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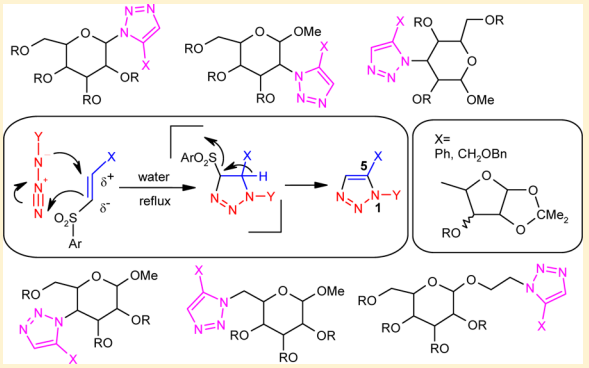
1,5-Disubstituted 1,2,3-Triazolylation at C1, C2, C3, C4, and C6 of Pyranosides: A Metal-Free Route to Triazolylated Monosaccharides and Triazole-Linked Disaccharides

Anirban Kayet and Tanmaya Pathak*

Department of Chemistry, Indian Institute of Technology Kharagpur, Kharagpur 721 302, India

Supporting Information

ABSTRACT: A pair of easily accessible vinyl sulfones derived from styrene epoxide and monotosylated glycerol were reacted with six different azidopyranosides having an azido group at C1, C2, C3, C4, C6, and at the terminal position of an exocylic chain attached to C1. The reaction was performed mostly in water at elevated temperature without any metal catalyst to afford regioselectively 1,5-disubstituted triazolylated pyranosides in high yields. Another set of exocyclic vinyl sulfones prepared from 3-*O*-methylated- and 3-*O*-benzylated glucofuranosides as well as 3-*O*-benzylated allofuranoside were also subjected to 1,3-dipolar cycloaddition reactions with six azidopyranosides under similar reaction conditions to generate a series of 1,5-disubstituted triazole-linked disaccharides. The synthesis of all 1,5-disubstituted triazolylated monosaccharides as well as all 1,5-disubstituted triazole linked disaccharides are reported for the first time. Steric bulk around the azido and vinyl sulfone groups plays a significant role in deciding the outcome of the reactions. This powerful and practical route has the potential to be exploited for the synthesis of complex 1,5-disubstituted 1,2,3-triazolylated carbohydrates.



INTRODUCTION

The copper(I)-catalyzed azide−alkyne cycloaddition (CuAAC)[1] has been extensively used for linking two different organic molecules or building blocks with a 1,2,3-triazolyl ring[2] for accessing new chemical entities and found applications in biology[3] and material science.[4] The unique feature of CuAAC is that, unlike its uncatalyzed counterpart,[5] it yields exclusively 1,4-disubstituted 1,2,3-triazoles (1,4-DTs) at ambient temperature.[1−4] The 1,4-DTs may be considered as a nonclassical bioisostere of the *trans*-amide bonds, whereas 1,5-disubstituted 1,2,3-triazoles (1,5-DTs) and *cis*-amide bonds have striking structural similarities.[2c,i] It is therefore logical to design easy and practical synthetic routes affording 1,5-DTs. Synthetic approaches toward 1,5-DTs using halomagnesium acetylenes[6a,c] or trimethylsilylacetylenes[6b] have achieved limited success because of the requirement of expensive reagent, anhydrous reaction conditions, or simply because a wide variety of starting materials are unavailable. 1,5-DTs were obtained from the triazolium salts generated from 1-(3,4-dimethoxybenzyl)-4-substituted 1,2,3-triazoles by CuAAC strategy, and the 3,4-dimethoxybenzyl group was removed by NH_4NO_3/CAN treatment to afford 1,5-DTs.[6d] Although a ruthenium-catalyzed azide alkyne cycloaddition (RuAAC)[7a,b,d,e] afforded 1,5-DTs in the post-CuAAC era, the reaction conditions are not compatible with the "click" concept[2c,f] and were reportedly more sensitive to solvent and steric demands of the organic azides. An indirect route using Pd-catalyzed arylation of 4,5-unsubstituted *N*-monosubstituted 1,2,3-triazole regioselectively yielded only 1,5-DTs.[7c] $Sm[N(SiMe_3)_2]_3$-catalyzed cycloaddition reactions have recently been introduced for the regioselective synthesis of 1,5-DTs but require extensive experimentation to find general applications.[7f]

The requirement for the copper in CuAAC reaction for 1,4-DT synthesis and ruthenium, palladium, or samarium in 1,5-DT synthesis severely limits the scope of these reactions due to the potential for residual traces of toxic metals. Nevertheless, the widespread applications of 1,4-DTs and the potential usefulness of 1,5-DTs have triggered a demand for easier access to disubstituted 1,2,3-triazoles in general and also encouraged researchers to devise metal-free routes.[8,9] However, the best known metal-free method uses strained cycloalkyne but produces trisubstituted[8,9] and not 1,4- or 1,5-DTs. Among other methods, the ligation of aromatic azides and aromatic alkynes in the presence of a catalytic amount of tetraalkylammonium hydroxide did produce 1,5-DTs but the method has limited applications because alkyl acetylenes failed to react under these conditions.[7e]

Since carbohydrates are widely used as a major source of starting substrates in synthetic chemistry under the popular name "chiral pool"[10] and are increasingly considered as major source of drug molecules,[3f,11] it is no wonder that CuAAC has

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been extensively applied in the preparation of 1,4-DT-functionalized carbohydrate derivatives.[2b,g,3f,12] However, the current status of 1,2,3-triazoles in the literature undoubtedly shows that the worldwide research is overwhelmingly biased toward the synthesis and applications of 1,4-DTs in carbohydrate chemistry. As a result, there are only few scattered reports on the synthesis of 1,5-DT functionalized carbohydrates.[13−15] Therefore, researchers are looking for alternative strategies for generating these important class of 1,5-DT-carbohydrate conjugates.

A large number of pyranosides functionalized with 1,4-DTs and a moderate number of pyranosides with 1,5-DTs at C1 and C6 have been synthesized; some of these 1,5-ditriazolyl mono- and disaccharides,**C1A/C6A** and **C1B/C6B**, respectively, are shown in Figure 1.[13d,14c,15b,c] It appears from the literature that

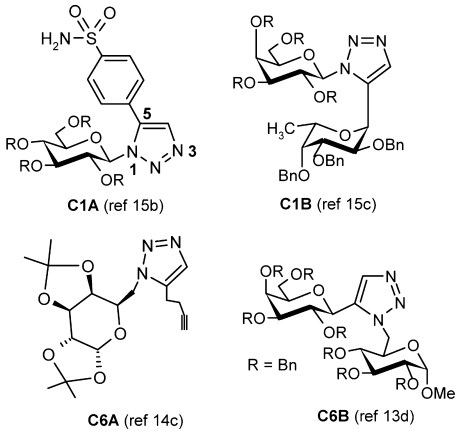


Figure 1. Pyranosides functionalized with 1,5-disubstituted 1,2,3-triazoles at C1 and C6.

for the synthesis of 1,5-DT-modified carbohydrates, heating a mixture of alkyne and azide and separating the required isomer from the mixture of products is still a popular strategy.[13] On the other hand, either $Ph_3P{=}CHCOCH_2R$-type reagents were coupled with azidosugars[14a,b] or allenylmagnesium bromide[14c] was used. There are only a few reports on the use of RuAAC in carbohydrate functionalization.[15a−c] However, as far as our knowledge goes into literature, there are no reports on pyranosides functionalized with 1,5-DTs at C2, C3, or C4, although many of the corresponding 1,4-triazolylated monosaccharides **C2A/C3A/C4A** and 1,4-DT linked disaccharides **C2B/C3B/C4B** have shown interesting biological properties (Figure 2).[16−18] Although the reasons for the nonexistence of these structures are not clear, we presume that none of the methods for the synthesis of 1,5-DT was efficient enough to provide such compounds. For example the disaccharide **C1B** was synthesized[15c] in 60−76% yield at 100 °C under microwave radiation whereas the sulfonamide **C1A** and its analogues were prepared[15b] in 21−63% yields at 100 °C in 18 h and both reactions required inert atmosphere for RuAAC-catalyzed conditions.[15b,c]

RESULTS AND DISCUSSION

For a metal-free strategy, we looked beyond alkynes to establish a regiospecific, general, and practical route to 1,5-DTs. Phenyl vinyl sulfoxide, considered as an acetylene equivalent,[19] reacted with 1-azidoadamantane to afford a monosubstituted 1,2,3-triazole.[20] In this context, our attention was drawn to vinyl

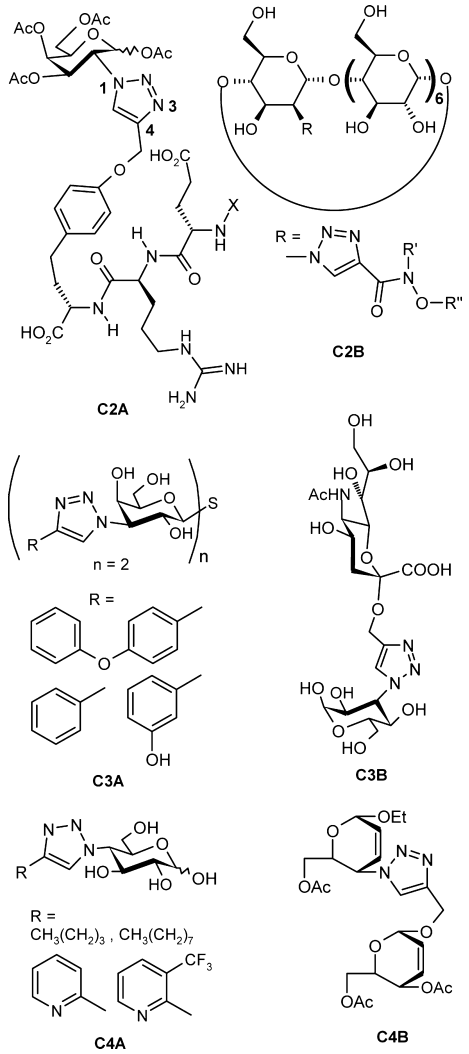
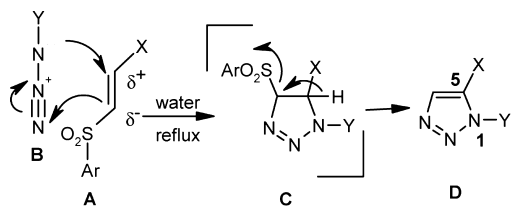


Figure 2. Pyranosides functionalized with 1,4-disubstituted 1,2,3-triazoles at C2, C3, and C4.

sulfones, a class of compounds more easily available than sulfoxides.[21] Although the (*E*)-1-perfluoroalkyl-2-phenylsulfonylethenes (e.g., *trans*-$PhO_2SCH{=}CHCF_3$) reacted with sugar azides to afford exclusively regioisomeric 1,4-DTs,[22a] due to the reported[22b] polarization pattern of the double bonds of nonfluorinated vinyl sulfones **A**, azides **B** are expected to attack the partially positively charged *β*-position to afford cyclic intermediates **C** which would eliminate the sulfinic acid to regioselectively afford 1,5-disubstituted 1,2,3-triazoles **D** (Scheme 1). We established that aryl/alkyl vinyl sulfones and alkyl azides afforded regioselectively 1,5-DTs following this mechanism.[23] This operationally less complicated reaction is

