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A target oriented expeditious approach towards synthesis of certain bacterial rare sugar derivatives

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Bacterial rare amino deoxy sugars are found in the cell surface polysaccharides of multiple pathogenic bacterial strains, but are absent in the human metabolism. This helps in the differentiation between pathogen and the host cell which can be exploited for target specific drug discovery and carbohydrate based vaccine development. The principal bacterial atypical sugar derivatives include 2-acetamido-4-amino-2,4,6-trideoxy-D-galactose (AAT), 2,4-diacetamido-2,4,6-trideoxy-D-galactose (DATDG) and N-acetylfucosamine (FucNAc). Herein, a highly streamlined protocol leading to the aforesaid derivatives is presented. The highlights of the method lie in radical mediated 6-deoxygenation along with a one-pot like protection profile manipulation on suitably derivatised D-glucosamine or D-mannose motifs to obtain a vital quinovosaminoside or rhamnoside from which rare sugar derivatives were synthesized in a diversity oriented manner.

Introduction

Bacterial rare sugars have been shown to be essential components of the cell surface polysaccharide profiles of various pathogenic bacterial strains like *Shigella sonnei, Streptococcus mitis, Streptococcus pneumonia, Neisseria meningitides, Pseudomonas aeruginosa.*[1,2] These rare sugars are mostly absent in the human metabolism. Hence, these can be considered as highly attractive candidates towards vaccine development against the aforesaid pathogenic bacteria.[3] Therefore access to these rare sugars in sizeable quantity and stereochemical purity is of great importance. However the aforesaid requirements cannot be met using available techniques of isolation from biological sources. It is hence imperative that efficient synthetic methods be devised so as to allow easy access to these compounds for further studies and research directed towards understanding the roles played by these sugars in the pathogenesis of virulent bacteria.

The derivatives in question include basic sugar units like AAT (2-acetamido-4-amino-2,4,6- trideoxygalactose),[4] DATDG (2,4-diamino-2,4,6-trideoxygalactose)[5] and FucNAc (N-acetylfucosamine).[6] Different synthetic strategies have been employed by researchers over the past three decades in their attempts to access the aforesaid synthetic targets.[7] A principal share of these strategies involves *C-6* deoxygenation on D-glucosamine[7a] and D-mannose[7c] derivatives followed by inversion at *C-4* position as well as d*e novo* approaches.[8] The deoxygenation protocols employed include reductive displacements of various leaving groups at the *C-6* position like bromide, iodide, -OMs and -OTs. On the other hand, the installation of nitrogenous functionalities at the *C-4* position has been carried out via nucleophilic displacements on leaving groups like –OTs, -OTf, or -OMs. Intramolecular displacement strategy has also been employed for the introduction amine function at the *C-4* position.[7b, 8c] These methods have been recently reviewed by Kulkarni *et al.*[1]

Despite the progress made, some of these strategies still suffer from limitations which include long drawn synthetic schemes requiring multiple steps, low overall yields or use of expensive and hazardous reagents in large quantities in the initial preparative stages. Considering the aforesaid limitations and lack of flexibility experienced in synthesizing appropriate amino sugar substrates there appears to be room left for further research with particular emphasis on step minimization through one-pot reactions. Herein, we wish to report an efficient target oriented approach (Figure 1) by which multiple rare sugar derivatives maybe accessed easily from the pivotal intermediates **1a-c** which are obtainable from the native sugars via the corresponding 4,6-*O*-benzylidene O-/S-glycosides.

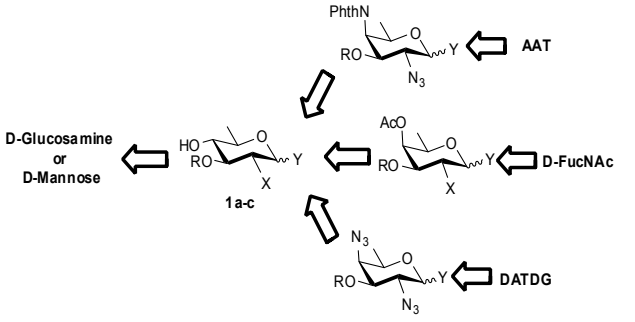

Fig. 1 Retrosynthetic analysis

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[b] Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

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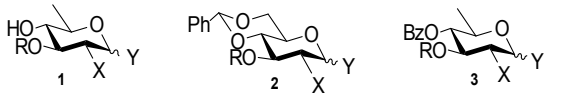
Results and discussion

Synthesis of D-quinovosamine derivatives 1a, 1b and 1c

In our previous studies related to the synthesis of D-rhamnosides radical based redox rearrangement 4,6-*O*-benzylidene derivatives[9] of D-*manno*-thioglycosides led to their corresponding 6-*O*-deoxy congeners in high yield and selectivity on treatment with DTBP (Di-*tert*-butyl peroxide)/ TIPST (Tri-isopropylsilane thiol) with minimal interference from the anomeric thioglycoside.[10] Using this deoxygenation protocol (Figure 2) on the D-glucosamine derived compounds **2a-c** we got the corresponding D-quinovosaminoside derivatives **3a-c** in 89 to 94% yields. Encouraged by this result we figured that access to the aforesaid bacterial rare sugars may be achieved via **1** (Fig. 1) if we could selectively deprotect the 4-*O*-benzoyl and then follow it up with an inversion at that position mediated via carbohydrate based triflates.[11a-e]

However, the *3-OH* of **3b/3c** (Figure 2) has to be suitably protected prior to the selective deprotection at *4-OH*. So, a protecting group which would be compatible with subsequent methoxide mediated debenzoylation at *O-4* had to be selected. This turned out to be rather difficult as the radical mediated deoxygenation protocol responds best when the other positions bear an acyl protection profile. But we cannot use acyl protection at *O-3* because that would rule out selective debenzoylation at *O-4* in the next step. The *O*-benzyl and related protecting groups which are typically used as orthogonal protection with respect to the acyl profile is also ruled out because of their incompatibility with the radical deoxygenation protocol.[12] The next option was silylation which was successfully carried out on **2b** (Figure 2). However, subsequent deoxygenation of the silylated derivative **2d**[11e] failed to give **3d** in satisfactory yield and purity**.**

At this point we decided to change the order of the reactions. Since the deoxygenation protocol is not affected by the presence of free –OH at *O-3*, as long as the solubility of the benzylidene substrate in octane is sufficient enough to permit complete dissolution under reflux, we deoxygenated **2b/2c** to get **3b/3c.** This opened up the option for acid mediated benzylation at *O-3*. But unfortunately this could not yield an efficient solution either as attempts made towards benzylation using benzyltrichloroacetimidate (BnOTCA) or 4-methoxybenzylation using 2,4,6-Tris-(*p*-methoxybenzyloxy)-



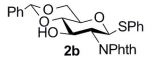
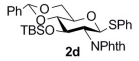
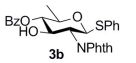
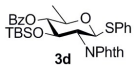
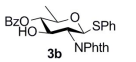
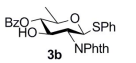
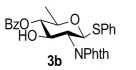
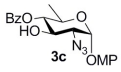
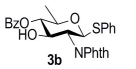
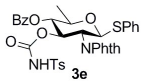
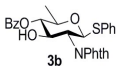
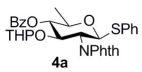
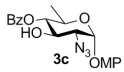
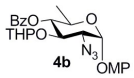
	X	Y	R
1a	NPhth	βSPh	THP
1b	N_3	αOMP	THP
1c	NPhth	βSPh	CONHTs

