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ORIGINAL ARTICLE

# Synthesis of Biologically Relevant β-Linked Hetryl C-Glycosides Using 1-Formyl Glucal

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## ABSTRACT

This chapter focuses on synthesizing biologically relevant β-linked hetryl C-glycosides using 1-formyl glucal. Glycals have many uses in synthetic carbohydrate chemistry. They are commonly used as glycosylation donors, meaning they can react with other monosaccharides to form a longer chain of monosaccharides called oligosaccharides. Glycals can also have interesting applications in studying biological systems, particularly enzymes. Glycoconjugates play a significant role in cell recognition processes and this has prompted the synthesis of many glycoconjugates via the glycal methodology. The presence of unsaturation and C-1 substitution make them good substrates in several reactions. In recent years C-1 functionalized glycalshave emerged as key carbohydrate precursors in a variety of synthetic transformations leading to carbohydrate mimetics. In such compounds broad structural variations are possible due to the presence of α–β unsaturation, offering the potential for improving drug metabolism and pharmacokinetic properties.

**KEY WORDS:** C-1 functionalized glucal, Glycomimetics, β-linked Hetryl C-Glycosides, Glycoconjugates

## INTRODUCTION

The scope of carbohydrates as chiral building blocks relies on the development of convenient key intermediates which are capable of meeting the requirement of stereocontrolled formation of oligosaccharide motifs (Marsault, *et al.,* 2004), *C*-glycosides (Well & Clendon, 2007; Horswill *et al.,* 2004), *C*-nucleosides (Driggers *et al.,* 2008; Wessjohann *et al.,* 2005; Butler, 2005), nucleosides (Veber *et al.,* 2002) and other biologically important molecules. Glycals have many uses in synthetic carbohydrate chemistry (Danishefsky *et al.,* 1993). They are commonly used as glycosylation donors, meaning that they can react with other glycosyl acceptors to form a longer chain of monosaccharides called oligosaccharides. Glycals can also have interesting applications in studying biological systems, particularly enzymes. D-glucal and radio-labeled D-galactal have been used to selectively bind with amino acids in the active sites of several enzymes. These enzyme-glycal complexes allow these amino acids essential for catalysis to be identified and allow for a better understanding of how these enzymes function (Sigman, 1992).

Glycoconjugates play a significant role in cell recognition processes and this has prompted the synthesis of many glycoconjugates through the glycal methodology. The presence of unsaturation and C-1 substitution make them good substrates in several reactions such as Claisen rearrangements (Liang *et al.,* 1996), hetero Diels–Alder reactions (Pettit *et al.,* 1986), acid-catalyzed spiroacetal formation (Smith *et al.,* 2005), selenium-induced spirocyclization (Smith *et al.,* 2011), radical addition of electrophilic radicals (Albert *et al.,* 1998), and Ferrier rearrangement (Konstantinoviæ *et al.,* 2001).

This has turned our attention to exploring the scope of the C-1 functionalized glycals for the synthesis of glycomimetics. In recent years *C*-1 functionalized glycals have emerged as key carbohydrate precursors in a variety of synthetic transformations leading to carbohydrate mimetics. It is worth mentioning here that Maiti *et al.*, 2001, have also reported recently the synthesis of benzimidazoles (including chiral ones) from reactions of aldehydes including glycal-derived aldehydes and *o*-phenylene diaminesbased on $VO(acac)_2$-$CeCl_3$-$Ti(OBu)_4$Combo catalyst. Similarly, Mishra *et al.,* 2020 reported that under the standard reaction condition, various glycal-2-carboxaldehydes in reaction with *o*-phenylene diamine or

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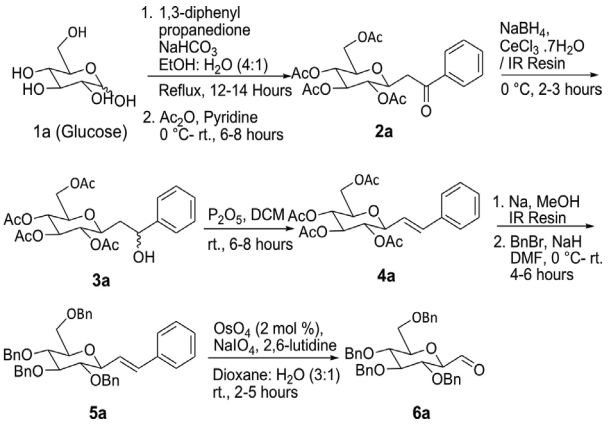
its analogs generated the corresponding optically pure benzimidazolesin good to excellent yields (70-90%) along with the results of antimicrobial assays of some selected chiral benzimidazoles.

