α-only). Rf (50% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.25 (m, 15H), 6.00 (dd, *J* = 10.0, 5.6 Hz, 1H), 5.69 (dd, *J* = 10.0, 3.0 Hz, 1H), 5.51-5.48 (m, 1H), 5.05 (d, *J* = 11.3 Hz, 1H), 4.90 (d, *J* = 5.6 Hz, 1H), 4.71 (dd, *J* = 20.0, 11.9 Hz, 3H), 4.63 (dd, *J* = 7.7, 4.2 Hz, 3H), 4.55 (d, *J* = 12.1 Hz, 1H), 4.08 (s, 2H), 3.95 (t, *J* = 9.2 Hz, 1H), 3.86-3.76 (m, 2H), 3.72-3.62 (m, 2H), 3.54 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.41 (s, 3H), 2.04 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 170.3, 138.5, 138.2, 137.8, 130.5, 128.4,

View Article Online
DOI: 10.1039/D0OB01042A

128.2, 128.1, 127.9, 127.6, 127.5, 127.5, 127.4, 124.4, 97.6, 95.1, 81.8, 80.1, 76.1, 75.5, 73.2, 72.9, 69.5, 69.4, 66.8, 62.6, 62.3, 55.2, 31.8, 22.6, 20.7, 20.7; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[16f]

5-O-(4,6-di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-2,3-O-isopropylidene uridine (42): Ferrier glycosylation of 3,4,6-tri-*O*-acetyl-D-galactal (100 mg, 0.367 mmol, 1.0 equiv.) with 2,3-*O*-isopropylidene uridine (124 mg, 0.440 mmol, 1.2 equiv.) at 50 °C for 3 h, purified by silica gel column chromatography to obtain glycoside **42** as a white semi solid (147 mg, 0.297mmol, 81% yield, α-only). Rf (60% EtOAc/Hexane) 0.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.48 (d, *J* = 8.1 Hz, 1H), 6.16 (ddd, *J* = 10.0, 5.5, 0.9 Hz, 1H), 5.97 (dd, *J* = 10.1, 3.0 Hz, 1H), 5.85 (d, *J* = 2.2 Hz, 1H), 5.69 (dd, *J* = 8.1, 2.1 Hz, 1H), 5.12-5.09 (m, 1H), 5.03 (dd, *J* = 5.5, 2.2 Hz, 1H), 4.82 (qd, *J* = 6.3, 2.7 Hz, 2H), 4.41 (q, *J* = 3.4 Hz, 1H), 4.32-4.26 (m, 1H), 4.26-4.20 (m, 2H), 4.02 (dd, *J* = 10.8, 3.8 Hz, 1H,), 3.80 (dd, *J* = 10.8, 3.3 Hz, 1H), 2.09 (s, 3H), 2.08 (s, 3H), 1.58 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 170.3, 163.1, 149.9, 141.3, 129.5, 126.0, 114.3, 102.0, 93.8, 93.3, 85.6, 84.9, 80.9, 67.7, 67.1, 62.7, 62.4, 27.2, 25.3, 20.8, 20.7; HRMS (ESI) m/z $[M + H]^+$ calculated for $[C_{22}H_{29}N_2O_{11}]^+$: 497.1766; found 497.1763.

Direct 1,2-addition reaction of armed glycal 1a and anomeric activation in One-pot: To a solution of glycal donor **1a** (100 mg, 0.240 mmol, 1.0 equiv.) and allyl alcohol **2b** (19 µL, 17 mg, 0.288 mmol, 1.2 equiv.) in Toluene (2 mL) was added 5 mol% $Cu(OTf)_2$ and the resulting mixture was stirred at 50 °C temperature under N_2 atmosphere. After the completion of the reaction the resulted allyl glycoside **5** was treated with L-Menthol (45 mg, 0.288 mmol, 1.2 equiv.) and NBS (51 mg, 0.288 mmol, 1.2 equiv.). The reaction mixture was stirred at 50 °C under inert atmosphere for 3 h. The reaction mixture after extraction with ethyl acetate, usual workup, purified by silica gel column chromatography to obtain pure compound **3a** in 62% yield over two-steps with α/β; 97:03.