	X	Y	R
2a	NPhth	βSPh	Ac
2b	NPhth	βSPh	H
2c	N_3	αOMP	H
2d	NPhth	βSPh	TBS

	X	Y	R
3a	NPhth	βSPh	Ac
3b	NPhth	βSPh	H
3c	N_3	αOMP	H
3d	NPhth	βSPh	TBS
3e	NPhth	βSPh	CONHTs
4a	NPhth	βSPh	THP
4b	N_3	αOMP	THP

Fig. 2 Synthesis of D-quinovosaminosides

Table 1 Optimisation of protocol for the protection of *O*-3

Entry	Reactant	Reaction Conditions	Expected Product	Yield
1	 **2b**	TBDMSOTf, Lutidine, DCM	 **2d**	88%
2	 **3b**	TBDMSOTf, Lutidine, DCM	 **3d**	63%
3	 **3b**	BnOTCA, DCM, TMSOTf	-	N.R.[a]
4	 **3b**	TriBOT-PM, TfOH cat., DCM	-	N.R.[b]
5	 **3b**	TriBOT-PM, CSA cat., DCM	-	N.R.[a]
6	 **3c**	TriBOT-PM, CSA cat., DCM	-	N.R.[a]
7	 **3b**	TsNCO, DCM	 **3e**	95%
8	 **3b**	DHP, *p*TSA, DCM	 **4a**	75%[c]
9	 **3c**	DHP, *p*TSA, DCM	 **4b**	77%[c]

[a] Starting material was recovered; [b] Starting material was decomposed; [c] Isolated yield of products obtained as anomeric mixture of THP ether.

1,3,5-triazine (TRIBOT-PM)[13] failed (Table 1, entries 3-6). Silylation of **3b** could be carried out but with a modest yield of **3d** in 63% only (Table 1, entry 2). Subsequent debenzoylation of **3d** led to a complex mixture from which the expected product could not be obtained in satisfactory yield (Table 2, entry 5). As a result this route had to be abandoned.

Protection with the recently reported *N*-Tosylcarbamoyl[13c] group led to **3e** in high yield of 95% (Table 1, entry 7) and then debenzoylated to **1c** in 87% yield (Table 2, entry 6). Protection of *O-3* was also successfully achieved by converting **3b/3c** to their corresponding tetrahydropyranyl ether (THP) derivatives by treatment with 3,4-di-hydro-2*H*-pyran (DHP) and *p*-toluenesulfonic acid (*p*-TSA)[14a] to give **4a/4b** (Table 1, entries 8 and 9).[14b] The next requirement was the selective debenzoylation at *O-4* (Table 2). After trying some variation of temperature, reagent concentration and reaction time, a suitable condition was found where the undesired deprotection of *N*-phthaloyl group could be minimised.

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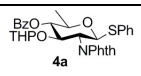
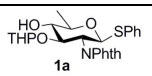
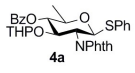
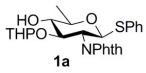
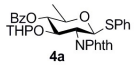
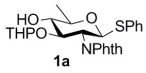
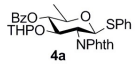
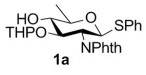
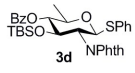
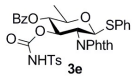
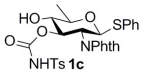
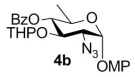
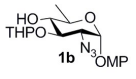
Table 2 Optimisation of conditions for deprotection at *O*-4

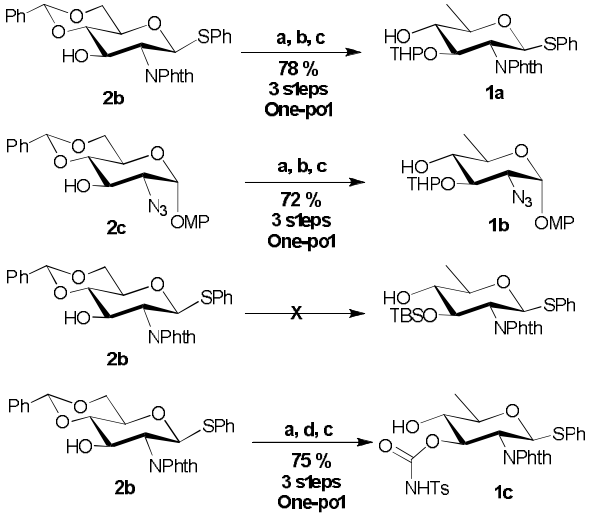
Entry	Reactant	Conc.[a]	Time (h)	Expected Product	Yield[c]
1	 **4a**	0.05	18	 **1a**	N.R.[d]
2	 **4a**	0.05	4[h]	 **1a**	N.R.[e]
3	 **4a**	0.2	1	 **1a**	N.R.[e]
4	 **4a**	0.08[f]	4	 **1a**	84%
5	 **3d**	0.2[g]	1[h]	-	N.R.[e]
6	 **3e**	0.1	12	 **1c**	87%
7	 **4b**	0.1	4	 **1b**	82%

[a] Molar concentration of NaOMe/MeOH solution. [b] All reaction were done at rt unless stated otherwise. [c] Isolated yield. [d] Starting material unconverted. [e] Starting material decomposed . [f] DCM was added as co-solvent. [g] Reaction was not initiated at lower concentration and rt. [h] Reaction was done at 40 °C

Development of one pot protocol for synthesis of 1a, 1b and 1c

After standardising the stepwise protocol for syntheses of **1a-1c** from **2b/2c**, a 3-step sequential one-pot procedure for synthesis of the same was envisioned. This involves deoxygenation at the *C-6* position, followed by acid catalyzed tetrahydropyranylation at *O-3*, and finally debenzoylation under Zémplen condition[15a] at *O-4*. Accordingly, compound **2b**[15b] was converted to **1a/1c** in 78% and 75% yields in one-pot, respectively (Scheme 1).

However, the yield was considerably lowered (<30%) when the protocol was scaled up (~3 fold) in case of **1a**. TLC analysis indicated that the first two steps responded well even on up scaling the protocol, but the overall yield was getting lowered possibly at the third step due to concomitant partial deprotection of the phthalimido group during the debenzoylation step. To address this problem, the conditions of the debenzoylation had to be optimised. Despite our efforts to address this problem with variation in reagent concentration, reaction temperature and time, the yield could not be improved upon scale up. The next option was to change the protection profile of the pendant amine at *C-2* position.



Scheme 1 One pot synthesis of compounds **1a**, **1b**, and **1c**. Reaction conditions: (a) DTBP, TIPST, octane, reflux; (b) pTSA, DHP, DCM, rt; (c) NaOMe 0.08 M, DCM-MeOH, rt; (d) TsNCO, DCM, rt.

This issue was, however, not observed with the *N*-Tosylcarbamoyl group (Table 2, entry 6) where the yield of **1c** was not compromised upon scale up.