Importance of such heterocycles originates from their broad application in chemistry, biology and material sciences (Hili *et al.,* 2006). Moreover heterocyclic motifs like benzimidazole, benzoxazole and benzthiazole occurs in many approved and in investigational drug and has generated considerable interest in many therapeutic area.

These results incited us to further explore this methodology towards synthesis of diversified optically pure benzimidazole scaffolds. As reported in our work on synthesis of heterocycles (chapter 3 of this thesis) and also in another work of our laboratory on glycal systemswe report herein chemo-selective synthesis of glucal fused benzimidazoles, glucal fused benzoxazoles and glucal fused benzthiazole by cyclocondensation of *o*-pheylene diamine, 2 amino phenol and 2 amino thiol, respectively with C-1 formylated glucal mediated by AcOH in DCM, proceeded in excellent yield. In such compounds broad structural variation are possible due to presence of α-β unsaturation, offering potential for improving drug metabolism and pharmacokinetic properties.

## RESULTS

The sugar-derived glycosyl aldehyde substrates was prepared from readily available glucose (Scheme 1). The peracylated β-C-gluco-benzoylmethane (2a) was obtained by the reaction of glucose(1a) and 1,3-diphenyl propanedione in the presence of sodium bicarbonate in ethanol: water (4:1) as solvent system was refluxed followed by acetylation with acetic anhydride in pyridine in excellent yields (90%). The 2a with sodium borohydride in the presence of cerium chloride heptahydrate/IR resin, led to the formation of glycosyl alcohol (3a) in very good yields (90%). The so-formed peracylated derivative (3a)




Scheme 1. Synthesis of glucosyl aldehydes (6a)

was reacted separately with phosphorous penataoxide in DCM at room temperature to provide the respective peracylated glycol-ethene derivative (4a) in good yields (81%). The peracylated alkene was converted in to perbenzylated alkene (5a) after deacetylation. Oxidation of this perbenzylated glycosyl ethene (5a) with osmium tetraoxide in presence of sodium meta periodate and lutidine in solution of dioxane-water (3:1) led to the formation of desired perbenzylated glycosyl aldehyde 6a (Khatri *et al.,* 2015) in good yields (75%).

After successfully synthesizing the glycosyl aldehyde (6a), we then synthesized C-1 functionalized glycal 7a (Arya & Khare, 2019) by base catalyzed elimination reaction for installing the required α, β- unsaturated system of glycal in preorganized sugar. As summarized in Table 1, several organic bases such as DBU, pyrolidine, and pipridine showed comparable reactivity in elimination reaction and provide the desired product 7a in 70-95% yields (entries 1-6, 15, 16). Decreasing the base loading produces little detrimental effect to yield with increased reaction time (entries 7, 8). It was found that removing or replacing the DBU by DABCO, TEA, DIPEA, Pyridine (entries 7, 8, 10, 11 respectively) was largely detrimental to the reaction and only traces of the product was formed, while use of pyrolidine and piperidine provides good yield of the products but not as good as with DBU (entries 13, 14). The use of potassium tertiary butoxide as base led to an inseparable complex mixture of products. Next, we

Table 1: Optimization of the reaction for C-1 formyl glucal (7a) from glycosyl aldehyde (6a)