Similarly, one-pot sequential glycosylation-anomeric activation employing **2n** as the acceptor in second step, purified by silica gel column chromatography to obtain the glycoside **18** in 65% yield with α/β; 96:04.

Ferrier Glycosylation of disarmed glycal 1b and anomeric activation in One-pot: To a solution of glycal donor **1b** (100 mg, 0.367 mmol, 1.0 equiv.) and allyl alcohol (30 µL, 25 mg, 0.440 mmol, 1.2 equiv.) in Acetonitrile (2 mL) was added 5 mol% $Cu(OTf)_2$ and the resulting mixture was stirred at 50 °C temperature under N_2 atmosphere. After the completion of the reaction the resulted allyl glycoside **29** was treated with L-Menthol (68 mg, 0.440 mmol, 1.2 equiv.) and NBS (78 mg, 0.440 mmol, 1.2 equiv.). After the completion of starting material, the reaction mixture was extracted with ethyl acetate and purification through column chromatography on silica to afford glycoside **4a** in 68% yield with α/β; 98:02. Similarly, one-pot sequential Ferrier glycosylation-anomeric activation employing **2n** as the acceptor in second step, purified by silica gel column chromatography to obtain the 2,3-unsaturated disaccharide **40** in 70% yield with complete α-selectivity.

Methyl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (43): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with methanol (13 µL, 10 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 3 h, purified by silica gel column chromatography to obtain glycoside **43** as an oil (98 mg, 0.218 mmol, 91% yield, $\alpha:\beta$; 97:03). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.25 (m, 15H), 4.94 (d, *J* = 11.6 Hz, 1H), 4.89 (d, *J* = 2.6 Hz, 1H), 4.63 (d, *J* = 11.7 Hz, 1H), 4.60 (s, 2H), 4.48 (dd, *J* = 36.0, 11.8 Hz, 2H), 3.90 (dd, *J* = 13.2, 7.3 Hz, 3H), 3.60 (d, *J* = 6.3 Hz, 2H), 3.33 (s, 3H), 2.24 (m, 1H), 2.01 (dd, *J* = 12.6, 3.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.5, 138.1, 128.4, 128.4, 128.3, 128.2, 128.2, 127.7, 127.6, 127.5, 127.2, 98.9, 74.7, 74.2, 73.4, 72.9, 70.4, 69.7, 69.6, 54.8, 31.1; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14g]

d_3-Methyl-3,4,6-tri-O-benzyl-2-deoxy-α-D-lyxo-hexapyranoside (44): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with methanol d^3 (11 µL, 10 mg, 0.288 mmol, 1.2 equiv.) at 50 °C for 3 h, purified by silica gel column chromatography to obtain glycoside **44** as an oil (100 mg, 0.223 mmol, 93% yield, $\alpha:\beta$; 91:09). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.36-7.25 (m, 15H), 4.93 (d, *J* = 11.6 Hz, 1H), 4.87 (m, 1H), 4.66-4.55 (m, 4H), 4.51 (d, *J* = 11.8 Hz, 1H), 4.43 (s, 1H), 3.94-3.85 (m, 2H), 3.59 (d, *J* = 6.1 Hz, 2H), 2.22 (m, 1H), 2.08-1.94 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.5, 138.1, 129.0, 128.4, 128.3, 128.2, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 127.2, 98.8, 74.7, 74.6, 74.2, 73.4, 72.9, 70.4, 69.7, 69.6, 31.1; HRMS (ESI) m/z $[M + H]^+$ calculated for $[C_{28}H_{30}D_3O_5]^+$: 452.2511; found 452.2510.