Scheme 1. Plausible Mechanism of 1,5-DT Formation from Organic Azides and Vinyl Sulfones



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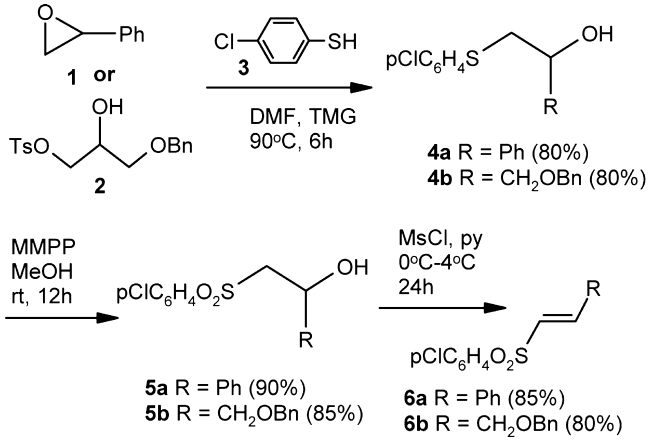
applicable to both phenyl- and alkylvinyl sulfones, avoids the use of any metal salts, and in most of the cases can be carried out using water as the solvent. Since the applications of vinyl sulfone in synthetic chemistry has proliferated during last three decades, it is possible to access a wide range of organic molecules decorated with this functional group from 1, 2-diols, olefins, epoxides, and aldehydes.[21] This is particularly practicable with carbohydrates, and a wide variety of vinyl sulfones have already been synthesized.[24] We therefore planned to study the efficiency of our method[23] by incorporating a 1,5-disubstituted triazole group at all positions of a pyranosyl system. In order to check the utility of our method for the synthesis of 1,5-disubstituted 1,2,3-triazolylated carbohydrates and 1,5-disubstituted 1,2,3-triazole-linked disaccharides, we intended to generate a triazolyl group at the C1, C2, C3, C4, and C6 positions of pyranosides using simple vinyl sulfones **6a** and **6b** (Scheme 2). Thus, either the epoxide **1** or partially

Scheme 2. Synthesis of Aryl-/Alkylvinyl Sulfone



functionalized glycerol **2** was efficiently thiolated with **3** to afford **4a** and **4b**, respectively. Sufides **4a** and **4b** were oxidized to sulfones **5a** and **5b**, respectively. Mesylation followed by elimination of these sulfones afforded the vinyl sulfones **6a** and **6b**. It should be noted that we have selected an aryl vinyl sulfone **6a** and alkyl vinyl sulfone **6b** to establish the general applicability of our strategy in both aromatic and aliphatic systems which is lacking with many of the strategies discussed previously.[7a,b,d,15b,c]

A series of known sugar derived azides **7**,[25e] **9**,[25d] **10**,[25c] **11**,[25b] and a new azidosugar **8** obtained by the benzylation of the corresponding hydroxyazido sugar[25a] (Figure 3) were selected to react with vinyl sulfones **6a** or **6b**. Another sugar

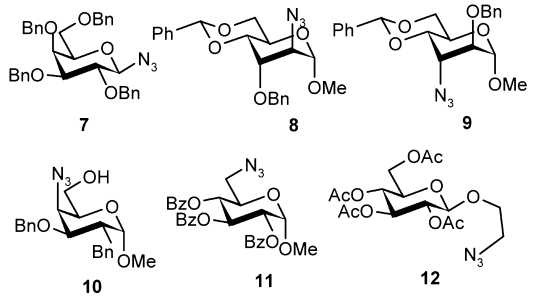
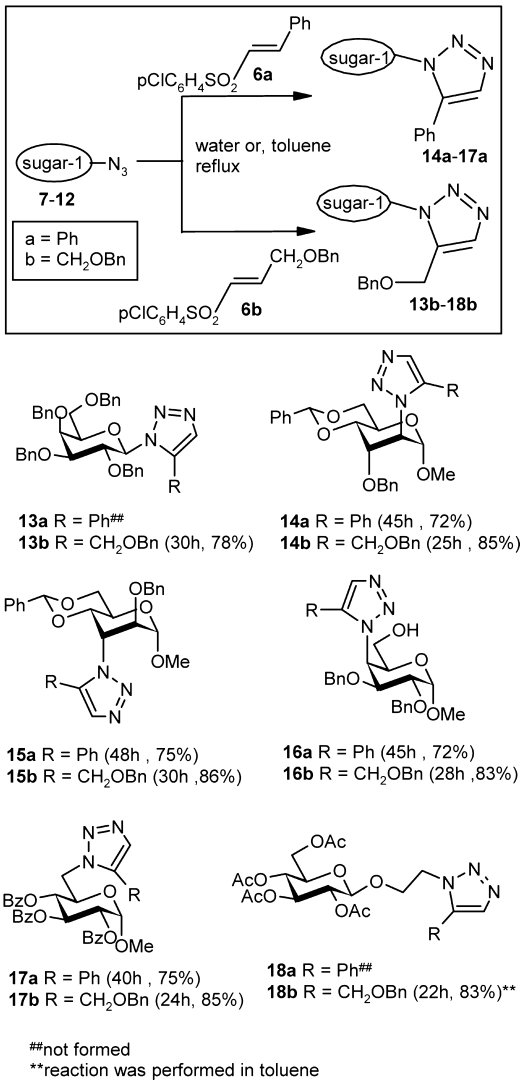


Figure 3. Azidosugars used for the synthesis of 1,5-disubstituted 1,2,3-triazolylated pyranosides.

molecule **12**[2a] carrying an azido group far removed from the sugar moiety was also used in this study to see the effect of steric bulk, if any, on the 1,3-dipolar cycloaddition reactions. Thus, a mixture of **6a** or **6b** and 1.5 equiv of each of the azido pyranosides **7**−**12** were heated under reflux in aqueous media to afford **14a**−**17a** and **13b**−**18b**. Reaction times and yields of the products are shown in Scheme 3. The bulkier arylvinyl

Scheme 3. 1,5-Disubstituted 1,2,3-Triazoles as Linkers of Alkyl/Aryl Groups at C1, C2, C3, C4, and C6 of Monosaccharides



sulfone **6a** reacted with **8**−**11** over a period of 40−48 h to afford 1,5-DTs **14a**−**17a** and did not react with **7** and **12** at all. The alkylvinyl sulfone **6b**, however, underwent triazolylation by reacting with all azidosugars to yield 1,5-DTs **13b**−**18b**. Since the reaction is expected to produce *p*-chlorophenylsulfinic acid, the acid labile benzylidine groups of **8** and **9** were stabilized by addition of 1.5 equiv of $NaHCO_3$ in this reaction mixture. The acetyl protections of **12** were unstable under these reaction conditions, and therefore, the reaction was carried out in toluene (Scheme 3). We were unable to detect any 1,4-isomer from these reactions either during purification (TLC analysis) or in the ^1H NMR spectra of the final products. However, it was necessary to unambiguously establish the structures of

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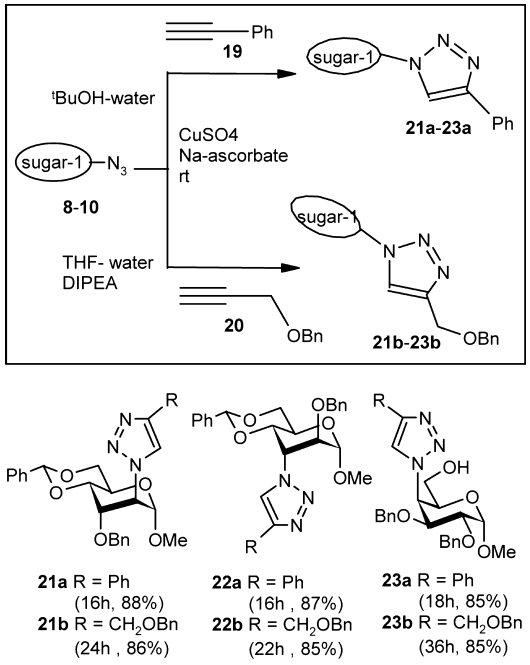
these 1,5-regioisomers. We therefore synthesized the 1,4-regioisomers of some of the compounds **14a**−**17a** and **13b**−**18b** using the well-known CuAAC route.[1] Thus, azidosugars **8**−**10** were reacted with phenylacetylene **19** or benzyl-protected propargyl alcohol[26] **20** under click conditions to obtain aryl series **21a**−**23a** and the alkyl series **21b**−**23b** in high yields (Scheme 4). The reactions of **20** with **8**−**10**

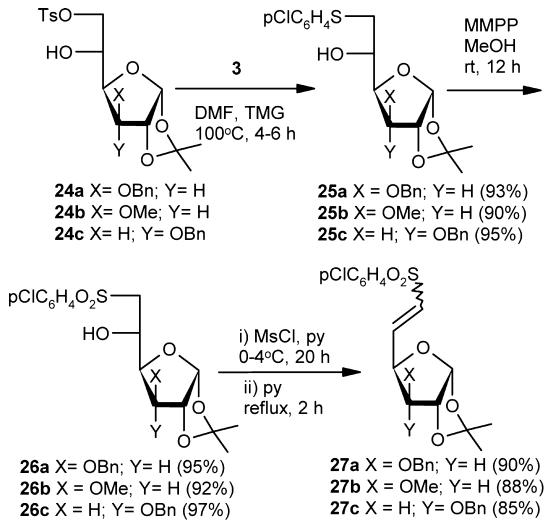
Scheme 4. Synthesis of 1,4-Disubstituted 1,2,3-Triazolylated Monosaccharides Using CuAAC Strategy



required the addition of 1.5 equiv of diisopropylethylamine and a relatively longer reaction period than that of phenylacetylene **19**. A comparison of NMR data of **14a**/**21a**, **14b**/**21b**, **15a**/**22a**, **15b**/**22b**, **16a**/**23a**, and **16b**/**23b** established that our strategy did indeed produce the desired 1,5-DT-functionalized carbohydrates. The selective formation of 1,5-regioisomers **13**−**18** prompted us to extend our strategy for coupling two sugar units for the synthesis of backbone-modified linkers. Since we required vinyl sulfone-modified carbohydrates for the cyclo-addition reactions, we synthesized vinyl sulfone-modified hexofuranosides **27a**−**c**. In all cases, C−S bond formation of the known tosylates **24a**−**c** at elevated temperature followed by oxidation of the sulfides **25a**−**c** to sulfones **26a**−**c** followed by mesylation and elimination of the mesylates from sulfones yielded the desired vinyl sulfones **27a**−**c** in relatively large quantities (Scheme 5).