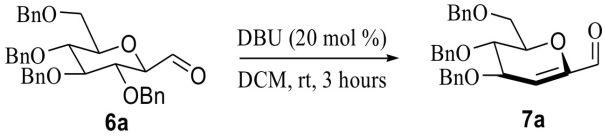
| Entry | Base (mol%) | Solvent | Time (h) | Yield (%) |
|---|---|---|---|---|
| 1 | DBU (20) | THF | 3 | 89 |
| 2 | DBU (20) | MeOH | 3 | 80 |
| 3 | DBU (20) | $CH_3CN$ | 3 | 83 |
| 4 | DBU (20) | DCM | 3 | 95 |
| 5 | DBU (20) | DMF | 3 | 78 |
| 6 | DBU (20) | Dioxane | 3 | 70 |
| 7 | DBU (5) | DCM | 6 | 73 |
| 8 | DBU (10) | DCM | 5 | 80 |
| 9 | DABCO (20) | DCM | 8 | Trace |
| 10 | TEA (20) | DCM | 8 | - |
| 11 | TEA | TEA | 6 | 5 |
| 12 | DIPEA (20) | DCM | 8 | 5 |
| 13 | Pyridine (20) | DCM | 8 | - |
| 14 | Pyridine | Pyridine | 6 | 5 |
| 15 | Pyrolidine (20) | DCM | 2 | 90 |
| 16 | Pipridine (20) | DCM | 2 | 86 |
| 17 | KO*t*-Bu (20) | DCM | 1 | - |

decided to explore solvent effects. The use of THF, MeOH and acetonitrile as the solvent at room temperature was detrimental to the yield (entries 1, 2, 3), and the use of DMF and dioxane as solvent was little more detrimental to the yield (entries 5, 6). The 20 mol% proved to be the optimum base loading for reactions that used DBU in DCM (95% yield, entry 4).

Under the above conditions, it is expected that C-2 equatorial benzyl ether group in 6a was eliminated smoothly and demonstrated that the stereochemistry of C-1 and of C-2 has no impact on elimination reaction and product formation.

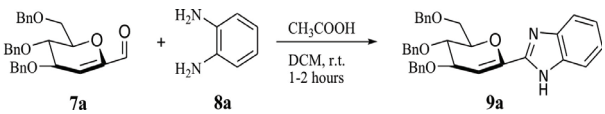
Our initial efforts of screening a series of commercial bases as catalysts for their ability to abstract the anomeric proton in the elimination reaction of perbenzylated glycosyl aldehyde (6a) into the desired C-1 functionalized glycal (7a) in the presence of different catalyst loadings and solvents at room temperature was tried and summarized in Table 1.

The reactions proceeded smoothly within 3-4 hours and in excellent yield (80%) without disturbing the stereochemistry of 6a.The DBU in DCM was ideally used as a base (Entry 4 in Table 1).

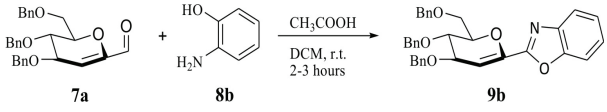



Scheme 2. Synthesis of Formyl Glycal(7a)

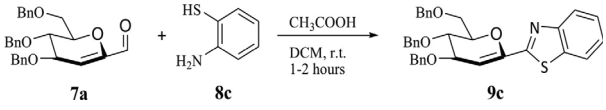
The compound C-1 formylated glucal (7a) was then reactedwith 1,2-diaminobenzene (8a) using DCMas a solvent and one or two drops acetic acid was added tothe stirring solution. Acetic acid was used as a catalyst to speed up the reaction. It is non-toxic, less expensive and easily available. Further, the reaction mixture was stirred vigorously for 1 to 2 hours at room temperature (25-30°C). After completion of the reaction work up was done with 5% NaOH solution and ethyl acetate, all the unreacted phenylene diamnine went to 5% NaOH solution and 3, 4, 6 Tri *O*-benzyl 1, 2-di-deoxy D-arabino-hex-1-en-pyranoside 1-benzimidazole (9a) was obtained as a crude product which was purified by column chromatography.