d_3-Methyl-3,4,6-tri-O-benzyl-2-deoxy-2-dutero-α-D-lyxo-hexapyranoside (45): Glycosylation of 3,4,6-tri-*O*-benzyl-D-galactal (100 mg, 0.240 mmol, 1.0 equiv.) with methanol d^4 (11 µL, 10 mg, 0.288mmol, 1.2 equiv.) at 50 °C for 3 h, purified by silica gel column chromatography to obtain glycoside **45** as an oil (98 mg, 0.223 mmol, 91% yield, $\alpha:\beta$; 91:09). Rf (20% EtOAc/Hexane) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.21(m, 15H), 4.93 (d, *J* = 11.8 Hz, 1H), 4.87 (d, *J* = 11.8 Hz, 1H), 4.66-4.55 (m, 3H), 4.52 (d, *J* = 11.8 Hz, 1H), 4.43 (d, *J* = 11.8 Hz, 1H), 3.87-3.76 (m, 2H), 3.52 (dd, *J* = 6.1, 1.6 Hz, 2H), 2.17 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 138.5, 138.1, 129.0, 128.4, 128.3, 128.2, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 127.2, 97.8, 73.7, 73.6, 73.2, 72.4, 71.9, 69.4, 68.7, 68.6, 30.1; the overall spectroscopic data are in complete agreement with assigned structures and consistent with literature.[14g]

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

SK gratefully acknowledges the Department of Science and Technology, India for the Early Career Research Award and Research Grant for Young Scientists (SERB-ECR/2017/001477). The author thanks TEQIP-III for generous support and MRC MNIT (Advanced Analytical and Characterization Centre) for providing NMR spectroscopic and analytical data. The authors are also grateful to the Director MNIT for providing necessary infrastructure. AG acknowledges a UGC Fellowship.

Notes and references

1 For selected reviews and articles; (a) R. M. De Lederkremer and C. Marino, *Adv. Carbohydr. Chem. Biochem.,* 2007, ***61***, 143; (b) A. Kirschning, A. F.-W. Bechthold and J. Rohr, *Top. Curr. Chem.*, 1997, ***188***, 1; (c) M. S. Butler, *Nat. Prod. Rep.,* 2005, ***22***, 162; (d) J. Thiem and W. Klaffke, *Top. Curr. Chem.,* 1990, ***154***, 285; (e) D. Hou and T. L. Lowary, *Carbohydr. Res.,* 2009, ***344***, 1911; (f) C. S. Bennett and M. C. Galan, *Chem. Rev.*, 2018, ***118***, 7931.

2 (a) J. M. Langenhan, N. R. Peters, I. A. Guzei, M. Hoffmann and J. S. Thorson, *Proc. Natl. Acad. Sci., U. S. A.* 2005, ***102***, 12305; (b) P. T. Daniel, U. Koert and J. Schuppan, *Angew. Chem., Int. Ed.,* 2006, ***45***, 872; (c) A. K. V. Iyer, M. Zhou, N. Azad, H. Elbaz, L. Wang, D. K. Rogalsky, Y. Rojanasakul, G. A. O'Doherty and J. M. Langenhan, *ACS Med. Chem. Lett.,* 2010, ***1***, 326; (d) V. Krěn and T. Řezanka, *FEMS Microbiol. Rev.,* 2008, ***32***, 858; (e) J. M. Langenhan, B. R. Griffith and J. S. Thorson, *J. Nat. Prod.,* 2005, ***68***, 1696.

3 (a) K. C. Nicolaou, and H. J. Mitchel, *Angew. Chem., Int. Ed*., 2001, ***40***, 1576; (b) H. Xi, M. Kurtoglu and T. J. Lampidis, *IUBMB Life,* 2014, ***66***, 110.

4 (a) C. H. Marzabadi and R. W. Franck, *Tetrahedron,* 2000, ***56***, 8385; (b) A. Veyriéres, In Carbohydrates in Chemistry and Biology; B. Ernst, G. W. Hart, P. Sinay, Eds.; Wiley-VCH: Weinheim, 2000; p 367; (c) A. Borovika and P. J. Nagorny, *Carbohydr. Chem*., 2012, ***31***, 255.

5 (a) W. G. Overend, C. W. Rees and J. S. Sequeira, *J. Chem. Soc.,* 1962, 3429; (b) R. Williams and M. C. Galan, *Eur. J. Org. Chem.,* 2017, 6247.

6 (a) M. Zhou and G. A. O'Doherty, *J. Org. Chem.,* 2007, ***72***, 2485; (b) F. E. McDonald and K. S. Reddy, *Angew. Chem. Int. Ed*., 2001, ***40***, 3653.