Mixtures of **27a**, **27b**, or **27c** and 1.5 equiv of each of the azido pyranosides **7**−**12** were heated under reflux in aqueous media (Scheme 6). None of the vinyl sulfone-modified carbohydrates **27a**−**c** reacted with the anomeric azidosugar **7**. Interestingly, the vinyl sulfone **27a** with "up" benzyl protection at C3 reacted only with azidosugars **11** and **12** containing primary azido groups far removed from the sugar ring to afford **31a** and **32a** but did not react with secondary azido groups of azidosugars **7**−**10**. Unreacted starting material **27a** was recovered where reactions did not take place. However, two other vinyl sulfones **27b** and **27c** with smaller "up" methyl protection at C3 and allo-configuration, respectively, reacted with azidosugars **8**−**12** to afford the desired 1,5-disubstituted

Scheme 5. Synthesis of Vinyl Sulfone Modified Hexofuranosides as Building Blocks for Disaccharide Synthesis



triazolyl-linked disaccharides **28b**−**32b** and **28c**−**32c**, respectively. Although the desired disaccharides did form to some extent, the ester protections of azidosugars **11** and **12** were found to be unstable in refluxing aqueous system. Therefore, triazolylations using **11**/**12** and vinyl sulfone-modified **27a**−**c** were carried out in toluene to obtain the disaccharides **31a**−**c** and **32a**−**c**, respectively, in high yields. It should be noted that only during the formation of 1,5-DT linked disaccharide **32b**, its 1,4-regioisomer **32b′** also formed in 30% yield (Scheme 6).

Although 1,4-DT-functionalized carbohydrates **21**−**23** were synthesized (Scheme 4) to unambiguously establish the structures of 1,5-DT-functionalized carbohydrates **13**−**18** (Scheme 3), we also used the ^{13}C NMR data for establishing the structures using reported strategies.[27] Thus, the chemical shift values of C4 and quaternary C5 of 1,5-DTs **13**−**18** ranging between 132.3 and 135.0 ppm and 133.6−141.1 ppm made Δ (δ_{C4}−δ_{C5}) values significantly smaller (ca. −8.7 ppm to +0.3 ppm). The chemical shift values of quaternary C4 and C5 of 1,4-DTs **21**−**23** ranges between 144.4 and 147.7 ppm and 119.4−123.9 ppm, respectively, and provides larger Δ (δ_{C4}−δ_{C5}) values (ca. 20−26 ppm). These comparisons are in line with the proposed strategy[27] for structural analysis to differentiate between 1,4-DTs and 1,5-DTs, and we also looked into the corresponding ^{13}C chemical shifts of disaccharides. Thus, the chemical shift values of C4 and quaternary C5 of disaccharides **28**−**32** ranging between 131.7 and 134.1 ppm and 131.4−136.4 ppm made Δ (δ_{C4}−δ_{C5}) values significantly smaller (ca. −4.5 ppm to +2.3 ppm), confirming that all these compounds contain 1,5-DT moiety. The only 1,4-DT-linked disaccharide **32b′** having C4 at 143.4 ppm and C5 at 124.8 ppm generated a large and positive Δ (δ_{C4}−δ_{C5}) value (18 ppm) as expected.[27]

It appears that azido sugar **7** is the least reactive of all, but it is not clear whether its reactivity may be attributed to steric factors alone because **6a** reacts with other azido sugars **8**−**10** having secondary azido groups. In addition, the failure of the reaction between **6a** and **12** is a surprising observation. However, the "up" OBn group of **27a** does carry a large steric bulk at C3 in the proximity of the vinyl sulfone group and therefore does not react with secondary azido functions (Figure 4). It is quite clear from Figure 4 that the "up" OBn groups of

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Scheme 6. Synthesis of 1,5-Disubstituted 1,2,3-Triazole-Linked Disaccharides

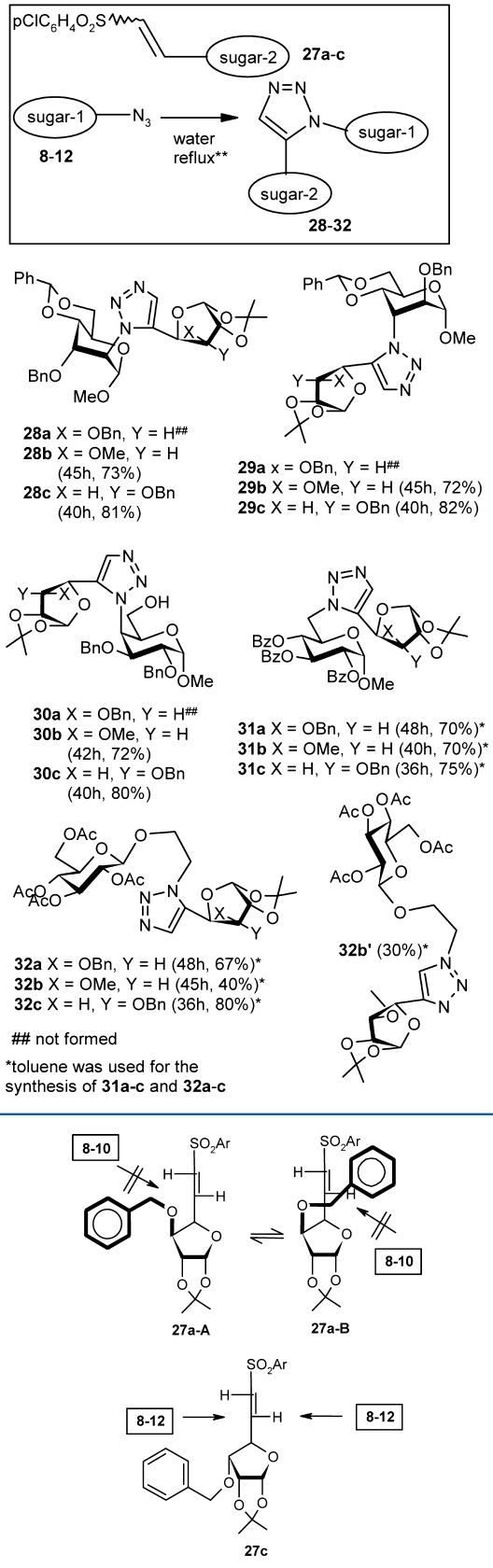

Figure 4. Steric effects of "up" *O*-benzyl and "down" *O*-benzyl groups on the cycloaddition reactions with azidosugars.

27a-A and **27a-B** completely blocks the approach of all secondary azido groups to the vinyl sulfone functionality. The effect of steric interference has been conclusively established by the reactions of **27b** and **27c** with azido sugars **8**–**10** having secondary azido groups. It is obvious that there is no such steric repulsion in the case of **27c** with a "down" OBn group because in this case the vinyl sulfone group has easy access to azidosugars **8**–**12** (Figure 4). However, a critical situation arises in the case of **27b**, which reacted with **12** in the cycloaddition step (Scheme 1) to afford **32b′**, the only 1,4-DT isolated in this study. Whether unreactive nature of **12** toward **6a** or unusual formation of **32b′** from **12** indicate a special structural feature of this azidosugar remains to be established.

CONCLUSION

Thus, in the absence of suitable and general methods for the synthesis of 1,5-DT-functionalized pyranosides we reacted vinyl sulfones derived from styrene epoxide and monotosylated glycerol with six different azidopyranosides to generate 1,5-DTs. A similar strategy efficiently couples the azidosugars with three different vinyl sulfone-modified carbohydrates to afford furanoside–pyranoside dimers. Both approaches gave access to 1,5-disubstituted 1,2,3-triazolylated monosaccharides and disaccharides corresponding to C1, C2, C3, C4, and C6 of pyranosides. Since most of these reactions were carried out in aqueous media[28] in the absence of any metal-based reagents, this less hazardous strategy adds to the arsenals of synthetic chemists interested in carbohydrate-based 1,5-DTs. All 1,5-triazolylated monosaccharides and 1,5-triazole-linked disaccharides reported in this paper are synthesized for the first time. Synthesis of more complex carbohydrate-based 1,5-DTs using our strategy is currently in progress.

EXPERIMENTAL SECTION

Genaral Methods. All reactions were conducted under nitrogen atmosphere. Melting points were determined in open-end-capillary tubes and uncorrected. Carbohydrates and other fine chemicals were obtained from commercial suppliers and were used without purification. Solvents were dried and distilled following the standard procedures. TLC was carried out on precoated silica gel plates, and the spots were visualized with UV light or by charring the plates dipped in 5% H_2SO_4–MeOH solution or in 5% H_2SO_4–vaniline–EtOH solution. Column chromatography was performed on silica gel (230–400 mesh). ^1H and ^{13}C NMR for compounds were recorded at 200/400 MHz instrument using $CDCl_3$ as the solvent. DEPT experiments have been carried out to identify the methylene carbons. Optical rotations were recorded at 589 nm. High-resolution mass spectra (HRMS) were recorded by quadrupole-equipped TOF mass spectrometer.

Compound ***4a***. To a well-stirred solution of the epoxide **1** (2.00 g, 16.66 mmol) in DMF (20 mL) was added 4-chlorothiophenol (3.61 g, 24.99 mmol) and 1,1,3,3-tetramethylguanidine (TMG) (2.50 mL, 19.99 mmol). The mixture was heated at 100 °C with stirring under N_2. After 5 h, the reaction mixture was cooled and poured into an aqueous saturated solution of $NaHCO_3$, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified over silica gel to afford the sulfide **4a** (3.30 g, 80%). Eluent: EtOAc/petroleum ether (1:5). Yellow oil. ^1H NMR (200 MHz, $CDCl_3$): δ 2.99–3.23 (m, 3H), 4.62–4.68 (m, 1H), 7.22–7.27 (m, 9H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 43.8 (CH_2), 71.9, 125.9, 128.1, 128.6, 129.2, 131.3, 132.6, 133.9, 142.1. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{14}H_{14}OSClNa$ found 288.0378, calcd 288.0376.

Compound ***4b***. Following the procedure described for **4a**, over 4 h compound **2** (2.00 g, 5.95 mmol) was converted to the sulfide **4b**

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(1.46 g, 80%). Eluent: EtOAc/petroleum ether (1:4). Yellow jelly. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.75 (d, 1H, J = 4.6 Hz), 2.94−3.14 (m, 2H), 3.46−3.60 (m, 2H), 3.85−3.90 (m, 1H). 4.51 (s, 2H), 7.20−7.38 (m 10H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 37.2 (CH_2), 68.9, 72.4 (CH_2), 73.1 (CH_2), 127.6 (2 × C), 128.3, 128.9, 130.3, 131.8, 134.5, 137.6. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{16}H_{17}O_2SClNa$ found 331.0548, calcd 331.0535.

Compound ***5a***. To a well stirred solution of sulfide **4a** (2.00 g, 8.06 mmol) in dry MeOH (20 mL) was added magnesium bis-(monoperoxyphthalate) hexahydrate (MMPP) (8.00 g, 16.13 mmol), and the mixture was stirred at room temperature under N_2. After 10 h, MeOH was evaporated to dryness under reduced pressure and the residue dissolved in an aqueous saturated solution of $NaHCO_3$. The aqueous part was washed with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure to get a residue. The residue was purified over silica gel to afford sulfone **5a** (2.03 g, 90%). Eluent: EtOAc/petroleum ether (1:3). White solid. Mp: 90−92 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.29 (dd, 1H, J = 2.3 Hz, 14.5 Hz), 3.45−3.57 (m, 1H), 3.65 (d, 1H, J = 2.8 Hz), 5.19−5.26 (m, 1H), 7.21 7.28 (m, 5H). 7.48 (d, 2H, J = 8.4 Hz), 7.82 (d, 2H, J = 8.4 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 63.9 (CH_2), 68.6, 125.7, 128.4, 128.8, 129.6, 129.7, 137.9, 140.7, 140.8. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{14}H_{13}O_3SClNa$ found 319.0150, calcd 319.0172.