Scheme 3. Synthesis of biologically relevant β- linked HetrylC Glycosides (9a)




Scheme 4. Synthesis of biologically relevant β- linked HetrylC Glycosides (9b)




Scheme 5. Synthesis of biologically relevant β- linked HetrylC Glycosides (9c)

Similarly, under standard conditions 2-aminophenol (8b) was mixed with 7a in the presence of DCM at room temperature in a similar manner as reported in the synthesis of 9a. A few drops of acetic acid were added and the reaction mixture was stirred for 2-3 hours to give 3, 4, 6 –*O*-benzyl 1, 2-di-deoxy arabino-hex-1-enopyranoside 1-benzoxazole (9b). It was observed that the formation of 9b took more time than 9a. It is noteworthy here that increasing the reaction temperature upto 50°C decreases the reaction time. On completion of the reaction, workup was done as mentioned above and purification of the crude product was done with the help of column chromatography.

In the same manner, as mentioned above, 7a was reacted with 2-aminothiophenol (8c) at room temperature in the presence of DCM (solvent) to generate3, 4, 6 –*O*-benzyl 1, 2-di-deoxy arabino-hex-1-enopyranoside 1-benzthiazole (9c) in 1-2 hours. Workup was done in the same manner as in the case of 9a and 9c. Many side products were also formed in case of 9c which were removed by column chromatography.

## DISCUSSION

### $^{1}$H NMR and $^{13}$C NMR Spectroscopy

The characterization of all the synthesized compounds was done with the help of $^{1}$H and $^{13}$C NMR spectroscopy.For the characterization of the structure of 7a, the presence of a singlet at δ 9.214 in the $^{1}$H NMR spectrum of 7a, confirmed the presence of –CHO group, which was also supported by the presence of a characteristic carbonyl carbon peak at δ 186.22 ppm in the $^{13}$C NMR spectrum of 7a. Appearance of a multiplet in the region δ 7.225 to δ 7.337 ppm in the $^{1}$H NMR spectrum of 7a, confirmed the presence of aromatic rings protons while the presence of peaks in the region δ 117.28 to δ 139.29 ppm in the $^{13}$C NMR spectrum of 7a, substantiated the presence of aromatic carbons. The presence of six methylene protons ofthe three benzyl groups was confirmed by a multiplet of six protons at δ 4.525-δ 4.727 ppm in the $^{1}$H NMR spectrum of 7a while the complementary

three methylene carbons were attributed to the presence of peaks at δ 73.55, 74.10 and 75.69 ppm in the $^{13}C$ NMR spectrum of 7a. The structure of the C-1 functionalized glucal(7a) is also confirmed by the presence of a doublet (J=2.4 Hz) at δ 5.840 ppm in $^{1}H$ NMR spectrum of 7a, attributed to H-2 proton which was also verified by the C-2 carbon signal at δ 114.07 and C-1 carbon signal at δ 151.53 in its $^{13}C$ NMR spectrum. Other characteristic peaks of 7a were also observed in both the $^{1}H$ and $^{13}C$ NMR spectra of 7a (please see the experimental section).

For the characterization of synthesized compound 9a, the disappearance of diagnostic signals due to carbonyl group of 7a indicated the conjugation of C-1 formylated glucal 7a with o-phenylene diamine (8a). The appearance of a doublet (J=2.4 Hz) at δ 5.985 ppm in the $^{1}H$ NMR spectrum of 9a resulted due to the presence of H-2 proton in 9a which is substantiated by the absence of H-1 anomeric proton in 9a. This confirmed the presence of a double bond between C-1 and C-2 in 9a. It was also supplemented by a carbon signal due to C-2 at δ 96.21 ppm and C-1 at δ 156.27 in the $^{13}C$ NMR spectrum of 9a. The presence of six methylene protons ofthe three benzyl groups was confirmed by the multiplet of six protons at δ 4.670-δ 4.982 ppm in the $^{1}H$ NMR spectrum of 9a while the complementary three methylene carbons were attributed by the presence of peaks at δ 73.58, 74.13 and 75.71 ppm in the $^{13}C$ NMR spectrum of 9a. Characteristic benzimidazole C-1´ carbon for 9a appeared at δ 143.31 ppm in its $^{13}C$ NMR spectrum. The presence of a multiplet of 20 protons in the $^{1}H$ NMR spectrum of 9a at δ 7.252 to δ 7.684 ppm, indicated the presence of nineteen aromatic rings protons and one –NH proton present in the synthesized compound 9a, which was also confirmed by the presence of aromatic carbon peaks in the range of δ 117.58 – 137.85 in the $^{13}C$ NMR spectrum of 9a (please see the experimental section).