The phthalimide protecting group at the *C-2* position is a participating group which leads to 1,2-*trans* glycosides. Since many bacterial rare sugar derivatives found in Nature bear 1,2-*cis* glycosidic linkages, a non-participating group has to be introduced at *C-2* position. Accordingly, the amino group at *C-2* position of D-glucosamine was converted to its corresponding azide,[16a] and then the resulting product was transformed to its corresponding 4,6-*O*-benzylidene derivative **2c**.[16b] On this occasion the one-pot three-step protocol (Scheme 1) led to the intermediate **1b** in fairly high yield of 72% even when the reaction was scaled up (~3 fold).

Synthesis of Rare sugar derivatives via triflate displacement

We next attempted the synthesis of the various rare sugar derivatives via triflate mediated inversion at *C-4* to reach AAT, D-FucNAc and DATDG equivalents**.** Accordingly, compound **1a** was converted to its corresponding triflate derivative by treatment with triflic anhydride and pyridine. The triflate so obtained was then displaced by different nucleophiles like acetate, azide and phthalimidate. However, similar attempts with **1c** (Table 2, entry 6) led to complex mixtures from which desired products could not be obtained. The triflate mediated displacements were excellent in terms of yield for compounds **5** (90%) and **10** (92%) where tetrabutylammonium acetate (TBAOAc) was the nucleophile. Fairly high yields were obtained for compounds **6** (73%)**, 7** (73%), **8** (78%), and **9** (80%) using azide and phthalimide as nucleophiles. (Scheme 3) The reactions could all be carried out under ambient conditions.

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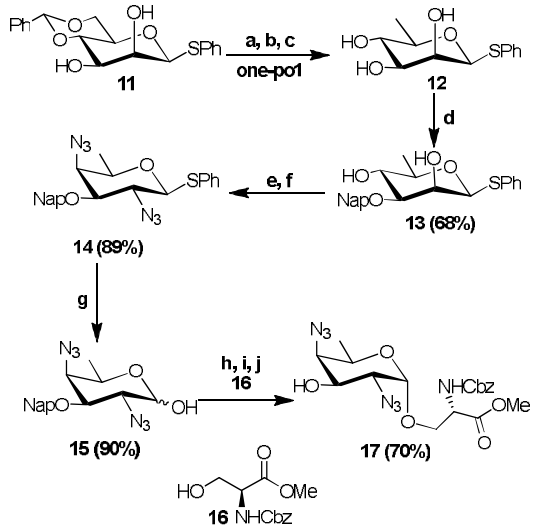
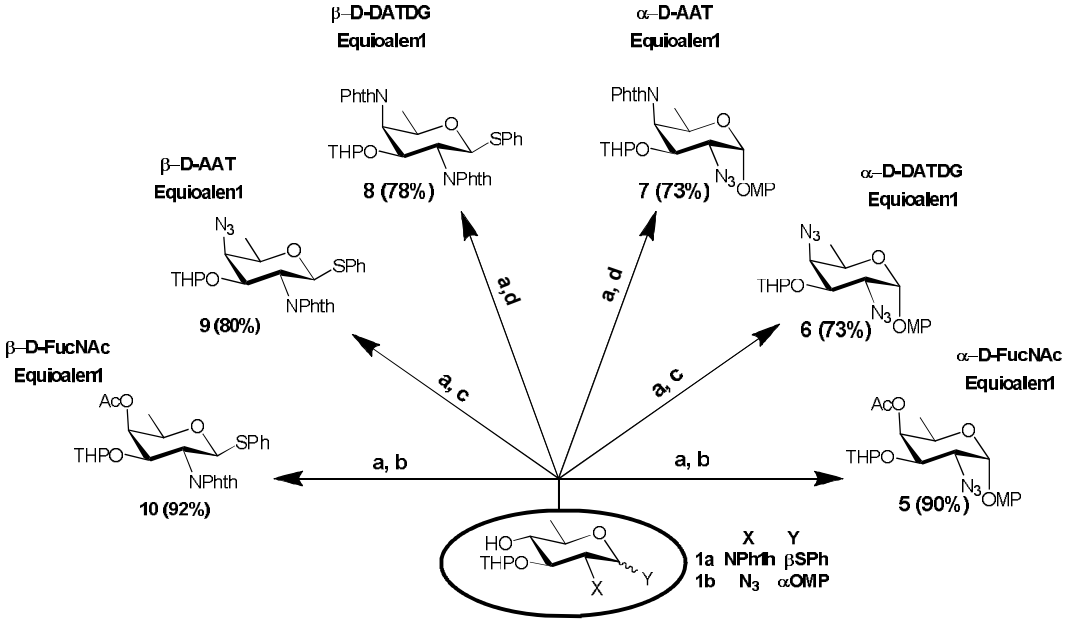
In a different approach, a DATDG-thioglycoside derivative was synthesized starting from D-mannose and subsequently glycosylated with the methyl ester L-serine. We began with the known D-mannose based 4,6-*O*-benzylidene derivative **11**[17] which was further elaborated to the 2,3,4-triol derivative **12**[7c] in one-pot over 3 steps. The steps include benzoyl protection at *O-2* and *O-3*,[18] followed by deoxygenation, and debenzoylation. Finally, selective introduction of the naphthylmethyl group at the *O-3* with Bu_2SnO in toluene generated **13** with an overall 68% yield over 4 steps. The diol intermediate **13** was then converted to the DATDG-thioglycoside derivative **14** via triflate mediated double parallel inversion[7c] using sodium azide as the nucleophile in 89% yield. The thioglycoside **14** was further hydrolyzed to its corresponding hemiacetal[19] **15** in 90% yield. Compound **15** was then directly converted to its corresponding trichloroacetimidate which was subsequently glycosylated with the serine derivative **16** in the presence of TMSOTf in THF after which deprotection of the naphthylmethyl group yielded the amino ester glycoside derivative **17** in 70% yield over three steps (Scheme 2). It is to be noted that **17** can be utilised in the total synthesis of the trisaccharide unit associated with the pilin of *N. meningitidis.*[19]



Scheme 2 Synthesis of Serine linked DATDG derivative. Reaction Conditions: (a)BzCl, Pyridine; (b) DTBP, TIPST, octane, reflux, 2h; (c) NaOMe 0.1 M, MeOH, rt, 12h; (d) Bu_2SnO, Toluene, reflux, 4h, 2-Bromomethylnaphthalene, CsF, DMF, rt, 12h; (e) Pyridine., Tf_2O, DCM, RT, 4h; (f) NaN_3, DMF, rt, 12h; (g) NBS, THF-H_2O, rt, 1h; (h) CCl_3CN, DBU, DCM, rt; (i) 16, TMSOTf, THF, -78 °C, 2h; (j) DDQ, DCM-H_2O (19:1), rt, 2h.



Scheme 3 Diversity oriented synthesis of rare sugar derivatives. Reaction conditions: (a) Pyridine, DCM, Tf_2O, rt; (b) TBAOAc, DMF, rt; (c) NaN_3, DMF, rt; (d) PhthNK, DMF, rt.

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Conclusions

In short an efficient protocol has been described whereby certain routinely prepared D-glucosamine or D-mannose derived compounds can be converted into various bacterial rare sugar derivatives in a target oriented manner; these derivatives are pertinent to the total synthesis of cell surface polysaccharides present in a variety of pathogenic bacterial strains. The synthesis of bacterial cell surface polysaccharides bearing such rare sugar residues has attracted a lot of attention in recent times [16a,20] because these polysaccharides are implicated in various stages of bacterial pathogenesis. The one-pot protocol used to arrive at the vital intermediates **1a/1b** is operationally simple and only requires solvent removal in the intermediate steps. This method is likely to lend flexibility in obtaining rare sugar derivatives and in turn aids the cause of oligosaccharide synthesis involving such sugar residues.