7 (a) M. Islam, N. D. Tirukoti, S. Nandi and S. Hotha, *J. Org. Chem.,* 2014, ***79***, 4470; (b) Y.-S. Lu, Q. Li, L.-H. Zhang and X.-S. Ye, *Org. Lett.*, 2008, ***10***, 3445; (c) R. Bandi, S. Chalapalaa and S. Chandrasekaran, *Org. Biomol. Chem.,* 2018, ***16***, 2248; (d) B. Kumar, M. A. Aga, A. Rouf, B. A. Shah and S. C. Taneja, *J. Org. Chem.,* 2011, ***76***, 3506; (e) D.-M. Yang, Y. Chen, R. P. Sweeney, T. L. Lowary and X.-Y. Liang, *Org. Lett.,* 2018, ***20***, 2287; (f) S. Adhikari, K. N. Baryal, D. Zhu, X. Li and J. Zhu, *ACS Catal*., 2013, ***3***, 57; (g) D. Zhu, S. Adhikari, K. N. Baryal, B. N. Abdullah and J. Zhu, *J. Carbohydr. Chem.,* 2014, ***33***, 438; (h) D. Liu, S. Sarrafpour, W. Guo, B. Goulart and C. S. Bennett, *J. Carbohydr. Chem*., 2014, ***33***, 423; (i) D. Zhu, K. N. Baryal, S. Adhikari and J. Zhu, *J. Am. Chem. Soc*., 2014, ***136***, 3172; (j) J.-H. Chen, J.-H. Ruei and K.-K. T. Mong, *Eur. J. Org. Chem.,* 2014, 1827; (k) M. Kaneko and S. B. Herzon, *Org. Lett*., 2014, ***16***, 2776; (l) T. M. Beale, P. J. Moon and M. S. Taylor, *Org. Lett*., 2014, ***16***, 3604; (m) M. Shaw and A. Kumar, *Chem. Asian J.,* 2019, ***14***, 4651.

8 H. Wang, J. Tao, X. Cai, W. Chen, Y. Zhao, Y. Xu and W. Tao, *Chem. -Eur. J.*, 2014, ***20***, 17319 and reference cited therein.

9 (a) R. W. Binkley and D. J. Koholic, *J. Org. Chem.,* 1989, ***54***, 3577; (b) K. Toshima, M. Misawa, K. Ohta, K. Tatsuta and M. Kinoshita, *Tetrahedron Lett*., 1989, ***30***, 6417.

10 H. Tanaka, A. Yoshizawa and T. Takahashi, *Angew. Chem., Int. Ed*., 2007, ***46***, 2505.

11 (a) L. Sun, P. Li and K. Zhao, *Tetrahedron Lett*., 1994, ***35***, 7147; (b) M. J. Lear, F. Yoshimura and M. Hirama, *Angew. Chem., Int. Ed*., 2001, ***40***, 946; (c) J. Jaunzems and A. Kirschning, *Tetrahedron Lett.,* 2003, ***44***, 637.

12 (a) R. Pongdee, B. Wu and G. A. Sulikowski, *Org. Lett.,* 2001, ***3***, 3523; (b) S. Hashimoto, Y. Yanagiya, T. Honda and S. Ikegami, *Chem. Lett*., 1992, 1511; (c) A. Koch, C. Lamberth, F. Wetterich and B. Giese, *J. Org. Chem.,* 1993, ***58***, 1083; (d) L. Hao, C. Meijin and Z. Kang, *Tetrahedron Lett.,* 1997, ***38***, 6143; (e) S.-I. Hashimoto, A. Sano, H. Sakamoto and S. Ikegami, *Synlett,* 1995, 1271; (f) L. Laupichler, H. Sajus and J. Thiem, *Synthesis,* 1992, 1133.