For the characterization of synthesized compound 9b, the disappearance of diagnostic signals due to carbonyl group of 7a indicated the conjugation of C-1 formylated glucal 7a with o-amino phenol (8b). The appearance of a doublet (J=2.4 Hz) at δ 5.983 ppm in the $^{1}H$ NMR spectrum of 9b resulted from the presence of H-2 proton in 9b which is substantiated by the absence of H-1 anomeric proton in 9b. This confirmed the presence of a double bond between C-1 and C-2 in 9b. It was also supplemented by a carbon signal due to C-2 at δ 96.17 ppm and C-1 at δ 159.87 in the $^{13}C$ NMR spectrum of 9b. The presence of six methylene protons ofthe three benzyl groups was confirmed by the multiplet of six protons at δ 4.508-4.823 ppm in the $^{1}H$ NMR spectrum of 9b while the complementary three methylene carbons were attributed to the presence of peaks at δ 73.55, 74.09 and 75.69 ppm in the $^{13}C$ NMR spectrum of 9b. Characteristic benzoxazole C-1´ carbon for 9b appeared at δ 156.21 ppm in its $^{13}C$ NMR spectrum. The presence of a multiplet of 20 protons in the $^{1}H$ NMR spectrum of 9b at δ 7.266 to δ 8.144 ppm, indicated the presence of nineteen aromatic rings protons in the synthesized compound 9b, which was also confirmed by the presence of aromatic carbon peaks in the range of δ 111.32-150.92 in the $^{13}C$ NMR spectrum of 9b (please see the experimental section).

For the characterization of synthesized compound 9c, the disappearance of diagnostic signals due to carbonyl group of 7a indicated the conjugation of C-1 formylated glucal 7a with o-amino thiophenol (8c). The appearance of an unresolved doublet at δ 5.982 ppm in the $^{1}H$ NMR spectrum of 9c resulted due to the presence of H-2 proton in 9c which is substantiated by the absence of H-1 anomeric proton in 9c. This confirmed the presence of a double bond between C-1 and C-2 in 9c. It was also supplemented by a carbon signal due to C-2 at δ 96.13 ppm and C-1 at ä 165.11 in the $^{13}C$ NMR spectrum of 9c. The presence of six methylene protons ofthe three benzyl groups was confirmed by the multiplet of six protons at δ 4.667-4.958 ppm in the $^{1}H$ NMR spectrum of 9c while the complementary three methylene carbons were attributed to the presence of peaks at δ 73.52, 74.06 and 75.67 ppm in the $^{13}C$ NMR spectrum of 9c. Characteristic benzthiazole C-1´ carbon for 9c appeared at δ 153.58 ppm in its $^{13}C$ NMR spectrum. Presence of a multiplet of 19 protons in the $^{1}H$ NMR spectrum of 9c at δ 7.122 to δ 7.940 ppm, indicated the presence of nineteen aromatic rings protons in the synthesized compound 9c, which was also confirmed by the presence of aromatic carbon peaks in the range of δ 121.51-144.43 in the $^{13}C$ NMR spectrum of 9c (please see the experimental section).

## CONCLUSION

In conclusion, we developed a general and highly regioselective method for cycloaddition reaction involving C-1 formylated glucal to form nitrogen-containing C-glycosidesand by this approach, several series of 2-heteroaryl-C-glycosides can be prepared. Diversified subsequent modifications can be made in such glycosides, by it allowing the conversion of the double bond into other functional groups. Based on these results, we believe that this protocol will find wide applications in preparing biologically important compounds.

## EXPERIMENTAL

All reactions were monitored by thin layer chromatography (TLC) Merck silica gel 60 $F_{254}$, spots were visualized by UV light. All products were purified by column chromatography over silica gel (SRL, 60-120 mesh) using a gradient of n-hexane and ethyl acetate as eluent. Optical rotations were measured with an automatic polarimeter, Optical Activity (Model: AA-5 series) at room

temperature. Melting points were determined on Buchi540 melting point apparatus. Synthesized products were characterized by their spectral data. The $^{1}H$ NMR and $^{13}C$ NMR spectra were recorded on Bruker DPX 300 MHz spectrometer using $CDCl_3$ (ppm) and TMS was used as the internal standard. Coupling constant (J) were recorded in Hz. Multiplicities are given as follows singlet (s), double (d), doublet of doublets (dd), triplet (t), quartet (q), multiplet (m).

