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# Cu(I)-CATALYZED FORMATION OF D-MANNOFURANOSYL 1,4-DISUBSTITUTED 1,2,3-TRIAZOLECARBOHYBRIDS

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**Abstract** – 2,3:5,6-Di-*O*-isopropylidene-D-mannofuranose has been exploited as a platform for the synthesis of new 1,2,3-triazolecarbohybrids. Placement of an azide group at C-1 (and C-6) of the carbohydrate allows for reaction with various alkynes in the presence of a Cu(I) catalyst to generate 1,4-disubstituted triazoles regiospecifically. The use of sugar-derived alkynes leads to 1,2,3-triazole-linked di- and trisaccharide carbohybrid analogs with retention of the β-D-*manno* configuration.

## INTRODUCTION

The Huisgen 1,3-dipolar cycloaddition reaction[1] between an azide and an acetylene has often been used to introduce the aromatic 1,2,3-triazole group onto saccharide frameworks with a view to the formation of potential nucleoside analogs.[2] Although this chemistry is exceedingly easy to carry out in practice, usually by simply heating the two reactants in a suitable solvent, a major drawback is the formation of mixtures of regioisomeric (1,4-disubstituted and 1,5-disubstituted) triazoles when unsymmetrical alkynes are employed.[3,4] Additionally, the use of electron-deficient alkynes works well, however unactivated alkynes often require very long reaction times for completion.

Recently the 1,2,3-triazole system has been the subject of intense study following the realization that the heterocycle is capable of being a useful linker for the conjugation of biologically active groups. Indeed, Sharpless and coworkers[5] have defined the cycloaddition route to 1,2,3-triazoles as a near perfect reaction in terms of such factors as atom economy and the large driving force inherent in the formation of an aromatic ring. Considering the robust nature of the resultant triazole ring, Sharpless has suggested the system as a key component of his "Click Chemistry" paradigm for potential drug discovery.[5]

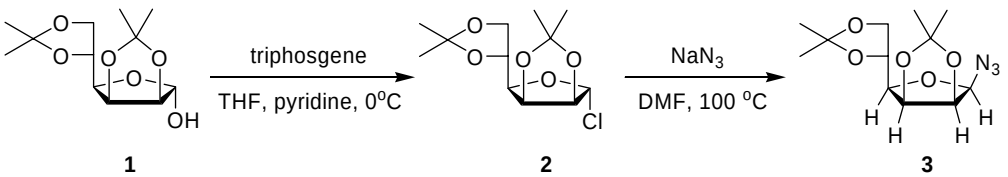
The problem of regiocontrol in the reaction between azides and unsymmetrical acetylenes has been

addressed in a number of key reports and has lead to reliable syntheses of either the 1,4-disubstituted isomer or its 1,5-disubstituted relative. Meldal has used Cu(I) salts to produce the 1,4-isomer exclusively[6] and Fokin and Sharpless have reported an azide-alkyne "ligation" process that gives the 1,4-isomer when a $CuSO_4$/sodium ascorbate mixture is used to generate the Cu(I) catalyst *in situ*.[7] This chemistry, which may be carried out in water as the solvent, has recently been applied to the synthesis of triazole-linked glycopeptides.[8] Also, a useful organic-soluble catalyst, $(PPh_3)_3$•CuBr, has been developed by Santoyo-Gonzalez and coworkers[9] that allows for homogenous catalysis in the synthesis of various 1,4-triazole-linked neoglycoconjugates.

The "Click Chemistry" concept requires suitable building blocks on which to introduce functionality[5] and the azidodeoxy sugars represent a potentially vast source of furanose and pyranose core structures for such manipulation. Since the literature contains many hundreds of such compounds, which most often serve as precursors to aminodeoxy sugars, we are interested in exploiting these platforms in order to build spatially well-defined chiral structures by using chemistry such as the newly developed methods for regioselective 1,2,3-triazole formation.[6-9] We chose 1-azido-1-deoxy-2,3:5,6-di-*O*-isopropylidene-β-D-mannofuranose (**3**, Scheme 1) as a platform for several reasons. Firstly, to the best of our knowledge, there are no examples of *furanosyl* azides being employed in metal-mediated 1,2,3-triazole synthesis. Secondly, all of the functionality in **3** is above the plane of the furanose ring, which makes the compound quite strained compared to the corresponding α-anomers; any epimerization at C-1 during triazole formation may provide useful mechanistic information about the organometallic-mediated formation of 1,2,3-triazoles. Lastly, the isopropylidene protecting groups should be stable to the required chemistry (Cu-acetylides) and the 5,6-acetal should be hydrolyzed selectively thus opening up O-5 and O-6 for further manipulation.

## RESULTS AND DISCUSSION

Synthesis of azide (**3**) (Scheme 1) begins with 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**1**), which is the product of thermodynamic acetalization of D-mannose with acetone and sulfuric acid. Diacetonide (**1**) crystallizes as the α-anomer and its $^1$H NMR spectrum reveals a narrow doublet at 5.38 ppm, which corresponds to H-1 of the furanose ring coupling with the OH proton. The lack of any coupling with H-2 is consistent for α-anomers in this system due to the ~90$^o$ torsional angle between H-1 and H-2.

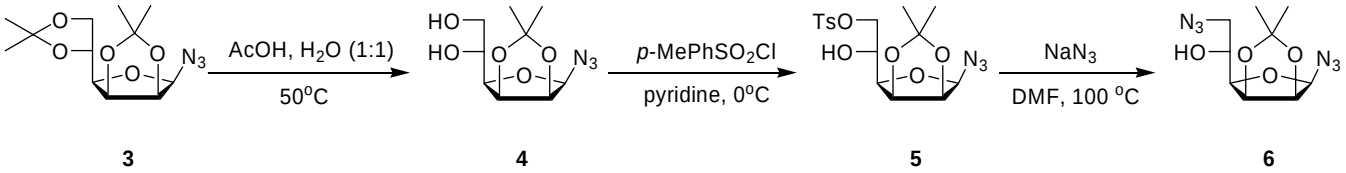



**Scheme 1.**

To introduce an azide group at C-1 of the mannofuranose skeleton we employed our glycosyl chloride synthesis,[10] which uses solid triphosgene as the chlorine source. Thus, chloride (**2**) (Scheme 1) was

produced on a 20 g scale in 87% yield. The $^1$H NMR spectrum of **2** shows a singlet for H-1 at 6.08 ppm thus identifying the chloride as the α-anomer. Finally, stereospecific $S_N2$ displacement of chloride with sodium azide gave compound (**3**) as a waxy solid.[11] That **3** is the β-anomer follows from its $^1$H NMR spectrum in which the signal at 4.40 ppm for H-1 is split by H-2 ($J$ = 3.7 Hz). The anomeric identity of the azide is supported by the crystal structure of one of the derived 1,2,3-triazoles formed herein.