Experimental

General

For reactions under anhydrous condition, all glassware was stored in the oven and was flame-dried prior to use. All reagents and solvents were commercially available. Reagents were used without further purification, and solvents were distilled prior to use. Dry dichloromethane (DCM) was obtained by distillation over P_2O_5. Dimethylformamide (DMF) was distilled over calcium hydride and methanol (MeOH) was dried over magnesium turnings. Thin layer chromatography (TLC) was done on glass plates coated with silica gel or on Merck silica gel plates (60-F_{254}) to monitor the reactions. Elution was carried out with ethyl acetate/pet.ether (EA/PE) unless specified otherwise. Visualization of spots was accomplished by spraying the chromatograms with 5% ethanolic solution of sulfuric acid followed by charring on a hot-plate. Column chromatography and flash column chromatography were performed using 60-120 and 230-400 mesh silica, respectively. Petroleum ether (PE, 60-80°C) was used for chromatographic purpose. Melting points recorded are uncorrected. NMR spectra were recorded on NMR spectrometers operating at 300 MHz, 500 MHz and 600 MHz for 1H-NMR and at 75 MHz, 125 MHz and 150 MHz for ^{13}C-NMR in $CDCl_3$ / DMSO-d_6. Peak assignments were obtained using ^{1}H -^{1}H COSY, and ^{1}H -^{13}C HSQC experiments for **1a** and **1b**. Mass spectral data were recorded by HRMS (ESI-TOF). Specific rotations were measured on a JASCO (P-1020) digital polarimeter using a cell of 50 mm-path length.

Representative procedure for the synthesis of 3a from 2a.

Compound **2a** (70 mg, 0.13 mmol) was suspended in octane (5 ml) and di-tert-butylperoxide (DTBP) (0.02 ml, 0.13 mmol) and tri-isopropylsilanethiol (TIPST) (3 l, 0.013 mmol) were added, and the reaction mixture was refluxed under argon atmosphere for 2 h. TLC at this point showed the reaction to be complete. The octane was removed under reduced pressure, and the residue was purified by column chromatography (10% EA/PE) to yield the product **3a**.

Phenyl 3-*O*-acetyl-4-*O*-benzoyl-2,6-di-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (3a). White foamy solid (66.4 mg, 94%). $[\alpha]^{28.3}_D$ = +25.48 (c 7.02, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 1.36 (3H, d, *J* = 6.0 Hz, H-6), 1.73 (3H, s, -OAc), 3.92 (1H, m), 4.41 (1H, app. t, *J* = 10.5 Hz), 5.17 (1H, app. t, *J* = 9.5 Hz), 5.79 (1H, d, *J* = 10.5 Hz), 5.95 (1H, t, *J* = 10.0 Hz), 7.27-7.29 (3H, m), 7.41-7.44 (4H, m), 7.56 (1H, t, *J* = 7.5 Hz), 7.74-7.75 (2H, m), 7.86 (2H, s), 7.99 (2H, d, *J* = 8.0 Hz). ^{13}C NMR (125 MHz $CDCl_3$): δ (ppm) 18.0, 20.5, 54.2, 71.6, 74.3, 74.8, 83.0, 123.8, 128.4, 128.7, 129.1, 129.2, 129.9, 131.4, 131.8, 133.2, 133.6, 134.4, 134.5, 165.5, 167.1, 168.1, 170.2. HRMS (ESI-TOF, *m/z*) $[M + Na]^+$ calculated for $C_{29}H_{25}NO_7SNa$ 554.1249 found 554.1234.

Phenyl 4-*O*-benzoyl-2,6-di-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (3b): White foam (110 mg, 92%). $[\alpha]^{28}_D$= +39.44 (*c* 1.10, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.35, (3H, d, *J* = 6.1 Hz, H-6), 2.92 (1H. br s, -OH), 3.85 (1H, m), 4.37 (1H, m), 4.59 (1H, m), 4.98 (1H, m), 5.67 (1H, d, *J* = 10.4 Hz), 7.23-7.26 (3H, m), 7.38-7.42 (4H, m), 7.53 (1H, m), 7.65-7.69 (2H, m), 7.77-7.83 (2H, m), 7.99-8.02 (2H, m). ^{13}C NMR (75 MHz $CDCl_3$) δ (ppm) 18.0, 56.5, 71.2, 74.6, 77.6, 83.4, 123.3, 123.9, 127.9, 128.5, 128.9, 129.3, 129.8, 129.9, 131.5, 132.0, 132.1, 132.4, 133.5, 134.3, 166.6, 167.8, 168.5. HRMS (ESI-TOF, *m/z*) $[M + Na]^+$ calculated for $C_{27}H_{23}NO_6SNa$ 512.1144 found 512.1146.

Phenyl 2-azido-4-*O*-benzoyl-2,6-di-deoxy-1-thio-β-D-glucopyranoside (3c). (Colorless syrup 89%). $[\alpha]^{29}_D$ = +144.42 (c 2.15, $CHCl_3$) ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.25 (3H, d, *J* = 6.2 Hz, H-6), 2.83 (1H, br s), 3.45 (1H, m), 3.79 (s, 3H), 4.20 (1H, m), 4.43 (1H, m), 4.97 (1H, m), 5.43 (d, *J* = 3.4 Hz, 1H), 6.85-6.88 (2H, m), 7.05-7.09 (2H, m), 7.45-7.50 (2H, m), 7.59-7.64 (1H, m), 8.06-8.09 (2H, m). ^{13}C NMR (75 MHz $CDCl_3$) δ (ppm) 17.5, 55.7, 63.5, 66.4, 70.1, 97.6, 114.8, 118.1, 128.6, 129.2, 129.9, 133.6, 150.6, 155.4, 166.7. HRMS (ESI-TOF, *m/z*) $[M + Na]^+$ calculated for $C_{20}H_{21}N_3O_6Na$ 422.1328 found 422.1327.

Phenyl 4-*O*-benzoyl-3-*O*-tert-butyldimethylsilyl--2,6-di-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (3d). Compound **3b** (180 mg, 0.37 mmol) was dissolved in DCM (10 ml) and stirred with 4Å MS at room temperature for 10 mins. The temeperature was lowered to 0 °C and then 2,6-lutidine (0.1 ml, 0.44 mmol) and TBDMSOTf (0.1 ml, 0.74 mmol) were added successively. The reaction mixture was allowed to stir at the same temperature for 4 h and then slowly brought up to room temperature and stirred for another 4 h. TLC at this point showed optimum conversion of starting material to product. The reaction mixture was diluted with DCM (20 ml) and the organic layer was washed with saturated NH_4Cl solution (100 ml). The aqueous layer was extracted with DCM (20 ml x 4) and the combined organic layer was dried over anhydrous Na_2SO_4. The DCM was removed under reduced pressure and the crude residue was purified by column chromatography to give the product **3d.** White foam (140 mg, 63%). $[\alpha]^{25}_D$ = +24.04 (*c* 2.01, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) -0.46

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(3H, s), -0.29 (3H, s), 0.56 (9H, s), 1.29 (3H, d, *J* = 5.9 Hz, H-6), 3.82 (1H, m), 4.39 (1H, m), 4.74 (1H, m), 5.14 (1H, m), 5.61 (1H, d, *J* = 10.7 Hz), 7.25 (1H, m), 7.37-7.48 (5H, m), 7.57 (1H, m), 7.76-7.88 (5H, m), 8.04 (2H, d, *J* = 7.1 Hz). ^{13}C NMR (75 MHz $CDCl_3$) δ (ppm) -4.4, -4.1, 17.5, 18.0, 25.4, 56.8, 71.3, 74.8, 77.3, 83.5, 123.2, 123.7, 126.4, 127.8, 127.9, 128.2, 128.5, 128.8, 128.9, 129.8, 129.9, 131.7, 131.9, 132.3, 133.3, 134.3, 134.4, 165.5, 167.2, 168.7. HRMS (ESI-TOF, *m/z*) $[M + Na]^+$ calculated for $C_{33}H_{37}NO_6SSiNa$ 626.2009 found 626.2016.