Compound ***5b***. Following the procedure described for **5a**, over 12 h the sulfide **4b** (2.00 g, 6.49 mmol) was converted to sulfone **5b** (1.87 g, 85%). Eluent: EtOAc/petroleum ether (3:7). Brownish gum. ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.06 (d, 1H, J = 3.8 Hz), 3.33 (d, 2H, J = 6.0 Hz), 3.51 (d, 2H, J = 5.0 Hz), 4.28−4.35 (m, 1H), 4.45−4.58 (m, 2H), 7.24−7.35 (m, 5H), 7.54 (d, 2H, J = 8.4 Hz), 7.87 (d, 2H, J = 8.4 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 59.7 (CH_2), 65.6, 72.4 (CH_2), 73.6 (CH_2), 127.9, 128.1, 128.6, 129.7 (2 × C), 137.5, 138.0, 140.8. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{16}H_{17}O_4SClNa$ found 363.0453, calcd 363.0434.

Compound ***6a***. To a well-stirred solution of sulfone **5a** (2.00 g, 7.14 mmol) in pyridine (15 mL) was added methanesulfonyl chloride (1.10 mL, 14.28 mmol) in pyridine (5 mL) dropwise at 0 °C under N_2. After completion of the addition, the reaction mixture was kept at +4 °C. After 24 h (TLC), the reaction mixture was poured into an aqueous saturated solution of $NaHCO_3$, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure to get a residue. The residue was dissolved in dry DCM (20 mL), Et_3N (1.5 equivalent) was added, and the mixture was stirred at room temperature. After 1 h, the solvent was evaporated to dryness to get a residue. The residue was purified over silica gel to afford the vinyl sulfone **6a** (1.66 g, 85%). Eluent: EtOAc/petroleum ether (1:4). White solid. Mp: 80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.87 (d, 1H, J = 15.2 Hz), 7.36−7.39 (m, 3H), 7.45−7.49 (m, 4H), 7.67 (d, 1H, J = 15.6 Hz), 7.87 (d, 2H, J = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 126.9, 128.6, 129.1 (2 × C), 129.6, 131.4, 132.1. HRMS [ES$^+$, (M + H)$^+$]: for $C_{14}H_{12}O_2SCl$ found 279.0255, calcd 279.0247.

Compound ***6b***. Following the procedure described for **6a**, over 24 h the sulfone **5b** (2.30 g, 6.76 mmol) was converted to the vinyl sulfone **6b** (1.74 g, 80%). Eluent: EtOAc/petroleum ether (1:4). Brown solid. Mp: 75−76 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.20−4.22 (m, 2H), 4.54 (s, 2H), 6.60−6.70 (m, 1H), 6.96−7.01 (m, 1H), 7.26−7.34 (m, 5H), 7.48−7.52 (m, 2H), 7.79−7.83 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 67.6 (CH_2), 73.0 (CH_2), 127.6, 127.9, 128.4, 129.1, 129.5, 129.8, 137.1, 138.8, 139.9, 143.3. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{16}H_{15}O_3SClNa$ found 345.0339, calcd 345.0328.

Compound ***8***. To a well-stirred solution of the known 2-azido-2-deoxy-4,6-*O*-(phenylmethylene)methyl-α-D-altropyranoside[25a] (2.00 g, 6.51 mmol) in DMF (20 mL) was added NaH (0.47 g, 9.77 mmol) at 0 °C and he mixture stirred for 20 min at the same temperature. Then benzyl bromide (1.32 mL, 11.07 mmol) was added at 0 °C, and after complete addition the reaction mixture was stirred for 3 h at room temperature. After 3 h, the reaction mixture was poured into an aqueous saturated solution of $NaHCO_3$ and extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified over silica gel to afford compound **8** (2.33 g, 90%). Eluent: EtOAc/petroleum ether (1:9). White solid. Mp: 65 °C. $[\alpha]^{25.2}_D$ (+): 5.0 (c 0.3, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.34 (s, 3H), 3.65−3.87 (m, 4H), 4.23−4.41 (m, 2H), 4.59 (s, 1H), 4.67 (d, 1H, J = 12.4 Hz), 4.80 (d, 1H, J = 12.6 Hz), 5.50 (s, 1H), 7.18−7.32 (m, 9H), 7.45−7.49 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.6, 58.4, 61.4, 69.1 (CH_2), 73.0 (CH_2), 73.4, 76.5, 99.2, 102.2, 126.2, 127.6, 128.2 (2 × C), 129.0, 137.6, 138.1. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{21}H_{23}N_3O_5Na$ found 420.1544, calcd 420.1535.

General Procedure for the Synthesis of 1,5-Disubstituted Triazolyl Monosaccharides 13−18. A mixture of a vinyl sulfone (1 equiv) and azidosugar (1.5 equiv) in water (5 mL/mmol) was heated under reflux for 22−48 h to afford 1,5-disubstituted triazolylated monosaccharides. For azidosugars **8** and **9**, $NaHCO_3$ (1.5 equiv) was added to the reaction mixture. For azidosugars **11** and **12**, the reaction was performed in refluxing toluene.

Compound ***14a***. Following the general procedure, over 45 h compound **6a** (0.20 g, 0.73 mmol) was converted to **14a** (0.26 g, 72%). Eluent: EtOAc/petroleum ether (1:3). Yellow gum. $[\alpha]^{25.2}_D$ (+): 72.4 (c 0.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.36 (s, 3H), 3.89−4.02 (m, 2H), 4.36−4.45 (m, 1H), 4.48−4.58 (m, 1H), 4.63 (s, 2H), 4.70 (dd, 1H, J = 3.2 Hz, 9.6 Hz), 4.84 (s, 2H), 5.65 (s, 1H) 7.11−7.49 (m, 17H), 7.69 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.6, 58.3, 60.2, 69.3 (CH_2), 73.2 (CH_2), 73.6, 76.2, 99.5, 102.1, 126.2, 127.6, 127.9, 128.2, 129.0, 129.4, 129.9, 133.0, 137.7, 138.4. HRMS [ES$^+$, (M + H)$^+$]: for $C_{29}H_{30}N_3O_5$ found 500.2168, calcd 500.2185.

Compound ***15a***. Following the general procedure, over 48 h compound **6a** (0.20 g, 0.73 mmol) was converted to **15a** (0.27 g, 75%). Eluent: EtOAc/petroleum ether (1:3). Yellow gum. $[\alpha]^{25.2}_D$ (+): 80.3 (c 0.7, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.37 (s, 3H), 3.69−3.85 (m, 2H), 4.20−4.28 (m, 3H), 4.35−4.42 (m, 1H), 4.72 (d, 1H, J = 1.6 Hz), 5.02−5.20 (m, 2H), 5.56 (s, 1H), 7.02−7.06 (m, 2H), 7.25−7.31 (m, 11H), 7.44−7.47 (m, 3H), 7.65 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.3, 56.0, 60.0, 69.8 (CH_2), 72.9 (CH_2), 74.4, 77.8, 99.8, 102.3, 126.5, 127.5, 127.8, 128.2, 128.3, 128.6, 129.2, 129.7, 132.3, 136.8, 137.3, 139.3. HRMS [ES$^+$, (M + H)$^+$]: for $C_{29}H_{30}N_3O_5$ found 500.2204, calcd 500.2185

Compound ***16a***. Following the general procedure, over 45 h compound **6a** (0.20 g, 0.73 mmol) was converted to **16a** (0.26 g, 72%). Eluent: EtOAc/petroleum ether (1:4). White solid. Mp: 138−140 °C. $[\alpha]^{25.2}_D$ (+): 58.3 (c 0.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.62 (bs, 1H), 3.21−3.37 (m, 5H), 4.14−4.22 (m, 2H), 4.40−4.79 (m, 5H), 4.89−4.97 (m, 2H), 7.01−7.03 (m, 2H), 7.21−7.42 (m, 13H), 7.62 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.6, 57.6, 61.2 (CH_2), 68.7, 73.8 (2 × CH_2), 74.8, 77.2, 99.0, 127.3, 127.6, 127.7, 127.9, 128.2, 128.4, 128.5, 129.0, 129.5, 129.8, 132.4, 138.0, 138.3, 141.1. HRMS [ES$^+$, (M + H)$^+$]: for $C_{29}H_{32}N_3O_5$ found 502.2321, calcd 502.2342.

Compound ***17a***. Following the general procedure, over 40 h compound **6a** (0.20 g, 0.73 mmol) was converted to **17a** (0.34 g, 75%). Eluent: EtOAc/petroleum ether (1:4). Yellowish gum. $[\alpha]^{25.2}_D$ (+): 36.8 (c 0.9, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.12 (s, 3H), 4.56 (d, 2H, J = 6.0 Hz), 4.72−4.83 (m, 1H), 5.11 (d, 1H, J = 3.6 Hz), 5.27 (dd, 1H, J = 3.7 Hz, 10.0 Hz), 5.45 (t, 1H, J = 9.8 Hz), 6.18 (t, 1H, J = 9.8 Hz), 7.23−7.58 (m, 14H), 7.70 (s, 1H), 7.82−7.97 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 48.9 (CH_2), 55.5, 68.8, 70.3, 71.3, 72.0, 96.7, 126.8, 128.4, 128.5, 128.6, 128.7, 129.0, 129.2 (2 × C), 129.7, 130.0, 130.1, 133.0, 133.3, 133.6, 133.9, 139.4, 165.7, 165.9, 166.0. HRMS [ES$^+$, (M + H)$^+$]: for $C_{36}H_{32}N_3O_8$ found 634.2208, calcd 634.2189.

Compound ***13b***. Following the general procedure, over 30 h compound **6b** (0.20 g, 0.62 mmol) was converted to **13b** (0.26 g, 72%). Eluent: EtOAc/petroleum ether (1:3). Brownish yellow gum. $[\alpha]^{26}_D$ (+): 40.4 (c 0.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.49−3.79 (m, 4H), 4.06−4.27 (m, 4H), 4.42 (d, 2H, J = 2.8 Hz), 4.50−4.72 (m, 5H), 4.77 (s, 2H), 4.97−5.03 (m, 1H), 5.69 (d, 1H, J = 9.0 Hz), 6.93−6.98 (m, 2H), 7.16−7.35 (m, 24H), 7.64 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 59.9 (CH_2), 68.3 (CH_2), 72.4 (CH_2), 72.9

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(CH_2), 73.5, 73.8 (CH_2), 75.1 (CH_2), 76.2, 77.1, 83.2, 87.8, 127.7, 127.9, 128.1, 128.3, 128.5 (2 × C), 128.7, 134.7, 135.0, 137.4, 137.7, 137.9, 138.2, 138.6. HRMS [ES^+, $(M + H)^+$]: for $C_{44}H_{46}N_3O_6$ found 712.3403, calcd 712.3387.

Compound ***14b***. Following the general procedure, over 25 h compound **6b** (0.20 g, 0.62 mmol) was converted to **14b** (0.286 g, 85%). Eluent: EtOAc/petroleum ether (1:3). Yellow gum. $[\alpha]^{26}_D$ (+): 70.3 (*c* 0.8, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 3.35 (s, 3H), 3.91 (t, 1H, *J* = 10.4 Hz), 4.06 (bs, 1H), 4.25−4.42 (m, 3H), 4.47 (s, 2H), 4.53−4.64 (m, 1H), 4.70−4.78 (m, 2H), 4.82−4.88 (m, 2H), 5.66 (s, 1H), 7.23−7.36 (m, 13H), 7.47−7.50 (m, 2H), 7.61 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.6, 58.3, 59.4 (CH_2), 60.7, 69.4 (CH_2), 72.9 (CH_2), 73.5 (CH_2), 74.0 (CH_2), 76.3, 99.8, 102.2, 126.4, 127.3, 127.9, 128.1, 128.3, 128.4, 128.8, 129.1, 133.6, 133.9, 136.7, 137.8, 138.3. HRMS [ES^+, $(M + H)^+$]: for $C_{31}H_{34}N_3O_6$ found 544.2435, calcd 544.2448.