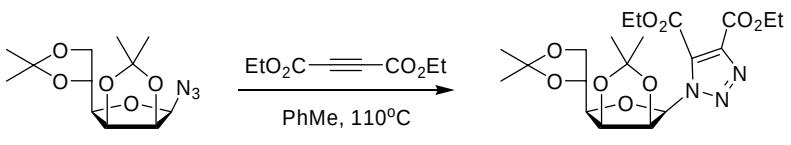
In order to introduce a second azide group onto the D-mannose backbone we decided to deprotect and then activate at O-6. Firstly, selective hydrolysis of the 5,6-*O*-isopropylidene group using AcOH-water was successful with monoacetal (**4**) (Scheme 2) being isolated in 84% yield.[12] Activation at O-6 proved problematic with the labile tosylate (**5**) decomposing upon silica gel chromatography; the best yield achieved for clean **5** was 30%. Subsequent conversion to the bis(azide) (**6**) was uneventful and **6** was isolated in 89% yield after chromatography.




**3** **4** **5** **6**

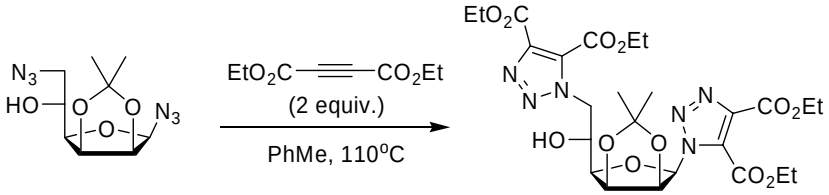
**Scheme 2.**

With azides (**3**) and (**6**) in hand we began to explore uncatalyzed Huisgen dipolar cycloaddition reactions with various acetylenes. Thus, monoazide (**3**) reacts with diethyl acetylenedicarboxylate (DEAD) to give the 1,2,3-triazole (**7**) as a crystalline solid (Equation 1) in 90% yield. The $^1$H NMR spectrum of triazole (**7**) shows a doublet at 6.29 ppm with a coupling constant of 4.7 Hz, which identifies **7** as being the *beta* anomer. Retention of the β-D-*manno* stereochemistry would be expected as there is no likelihood of anomeric interconversion during a concerted Huisgen dipolar cycloaddition. In similar fashion bis(azide) (**6**) reacts with two equivalents of DEAD to afford the bis(triazole) (**8**) (Equation 2). The proton for H-1 of the mannofuranosyl ring in **8** appears as a doublet at 6.42 ppm and the corresponding signal for H-1 in triazole (**7**) appears at 6.29 ppm. The fact that the coupling constants for these signals are so similar (4.8 and 4.7 Hz respectively) suggests that the second triazole ring in bis(triazole) (**8**) does not distort the mannofuranose ring compared with compound (**7**).




**3** **7**

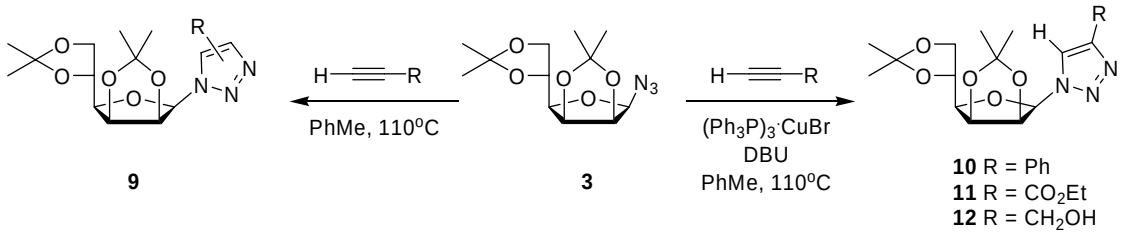
**Equation 1.**




**6** **8**

**Equation 2.**

Since DEAD is symmetrical it can only give one triazole upon cycloaddition however conventional (i.e. uncatalyzed) reaction of azide (**3**) with terminal acetylenes (Scheme 3) gave mixtures of 1,4- and 1,5-disubstituted isomers (**9**) in which the 1,4-isomer predominates.[1] When the organic-soluble catalyst $(PPh_3)_3$•CuBr[9] was employed reaction of azide (**3**) with phenyl acetylene, ethyl propiolate, and propargyl alcohol in toluene gave only one triazole product (**10-12** respectively, Scheme 3) in good yield. In each case triazoles (**10**) through (**12**) matched the major isomer formed in the uncatalyzed reactions.




**9** **3**

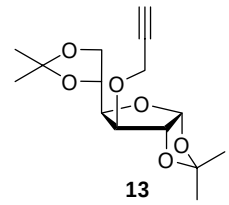
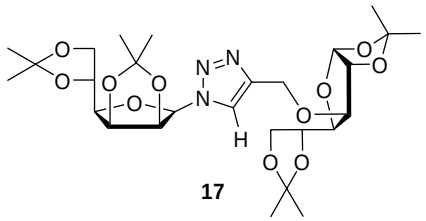
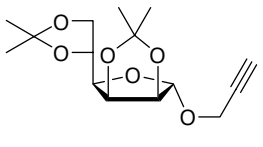
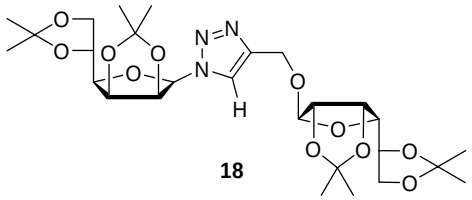
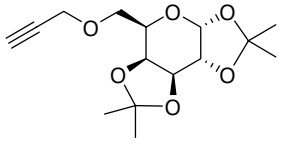
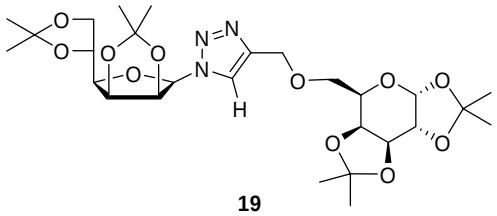
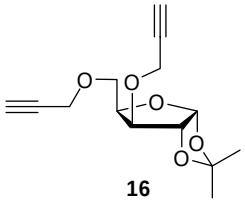
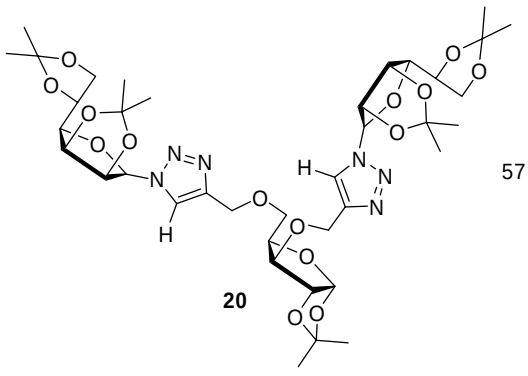
**Scheme 3.**

Encouraged by the efficiency of the Cu(I)-catalyzed triazole formation, and the fact that the β-mannofuranosyl configuration is retained, we turned our attention to the synthesis of several triazole-linked disaccharide and trisaccharide analogs. The term *carbohybrid* has been coined to describe compounds in which portions of oligosaccharides are replaced by non-carbohydrate groups,[13] and within that potentially vast family we refer to 1,2,3-triazole-linked sugars as *glycazoles*.