Phenyl 4-*O*-benzoyl-3-*O*-(*N*-Tosyl)carbamoyl-2,6-di-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (3e). Compound **3b** (240 mg, 0.49 mmol) was dissolved in DCM (5 ml) and TsNCO (0.24 ml, 1.48 mmol) was added at room temperature. The reaction mixture was allowed stir at room temperature for 4 h. TLC (1:2 EA/PE) at this point indicated completion of the reaction. The reaction mixture was diluted with DCM (20 ml) and the organic layer was washed with water (100 ml). The aqueous layer was extracted thrice with DCM (20 ml). The combined organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (33% EA/PE) to give the desired product **3e**. White foam (320 mg, 95%). $[\alpha]^{27.4}_D$ = +14.60 (c 1.42, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.30 (3H, d, *J* = 6.1 Hz, H-6), 2.28 (3H, s, -Me), 3.87 (1H, m), 4.35 (1H, m), 5.05 (1H, m), 5.71 (1H, d, *J* = 10.5 Hz), 5.79 (1H, m), 6.88 (2H, d, *J* = 7.9 Hz), 7.25-7.31 (3H, m), 7.37-7.42 (4H, m), 7.51-7.58 (3H, m), 7.73-7.88 (6H, m), 8.27 (1H, m). ^{13}C NMR (75 MHz $CDCl_3$) δ (ppm) 17.8, 21.7, 53.9, 73.8, 73.9, 74.6, 83.1, 123.7, 123.9, 126.5, 127.7, 128.3, 128.5, 128.8, 128.9, 129.2, 129.7, 129.8, 131.1, 131.3, 133.0, 133.4, 134.2, 134.3, 135.1, 143.4, 144.3, 149.6, 165.5, 167.1, 167.9. HRMS (ESI-TOF, *m/z*) $[M + Na]^+$ calculated for $C_{35}H_{20}N_2O_9S_2Na$ 686.1393 found 686.1389.

Representative one-pot protocol for the synthesis of 1a from 2b. Compound **2b** (355 mg, 0.7 mmol) was suspended in octane (15 ml), and DTBP (0.14 ml, 0.7 mmol) and TIPST (0.02 ml, 0.08 mmol) were added. The reaction mixture was refluxed for 2 h under argon atmosphere. TLC at this point showed the reaction to be complete. The solvent was removed under reduced pressure. The crude residue was dissolved in DCM (6 ml), and DHP (0.08ml, 0.09 mmol) was added. The temperature was lowered to 0 °C, and pTSA (14 mg, 7 mol) was added. The temperature was then raised to room temperature, and the reaction mixture was stirred for 2 h. TLC at this point showed completion of the second step. The solvent was removed under reduced pressure. The crude residue was dissolved in methanol (5 ml), and NaOMe/MeOH solution (1 ml, 1M) was added followed by DCM (2 ml). The reaction was carried on for 4 h at which point the optimum conversion of starting materials to product was observed. The reaction mixture was quenched with DOWEX 50W resin and subsequently filtered under suction. The filtrate was evaporated to dryness under reduced pressure and the crude residue was co-evaporated with toluene to ensure dryness. The dry mass was purified by flash column chromatography (32% EA/PE) to give the product **1a**. The product was further crystallized from DCM/PE.

Phenyl 2, 6-di-deoxy-2-phthalimido-3-*O*-tetrahydropyranyl-1-thio-β-D-glucopyranoside (1a). White needle shaped crystals (265 mg, 78%). Mp 138 °C. $[\alpha]^{29}_D$ = +73.46 (c 0.84, CH_3CN) ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 0.86 (1H, m, *H*-THP), 1.10-1.23 (3H, m, *H*-THP), 1.27 (3H, d, *J* = 5.9 Hz, H-6), 1.49-1.61 (2H, m, *H*-THP), 2.83 (2H, m, -OC*H*$_2$-THP), 3.12 (1H, m, H-4), 3.50 (1H, m, H-5), 3.99 (1H, m, H-2), 4.17 (1H, m, H-3), 4.47 (1H, m, O*H*-4), 5.49 (1H, m, *H*-1-THP), 5.59 (1H, d, *J* = 10.2 Hz, H-1), 7.28-7.32 (5H, m, arom.-*H*), 7.86-7.92 (4H, m, arom.-*H*). ^{13}C NMR (75 MHz DMSO-d_6) δ (ppm) 18.4 (C-6), 20.6 (THP), 25.0 (THP), 31.0 (THP), 55.2 (C-2), 63.6 (5-OC*H*$_2$-THP), 75.9 (C-4), 76.8 (C-5), 79.9 (C-3), 82.9 (C-1), 102.1(C-1 THP), 123.2 (arom.-C), 123.7, 127.8, 129.6, 130.9, 131.7, 131.9, 133.2, 135.0, 167.8 (-CO- NPhth), 168.5 (-CO- NPhth). HRMS (ESI-TOF, *m/z*) $[M + Na]^+$ calculated for $C_{25}H_{27}NO_6SNa$ 492.1457 found 492.1456.

4'-Methoxyphenyl 2-azido -2, 6-di-deoxy -3-*O*-tetrahydropyranyl-α-D-glucopyranoside (1b). White crystals (683 mg, 72%). Mp 124 °C. $[\alpha]^{29}_D$ = +111.58 (c 1.03, CH_3CN). ^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm) 1.14 (3H, d, *J* = 6.3 Hz, H-6), 1.49-1.57 (4H, m, H-THP), 1.70-1.75 (2H, m, H-THP), 3.14 (1H, m, H-4), 3.34 (1H, m, H-2), 3.51 (1H, m, -OC*H*$_2$-THP), 3.71 (4H, s, -OMe, H-5), 3.97 (1H, m, -OC*H*$_2$-THP), 4.02 (1H, m, H-3), 5.14 (1H, s, H-1-THP), 5.47 (2H, s, OH-4, H-1), 6.89 (2H, d, *J* = 8.4 Hz, arom. H-OMP), 7.00 (2H, d, *J* = 7.8 Hz, arom. H-OMP). ^{13}C NMR (150 MHz DMSO-d_6) δ (ppm) 17.9 (C-6), 19.6 (C-THP), 25.5 (C-THP), 30.8 (C-THP), 55.8 (-OMe), 61.8 (C-2), 61.9 (OCH2-THP), 68.9 (C-5), 75.4 (C-3), 76.8 (C-4), 97.9 (C-1), 99.5 (C-1 THP), 115.2 (arom. C-OMP), 118.5 (arom. C-OMP), 150.5 (arom. C-OMP), 155.2 (arom. C-OMP). HRMS (ESI-TOF, *m/z*) $[M + Na]^+$ calculated for $C_{18}H_{25}N_3O_6Na$ 402.1641 found 402.1638.