13 K. S. Kim, J. Park, Y. J. Lee and Y. S. Seo, *Angew. Chem., Int. Ed.*, 2003, ***42***, 459.

14 (a) G. Zhao and T. Wang, *Angew. Chem., Int. Ed*., 2018, ***57***, 6120; (b) M. R. Gupta, K. Thakur and N. K. Khare, *Carbohydr. Res*., 2018, ***457***, 51; (c) M.-Y. Hsu, Y.-P. Liu, S. Lam, S.-C. Lin and C.-C. Wang, *Beilstein J. Org. Chem.,* 2016, ***12***, 1758; (d) H. Tanaka, A. Yoshizawa and T. Takahashi, *Angew. Chem. Int. Ed.,* 2007, ***46***, 2505; (e) J. Park, T. J. Boltje and G.-J. Boons, *Org. Lett*., 2008, ***10***, 4367; (f) H.-C. Lin, J.-F. Pan, Y.-B. Chen, Z.-P. Lin and C.H. Lin, *Tetrahedron,* 2011, ***67***, 6362; (g) E. I. Balmond, D. M. Coe, M. C. Galan and E. M. McGarrigle, *Angew. Chem. Int. Ed.,* 2012, ***51***, 9152; (h) X.-K. Cui, M. Zhong, X.-B. Meng and Z.-J. Li, *Carbohydr. Res*., 2012, ***358***, 19; (i) E. I. Balmond, D. Benito-Alifonso, D. M. Coe, R. W. Alder, E. M. McGarrigle and M. C. Galan, *Angew. Chem. Int. Ed*., 2014, ***53***, 8190; (j) A. Sau, R. Williams, C. Palo-Nieto, A. Franconetti, S. Medina and M. C. Galan, *Angew. Chem. Int. Ed*., 2017, ***56***, 1; (k) A. Sau, C. Palo-Nieto and M. C. Galan, *J. Org. Chem.,* 2019, ***84***, 2415; (l) M. B. Tatina, Z. Moussa, M. Xiaa and Z. M. A. Judeh, *Chem. Commun.,* 2019, ***55***, 12204; (m) C. Palo-Nieto, A. Sau and M. C. Galan, *J. Am. Chem. Soc.,* 2017, ***139***, 14041; (n) K. B. Mishra and J. Kandasamy, *Asian J. Org. Chem.,* 2019, ***8***, 549; (o) C. Palo-Nieto, A. Sau, R. Jeanneret, P-A. Payard, A. Salame´, M. B. Martins-Teixeira, I. Carvalho, L. Grimaud, and M. C. Galan, *Org. Lett*., 2020, **22**, 1991.

15 (a) R. J. Ferrier, *Top. Curr. Chem*., 2001, ***215***, 153; (b) A. M. Gomez, F. Lobo, C. Uriel and J. C.´Lopez, *Eur. J. Org. Chem*., 2013, 7221. (c) R. J. Ferrier and J. O. Hoberg, *Adv. Carbohydr. Chem. Biochem*., 2003, ***58***, 55.

16 (a) D. B. G. Williams, S. B. Simelane and H. H. Kinfe, *Org. Biomol. Chem.,* 2012, ***10***, 5636; (b) O. Rosati, M. Curini, F. Messina, M. C. Marcotullio and G. Cravotto, *Catal. Lett*., 2013, ***143***, 169; (c) A. Sau and M. C. Galan, *Org. Lett*., 2017, ***19***, 2857; (d) J. Wang, C. Deng, Q. Zhang, and Y. Chai, *Org. Lett.,* 2019, ***21***, 1103; (e) R. S. Thombal and V. H. Jadhav, *RSC Adv.,* 2016, ***6***, 30846; (f) R. Balamurugan and S. R. Koppolu, *Tetrahedron Lett.,* 2009, ***65***, 8139; (g) K. Anil Kumar, M. Tatina, S. K. Yousuf and D. Mukherjee, *Chem. Commun*., 2013, ***49***, 10154.

17 (a) R. J. Ferrier, *J. Chem. Soc.* 1964, 5443; (b) D. M. Ciment and R. J. Ferrier, *J. Chem. Soc. C,* 1966, 441; (c) R. J. Ferrier and G. H. Sankey, *J. Chem. Soc. C,* 1966, 2345.

18 (a) V. D. Bussolo, Y. J. Kim and D. Y. Gin, *J. Am. Chem. Soc.,* 1998, ***120***, 13515; (b) R. R. Schmidt and R. Angerbauer, *Carbohydr. Res.,* 1979, ***89***, 272; (c) R. R. Schmidt and R. Angerbauer, *Angew. Chem., Int. Ed*., 1977, ***16***, 783. (d) B. Fraser-Reid, *Acc. Chem. Res.*, 1996, ***29***, 57; (e) M. P. Bracherro, E. F. Cabrera, G. M. Gómez and L. M. R. Peredes, *Carbohydr. Res.,* 1998, ***308***, 181; (f) D. J. Chambers, G. R. Evans and A. J. Fairbanks, *Tetrahedron: Asymmetry,* 2005, ***16***, 45.