Compound ***15b***. Following the general procedure, over 30 h compound **6b** (0.20 g, 0.62 mmol) was converted to **15b** (0.29 g, 86%). Eluent: EtOAc/petroleum ether (1:3). Brownish yellow gum. $[\alpha]^{26}_D$ (+): 46.0 (*c* 0.6, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 3.38 (s, 3H), 3.75 (t, 1H, *J* = 10.2 Hz), 4.04 (s, 1H), 4.25−4.40 (m, 4H), 4.46−4.67 (m, 4H), 4.78 (s, 1H), 4.97−5.16 (m, 2H), 5.52 (s, 1H), 7.24−7.28 (m, 14H), 7.57 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.4, 56.8, 59.9 (CH_2), 69.8 (CH_2), 72.0 (CH_2), 73.0 (CH_2), 74.6, 77.9, 99.9, 102.5, 126.5, 127.1, 127.9, 128.1, 128.2, 128.3, 128.7, 129.3, 133.5, 134.5, 137.0, 137.3. HRMS [ES^+, $(M + H)^+$]: for $C_{31}H_{34}N_3O_6$ found 544.2468, calcd 544.2448.

Compound ***16b***. Following the general procedure, over 28 h compound **6b** (0.20 g, 0.62 mmol) was converted to **16b** (0.28 g, 83%). Eluent: EtOAc/petroleum ether (1:4). Yellow gum. $[\alpha]^{26}_D$ (+): 54.0 (*c* 0.8, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 2.79−3.05 (m, 2H), 3.35 (bs, 1H), 3.42 (s, 3H), 4.17−4.28 (m, 3H), 4.37−4.43 (m, 2H), 4.47−4.63 (m 5H), 4.67−4.77 (m, 2H), 4.87−4.91 (m, 2H), 7.02−7.07 (m, 2H), 7.24−7.39 (m, 15H), 7.62 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.3, 57.5, 59.1 (CH_2), 60.2 (CH_2), 68.3, 72.6 (CH_2), 73.3 (CH_2), 73.4 (CH_2), 75.1, 76.8, 98.7, 127.1, 127.4, 127.6, 127.8, 128.2, 128.3, 128.5, 132.9, 135.5, 136.1, 138.0, 138.1. HRMS [ES^+, $(M + H)^+$]: for $C_{31}H_{36}N_3O_6$ found 546.2622, calcd 546.2604.

Compound ***17b***. Following the general procedure, over 24 h compound **6b** (0.20 g, 0.62 mmol) was converted to **17b** (0.36 g, 85%). Eluent: EtOAc/petroleum ether (1:4). Yellow gum. $[\alpha]^{26}_D$ (+): 70.0 (*c* 0.8 $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 2.99 (s, 3H), 4.45−4.76 (m, 7H), 5.06 (d, 1H, *J* = 3.4 Hz), 5.26 (dd, 1H, *J* = 3.6 Hz, 10.2 Hz), 5.44−5.53 (m, 1H), 6.20 (t, 1H, *J* = 10.0 Hz), 7.20−7.53 (m, 14H), 7.62 (s, 1H), 7.86−8.01 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 49.0 (CH_2), 55.0, 59.5 (CH_2), 68.8, 70.0, 70.9, 71.8, 72.5 (CH_2), 96.5, 128.1, 128.3, 128.4, 128.5, 128.7 (2 × C), 129.0, 129.5, 129.8, 129.9, 133.2, 133.4, 133.6, 133.7, 134.7, 136.8, 165.6 (2 × C), 165.7. HRMS [ES^+, $(M + H)^+$]: for $C_{38}H_{36}N_3O_9$ found 678,2462, calcd 678.2452.

Compound ***18b:*** Following the general procedure, over 22 h compound **6b** (0.20 g, 0.62 mmol) was converted to **18b** (0.29 g, 83%). Eluent: EtOAc/petroleum ether (1:1). Brown gum. $[\alpha]^{26}_D$ (+): 65.0 (*c* 1.0, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 1.87 (s, 3H), 1.98 (s, 3H), 2.01(s, 3H), 2.08 (s, 3H), 3.61−3.67 (m, 1H), 3.94−4.05 (m, 1H), 4.11 (d, 1H, *J* = 1.8 Hz), 4.20−4.29 (m, 2H), 4.40 (d, 1H, *J* = 7.8 Hz), 4.52−4.69 (m, 6H), 4.86−4.99 (m, 1H), 5.03−5.18 (m, 2H), 7.30−7.41 (m, 5H), 7.58 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.6, 20.8, 47.9 (CH_2), 59.9 (CH_2), 61.8 (CH_2), 68.2, 68.6 (CH_2), 70.9, 71.9, 72.5 (CH_2), 72.6, 100.7, 128.0, 128.2, 128.7, 133.7, 134.6, 137.2, 169.3, 169.5, 170.2, 170.7. HRMS [ES^+, $(M + H)^+$]: for $C_{26}H_{34}N_3O_{11}$ found 564.2183, calcd 564.2193.

General Procedure for the Synthesis of 1,4-Disubstituted Triazolyl Monosaccharides 21−23. To a well-stirred solution of azidosugars **8−10** (1 equiv) and alkyne **19** (1 equiv) in $^tBuOH/H_2O$ (1:1) were added $CuSO_4$ (0.5 equiv) and sodium ascorbate (1 equiv). The reaction mixture was stirred at room temperature for 16−18 h. After completion of the reaction (TLC), the reaction mixture was poured into aqueous saturated solution of $NaHCO_3$ and extracted with EtOAc (3 × 10 mL). The organic phase was dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The residue was purified over silica gel column to afford the 1,4-disubstituted triazoles (1,4-DTs) **21a−23a**. In case of alkyne **20** (1 equiv) the reaction was performed in THF/H_2O (1:1), and DIPEA (1.5 equiv) was added to afford the 1,4-DTs **21b−23b** in 22−36 h.

Compound ***21a***. Following the general procedure, over 16 h compound **19** (0.20 g, 1.96 mmol) was converted to **21a** (0.84 g, 88%). Eluent: EtOAc/petroleum ether (1:3). Yellow gum. $[\alpha]^{25}_D$ (−): 23.4 (*c* 0.8, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 3.42 (s, 3H), 3.80 (t, 1H, *J* = 10.3 Hz), 4.02 (dd, 1H, *J* = 3.2 Hz, 9.6 Hz), 4.19 (bs, 1H), 4.33−4.41 (m, 1H), 4.50−4.63 (m, 1H), 4.74−4.86 (m, 2H), 4.93 (s, 1H), 5.02 (d, 1H, *J* = 2.2 Hz), 5.49 (s, 1H), 7.18−7.46 (m, 13H), 7.79−7.87 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.7, 58.6, 61.9, 69.1 (CH_2), 73.4 (CH_2), 74.5, 76.0, 99.1, 102.1, 119.4, 125.7, 126.2, 127.7 (2 × C), 128.2, 128.3, 128.4, 128.9, 129.1, 130.1, 137.4, 137.9, 147.7. HRMS [ES^+, $(M + H)^+$]: for $C_{29}H_{30}N_3O_5$ found 500.2179, calcd 500.2185.

Compound ***22a***. Following the general procedure, over 16 h compound **19** (0.20 g, 1.96 mmol) was converted to **22a** (0.83 g, 87%). Eluent: EtOAc/petroleum ether (1:3). Yellow gum. $[\alpha]^{25}_D$ (−): 58.0 (*c* 0.8, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 3.25 (s, 3H), 3.87 (t, 1H, *J* = 9.6 Hz), 4.22−4.51 (m, 4H), 4.68−4.84 (m, 3H), 5.33−5.35 (m, 1H), 5.65 (s, 1H), 7.29−7.43 (m, 14H), 7.81−7.85 (m, 2H), 8.42 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.4, 57.9, 59.0, 69.5 (CH_2), 73.2 (CH_2), 73.9, 76.8, 99.5, 102.5, 120.7, 125.8, 126.0, 128.0, 128.2, 128.4, 128.7, 128.8, 129.3, 130.9, 136.8, 147.0. HRMS [ES^+, $(M + H)^+$]: for $C_{29}H_{30}N_3O_5$ found 500.2177, calcd 500.2185.

Compound ***23a***. Following the general procedure, over 18 h compound **19** (0.20 g, 1.96 mmol) was converted to **23a** (0.83 g, 85%). Eluent: EtOAc/petroleum ether (1:3). White solid. Mp: 172 °C. $[\alpha]^{25}_D$ (−): 78.0 (*c* 0.7, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 3.16−3.48 (m, 6H), 3.89 (dd, 1H, *J* = 3.2 Hz, 9.6 Hz), 4.19−4.24 (m, 2H), 4.55−4.64 (m, 2H), 4.74−4.84 (m, 3H), 5.36 (d, 1H, *J* = 4.6 Hz), 7.26−7.42 (m, 14H), 7.74 (d, 2H, *J* = 7.2 Hz), 7.85 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.7, 59.8, 60.7 (CH_2), 68.0, 72.1 (CH_2), 73.9 (CH_2), 75.2, 75.3, 99.0, 120.8, 125.9, 127.9, 128.0, 128.3, 128.5, 128.9, 130.4, 137.6, 138.0, 147.5. HRMS [ES^+, $(M + H)^+$]: for $C_{29}H_{32}N_3O_5$ found 502.2345, calcd 502.2342.

Compound ***21b***. Following the general procedure, over 24 h compound **20** (0.25 g, 1.71 mmol) was converted to **21b** (0.80 g, 86%). Eluent: EtOAc/petroleum ether (3:7). White solid. Mp: 122−124 °C. $[\alpha]^{25}_D$ (−): 16.0 (*c* 0.8, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 3.47 (s, 3H), 3.82 (t, 1H, *J* = 10.4 Hz), 3.97 (dd, 1H, *J* = 3.0 Hz, 9.6 Hz), 4.14 (bs, 1H), 4.35−4.43 (m, 1H), 4.50−4.68 (m, 5H), 4.78−5.03 (m, 4H), 5.54 (s, 1H), 7.25−7.46 (m, 16H), 7.69 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.5, 58.3, 61.6, 63.4 (CH_2), 68.9 (CH_2), 72.5 (CH_2), 73.1 (CH_2), 74.3, 75.7, 98.9, 101.9, 122.2, 126.0, 127.4, 127.6, 127.7, 128.0, 128.1, 128.3, 128.9, 137.3, 137.6, 137.8, 145.1. HRMS [ES^+, $(M + H)^+$]: for $C_{31}H_{34}N_3O_6$ found 544.2435, calcd 544.2448.