The required sugar-derived alkyne partners were prepared by alkylation of several readily available carbohydrate platforms with propargyl bromide. Thus, 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose, 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose, 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose, and 1,2-*O*-isopropylidene-D-xylofuranose where alkylated to give alkynes (**13**)-(**16**) respectively in the yields shown in Table 1. With suitable alkynes in hand we treated each with mannofuranosyl azide (**3**) in the presence of $(PPh_3)_3$•CuBr and DBU to generate the glycazoles (**17**)-(**20**) shown in Table 1. In each case only the 1,4-disubstituted triazole was formed and analysis of $^1$H NMR spectra of the crude reaction mixtures did not give any evidence for the formation of the 1,5-disubstituted isomers during these reactions. In each case the anomeric proton on the mannofuranosyl ring in compounds (**17-20**) appears around 6.0 ppm as doublets with $J \sim 3.3$ Hz again proving that the β configuration of the azide precursor (i.e. **3**) had

been retained during the formation of the 1,2,3-triazole products. Each of the signals for the proton attached at C-5 of the triazole rings in **17-20** appears as a singlet at 7.8-7.9 ppm, which indicates that they are the same regioisomer in each case. Further evidence for these regioisomeric assignments is provided by the X-Ray crystal structure of compound (**17**), which clearly shows it to be the 1,4-disubstituted triazole (Figure 1, Tables 2 and 3).

**Table 1.** Monosaccharide-derived alkynes used in this work and yields for resultant triazole carbohybrids.

| Alkyne precursor | %Yield | Addition product with **3** | %Yield |
|---|---|---|---|
|  **13** | 62 |  **17** | 73 |
|  **14** | 69 |  **18** | 70 |
|  **15** | 67 |  **19** | 72 |
|  **16** | 73 |  **20** | 57 |

In conclusion, we have applied recently reported methods for regiocontrolled synthesis of disubstituted 1,2,3-triazoles to the formation of a variety of novel carbohybrids (glycazoles) derived from the β-D-mannofuranosyl skeleton. The β-D-*manno* configuration is retained in each case. We are presently applying these methods to the regioselective synthesis of both furanosyl and pyranosyl substrates with a view to creating compounds with glycomimetic potential.

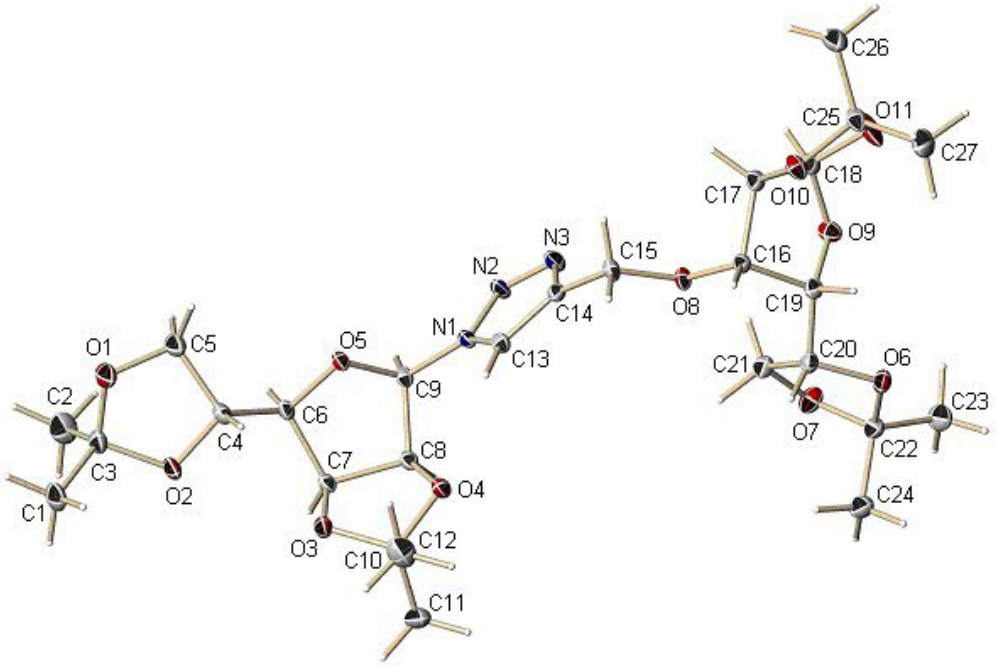



**Figure 1.** ORTEP representation of **17** at the 50% probability level.

**Table 2**. Crystal data and structure refinement for **17**.

| | |
|---|---|
| Empirical formula | $C_{27}H_{41}N_3O_{11}$ |
| Formula weight | 583.63 |
| Temperature | 100(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Monoclinic |
| Space group | *P* $2_1$ (No. 4) |
| Unit cell dimensions | $a$ = 10.0048(13) Å $\alpha$ = 90°. |
| | $b$ = 10.3781(13) Å $\beta$ = 107.051(2)°. |
| | $c$ = 14.6612(19) Å $\gamma$ = 90°. |
| Volume, $Z$ | 1455.4(3) Å$^3$, 2 |
| Density (calculated) | 1.332 g/cm$^3$ |
| Absorption coefficient | 0.103 mm$^{-1}$ |
| $F$(000) | 624 |
| Crystal size | 0.407 x 0.275 x 0.154 mm |
| Theta range for data collection | 1.45 to 28.33°. |
| Limiting indices | -13<=$h$<=13, -13<=$k$<=13, -19<=$l$<=19 |
| Reflections collected | 15527 |
| Independent reflections | 7134 [$R$(int) = 0.0212] |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 7134 / 1 / 426 |
| Goodness-of-fit on $F^2$ | 1.078 |
| Final $R$ indices [$I$>2σ($I$)] | $R_1$ = 0.0425, $wR_2$ = 0.1088 |
| $R$ indices (all data) | $R_1$ = 0.0436, $wR_2$ = 0.1098 |
| Absolute structure parameter | 0.6(5) |
| Largest diff. peak and hole | 0.374 and -0.256 e·Å$^{-3}$ |