19 (a) T. R. Reddy, D. S. Rao, K. Babachary and S. Kashyap, *Eur. J. Org. Chem.,* 2016, 291; (b) T. R. Reddy, S. K. Battina and S.

View Article Online
DOI: 10.1039/D0OB01042A

Kashyap, *J. Carbohydr. Chem.,* 2015, ***34***, 133; (c) G. Kundoor, D. S. Rao and S. Kashyap*, Asian J. Org. Chem.,* 2016, ***5***, 264; (d) S. K. Battina and S. Kashyap, *Tetrahedron Lett.,* 2016, ***57***, 811; (e) S. Chittela, T. R. Reddy, P. R. Krishna and S. Kashyap, *J. Org. Chem.,* 2015, ***80***, 7108; (f) T. R. Reddy, D. S. Rao and S. Kashyap, *RSC Adv.,* 2015, ***5***, 28338; (g) B. Srinivas, T. R. Reddy and S. Kashyap, *Carbohydr. Res.,* 2015, ***406***, 86; (h) T. R. Reddy, S. Chittela and S. Kashyap, *Tetrahedron,* 2014, ***70***, 9224; (i) S. Chittela, T. R. Reddy, P. R. Krishna and S. Kashyap, *RSC Adv.,* 2014, ***4***, 46327; (j) B. Srinivas, T. R. Reddy, P. R. Krishna and S. Kashyap, *Synlett,* 2014, 1325.

20 (a) S. Sato, M. Mori, Y. Ito and T Ogawa, *Carbohydr. Res.,* 1986, ***155***, C6-C10; (b) H. Yamada and T. Hayashi *Carbohydr. Res.,* 2002, ***337***, 581; (c) D. Frem, D. Urban,S. Norsikian and J-M. Beau*, Eur. J. Org. Chem*., 2017, ***2017***, 5094; (d) **R**. Sommer, D. Hauck and A. Titz, *Chemistry Select,* 2017, ***2***, 4187.

21 See the supporting information.

22 (a) M. Thomas, F. Rivault, I. Tranoy-Opalinski, J. Roche, J.-P. Gesson and S. Papot, *Bioorg. Med. Chem. Lett.,* 2007, ***17***, 983; (b) J. Tejler, H. Leffler and U. J. Nilsson, *Bioorg. Med. Chem. Lett.,* 2005, ***15***, 2343.

View Article Online
DOI: 10.1039/D0OB01042A

Copper(II)-Catalyzed Stereoselective 1,2-Addition *vs* Ferrier Glycosylation of "Armed" and "Disarmed" Glycal Donors

Manoj Kumar, Thurpu Raghavender Reddy, Aakanksha Gurawa and

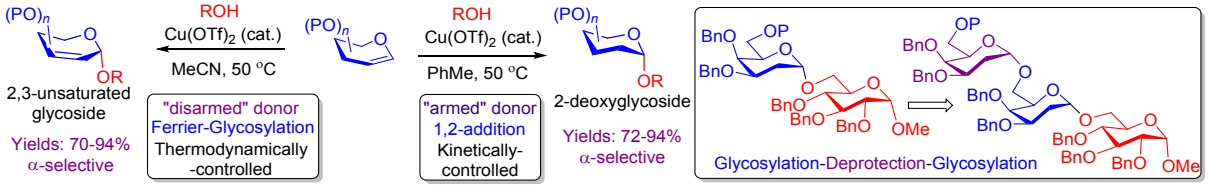
*Dr. Sudhir Kashyap**

Carbohydrate Chemistry Research Laboratory (CCRL), Department of Chemistry,

Malaviya National Institute of Technology (MNIT), Jaipur-302017, INDIA.

Email: skashyap.chy@mnit.ac.in, skr.kashyap@gmail.com

Graphical Abstract for Table of Contents



Précising the selectivity: The thermodynamic-kinetic switch model enables the selective activation of enol-ether moiety in "armed" and "disarmed" glycal donor leading to *syn*-diastereoselective direct addition or an allylic rearrangement.