Phenyl 3-*O*-(*N*-Tosyl)carbamoyl-2,6-di-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (1c). Compound **3e** (300 mg, 0.44 mmol) was dissolved in NaOMe/MeOH (0.1M, 6ml) solution at room temperature. The reaction mixture was allowed to stir overnight at room temperature. TLC (1:2 EA/PE) at this point indicated completion of the reaction. The reaction mixture was neutralised with DOWEX 50W resin and then filtered under suction. The filtrate was concentrated under reduced pressure and the crude residue was purified by column chromatography (EA) to give the desired product **1c**. White foam (220 mg, 87%). $[\alpha]^{28}$D = 39.29 (c 1.54, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.36 (3H, d, J = 6.0 Hz, H-6), 2.35 (3H, s, Me), 3.32 (1H, m), 3.60 (1H, m), 4.20 (1H, m), 5.46 (1H, m), 5.63 (1H, d, *J* = 10.5 Hz), 7.06-7.36 (7H, m), 7.65-7.75 (6H, m). ^{13}C NMR (75 MHz $CDCl_3$) δ (ppm) 17.9, 21.7, 53.8, 74.3, 76.2, 82.9, 123.7, 127.9, 128.0, 128.9, 129.4, 131.1, 131.4, 131.9, 132.4, 134.0, 134.2, 135.3, 144.5, 151.1, 167.3, 167.9. HRMS (ESI-TOF, m/z) $[M + Na]^+$ calculated for $C_{28}H_{26}NO_8S_2Na$ 582.1131 found 582.1129.

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One-pot protocol for the synthesis of 1c from 2b. Compound **2b** (1.0 g, 2.06 mmol) was suspended in n-Octane (50 ml) along with DTBP (0.38 ml, 2.06 mmol) and TIPST (0.05 ml, 0.2 mmol). The reaction mixture was refluxed for 2 h. The solvent was removed under the reduced pressure and the residue was co-evaporated twice with Toluene (10 ml). The dried residue was dissolved in DCM (15 ml) and TsNCO (0.9 ml, 6.1 mmol) was added. The reaction mixture was allowed to stir at room temperature for 4 h. The DCM was removed under reduced pressure and the residue was again co-evaporated twice with Toluene (10 ml). The dried residue was next dissolved in NaOMe/ MeOH (0.1M, 20 ml). The reaction mixture was allowed to stir overnight at room temperature. The reaction mixture was neutralised with DOWEX 50W resin and then filtered under suction. The filtrate was concentrated under reduced pressure and the crude residue was purified by column chromatography (EA) to give the desired product **1c**. White foam (893 mg, 75%). NMR and other characterisation data were found to be in agreement with that obtained for the same compound synthesized via step wise protocol.

Representative procedure for triflate mediated displacement for the synthesis of compound 5 from 1b. Compound **1b** (40 mg, 0.1 mmol) was dissolved in DCM (5 ml) and pyridine (0.02 ml, 0.2 mmol). The temperature was lowered to 0 °C, triflic anhydride (0.05 ml, 0.3 mmol) was added, and the reaction mixture was allowed to attain room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of the reaction (monitored by TLC), the mixture was diluted with DCM (10 ml), and the solution was washed with water (50 ml). The organic layer was dried over Na_2SO_4, and then the solvent was evaporated under reduced pressure. The crude residue was co-evaporated with dry toluene (5 ml), and the dried residue was dissolved in DMF (5 ml). Tetrabutylammonium Acetate (TBAOAc) (49 mg, 0.16 mmol) was added, and the reaction mixture was stirred rigorously for 12 h at room temperature. After the completion of the reaction (monitored by TLC) the solvent was removed under reduced pressure, and the crude residue was dissolved in DCM (15 ml). The organic layer was washed with water (50 ml) and collected. The aqueous layer was extracted thrice with DCM (10 ml) and the combined organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (5% EA/PE) to give the desired product **5**.

4'-Methoxyphenyl 4-*O*-acetyl 2- azido- 2, 6- di-deoxy- 3- *O*- tetrahydropyranyl - α- D- galactopyranoside (5). White foam (40 mg, 90%). $[\alpha]^{29.2}_D$ = +122.75 (c 1.23, CH_3CN). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 0.99 (3H , d, *J* = 6.2 Hz, H-6), 1.21-1.70 (6H, m), 2.09 (3H, s), 3.55 (1H, br s), 3.64-3.70 (4H, m), 3.87 (1H, m), 4.20 (1H, m), 4.36 (1H, m), 4.83 (1H, s), 5.35 (1H, s), 5.55 (1H, d, *J* = 3.2 Hz), 6.88 (2H, d, *J* = 8.9 Hz), 6.98 (2H, d, *J* = 8.9 Hz). ^{13}C NMR (75 MHz DMSO-d_6) δ (ppm) 16.3, 19.0, 20.9, 25.4, 30.1, 55.8, 58.8, 61.6, 65.6, 69.4, 69.8, 94.7, 97.9, 115.2, 118.8, 150.5, 155.3, 170.7. HRMS (ESI-TOF, *m/z*) [M + Na]$^+$ calculated for $C_{20}H_{27}N_3O_7Na$ 444.1747 found 444.1749.

4'-Methoxyphenyl 2, 4- di- azido- 3- *O*- tetrahydropyranyl- 2, 4, 6- tri-deoxy- α- D- galactopyranoside (6). Colorless oil (77.3 mg, 73%). $[\alpha]^{27.7}_D$ = +85.03 (c 3.48, CH_3CN). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 1.11 (3H, d, *J* = 6.1 Hz, H-6), 1.52 (4H, m), 1.69-1.77 (2H, m), 3.57 (1H, m), 3.68-3.75 (4H, m), 3.92 (1H, m), 4.10 (1H, m), 4.41-4.44 (2H, m), 5.06 (1H, s), 5.48 (1H, d, *J* = 3.2 Hz), 6.85 (2H, d, *J* = 8.9 Hz), 6.96 (2H, d, *J* = 8.8 Hz). ^{13}C NMR (75 MHz DMSO-d_6) δ (ppm) 17.6, 18.9, 25.3, 29.7, 55.8, 58.7, 61.6, 62.3, 65.5, 71.8, 94.5, 97.8, 115.1, 118.8, 150.4, 155.3. HRMS (ESI-TOF, *m/z*) [M + Na]$^+$ calculated for $C_{18}H_{24}N_6O_5Na$ 427.1706 found 427.1705.