**Table 3**. Selected bond lengths (Å) and angles (°) for **17**.

| | | | |
|---|---|---|---|
| C(6)-C(7) | 1.535(2) | C(9)-O(5)-C(6) | 102.99(11) |
| C(7)-C(8) | 1.548(2) | O(5)-C(6)-C(7) | 104.86(11) |
| C(8)-C(9) | 1.529(2) | C(6)-C(7)-C(8) | 103.88(12) |
| O(5)-C(6) | 1.4398(17) | C(9)-C(8)-C(7) | 102.30(12) |
| O(5)-C(9) | 1.4283(17) | O(5)-C(9)-C(8) | 105.14(12) |
| N(1)-C(9) | 1.4421(19) | N(1)-C(9)-C(8) | 116.49(12) |
| N(1)-C(13) | 1.3515(19) | O(5)-C(9)-N(1) | 109.66(11) |
| C(13)-C(14) | 1.372(2) | N(2)-N(1)-C(9) | 116.63(12) |
| N(3)-C(14) | 1.361(2) | N(3)-N(2)-N(1) | 107.08(12) |
| N(1)-N(2) | 1.3540(18) | C(13)-N(1)-N(2) | 110.95(12) |
| N(2)-N(3) | 1.3033(19) | N(1)-C(13)-C(14) | 104.12(13) |
| C(14)-C(15) | 1.493(2) | N(2)-N(3)-C(14) | 109.17(12) |
| O(8)-C(15) | 1.4320(18) | N(3)-C(14)-C(15) | 121.51(13) |
| O(8)-C(16) | 1.4244(17) | C(13)-C(14)-C(15) | 129.81(14) |
| C(16)-C(17) | 1.533(2) | O(8)-C(15)-C(14) | 107.48(12) |
| C(17)-C(18) | 1.543(2) | O(8)-C(16)-C(17) | 111.29(12) |
| C(16)-C(19) | 1.530(2) | C(19)-C(16)-C(17) | 100.96(12) |
| O(9)-C(18) | 1.406(2) | O(9)-C(18)-C(17) | 107.35(13) |
| O(9)-C(19) | 1.4329(19) | O(9)-C(19)-C(16) | 104.20(12) |

## EXPERIMENTAL

**General:** Reaction progress was monitored by TLC with UV light detection or the TLC plate was treated

with a 5% sulfuric acid/ethanol solution to burn the reaction material to provide indication of the carbohydrate product. Flash chromatography was performed on 32-63 μm, 60-Å silica gel. All products are homogeneous by TLC. A Bruker Esquire-HP 1100 mass spectrometer was used for low-resolution MS and a Micromass LCT was used for high resolution. A Varian Gemini 2000 NMR system was employed for measurement of $^1$H and $^{13}$C NMR spectra at 400 MHz and 100 MHz respectively, using $CDCl_3$ or DMSO-$d_6$ as solvents. X-Ray diffraction data was collected on a Bruker SMART APEX 4K CCD Single Crystal Diffractometer at 100 K; Mo ($K_\alpha$) radiation. The structure was solved using the *SMART*, *SAINT*, *SADABS*, *SHELXL*, and *SHELXP* software.[14] Melting points were recorded on a MelTemp apparatus and are uncorrected. Optical rotations were recorded on a Perkin Elmer model 343 automatic polarimeter.

**2,3:5,6-Di-*O*-isopropylidene-α-D-mannofuranose (1).**

In a flame-dried 2000 mL Erlenmeyer flask equipped with a drying tube and magnetic stir bar, D-mannose (20.0 g, 107.4 mmol) was dissolved in acetone (750 mL) at rt. Concentrated $H_2SO_4$ (14 mL) was added in 2 mL portions every five minutes and the reaction was allowed to stir for 12 h when TLC (EtOAc) showed consumption of starting material. The reaction was neutralized with $Na_2CO_3$ and filtered. Charcoal (5 g) and $Na_2CO_3$ (10 g) were added to the filtrate and the mixture was refluxed for 1 h. The reaction was cooled, filtered, and evaporated and the remaining solid was recrystallized from methanol to afford 18.8 g of **1** (67%). mp = 119-121 ˚C. $^1$H NMR ($CDCl_3$): $\delta$ 1.32 (s, 3H, -$CH_3$), 1.37 (s, 3H, -$CH_3$), 1.45 (s, 3H, -$CH_3$), 1.46 (s, 3H, -$CH_3$), 2.77 (d, 1H, -OH, $J$ = 2.6 Hz), 4.06 (m, 2H, H-6, H-6'), 4.18 (dd, 1H, H-4, $J$ = 3.7, 7.3 Hz), 4.40 (m, 1H, H-5), 4.61 (d, 1H, H-2, $J$ = 5.9 Hz), 4.81 (dd, 1H, H-3, $J$ = 3.7, 5.9 Hz), 5.38 (d, 1H, H-1, $J$ = 2.2 Hz). This data match that of a commercially available sample of **1**.

**2,3:5,6-Di-*O*-isopropylidene-α-D-mannofuranosyl chloride (2).**

In a 500 mL flame-dried round bottom flask fitted with a septum and magnetic stir bar, 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**1**) (24.0 g, 92.2 mmol) was dissolved in THF (250 mL). Triphosgene (10.9 g, 36.9 mmol) was added and the flask placed in an ice bath. Pyridine (4.8 mL) was added dropwise (**CAUTION** – $CO_2$ gas evolved), and the mixture was allowed to stir for 4 h when TLC (3:1 hexane: EtOAc, product $R_f$ = 0.58) showed consumption of the starting material. The mixture was filtered and the precipitate washed with THF. The filtrate was reduced to produce 22.85 g of **3** as a yellow syrup (87%), which was used without further purification. $^1$H NMR ($CDCl_3$): $\delta$ 1.35 (s, 3H, -$CH_3$), 1.41 (s, 3H, -$CH_3$), 1.48 (s, 6H, 2 x -$CH_3$), 4.00 (dd, 1H, H-6, $J$ = 4.4, 8.8 Hz), 4.08 (dd, 1H, H-6', $J$ = 6.2, 8.8 Hz), 4.19 (dd, 1H, H-4, $J$ = 3.7, 7.9 Hz), 4.42 (ddd, 1H, H-5, $J$ = 4.4, 6.2, 10.6 Hz), 4.87 (dd, 1H, H-3, $J$ = 3.7, 5.9 Hz), 4.93 (d, 1H, H-2, $J$ = 5.9 Hz), 6.08 (s, 1H, H-1). This data match that reported previously for compound (**2**).[10]