Compound ***22b:*** Following the general procedure, in 22 h compound **20** (0.25 g, 1.71 mmol) was converted to **22b** (0.79 g, 85%). Eluent: EtOAc/petroleum ether (3:7). White solid. Mp: 120−122 °C. $[\alpha]^{25}_D$ (−): 60.0 (*c* 0.8, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 3.25 (s, 3H), 3.87 (t, 1H, *J* = 10.0 Hz), 4.18−4.28 (m, 2H), 4.33−4.49 (m, 4H), 4.55 (s, 2H), 4.70−4.86 (m, 5H), 5.30−5.33 (m, 1H), 5.66 (s, 1H), 7.25−7.39 (m, 17H), 8.22 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.5, 57.9, 59.0, 63.7 (CH_2), 69.6 (CH_2), 72.1 (CH_2), 73.3 (CH_2), 74.0, 76.9, 99.5, 102.6, 123.9, 126.2, 127.8, 128.0, 128.2, 128.5, 128.6, 128.9, 129.4, 136.8, 136.9, 138.1, 144.4. HRMS [ES^+, $(M + H)^+$]: for $C_{31}H_{34}N_3O_6$ found 544.2435, calcd 544.2448.

Compound ***23b***. Following the general procedure, over 36 h compound **20** (0.25 g, 1.71 mmol) was converted to **23b** (0.79 g, 85%). Eluent: EtOAc/petroleum ether (3:7). Yellowish gum. $[\alpha]^{25}_D$ (−): 36.5 (*c* 0.8, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ 3.00−3.09 (m, 1H), 3.31−3.36 (m, 1H), 3.42 (s, 3H), 3.92 (dd, 1H, *J* = 3.8 Hz, 10.0 Hz), 4.17−4.42 (m, 5H), 4.54−4.84 (m, 7H), 5.31 (d, 1H, *J* = 3.6 Hz), 7.17−7.29 (m, 16H), 7.63 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.9, 56.6 (CH_2), 60.2, 66.6, 68.2 (CH_2), 72.3 (CH_2), 73.7 (CH_2),

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74.1 (CH_2), 75.2, 75.8, 99.1, 123.1, 127.9, 128.0 (2 × C), 128.2, 128.6 (2 × C), 137.5, 137.7, 138.2, 147.3. HRMS [ES$^+$, (M + H)$^+$]: for $C_{31}H_{36}N_3O_6$ found 546.2582, calcd 546.2604.

Compound ***25a***. To a well-stirred solution of the known monotosylated compound **24a** (2.00 g, 4.31 mmol) in DMF (20 mL) were added 4-chlorothiophenol (0.93 g, 6.46 mmol) and TMG (0.65 mL, 5.17 mmol). The mixture was heated at 100 °C with stirring under N_2. After 6 h, the reaction mixture was cooled and poured into an aqueous saturated solution of $NaHCO_3$, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified over silica gel to afford the sulfide **25a** (1.74 g, 93%). Eluent: EtOAc/petroleum ether (1:5). Yellowish gum. $[\alpha]^{25}_D$ (−): 56.5 (*c* 0.9, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.45 (s, 3H), 2.60 (d, 1H, *J* = 4.2 Hz), 2.94−3.05 (m, 1H), 3.31−3.39 (m, 1H), 4.07 (s, 3H), 4.49−4.73 (m, 3H), 5.92 (d, 1H, *J* = 3.6 Hz), 7.19−7.39 (m, 9H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.2, 26.7, 39.0 (CH_2), 67.1, 72.0 (CH_2), 81.5, 82.1, 105.1, 111.7, 127.7, 128.1, 128.6, 129.0, 130.5, 131.9, 134.2, 137.1. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{22}H_{25}O_5NaSCl$ found 459.0980, calcd 459.1009.

Compound ***25b***. Following the procedure described for the preparation of **25a**, over 5 h compound **24b** (2.00 g, 5.15 mmol) was converted to **25b** (1.66 g, 90%). Eluent: EtOAc/petroleum ether (1:5). Colorless gum. $[\alpha]^{25}_D$ (−): 46.4 (*c* 1.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.46 (s, 3H), 2.79 (d, 1H, *J* = 4.8 Hz), 2.95−3.08 (m, 1H), 3.36 (d, 1H, *J* = 3.0 Hz), 3.43 (s, 3H), 3.86 (d, 1H, *J* = 3.0 Hz), 3.95−4.12 (m, 2H), 4.58 (d, 1H, *J* = 3.8 Hz), 5.90 (d, 1H, *J* = 3.8 Hz), 7.20−7.35 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.1, 26.6, 38.9 (CH_2), 57.7, 67.1, 81.2, 81.5, 83.8, 104.9, 111.6, 128.9, 130.1, 131.7, 134.5. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{16}H_{21}O_5NaSCl$ found 383.0681, calcd 383.0696.

Compound ***25c***. Following the procedure described for the preparation of **25a**, over 4 h compound **24c** (2.00 g, 4.31 mmol) was converted to **25c** (1.78 g, 95%). Eluent: EtOAc/petroleum ether (1:5). Yellow gum. $[\alpha]^{25}_D$ (+): 56.4 (*c* 1.3, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (s, 3H), 1.58 (s, 3H), 2.64 (bs, 1H), 2.91−3.03 (m, 1H), 3.15 (dd, 1H, *J* = 3.7 Hz, 13.8 Hz), 3.91−3.98 (m, 2H), 4.07−4.14 (m, 1H), 4.51−4.60 (m, 2H), 4.77 (d, 1H, *J* = 11.6 Hz), 5.72 (d, 1H, *J* = 3.8 Hz), 7.18−7.37 (m, 9H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.5, 26.7, 36.7 (CH_2), 69.2, 71.9 (CH_2), 77.1, 77.5, 79.6, 104.0, 113.0, 128.0, 128.4, 128.9, 130.6, 131.9, 134.5, 137.2. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{22}H_{25}O_5NaSCl$ found 459.0980, calcd 459.1009.

Compound ***26a***. To a well-stirred solution of sulfide **25a** (1.00 g, 2.29 mmol) in dry MeOH (10 mL) was added MMPP (2.26 g, 4.59 mmol), and the mixture was stirred at room temperature under N_2. After 12 h, MeOH was evaporated to dryness under reduced pressure, and the residue was dissolved in an aqueous saturated solution of $NaHCO_3$. The aqueous part was washed with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure to obtain a residue. The residue was purified over silica gel to afford sulfone **26a** (1.00 g, 95%). Eluent: EtOAc/petroleum ether (3:7). Colorless gum. $[\alpha]^{25}_D$ (+): 48.4 (*c* 1.2, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.29 (s, 3H), 1.44 (s, 3H), 3.23−3.35 (m, 2H), 3.59 (dd, 1H, *J* = 1.8 Hz, 14.4 Hz), 4.02−4.08 (m, 2H), 4.42−4.71 (m, 4H), 5.82 (d, 1H, *J* = 3.6 Hz), 7.26−7.39 (m, 5H), 7.46−7.50 (m, 2H), 7.77−7.82 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.1, 26.7, 59.8 (CH_2), 64.0, 72.2 (CH_2), 81.0, 81.4, 82.1, 104.9, 111.8, 127.6, 127.9, 128.4, 129.4, 137.2, 137.9, 140.2. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{22}H_{25}O_7NaSCl$ found 491.0891, calcd 491.0907.

Compound ***26b***. Following the procedure described for the preparation of **26a**, over 12 h compound **25b** (2.00 g, 5.57 mmol) was converted to **26b** (2.00 g, 92%). Eluent: EtOAc/petroleum ether (3:7). White solid. Mp: 100−105 °C. $[\alpha]^{25}_D$ (+) 54.4 (*c* 0.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.30 (s, 3H), 1.45 (s, 3H), 3.26−3.39 (m, 2H), 3.42 (s, 3H), 3.61 (dd, 1H, *J* = 1.6 Hz, 14.4 Hz), 3.84 (d, 1H, *J* = 3.2 Hz), 4.03 (dd, 1H, *J* = 3.2 Hz, 8.0 Hz), 4.44 (t, 1H, *J* = 8.4 Hz), 4.55 (d, 1H, *J* = 3.8 Hz), 5.80 (d, 1H, *J* = 3.6 Hz), 7.52−7.58 (m, 2H), 7.85−7.91 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.1, 26.7, 57.9, 60.1 (CH_2), 63.9, 81.3, 83.1, 104.9, 111.8, 129.5, 138.2, 140.3. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{16}H_{21}O_7NaSCl$ found 415.0604, calcd 415.0594.

Compound ***26c***. Following the procedure described for the preparation of **26a**, over 12 h compound **25c** (1.00 g, 2.29 mmol) was converted to **26c** (1.04 g, 97%). Eluent: EtOAc/petroleum ether (3:7). Colorless gum. $[\alpha]^{25}_D$ (+): 72.4 (*c* 0.9, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.34 (s, 3H), 1.54 (s, 3H), 2.98 (d, 1H, *J* = 2.2 Hz), 3.18−3.36 (m, 2H), 3.90−3.92 (m, 2H), 4.38−4.43 (m, 1H), 4.50 (d, 1H, *J* = 11.6 Hz), 4.55−4.58 (m, 1H), 4.74 (d, 1H, *J* = 11.6 Hz), 5.70 (d, 1H, *J* = 3.6 Hz), 7.33 (s, 5H), 7.49−7.53 (m, 2H), 7.78−7.84 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.5, 26.7, 58.5 (CH_2), 65.3, 71.9 (CH_2), 76.7, 77.3, 79.8, 104.1, 113.1, 128.1, 128.4, 129.4, 129.6, 137.0, 138.1, 140.3. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{22}H_{25}O_7NaSCl$ found 491.0880, calcd 491.0907.

Compound ***27a***. To a well-stirred solution of sulfone **26a** (1.20 g, 2.56 mmol) in pyridine (10 mL) was added methanesulfonyl chloride (0.40 mL, 5.13 mmol) in pyridine (2 mL) dropwise at 0 °C under N_2. After completion of the addition, the reaction mixture was kept at +4 °C. After 20 h (TLC), the reaction mixture was poured into an aqueous saturated solution of $NaHCO_3$, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure to get a residue. The residue was heated under reflux with pyridine. After 2 h (TLC), the reaction mixture poured into ice-cold water, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhyd Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The residue was purified over silica gel to afford the vinyl sulfone **27a** (1.03 g, 90%, mixture). Eluent: EtOAc/petroleum ether (1:4). Brownish gum, ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.47 (s, 3H), 4.05 (d, 1H, *J* = 3.4 Hz), 4.42−4.66 (m, 3H), 4.86−4.90 (m, 1H), 5.95 (d, 1H, *J* = 3.6 Hz), 6.68 (dd, 1H, *J* = 1.9 Hz, 14.8 Hz), 6.99 (dd, 1H, *J* = 3.6 Hz, 15.0 Hz), 7.22−7.41 (m, 8H), 7.71−7.77 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.2, 26.8, 72.1 (CH_2), 78.7, 82.4, 82.6, 104.9, 112.2, 127.7, 128.1, 128.6, 129.1, 129.5, 131.6, 136.8, 138.7, 139.8, 140.7. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{22}H_{23}O_6NaSCl$ found 473.0824, calcd 473.0802 (E). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.33 (s, 3H), 1.55 (s, 3H), 4.31 (d, 1H, *J* = 3.4 Hz), 4.49−4.66 (m, 3H), 5.72−5.77 (m, 1H), 5.98 (d, 1H, *J* = 3.8 Hz), 6.34−6.51 (m, 2H), 7.24−7.36 (m, 6H), 7.45−7.52 (m, 2H), 7.78−7.84 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.6, 27.2, 72.6 (CH_2), 75.9, 83.1, 85.3, 105.5, 112.3, 127.7, 128.1, 128.6, 129.0, 129.8, 131.1, 137.3, 139.1, 140.6, 142.5. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{22}H_{23}O_6NaSCl$ found 473.0808, calcd 473.0802 (Z).