4'-Methoxyphenyl 2- azido- 4- phthalimido- 3-*O*- tetrahydropyranyl- 2, 4, 6- tri-deoxy- α- D- galactopyranoside (7). Yellowish oil. (89 mg, 73%). $[\alpha]^{25}_D$ = +113.67 (c 1.17, CH_3CN). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 0.91 (3H, d, *J*= 6.2 Hz, H-6), 1.07-1.24 (2H, m), 1.35-1.41 (4H, m), 3.54 (1H, m), 3.70 (3H, s), 3.86 (1H, m), 4.25 (1H, m), 4.44 (1H, m), 4.63 (1H, m), 4.70 (1H, m), 4.99 (1H, m), 5.72 (1H, d, *J*= 3.5 Hz), 6.89 (2H, d, *J*= 8.9 Hz), 7.04 (2H, d, *J*= 8.9 Hz), 7.92 (m, 4H). ^{13}C NMR (75 MHz DMSO-d_6) δ (ppm) 16.8, 18.9, 25.2, 30.4, 51.5, 55.8, 59.5, 61.7, 64.5, 69.4, 95.1, 98.3, 115.2, 118.7, 123.9, 131.4, 135.6, 150.6, 155.3, 168.4, 169.7. HRMS (ESI-TOF, *m/z*) [M + Na]$^+$ calculated for $C_{26}H_{28}N_4O_7Na$ 531.1856 found 531.1847.

Phenyl 2,4- di- phthalimido-3-*O*-tetrahydropyranyl-2, 4, 6- tri-deoxy- 1-thio-β-D-galactopyranoside (8). Colorless viscous gel (48 mg, 78%). $[\alpha]^{25}_D$ = +44.67 (c 1.04, CH_3CN). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 0.94 (1H, m), 1.13-1.23 (4H, m), 1.29-1.34 (4H, m), 3.01 (1H, m), 3.77-3.82 (2H, m), 4.36-4.46 (2H, m), 4.62 (1H, s), 4.94 (1H, d, *J* = 3.2 Hz), 5.61 (1H, d, *J* = 10.2 Hz), 7.19-7.33 (7H, m), 7.81-7.92 (6H, m). ^{13}C NMR (75 MHz DMSO-d_6) δ (ppm) 17.5, 19.5, 25.2, 30.7, 51.0, 61.9, 67.5, 74.4, 75.1, 83.2, 96.0, 123.4, 123.8, 127.5, 129.5, 130.5, 131.4, 131.7, 133.8, 135.2, 135.2, 167.9, 168.5. HRMS (ESI-TOF, *m/z*) [M + Na]$^+$ calculated for $C_{33}H_{30}N_2O_7SNa$ 621.1671 found 621.1678.

Phenyl 4- azido- 2- phthalimido- 3- *O*- tetrahydropyranyl- 2,4,6- tri-deoxy- 1- thio- β- D-galactopyranoside (9). Colorless syrup (110 mg, 80%). $[\alpha]^{29.3}_D$ = +64.46 (c 0.71, CH_3CN). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 0.93 (1H, m), 1.15-1.32 (6H, m), 1.44-1.56 (2H, m), 2.87-3.02 (2H, m), 3.94 (1H, m), 4.28-4.35 (2H, m), 4.69-4.73 (2H, m), 5.58 (1H, d, *J*= 10.5 Hz), 7.18-7.32 (5H, m), 7.84-7.94 (4H, m). ^{13}C NMR (75 MHz DMSO-d_6) δ (ppm) 17.6, 18.9, 24.4, 29.9, 50.9, 61.9, 63.2, 72.6, 74.7, 82.5, 97.3, 122.9, 123.3, 127.2, 129.0, 130.4, 130.8, 131.1, 132.5, 134.7, 134.7, 167.2, 167.8. HRMS (ESI-TOF, *m/z*) [M + Na]$^+$ calculated for $C_{25}H_{26}N_4O_5SNa$ 517.1522 found 517.1525.

Phenyl 4- *O*- acetyl- 2- phthalimido-3- *O*- tetrahydropyranyl-2, 4, 6- tri-deoxy- 1-thio-β-D-galactopyranoside (10). Colorless oil (93.7

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mg, 92%). $[\alpha]^{29}_{D}$ = +47.29 (c 3.07, CH_3CN). ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 0.89 (1H, m), 1.11-1.13 (4H, m), 1.19-1.39 (4H, m), 2.11 (3H, s), 2.93-2.97 (2H, m), 4.03 (1H, m), 4.29 (1H, m), 4.57-4.64 (2H, m), 5.33 (1H, m), 5.65 (1H, d, *J* = 10.6 Hz), 7.22-7.35 (5H, m), 7.84-7.92 (4H, m). ^{13}C NMR (75 MHz DMSO-d_6) δ (ppm) 16.9, 19.4, 21.0, 25.0, 30.4, 51.5, 62.2, 70.0, 72.4, 73.2, 83.0, 96.9, 123.5, 123.9, 127.8, 129.5, 130.9, 131.2, 131.6, 133.1, 135.3, 135.4, 167.7, 168.3, 170.6. HRMS (ESI-TOF, *m/z*) [M + Na]$^+$ calculated for $C_{27}H_{29}NO_7SNa$ 534.1562 found 534.1565.

One-pot protocol on the D-Mannose based scaffold 11.

Phenyl 3- *O*- (2'-methyl)naphthyl- 1- thio- β- D-rhamnopyranoside (13). Compound **11** (960 mg, 2.67 mmol) was dissolved in DCM (20 ml) and pyridine (4 ml). The reaction mixture was cooled to 0 °C, and benzoyl chloride (0.68 ml, 5.86 mmol) was added dropwise. The reaction vessel was brought to room temperature and stirred for 12 h. After completion of the reaction (monitored by TLC), the solvent was removed under reduced pressure, and the residue was co-evaporated thrice with toluene (10 ml) to ensure removal of pyridine. The crude residue was next suspended in dry octane (40 ml). DTBP (0.50 ml, 2.7 mmol) and TIPST (0.06 ml, 0.27 mmol) were added and then the reaction mixture was refluxed for 1.5 h. After completion of the reaction (monitored by TLC), the solvent was removed under reduced pressure, and the residue was co-evaporated with toluene (10 ml). The residue was next dissolved in methanol (18 ml) and NaOMe/MeOH 1M (2 ml) was added dropwise at 0°C. The reaction vessel was brought to room temperature and stirred for 14 h. After completion of the reaction (monitored by TLC), the reaction mixture was neutralized with Dowex 50W resin. The resin was filtered out, and the filtrate was collected. The solvent was evaporated under reduced pressure to give the product **12**.[7c] A part of the crude residue was purified by column chromatography (EA) for characterization by NMR. The remaining bulk of the material was carried forward to the next step without further purification. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 1.17 (3H, d, *J* = 5.4 Hz, H-6), 3.17-3.22 (2H, m), 3.83 (1H, m), 4.77-4.85 (2H, m), 4.98-5.01 (2H, m), 7.19 (1H, m), 7.27-7.37 (4H, m). ^{13}C NMR (75 MHz DMSO-d_6) δ (ppm) 18.1, 71.6, 72.4, 73.9, 75.9, 86.0, 125.9, 128.3, 128.9, 136.5. Compound **12** (0.67 g, 2.6 mmol) was suspended in toluene (35 ml) and dibutyl tin oxide (0.67 g, 2.7 mmol) was added. The reaction mixture was refluxed for 4 h and then cooled to room temperature. The solvent was next removed under reduced pressure, and DMF (30 ml) was added. CsF (0.8 g, 5.3 mmol) and 2-bromomethyl naphthalene (0.68 g, 2.9 mmol) were added. The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction (monitored by TLC), the solvent was removed under reduced pressure. The crude residue was dissolved in DCM (30 ml) and washed with brine solution (250 ml). The aqueous layer was extracted thrice with DCM (40 ml) and the combined organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography (30% EA/PE) to give the product **13** (0.55 g, 68%) over 4 steps. $[\alpha]^{27.8}_{D}$ = +89.22 (c 4.46, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.31 (3H, d, *J* = 6.2 Hz, H-6), 3.67-3.70 (2H, m), 4.16 (1H, m), 4.30 (1H, s), 4.77 (1H, d, *J* = 11.5 Hz), 4.89 (1H, d, *J* = 11.5 Hz), 5.54 (1H, s), 7.28 (2H, m), 7.44 (2H, d, *J* = 6.7 Hz), 7.48-7.53 (4H, m), 7.83-7.89 (4H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 17.6, 69.2, 69.5, 71.9, 72.0, 79.9, 87.4, 125.7, 126.3, 126.5, 127.1, 127.4, 127.8, 127.9, 128.7, 129.1, 131.4, 133.2, 133.3, 134.0, 134.7. HRMS (ESI-TOF, *m/z*) [M + Na]+ calculated for $C_{23}H_{24}O_4SNa$ 419.1293 found 419.1294.