**1-Azido-1-deoxy-2,3:5,6-di-*O*-isopropylidene-β-D-mannofuranose (3).**

In a 500 mL round bottom two neck flask equipped with a thermometer adapter and magnetic stir bar,

2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl chloride (**2**, 22.85 g, 82.2 mmol) and $NaN_3$ (26.7 g, 410.8 mmol) were heated at 80 ˚C in DMF (250 mL) for 12 h when TLC (3:1 hexane : EtOAc, product $R_f$ = 0.32) showed consumption of the starting material. The reaction was diluted with water (100 mL) and then extracted with $CH_2Cl_2$ (3 x 20 mL). The organic phase was washed with water (20 mL) and then dried using $MgSO_4$. Evaporation of the solvent gave a waxy homogenous solid identified as **3** (22.5 g, 96%). $^1$H NMR ($CDCl_3$*):* $\delta$ 1.36 (s, 3H, -$CH_3$), 1.38 (s, 3H, -$CH_3$), 1.44 (s, 3H, -$CH_3$), 1.55 (s, 3H, -$CH_3$), 3.59 (dd, 1H, H-4, *J* = 3.7, 7.7 Hz), 4.11 (m, 2H, H-6, H-6'), 4.40 (d, 1H, H-1, *J* = 3.7 Hz), 4.45 (m, 1H, H-5), 4.67 (dd, 1H, H-2, *J* = 3.7, 5.9 Hz), 4.77 (dd, 1H, H-3, *J* = 3.3, 5.9 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.6, 26.3, 26.4, 28.2, 67.9, 74.0, 79.6, 80.6, 82.2, 90.1, 110.3, 114.6. This data are consistent with an authentic sample of **3** prepared by a different route.[11]

**1-Azido-1-deoxy-2,3-*O*-isopropylidene-β-D-mannofuranose** (**4**).

In a 500 mL two neck round bottom flask equipped with a thermometer adapter and magnetic stir bar, azide (**3**) (6.0 g, 21.0 mmol) was dissolved in 1:1 glacial acetic acid and water (300 mL). The reaction was heated to 50 ˚C for 3 h after which time TLC (EtOAc, product $R_f$ = 0.34) showed complete disappearance of **3**. The residue after evaporation *in vacuo* was evaporated with toluene (2 x 100 mL) to afford **4** as a clear syrup in 84% yield (4.32 g). $^1$H NMR (DMSO-$d_6$): $\delta$ 1.37 (s, 3H, -$CH_3$), 1.56 (s, 3H, -$CH_3$), 3.67 (dd, 1H, H-4, *J* = 4.0, 8.4 Hz), 3.75 (dd, 1H, H-6, *J* = 5.5, 11.4 Hz), 3.90 (dd, 1H, H-6', *J* = 3.3, 11.7 Hz), 4.10 (m, 1H, H-5), 4.46 (d, 1H, H-1, *J* = 3.7 Hz), 4.69 (dd, 1H, H-2, *J* = 3.7, 6.2 Hz), 4.84 (dd, 1H, H-3, *J* = 4.0, 6.2 Hz). $^{13}$C NMR (DMSO-$d_6$): $\delta$ 26.0, 26.8, 65.2, 70.0, 78.8, 81.0, 82.0, 89.6, 103.2.

**1-Azido-1-deoxy-2,3-*O*-isopropylidene-6-*O*-*p*-toluenesulfonyl-β-D-mannofuranose** (**5**).

In a 100 mL round bottom flask equipped with a magnetic stir bar and septum 1-azido-1-deoxy-2,3-*O*-isopropylidene-β-D-mannofuranose (**4**) (3.25 g, 13.4 mmol) was dissolved in pyridine (60 mL). *p*-Toluenesulfonyl chloride (3.06 g, 16.0 mmol) was added and the temperature lowered to 0 ºC. The mixture was stirred for 12 h when TLC (ethyl acetate) showed the disappearance of the starting material. Water (12 mL) was mixed with the reaction for 10 min, the mixture was poured over ice and then extracted with methylene chloride (3 x 10 mL). The combined organic layers were washed with water (10 mL). The organic layer was dried over $MgSO_4$, evaporated, and purified by elution from a column of silica gel (1:1 hexane: ethyl acetate) to afford an unstable white solid in 30% yield. $^1$H NMR ($CDCl_3$): $\delta$ 1.34 (s, 3H, -$CH_3$), 1.50 (s, 3H, -$CH_3$), 2.45 (s, 3H, -PhC$\underline{H}_3$), 2.64 (d, 1H, -OH, *J* = 5.5 Hz), 3.58 (dd, 1H, H-4, *J* = 4.0, 8.1 Hz), 4.17 (m, 2H, H-6, H-6'), 4.34 (m, 2H, H-1, H-5), 4.66 (dd, 1H, H-2, *J* = 3.7, 5.9 Hz), 4.81 (dd, 1H, H-3, *J* = 4.0, 6.2 Hz), 7.35 (d, 2H, Ar-H), 7.81 (d, 2H, Ar-H). $^{13}$C NMR ($CDCl_3$): $\delta$ 22.9, 25.7, 26.4, 68.7, 72.7, 77.9, 80.6, 82.0, 90.2, 114.8, 129.1 (double intensity), 131.0 (double intensity), 133.4, 146.1. APCI-MS (*m/z*) calcd: 399.41, found: 391.3 (M–$N_2$+$H_2O$).

**1,6-Diazido-1,6-dideoxy-2,3-*O*-isopropylidene-β-D-mannofuranose** (**6**).

In a 50 mL two neck round bottom flask equipped with a magnetic stir bar and thermometer adapter,

tosylate (**5**) (0.50 g, 1.3 mmol) and $NaN_3$ (0.41 g, 6.3 mmol) in DMF (15 mL) were heated at 100 ºC for 12 h when TLC (2:1 hexane: EtOAc) showed no starting material. The reaction was poured over water (25 mL) and the mixture was extracted with $CH_2Cl_2$ (3 x 15 mL), which was then back extracted with water (10 mL). After drying over $MgSO_4$ removal of solvent gave **6** as a yellow syrup in 89% yield. $^1$H NMR ($CDCl_3$): $\delta$ 1.36 (s, 3H, -$CH_3$), 1.56 (s, 3H, -$CH_3$), 2.52 (d, 1H, -OH, $J$ = 5.1 Hz), 3.48 (dd, 1H, H-6, $J$ = 5.9, 12.8 Hz), 3.64 (m, 2H, H-4, H-6'), 4.18 (m, 1H, H-5), 4.48 (d, 1H, H-1, $J$ = 3.7 Hz), 4.70 (dd, 1H, H-2, $J$ = 3.7, 6.2 Hz), 4.84 (dd, 1H, H-3, $J$ = 4.0, 6.2 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.8, 26.5, 55.2, 70.1, 79.1, 80.8, 82.1, 90.2, 114.9. APCI-MS (*m/z*) calcd: 270.11, found: 243.1 (M-$N_2$,+H). HRMS (M+Na) calcd: 293.0974, found: 293.0962.