## Synthesis of per *O*-benzylated β-glycopyranoside 1-C-carbaldehyde (6a)

It was synthesized by a known multistep process[16] taking glucose as starting material. The characterization and identification of 6a was reported in chapter 3 of this thesis.

## Synthesis of 3, 4, 6 –Tri O-benzyl 1, 2-di-deoxy D-arabino-hex-1-en-pyranoside 1-C-carbaldehyde (7a)

The 1-formyl glucose (6a), 150 mg (0.302 mmol) was dissolved in DCM then two drops of DBU (20%mol) were added and the reaction mixture was refluxed at 60°C. Product (7a) was obtained as a dirty white semi-solid in 107 mg (80% yields), $[\alpha]_D$ -24.$^{1}H$ NMR ($CDCl_3$, 300MHz) δ 3.857-3.896 (m, 2H, H-6a, H-6b), 3.977- 4.028 (m, 1H, H-3), 4.154 - 4.183 (m, 1H, H-4), 4.367-4.368 (m, 1H, H-5), 4.525-4.727 (m, 6H, Benzyl –$CH_2$ Protons), 5.840 (d, 1H, J=2.4Hz, H-2), 7.225-7.337 (m, 15H, Aromatic Protons), 9.214 (s, 1H, -C<u>H</u>O). $^{13}C$ NMR ($CDCl_3$, 300MHz) δ 67.64 (C-6), 71.56 (C-3), 73.55, 74.10 and 75.69 (3xbenzyl –$CH_2$ carbons), 77.44 (C-4), 77.62 (C-5), 114.07 (C-2), 117.28-139.29 (Aromatic carbons), 151.53 (C-1), 186.22 (-<u>C</u>HO). Elemental Analysis: Calcd. For $C_{28}H_{28}O_5$, C, 75.65; H, 6.35; Found: C, 75.55; H, 6.31.

## Synthesis of 3,4,6 Tri *O*-benzyl 1,2-di-deoxy D-gluco-hex-1-en-pyranoside 1-*C*-benzimidazole(9a)

The C-1 formylated glucal (7a) (50 mg, 0.096 mM) was dissolved in DCM (20 ml) then *o*-Phenylene diamine (8a) 10mg (0.096mmol) was added to the reaction mixture, stirred at room temperature. One drop of acetic acid was added and the reaction mixture was further stirred at room temperature for 1-2 hours. The progress of reaction was monitored on TLC plate. The workup was done by adding 5% aq. NaOH solution and ethyl acetate to the reaction mixture. Most of the phenylene diamine went to 5% aq. NaOH solution and desired compound went to ethyl acetate layer followed by washing and drying. Ethyl acetate was evaporated under reduced pressure to get crude product. Crude product was purified by column chromatography to give pure product 9a as a dirty white solid in 39.32 mg (77% yields). $[\alpha]_D$ +21°(c0.2, $CH_3OH$);$^{1}H$ NMR ($CDCl_3$, 300MHz) δ 4.002-4.041 (m, 2H, H-6a, H-6b), 4.122- 4.173 (m, 1H, H-3), 4.299-4.328 (m, 1H, H-4), 4.512-4.533 (m, 1H, H-5), 4.670-4.982 (m, 6H, Benzyl –$CH_2$ Protons), 5.985 (d, 1H, J= 2.4Hz, H-2), 7.252-7.684 (m, 20H, Aromatic Protons, -N*H*). $^{13}C$ NMR ($CDCl_3$, 300MHz) δ 67.67 (C-6), 71.58 (C-3), 73.58, 74.13 and 75.71 (benzyl –$CH_2$ carbon), 77.46 (C-4), 77.63 (C-5), 96.21 (C-2), 117.58-137.85 (Aromatic carbons), 143.31 (C-1´), 156.27 (C-1). Elemental Analysis: Calcd. For $C_{34}H_{32}N_2O_4$, C, 76.67; H, 6.06; N, 5.26; Found: C, 76.59; H, 5.99; N, 5.22