Phenyl 2,4- di- azido- 3- O- (2'-methyl)naphthyl- 2,4,6- tri- deoxy- 1- thio- β- D-galactopyranoside (14). Diol **13** (0.55 g, 1.38 mmol) was dissolved in DCM (25 ml) and pyridine (2 ml). The temperature was lowered to 0 °C and triflic anhydride (1.38 ml, 8.2 mmol) was added, and the reaction mixture was allowed to attain room temperature. The reaction mixture was stirred at room temperature for 4 h. After completion of the reaction (monitored by TLC), the reaction mixture was diluted with DCM (30 ml), and the solution was washed with water (250 ml). The organic layer was dried over Na_2SO_4, and then the solvent was evaporated under reduced presure. The crude residue was co-evaporated with dry toluene (20 ml), and the dried residue was dissolved in DMF (15 ml). NaN_3 (0.45 g, 6.9 mmol) was added, and the reaction mixture was stirred rigorously for 12 h at room temperature. After the completion of the reaction (monitored by TLC) the solvent was removed under reduced pressure, and the crude residue was dissolved in DCM (30 ml). The organic layer was washed with water (250 ml) and collected. The aqueous layer was extracted thrice with DCM (30 ml), and the combined organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (10% EA/PE) to give the product **14**. (0.54 g, 90%). $[\alpha]^{27.7}_{D}$ = +85.73 (c 3.48, CH_3CN). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.32 (3H, d, *J* = 6.2 Hz, H-6), 3.47-3.69 (4H, m), 4.29 (1H, d, *J* = 9.8 Hz), 4.89 (2H, s), 7.31-7.33 (3H, m), 7.49-7.60 (5H, m), 7.83-7.89 (4H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 17.9, 61.2, 62.6, 72.8, 73.4, 81.3, 86.4, 125.8, 126.3, 126.4, 127.1, 127.8, 127.9, 128.3, 128.6, 128.9, 131.4, 133.2, 133.2, 133.3, 134.4. HRMS (ESI-TOF, *m/z*) [M + Na]+ calculated for $C_{23}H_{22}N_6O_2SNa$ 469.1423 found 469.1428.

***N*-(benzyloxycarbonyl)- 2,4- di- azido- 2,4,6- tri- deoxy-α- D-galactopyranosyl- L- serine methyl ester (17).** Compound **14** (0.54 g,1.36 mmol) was dissolved in THF/H_2O (4:1) (20 ml). The temperature was lowered to 0 °C, N-bromosuccinimide (0.65 g, 3.65 mmol) was added, and the reaction mixture was stirred at room temperature for 1 h. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure. The residue was dissolved in DCM (30 ml), and the solution was washed successively with $Na_2S_2O_3$ solution (200 ml) and $NaHCO_3$ solution (200 ml) after which

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the organic layer was collected. The aqueous layers were extracted thrice with DCM (30 ml), and the combined organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (15% EA/PE) to give the product **15** as an anomeric mixture (α:β 1: 1.46). The ratio of the isomers was determined by the ratio of the integration of ^{1}H NMR (300 MHz, $CDCl_3$) signals at δ 5.26 (d, *J*= 3.3 Hz) and δ4.39 (d, *J*= 8.0 Hz) corresponding to the α and β isomer respectively. (0.39 g, 90%). HRMS (ESI-TOF, *m/z*) $[M + Na]^+$ calculated for $C_{17}H_{18}N_6O_3Na$ 377.1338 found 377.1334. This inseparable anomeric mixture was used for the next step. Compound **15** (0.39 g, 1.10 mmol) was dissolved in DCM (10 ml).The temperature was brought down to -5 °C. CCl_3CN (0.25 ml, 2.5 mmol) and DBU (0.04 ml, 0.25 mmol) were added and the reaction mixture was stirred at -5 °C for 2 h. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure. The residue was chromatographed through a short silica bed to give the corresponding trichloroacetimidate (0.43 g, 79%). The trichloroacetimidate was carried forward to the next step. The trichloroacetimidate (0.33g, 0.67 mmol) was dissolved in THF (6 ml) along with the amino acid acceptor **16** (0.25 g, 1.00 mmol) and 3Å MS. The temperature was lowered to -78 °C. TMSOTf (0.06 ml, 0.33 mmol) was added and the reaction mixture was stirred for 2 h. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with Et_3N (0.1 ml, 0.72 mmol) at -78 °C. The solvent was evaporated under reduced pressure. The residue was dissolved in DCM/H_2O (19:1) (20 ml) and DDQ (0.18 g, 0.79 mmol) was added and the reaction mixture was stirred at room temperature for 2 h. After completion of the reaction (monitored by TLC), the reaction mixture was diluted with DCM (30 ml), washed successively with sodium bicarbonate (aq. sat.) (150 ml) and water (100 ml), and the organic layer was collected. The aqueous layers were extracted thrice with DCM (20 ml). The combined organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (30% EA/PE) to give the product **17**. White foam (0.20 g, 70%). $[\alpha]^{28.3}_D$ = +94.51 (*c* 1.83, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.24 (3H, d, *J* = 6.5 Hz, H-6), 3.39 (1H, dd, *J* = 10.5, 3.5 Hz), 3.70 (1H, d, *J* = 3.5 Hz), 3.78 (4H, br s), 3.95-4.01 (3H, m), 4.13 (1H, dd, *J* = 10.5, 3.5 Hz), 4.83 (1H, d, *J* = 3.5 Hz), 5.10-5.15 (2H, m), 5.73 (1H, d, *J* = 7.5 Hz), 7.31-7.37 (5H, m). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 17.2, 53.0, 54.5, 60.4, 66.1, 66.5, 67.4, 68.5, 69.1, 98.9, 128.3, 128.5, 128.7, 136.3, 156.0, 170.3. HRMS (ESI-TOF, *m/z*) $[M + Na]^+$ calculated for $C_{18}H_{23}N_7O_7Na$ 472.1557 found 472.1545. The data was found to be in agreement with that reported in literature.[19]

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