**1-(2,3:5,6-Di-*O*-isopropylidene-β-D-mannofuranosyl)-1*H*-[1,2,3]triazol-4,5-dicarboxylic acid diethyl ester** (**7**).

Azide (**3**) (210 mg, 0.74 mmol) and diethyl acetylenedicarboxylate (126 mg, 0.74 mmol) were refluxed in toluene (5 mL) overnight. Removal of solvent and purication by flash chromatography (3:1 hexane: EtOAc) gave triazole (**7**) as a colorless solid (190 mg, 90%). mp = 122-124 ˚C, recrystallized from ethanol. $^1$H NMR ($CDCl_3$): $\delta$ 1.27 (s, 3H, -$CH_3$), 1.29 (s, 3H, -$CH_3$), 1.39 (m, 9H, -$CH_3$, 2 x -$OCH_2C\underline{H}_3$), 1.47 (s, 3H, -$CH_3$), 4.00 (dd, 1H, H-4, $J$ = 4.0, 8.1 Hz), 4.17 (m, 2H, H-6, H-6'), 4.41 (m, 4H, -$OC\underline{H}_2CH_3$), 4.65 (m, 1H, H-5), 4.94 (dd, 1H, H-3, $J$ = 4.0, 5.9 Hz), 5.08 (dd, 1H, H-2, $J$ = 4.4, 6.2 Hz), 6.29 (d, 1H, H-1, $J$ = 4.7 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ 15.1, 15.4, 25.7, 26.1, 26.3, 28.2, 62.9, 64.0, 67.7, 73.7, 77.9, 80.5, 81.8, 91.7, 110.5, 115.8, 131.9, 140.1, 159.7, 160.9. APCI-MS (*m/z*) calcd: 455.19, found: 456.1 (M+H). HRMS (M+Na) calcd: 478.1801, found: 478.1826. Anal. Calcd for $C_{20}H_{29}N_3O_9$: C, 52.74; H, 6.42; N, 9.23. Found: C, 52.91; H, 6.46; N, 9.24.

**1-(2,3-*O*-Isopropylidene-β-D-mannofuranosyl)-1,6-di(1*H*-[1,2,3]triazol-4,5-dicarboxylic acid diethyl esters)** (**8**).

Refluxing azide (**6**) (270 mg, 1.0 mmol) with DEAD (340 mg, 2.0 mmol) in toluene (5 mL) overnight gave, after chromatography (3:1 hexane: EtOAc), bis(triazole) (**8**) as a colorless syrup (458 mg, 75%). $^1$H NMR ($CDCl_3$): $\delta$ 1.15 (s, 3H, -$CH_3$), 1.24 (s, 3H, -$CH_3$), 1.38 (m, 12H, 4 x -$OCH_2C\underline{H}_3$), 3.11 (d, 1H, -OH, $J$ = 5.5 Hz), 3.93 (dd, 1H, H-4, $J$ = 4.8, 8.8 Hz), 4.42 (m, 10H, H-6, H-6', 4 x -$OC\underline{H}_2CH_3$), 4.70 (m, 1H, H-5), 4.95 (m, 1H, H-3), 5.10 (dd, 1H, H-2, $J$ = 4.8, 5.9 Hz), 6.42 (d, 1H, H-1, $J$ = 4.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ 15.1 (double intensity), 15.4 (double intensity), 25.7, 26.0, 53.4, 62.9, 63.0, 64.1, 64.3, 69.1, 80.6, 81.3, 81.9, 91.9, 116.0, 131.8, 133.5, 140.30, 140.31, 159.6, 159.9, 160.9 (double intensity). APCI-MS (*m/z*) calcd: 610.57, found: 611.3 (M+H). HRMS (M+Na) calcd: 633.2132, found: 633.2146.

**Cu(I)-catalyzed 1,2,3-triazole synthesis.**

Azide (**3**) (0.5 g, 1.75 mmol), either phenyl acetylene, ethyl propiolate, or propargyl alcohol (1 equivalent), $(PPh_3)_3$•CuBr[9] (0.2 equivalent), and DBU (3 equivalents) were refluxed in toluene for 16 h. After chromatography (3:1 hexane : EtOAc) the triazoles were isolated as colorless syrups.

**1-(2,3:5,6-Di-*O*-isopropylidene-β-D-mannofuranosyl)-4-phenyl-1*H*-[1,2,3]triazole** (**10**). 67% yield. $^1$H NMR ($CDCl_3$): $\delta$ 1.36 (s, 3H, -$CH_3$), 1.41 (s, 3H, -$CH_3$), 1.48 (s, 3H, -$CH_3$), 1.61 (s, 3H, -$CH_3$), 3.80 (dd, 1H, H-4, $J$ = 3.7, 7.7 Hz), 4.11 (dd, 1H, H-6, $J$ = 4.4, 9.2 Hz), 4.15 (dd, 1H, H-6', $J$ = 6.2, 9.2 Hz), 4.53 (ddd, 1H, H-5, $J$ = 4.0, 6.2, 10.3 Hz), 4.92 (dd, 1H, H-2, $J$ = 3.7, 5.9 Hz), 4.98 (dd, 1H, H-3, $J$ = 3.7, 5.9 Hz), 6.14 (d, 1H, H-1, $J$ = 3.7 Hz), 7.32 (m, 5H, Ar-H), 8.08 (s, 1H, triazole-H). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.2, 26.4, 26.7, 28.2, 67.9, 73.8, 80.2, 80.3, 80.8, 89.9, 110.5, 114.7, 121.4, 126.7 (double intensity), 129.2 (double intensity), 129.8, 131.5, 148.2. APCI-MS (*m/z*) calcd: 387.43, found: 388.3 (M+H). HRMS (M+Na) calcd: 410.1692, found: 410.1703.