## Synthesis of 3,4,6 –*O*-benzyl 1,2-di-deoxy arabino-hex-1-enopyranoside 1-benzoxazole (9b)

The 1-formyl glucal (7a) (50 mg 0.096 mmol) was dissolved in DCM (20 ml) then 2-amino phenol (8b) (10.5 mg, 0.096 mmol) was added and reaction mixture was stirred thoroughly for 2-3 hours. The progress of reaction was monitored on TLC plate. After completion of reaction, the workup was done by adding 5% aq. NaOH solution and ethyl acetate to the reaction mixture. The organic layer was washed with water, dried and filtered. Ethyl acetate was evaporated under reduced pressure to get crude product. Crude product was purified by column chromatography using hexane/ethyl acetate gradient in 3:1 ratio to give the pure product 9b as a dirty white semi-solid in 37mg (73% yields),$[\alpha]_D$ -11° (c0.2,$CH_3OH$).$^{1}H$ NMR ($CDCl_3$, 300MHz) δ 3.853-3.875 (m, 2H, H-6a, H-6b), 3.967-4.008 (m, 1H, H-3), 4.126 - 4.177 (m, 1H, H-4), 4.368 - 4.398 (m, 1H, H-5), 4.508-4.823 (m, 6H, Benzyl –$CH_2$ Protons), 5.983 (d, 1H, J=2.4 Hz, H-2), 7.266-8.144 (m, 19H, Aromatic Protons). $^{13}C$ NMR ($CDCl_3$, 300MHz) δ 67.64 (C-6), 71.55 (C-3), 73.55, 74.09, 75.69 (3xbenzyl –$CH_2$ carbon), 77.42 (C-4), 77.60 (C-5), 96.17 (C-2), 111.32-150.92 (Aromatic carbons), 156.21 (C-1´), 159.87 (C-1). Elemental Analysis: Calcd. For $C_{34}H_{31}NO_5$, C, 76.53; H, 5.86; N, 2.62; Found: C, 76.50; H, 5.81; N, 2.60.

## Synthesis of 3,4,6–*O*-benzyl 1,2-di-deoxy arabino-hex-1-enopyranoside 1-benzthiazole (9c)

To the stirring solution of glucal(7a) (50 mg 0.096 mmol) in DCM (20 ml), 2-amino thiol (8c) (12.6 mg, 0.096 mmol) was added. One drop of acetic acid was added to speed up the reaction. The progress of reaction was monitored on TLC plate. After completion of reaction the workup was done by adding 5% aq. NaOH solution and ethyl acetate to the reaction mixture. Ethyl acetate was evaporated under reduced pressure after drying to get crude product. Crude product was purified by column chromatography using hexane/ethyl acetate gradient in 3:1 ratio to give pure product 9c. It was obtained as a pale yellow semi-solid in 36.41 mg (69% yields), $[\alpha]_D$ -15°.

$^{1}$H NMR ($CDCl_3$, 300MHz) δ 4.003 (m, 2H, H-6a, H-6b), 4.148 (m, 1H, H-3 ), 4.317 (m, 1H, H-4), 4.520 (m, 1H, H-5), 4.667-4.958 (m, 6H, Benzyl Protons), 5.982 (unresolved d, 1H, H-2), 7.122-7.940 (m, 19H, Aromatic Protons). $^{13}$C NMR ($CDCl_3$, 300MHz) δ 67.63 (C-6), 71.53 (C-3), 73.52, 74.06, 75.67 (benzyl –$CH_2$ carbon), 77.41 (C-4), 77.68 (C-5), 96.13 (C-2), 121.51-144.43 (Aromatic carbons), 153.58 (C-1´), 165.11 (C-1). Elemental Analysis: Calcd. For $C_{34}H_{31}NO_4S$: C, 74.29; H, 5.68; N, 2.55; Found: C, 74.25; H, 5.64; N, 2.51.

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