Compound ***27b***. Following the procedure described for the preparation of **27a**, over 22 h compound **26b** (2.00 g, 5.11 mmol) was converted to **27b** (1.68 g, 88%, mixture). Eluent: EtOAc/petroleum ether (1:4). Brownish gum. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.47 (s, 3H), 3.35 (s, 3H), 3.85 (d, 1H, *J* = 3.2 Hz), 4.61 (d, 1H, *J* = 3.6 Hz), 4.85−4.89 (m, 1H), 5.91 (d, 1H, *J* = 3.8 Hz), 6.67 (dd, 1H, *J* = 1.8 Hz, 15.0 Hz), 7.02 (dd, 1H, *J* = 3.7 Hz, 14.8 Hz), 7.46−7.52 (m, 2H), 7.78−7.84 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.3, 26.9, 58.3, 78.7, 81.9, 85.2, 104.9, 112.3, 129.3, 129.7, 131.8, 138.9, 140.2, 140.4. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{16}H_{19}O_6NaSCl$ found 397.0496, calcd 397.0489 (E). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (s, 3H), 1.56 (s, 3H), 3.39 (s, 3H), 4.08 (d, 1H, *J* = 3.4 Hz), 4.63 (d, 1H, *J* = 3.8 Hz), 5.69−5.74 (m, 1H), 5.96 (d, 1H, *J* = 3.6 Hz), 6.38−6.40 (m, 2H), 7.51−7.56 (m, 2H), 7.82−7.87 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.4, 27.0, 58.3, 75.7, 82.2, 87.2, 105.3, 112.1, 129.0, 129.8, 130.9, 139.0, 140.5, 142.2. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{16}H_{19}O_6NaSCl$ found 397.0490, calcd 397.0489 (Z).

Compound ***27c***. Following the procedure described for the preparation of **27a**, in 22 h compound **26c** (1.20 g, 2.56 mmol) was converted to **27c** (0.98 g, 85%). Eluent: EtOAc/petroleum ether (1:4). Yellowish gum. $[\alpha]^{29}_D$ (+): 22.3 (*c* 0.9, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (s, 3H), 1.57 (s, 3H), 3.53 (dd, 1H, *J* = 4.0 Hz, 9.2 Hz), 4.53−4.78 (m, 4H), 5.73 (d, 1H, *J* = 3.6 Hz), 6.61 (dd, 1H, *J* = 1.8 Hz, 15.0 Hz), 7.03 (dd, 1H, *J* = 3.8 Hz, 15.0 Hz), 7.32−7.38 (m,

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5H), 7.45−7.50 (m, 2H), 7.73−7.78 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.4, 26.7, 72.2 (CH_2), 76.1, 77.1, 81.4, 104.0, 113.4, 128.0, 128.2, 128.5, 129.1, 129.5, 130.7, 136.8, 138.5, 140.0, 142.2. HRMS [ES$^+$, (M + Na)$^+$]: for $C_{22}H_{23}O_6NaSCl$ found 473.0779, calcd 473.0802 (E).

General Procedure for the Synthesis of 1,5-Disubstituted Triazole-Linked Disaccharides 28−32. A mixture of vinyl sulfone (1 equiv) and azidosugar (1.5 equiv) in water (5 mL/mmol) was heated under reflux for 36−48 h to afford 1,5-disubstituted triazole-linked disaccharides. For vinyl sulfones **27a−c** and azidosugars **8** and **9**, $NaHCO_3$ (1.5 equiv) was added to the reaction mixture. For azidosugars **11** and **12** the reaction was performed in reluxing toluene.

*Compound **31a**.* Following the general procedure, over 48 h compound **27a** (0.25 g, 0.55 mmol) was converted to **31a** (0.31 g, 70%). Eluent: EtOAc/petroleum ether (1:4). White solid. Mp: 140 °C. $[\alpha]^{29}_D$ (−): 28.3 (*c* 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (s, 3H), 1.57 (s, 3H), 3.08 (s, 3H), 3.96 (d, 1H, *J* = 3.2 Hz), 4.22 (d, 1H, *J* = 12.0 Hz), 4.32−4.38 (m, 1H), 4.43 (d, 1H, *J* = 3.6 Hz), 4.49 (d, 1H, *J* = 12.4 Hz), 4.56−4.67 (m, 2H), 5.14 (d, 1H, *J* = 3.6 Hz), 5.24 (dd, 1H, *J* = 3.6 Hz, 10.0 Hz), 5.39−5.46 (m, 2H), 5.83 (d, 1H, *J* = 4.0 Hz), 6.17 (t, 1H, *J* = 9.8 Hz), 6.98 (d, 2H, *J* = 7.2 Hz), 7.17−7.59 (m, 12H), 7.69 (s, 1H), 7.88 (d, 2H, *J* = 7.2 Hz), 7.96 (d, 2H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 26.7, 50.1 (CH_2), 55.3, 68.7, 70.1, 70.9, 71.7, 72.0 (CH_2), 73.6, 82.1, 82.4, 96.5, 104.4, 112.0, 127.8, 128.2 (2 × C), 128.3, 128.5, 128.6, 128.7, 128.8, 129.0, 129.6, 129.8, 129.9, 132.4, 133.1, 133.3, 133.6, 134.1, 136.2, 165.6 (2 × C), 165.7. HRMS [ES$^+$, (M + H)$^+$]: for $C_{44}H_{44}N_3O_{12}$ found 806.2890, calcd 806.2925.

*Compound **32a**.* Following the general procedure, over 48 h compound **27a** (0.25 g, 0.55 mmol) was converted to **32a** (0.25 g, 67%). Eluent: EtOAc/petroleum ether (1:1). Brownish yellow gum. $[\alpha]^{29}_D$ (−) 40.0 (*c* 0.9, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.37 (s, 3H), 1.56 (s, 3H), 1.98 (s, 6H), 2.01 (s, 3H), 2.07 (s, 3H), 3.60−3.67 (m, 1H), 3.92−4.11 (m, 3H), 4.14−4.33 (m, 3H), 4.35−4.54 (m, 3H), 4.74 (d, 1H, *J* = 3.6 Hz), 4.86−4.99 (m, 1H), 5.03−5.18 (m, 2H), 5.36 (d, 1H, *J* = 3.2 Hz), 6.06 (d, 1H, *J* = 3.6 Hz), 6.97−7.02 (m, 2H), 7.27−7.30 (m, 4H), 7.63 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.6, 20.8, 26.2, 26.9, 48.7 (CH_2), 61.8 (CH_2), 68.2, 68.4 (CH_2), 70.9, 71.9, 72.2 (CH_2), 72.7, 73.9, 82.4, 100.9, 104.8, 112.4, 127.9, 128.3, 128.7, 132.3, 133.6, 136.4, 169.4, 170.2, 170.7. HRMS [ES$^+$, (M + H)$^+$]: for $C_{32}H_{42}N_3O_{14}$ found 692.2656, calcd 692.2667.

*Compound **28b**.* Following the general procedure, over 45 h compound **27b** (0.25 g, 0.67 mmol) was converted to **28b** (0.29 g, 73%). Eluent: EtOAc/petroleum ether (1:3). Brownish gum. $[\alpha]^{29}_D$ (−): 42.3 (*c* 0.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.36 (s, 3H), 1.57 (s, 3H), 3.27 (s, 3H), 3.42 (s, 3H), 3.77 (d, 1H, *J* = 3.4 Hz), 3.91−4.01 (m, 2H), 4.36−4.48 (m, 1H), 4.50−4.60 (m, 1H), 4.68−4.84 (m, 5H), 5.27 (d, 1H, *J* = 1.6 Hz), 5.40 (d, 1H, *J* = 3.2 Hz), 5.64 (s, 1H), 5.99 (d, 1H, *J* = 3.8 Hz), 7.20−7.50 (m, 11H), 7.66 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.2, 26.9, 55.6, 57.9, 58.3, 61.6, 69.6 (CH_2), 73.4 (CH_2), 73.7, 75.0, 76.2, 81.2, 85.8, 99.9, 102.2, 104.8, 112.4, 126.4, 127.6, 127.9, 128.3, 129.1, 131.4, 133.7, 138.0, 138.6. HRMS [ES$^+$, (M + H)$^+$]: for $C_{31}H_{38}N_3O_9$ found 596.2631, calcd 596.2608.

*Compound **29b**.* Following the general procedure, over 45 h compound **27b** (0.25 g, 0.67 mmol) was converted to **29b** (0.29 g, 72%). Eluent: EtOAc/petroleum ether (1:3). White solid. Mp: 162 °C. $[\alpha]^{29}_D$ (−): 55.8 (*c* 0.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.50 (s, 3H), 2.85 (s, 3H), 3.29 (s, 3H), 3.72−3.83 (m, 2H), 3.93 (s, 1H), 4.31−4.43 (m, 2H), 4.59 (d, 1H, *J* = 3.6 Hz), 4.71 (s, 3H), 5.30−5.40 (m, 1H), 5.44−5.49 (m, 2H), 5.59 (s, 1H), 5.93 (d, 1H, *J* = 3.8 Hz), 7.21−7.39 (m, 11H), 7.61 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.2, 26.9, 55.1, 57.8, 58.9, 60.5, 70.2 (CH_2), 73.3 (CH_2), 74.4, 74.7, 78.9, 82.5, 86.4, 98.9, 102.7, 104.8, 112.3, 126.5, 128.0, 128.1, 128.6, 129.0, 132.0, 132.6, 137.6 (2C). HRMS [ES$^+$, (M + H)$^+$]: for $C_{31}H_{38}N_3O_9$ found 596.2620, calcd 596.2608.

*Compound **30b**.* Following the general procedure, over 42 h compound **27b** (0.25 g, 0.67 mmol) was converted to **30b** (0.29g, 72%). Eluent: EtOAc/petroleum ether (1:1). Brownish yellow gum. $[\alpha]^{29}_D$ (+): 112.0 (*c* 0.6, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.33 (s, 3H), 1.44 (s, 3H), 3.34 (s, 3H), 3.38 (s, 3H), 3.44−3.52 (m, 1H), 3.96 (d, 1H, *J* = 3.0 Hz), 4.21−4.33 (m, 2H), 4.56−4.86 (m, 9H), 5.19−5.23 (m, 1H), 5.42 (d, 1H, *J* = 3.0 Hz), 5.96 (d, 1H, *J* = 3.8 Hz), 7.22−7.32 (m, 10H), 7.79 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.3, 26.9, 55.6, 57.6, 57.7, 60.8 (CH_2), 68.1, 72.4, 73.0 (CH_2), 74.1 (CH_2), 75.2, 76.7, 81.4, 84.5, 99.3, 104.8, 112.1, 127.5, 127.7, 127.8, 128.2, 128.4, 128.5, 133.4, 134.6, 138.1, 138.6. HRMS [ES$^+$, (M + H)$^+$]: for $C_{31}H_{40}N_3O_9$ found 598.2744, calcd 598.2765.