**1-(2,3:5,6-Di-*O*-isopropylidene-β-D-mannofuranosyl)-1*H*-[1,2,3]triazol-4-carboxylic acid ethyl ester** (**11**). 81% yield. $^1$H NMR ($CDCl_3$): $\delta$ 1.38 (s, 3H, -$CH_3$), 1.45 (m, 6H, -$CH_3$, -$OCH_2C\underline{H}_3$), 1.50 (s, 3H, -$CH_3$), 1.60 (s, 3H, -$CH_3$), 3.80 (dd, 1H, H-4, $J$ = 3.8, 7.8 Hz), 4.06 (dd, 1H, H-6, $J$ = 4.2, 9.0 Hz), 4.14 (dd, 1H, H-6', $J$ = 6.2, 9.2 Hz), 4.47 (m, 3H, H-5, -$OC\underline{H}_2CH_3$), 4.92 (dd, 1H, H-2, $J$ = 3.6, 5.9 Hz), 4.98 (dd, 1H, H-3, $J$ = 5.9, 3.7 Hz), 6.17 (d, 1H, H-1, $J$ = 3.6 Hz), 8.35 (s, 1H, triazole-H). $^{13}$C NMR ($CDCl_3$): $\delta$ 15.5, 25.2, 26.3, 26.6, 28.1, 62.4, 67.7, 73.7, 80.2, 80.4, 80.8, 89.8, 110.5, 114.8, 129.3, 140.7, 161.5. APCI-MS (*m/z*) calcd: 383.39, found: 384.2 (M+H). HRMS (M+Na) calcd: 406.1590, found: 406.1614.

**1-(2,3:5,6-Di-*O*-isopropylidene-β-D-mannofuranosyl)-1*H*-[1,2,3]triazol-4-ylmethanol** (**12**). 57% yield. $^1$H NMR ($CDCl_3$): $\delta$ 1.35 (s, 3H, -$CH_3$), 1.40 (s, 3H, -$CH_3$), 1.47 (s, 3H, -$CH_3$), 1.58 (s, 3H, -$CH_3$), 2.46 (s, 1H, -OH), 3.77 (dd, 1H, H-4, $J$ = 3.7, 7.7 Hz), 4.06 (dd, 1H, H-6, $J$ = 4.0, 8.8 Hz), 4.12 (dd, 1H, H-6', $J$ = 5.9, 8.8 Hz), 4.49 (ddd, 1H, H-5, $J$ = 4.0, 5.9, 7.7 Hz), 4.82 (d, 2H, -$C\underline{H}_2OH$, $J$ = 4.4 Hz), 4.88 (dd, 1H, H-2, $J$ = 3.7, 6.2 Hz), 4.96 (dd, 1H, H-3, $J$ = 4.0, 6.2 Hz), 6.10 (d, 1H, H-1, $J$ = 3.7 Hz), 7.87 (s, 1H, triazole-H). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.2, 26.3, 26.7, 28.1, 57.2, 67.7, 73.7, 80.1, 80.2, 80.7, 89.7, 110.5, 114.7, 123.7, 148.5. APCI-MS (*m/z*) calcd: 341.36, found: 342.1 (M+H). HRMS (M+Na) calcd: 364.1485, found: 364.1463.

**Synthesis of sugar-derived alkynes.**

1,2:5,6-Di-*O*-isopropylidene-D-glucofuranose, 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose, 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose, or 1,2-*O*-isopropylidene-D-xylofuranose (1.15 g), KOH (1.5 g, 26.5 mmol) and propargyl bromide (3.1 g, 26.5 mmol) in MeCN (10 mL) were stirred at rt for 24 h. The mixtures were evaporated *in vacuo* and partitioned between $CH_2Cl_2$ (25 mL) and water (25 mL). The aqueous phase was extracted with $CH_2Cl_2$ (3 x 20 mL) then the combined organic layers were dried over $MgSO_4$, reduced, and purified by chromatography (3:1 hexane : EtOAc) to give the alkynes as colorless syrups.

**1,2:5,6-Di-*O*-isopropylidene-3-*O*-(prop-2-ynyloxy)-D-glucofuranose** (**13**). 62% yield. $^1$H NMR ($CDCl_3$): $\delta$ 1.30 (s, 3H, -$CH_3$), 1.34 (s, 3H, -$CH_3$), 1.41 (s, 3H, -$CH_3$), 1.49 (s, 3H, -$CH_3$), 2.52 (t, 1H, -$OCH_2CC\underline{H}$, $J$ = 2.4 Hz), 3.98 (dd, 1H, H-4, $J$ = 5.4, 8.6 Hz), 4.11 (m, 3H, H-5, H-6, H-6'), 4.26 (m, 3H, H-3, -$OC\underline{H}_2CCH$), 4.62 (d, 1H, H-2, $J$ = 3.7 Hz), 5.87 (d, 1H, H-1, $J$ = 3.7 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ 26.6, 27.5, 28.0 (double intensity), 59.2, 68.3, 73.6, 76.1, 80.3, 82.1, 82.6, 83.9, 106.2, 110.0, 112.9. APCI-MS (*m/z*) calcd: 298.3, found: 299.3 (M+H). HRMS (M+Na) calcd: 321.1314, found: 321.1311.

**(Prop-2-ynyloxy) 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranoside** (**14**). 69% yield. $^1$H NMR ($CDCl_3$): $\delta$ 1.33 (s, 3H, -$CH_3$), 1.38 (s, 3H, -$CH_3$), 1.46 (s, 3H, -$CH_3$), 1.48 (s, 3H, -$CH_3$), 2.44 (t, 1H, $\underline{H}CCCH_2$, $J$ = 2.4 Hz), 3.96 (dd, 1H, H-4, $J$ = 3.6, 7.8 Hz), 4.06 (dd, 1H, H-6, $J$ = 4.2, 8.7 Hz), 4.11 (dd, 1H, H-6', $J$ = 6.2, 8.7 Hz), 4.19 (dd, 2H, -OC$\underline{H}_2$CCH, $J$ = 2.3, 4.3 Hz), 4.41 (ddd, 1H, H-5, $J$ = 4.3, 6.2, 7.8 Hz), 4.63 (d, 1H, H-2, $J$ = 5.9 Hz), 4.79 (dd, 1H, H-3, $J$ = 3.6, 5.9 Hz), 5.18 (s, 1H, H-1). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.7, 26.4, 27.1, 28.2, 55.3, 70.0, 74.1, 75.8, 78.8, 80.5, 81.7, 86.1, 105.9, 110.3, 113.7. APCI-MS (*m/z*) calcd: 298.33, found: 299.2 (M+H). HRMS (M+Na) calcd: 321.1314, found: 321.1306.