*Compound **31b**.* Following the general procedure, over 40 h compound **27b** (0.25 g, 0.67 mmol) was converted to **31b** (0.34 g, 70%). Eluent: EtOAc/petroleum ether (1:4). Colorless gum. $[\alpha]^{29}_D$ (+): 90.0 (*c* 0.9, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.26 (s, 3H), 1.55 (s, 3H), 3.10 (s, 3H), 3.18 (s, 3H), 3.75 (d, 1H, *J* = 3.2 Hz), 4.29 (d, 1H, *J* = 3.8 Hz), 4.57−4.63 (m, 2H), 4.81−4.91 (m, 1H), 5.18 (d, 1H, *J* = 3.6 Hz), 5.28 (dd, 1H, *J* = 3.6 Hz, 10.2 Hz), 5.41−5.50 (m, 2H), 5.75 (d, 1H, *J* = 3.6 Hz), 6.18 (t, 1H, *J* = 9.8 Hz), 7.25−7.60 (m, 10H), 7.69 (s, 1H), 7.85−8.03 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.1, 26.9, 50.5 (CH_2), 55.6, 58.1, 69.0, 70.3, 71.3, 72.0, 73.5, 81.7, 85.7, 96.8, 104.5, 112.1, 128.5, 128.6, 128.7, 129.0, 129.1, 129.3, 129.8, 130.1 (2 × C), 130.3, 132.3, 133.4, 133.6, 133.9, 165.9 (2C), 166.0. HRMS [ES$^+$, (M + H)$^+$]: for $C_{38}H_{40}N_3O_{12}$ found 730.2636, calcd 730.2612.

*Compound **32b**.* Following the general procedure, over 45 h compound **27b** (0.25 g, 0.67 mmol) was converted to **32b** (0.16 g, 40%). Eluent: EtOAc/petroleum ether (1:3). Brownish yellow gum. $[\alpha]^{29}_D$ (+): 62.9 (*c* 0.7, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.37 (s, 3H), 1.57 (s, 3H), 1.99 (s, 3H), 2.00 (s, 3H), 2.02 (s, 3H), 2.09 (s, 3H), 3.27 (s, 3H), 3.63−3.71 (m, 1H), 3.88 (d, 1H, *J* = 3.2 Hz), 4.05−4.31 (m, 4H), 4.48−4.71 (m, 4H), 4.90−5.21 (m, 4H), 5.35 (d, 1H, *J* = 3.0 Hz), 6.01 (d, 1H, *J* = 3.6 Hz), 7.65 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.8, 20.9, 26.3, 27.0, 48.9 (CH_2), 58.2, 62.0 (CH_2), 68.4, 68.5 (CH_2), 71.1, 72.1, 72.9, 73.6, 81.8, 85.6, 101.1, 104.8, 112.5, 132.1, 133.8, 169.6, 170.3, 170.8. HRMS [ES$^+$, (M + H)$^+$]: for $C_{26}H_{38}N_3O_{14}$ found 616.2357, calcd 616.2354.

*Compound **32b′**:* Following the general procedure, over 45 h compound **27b** (0.25 g, 0.67 mmol) was converted to **32b′** (0.12 g, 30%). Eluent: EtOAc/petroleum ether (1:3). Brownish yellow gum. $[\alpha]^{29}_D$ (+): 25.9 (*c* 0.5, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.36 (s, 3H), 1.56 (s, 3H), 2.00 (s, 3H), 2.01 (s, 3H), 2.02 (s, 3H), 2.10 (s, 3H), 3.28 (s, 3H), 3.66−3.73 (m, 2H), 3.90−4.05 (m, 3H), 4.10−4.29 (m, 4H), 4.48−4.59 (m, 4H), 4.69 (d, 1H, *J* = 3.8 Hz), 4.94−5.23 (m, 4H), 5.47 (d, 1H, *J* = 3.0 Hz), 5.96 (d, 1H, *J* = 3.8 Hz), 7.70 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.7 (3 × C), 20.9, 26.4, 26.9, 50.2 (CH_2), 58.3, 61.9 (CH_2), 67.9 (CH_2), 68.4, 71.1, 72.2, 72.8, 76.1, 82.3, 85.0, 100.8, 104.7, 112.1, 124.8, 143.4, 169.5, 170.3, 170.8. HRMS [ES$^+$, (M + H)$^+$]: for $C_{26}H_{38}N_3O_{14}$ found 616.2371, calcd 616.2354.

*Compound **28c**.* Following the general procedure, over 40 h compound **27c** (0.25 g, 0.55 mmol) was converted to **28c** (0.30 g, 81%). Eluent: EtOAc/petroleum ether (1:3). Yellowish gum. $[\alpha]^{27}_D$ (−): 38.2 (*c* 0.5, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.65 (s, 3H), 3.35 (s, 3H), 3.78−3.92 (m, 2H), 4.18 (bs, 1H), 4.32−4.39 (m, 1H), 4.46−4.52 (m, 2H), 4.60−4.91 (m, 7H), 5.08 (d, 1H, *J* = 9.2 Hz), 5.63 (s, 1H), 5.80 (d, 1H, *J* = 3.6 Hz), 7.20−7.49 (m, 17H), 7.55 (s, 1H).^{13}C NMR (50 MHz, $CDCl_3$): δ 26.4, 26.8, 55.6, 58.2, 61.0, 69.3 (CH_2), 70.0, 72.1 (CH_2), 73.5 (CH_2), 74.4, 76.3, 76.6, 80.9, 99.6, 102.1, 104.2, 113.6, 126.3, 127.5, 128.1, 128.2, 128.5, 128.7, 129.0, 132.8, 134.2, 136.4, 137.8, 138.2. HRMS [ES$^+$, (M + H)$^+$]: for $C_{37}H_{42}N_3O_9$ found 672.2941, calcd 672.2921.

*Compound **29c**.* Following the general procedure, over 40 h compound **27c** (0.25 g, 0.55 mmol) was converted to **29c** (0.30 g, 82%). Eluent: EtOAc/petroleum ether (1:3). Brownish yellow gum. $[\alpha]^{27}_D$ (−): 39.8 (*c* 0.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (s, 3H), 1.52 (s, 3H), 3.33 (s, 3H), 3.70−3.87 (m, 2H), 4.06−4.07 (m, 1H), 4.30−4.40 (m, 3H), 4.45−4.55 (m, 2H), 4.58−4.71 (m, 3H), 5.12−5.23 (m, 2H), 5.28−5.31 (m, 1H), 5.57 (s, 1H), 5.81 (d, 1H, *J* = 3.6 Hz), 7.13−7.37 (m, 17H), 7.56 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.4, 26.8, 55.2, 56.8, 60.0, 69.9 (CH_2), 71.0, 72.5 (CH_2), 73.2 (CH_2), 74.5, 76.7, 78.4, 82.5, 99.6, 102.7, 104.2, 113.3, 126.6, 127.9, 128.1, 128.3, 128.4, 128.6 (2 × C), 129.2, 132.0, 135.2, 136.7,

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137.3, 137.4. HRMS [ES$^+$, (M + H)$^+$]: for $C_{37}H_{42}N_3O_9$ found 672.2941, calcd 672.2921.

Compound ***30c***. Following the general procedure, over 40 h compound **27c** (0.25 g, 0.55 mmol) was converted to **30c** (0.30 g, 80%). Eluent: EtOAc/petroleum ether (1:1). Brown gum. $[\alpha]^{27}_D$ (+): 60.2 (*c* 0.6, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.39 (s, 3H), 1.60 (s, 3H), 3.27−3.36 (m, 2H), 3.38 (s, 3H), 3.88−3.95 (m, 1H), 4.11−4.19 (m, 1H), 4.23−4.31 (m, 1H), 4.44 (d, 1H, *J* = 11.6 Hz), 4.59−4.67 (m, 5H), 4.72−4.86 (m, 5H), 5.18−5.25 (m, 2H), 5.80 (d, 1H, *J* = 3.8 Hz), 7.16−7.37 (m, 17H), 7.57 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.6, 26.8, 55.4, 57.6, 60.3 (CH_2), 67.9, 69.6, 72.3 (CH_2), 72.8 (CH_2), 73.9 (CH_2), 75.0, 76.3, 76.7, 81.8, 99.1, 104.3, 113.4, 127.4, 127.5, 127.7, 128.1, 128.3, 128.4, 128.6, 128.7, 131.7, 136.2, 136.7, 138.2, 138.5. HRMS [ES$^+$, (M + H)$^+$]: for $C_{37}H_{44}N_3O_9$ found 674.3075, calcd 674.3078.

Compound ***31c***. Following the general procedure, over 36 h compound **27c** (0.25 g, 0.55 mmol) was converted to **31c** (0.33 g, 75%). Eluent: EtOAc/petroleum ether (1:4). Yellowish gum. $[\alpha]^{27}_D$ (+): 54.8 (*c* 0.8, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.42 (s, 3H), 1.72 (s, 3H), 3.03 (s, 3H), 3.74−3.80 (m, 1H), 4.47−4.75 (m, 6H), 5.09 (d, 1H, *J* = 3.4 Hz), 5.23 (dd, 1H, *J* = 3.6 Hz, 10.2 Hz), 5.36−5.51 (m, 2H), 5.84 (d, 1H, *J* = 3.6 Hz), 6.14 (t, 1H, *J* = 9.8 Hz), 7.18−7.55 (m, 15H), 7.59 (s, 1H), 7.83−8.02 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.6, 26.9, 49.6 (CH_2), 55.3, 69.1, 70.2, 70.9, 71.0, 71.8, 72.4 (CH_2), 77.1, 82.8, 96.6, 104.1, 113.6, 127.9, 128.3, 128.4, 128.5, 128.6, 128.9, 129.0, 129.6, 129.9, 130.0, 132.1, 133.2, 133.4, 133.7, 136.4, 136.6, 165.6 (2 × C), 165.7. HRMS [ES$^+$, (M + H)$^+$]: for $C_{44}H_{44}N_3O_{12}$ found 806.2953, calcd 806.2925.

Compound ***32c***. Following the general procedure, in 36 h compound **27c** (0.25 g, 0.55 mmol) was converted to **32c** (0.30 g, 80%). Eluent: EtOAc/petroleum ether (1:1). Brownish yellow gum. $[\alpha]^{27}_D$ (+): 74.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.41 (s, 3H), 1.68 (s, 3H), 1.92 (s, 3H), 1.97 (s, 3H), 2.01(s, 3H), 2.08 (s, 3H), 3.58−3.64 (m, 1H), 3.76−3.82 (m, 1H), 4.02−4.12 (m, 2H), 4.16−4.25 (m, 2H), 4.40−4.61 (m, 4H), 4.66−4.77 (m, 2H), 4.86−4.99 (m, 2H), 5.04−5.15 (m, 3H), 5.86 (d, 1H, *J* = 3.6 Hz), 7.24−7.36 (m, 6H), 7.48 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.6 (3xC), 20.8, 26.5, 26.9, 48.3 (CH_2), 61.8 (CH_2), 68.0 (CH_2), 68.2, 70.8 (2 × C), 71.9, 72.3 (CH_2), 72.8, 76.8, 82.3, 100.7, 104.3, 113.6, 128.2, 128.5, 128.7, 131.7, 135.7, 136.6, 169.3, 169.5, 170.2, 170.7. HRMS [ES$^+$, (M + H)$^+$]: for $C_{32}H_{42}N_3O_{14}$ found 692.2675, calcd 692.2667.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Full spectroscopic data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: tpathak@chem.iitkgp.ernet.in. Tel: +91-3222-283342. Fax: +91-3222-282252.

Notes

The authors declare no competing financial interest.

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