**1,2:3,4-Di-*O*-isopropylidene-6-*O*-(prop-2-ynyloxy)-D-galactopyranose** (**15**). 67% yield. $^1$H NMR ($CDCl_3$): $\delta$ 1.33 (s, 3H, -$CH_3$), 1.35 (s, 3H, -$CH_3$), 1.46 (s, 3H, -$CH_3$), 1.55 (s, 3H, -$CH_3$), 2.44 (t, 1H, $\underline{H}CCCH_2$, $J$ = 2.4 Hz), 3.67 (dd, 1H, H-6, $J$ = 7.1, 10.1 Hz), 3.78 (dd, 1H, H-6', $J$ = 5.2, 10.1 Hz), 4.00 (ddd, 1H, H-5, $J$ = 1.9, 5.2, 7.1 Hz), 4.21 (d, 1H, -OC$\underline{H}_2$CCH, $J$ = 2.4 Hz), 4.24 (d, 1H, -OC$\underline{H}_2$CCH, $J$ = 2.4 Hz), 4.26 (dd, 1H, H-4, $J$ = 1.8, 7.9 Hz), 4.32 (dd, 1H, H-2, $J$ = 2.4, 5.1 Hz), 4.61 (dd, 1H, H-3, $J$ = 2.4, 7.9 Hz), 5.55 (d, 1H, H-1, $J$ = 5.1 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.7, 26.2, 27.2, 27.3, 59.7, 67.9, 69.8, 71.6, 71.8, 72.3, 75.8, 80.7, 97.4, 109.6, 110.3. APCI-MS (*m/z*) calcd: 298.33, found: 299.0 (M+H). HRMS (M+Na) calcd: 321.1314, found: 321.1290.

**1,2-*O*-Isopropylidene-3,5-di-*O*-(prop-2-ynyloxy)-D-xylofuranose** (**16**). 73% yield. $^1$H NMR ($CDCl_3$): $\delta$ 1.32 (s, 3H, -$CH_3$), 1.50 (s, 3H, -$CH_3$), 2.47 (t, 1H, -$CH_2$C$\underline{C}$H, $J$ = 2.6 Hz), 2.50 (t, 1H, -$CH_2$C$\underline{C}$H, $J$ = 2.6 Hz), 3.72 (dd, 1H, H-5, $J$ = 6.6, 10.0 Hz), 3.81 (dd, 1H, H-5', $J$ = 5.6, 10.0 Hz), 4.11 (d, 1H, H-3, $J$ = 3.1 Hz), 4.19-4.25 (m, 4H, 2 x -OC$\underline{H}_2$CCH), 4.40 (m, 1H, H-4), 4.62 (d, 1H, H-2, $J$ = 3.8 Hz), 5.92 (d, 1H, H-1, $J$ = 3.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ 27.6, 28.0, 58.9, 59.8, 68.4, 75.8, 76.2, 80.0, 80.2, 80.6, 82.6, 83.4, 106.1, 112.9. APCI-MS (*m/z*) calcd: 266.29, found: 267.2 (M+H). HRMS (M+Na) calcd: 289.1052, found: 289.1039.

**1,4-Disubstituted triazole (17).**

Mannofuranosyl azide (**3**) (0.25 g, 0.88 mmol), alkyne (**13**) (0.288 g, 0.96 mmol), $(PPh_3)_3$•CuBr (0.268 g, 0.29 mmol) and DBU (0.432 mL) were refluxed in toluene (15 mL) overnight. The reaction was concentrated and purified by chromatography (2:1 hexane : EtOAc) to give 0.360 g (73%) of **17** as a colorless solid. mp = 196-198 ˚C, recrystallized from ethanol. $^1$H NMR ($CDCl_3$): $\delta$ 1.29 (s, 3H, -$CH_3$), 1.33, 1.34 (2s, 6H total, 2 x -$CH_3$), 1.39 (s, 6H, 2 x -$CH_3$), 1.46, 1.48, 1.56 (3s, 9H total, 3 x -$CH_3$), 3.76 (dd, 1H, H-4$_{man}$, $J$ = 3.7, 8.1 Hz), 4.07 (m, 9H, H-6 and H-6'$_{man}$, H-3, H-4, H-5, H-6, and H-6'$_{glc}$, -OC$\underline{H}_2$CNCH-), 4.50 (ddd, 1H, H-5$_{man}$, $J$ = 4.0, 5.9, 8.1 Hz), 4.61 (d, 1H, H-2$_{glc}$, $J$ = 3.7 Hz), 4.87 (dd, 1H, H-2$_{man}$, $J$ = 3.6, 5.9 Hz), 4.96 (dd, 1H, H-3$_{man}$, $J$ = 3.7, 5.9 Hz), 5.88 (d, 1H, H-1$_{glc}$, $J$ = 3.7 Hz), 6.10 (d, 1H, H-1$_{man}$, $J$ = 3.6 Hz), 7.87 (s, 1H, triazole-H). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.2, 26.3, 26.7 (double intensity), 27.4, 28.1 (double intensity), 28.3, 65.1, 68.0, 68.4, 73.7 (double intensity), 80.3, 80.35, 80.7, 82.2, 82.8, 83.6, 89.9, 106.3, 110.0, 100.7, 112.9, 114.8, 124.5, 145.2. APCI-MS (*m/z*) calcd: 583.27, found 584.3 (M+H). HRMS (M+Na) calcd: 606.2639, found: 606.2645. $[\alpha]_D$ = +55.6˚ (*c* 5.0, $CH_2Cl_2$). Anal. Calcd for $C_{27}H_{41}N_3O_{11}$: C,

55.56; H, 7.08; N, 7.20. Found: C, 55.39; H, 7.38; N, 7.21.

**1,4-Disubstituted triazole (18).**

Mannofuranosyl azide (**3**) (0.774 g, 2.7 mmol), alkyne (**14**) (0.89 g, 3.0 mmol), $(PPh_3)_3$•CuBr (0.554 g, 0.59 mmol) and DBU (1.33 mL) were refluxed in toluene (15 mL) overnight. The reaction was reduced and the residue purified by chromatography (2:1 hexane : EtOAc) to give 1.11 g (70%) of triazole (**18**) as a colorless syrup. $^1$H NMR[15] ($CDCl_3$): $\delta$ 1.29, 1.33, 1.36, 1.37 (4s, 12H, 4 x -$CH_3$), 1.44 (overlapping 3s, 9H, 3 x -$CH_3$), 1.56 (s, 3H, -$CH_3$), 3.74 (dd, 1H, H-4$_{ringB}$, $J$ = 3.7, 8.1 Hz), 3.96 (dd, 1H, H-4$_{ringA}$, $J$ = 3.7, 8.1 Hz), 4.06 (m, 6H, (H-6, H-6')$_{ringA}$, (H-6, H-6')$_{ringB}$, -OC$\underline{H}_2$CNCH-), 4.39 (ddd, 1H, H-5$_{ringB}$, $J$ = 4.4, 6.6, 8.1 Hz), 4.48 (m, 1H, H-5$_{ringA}$, $J$ = 4.0, 5.9, 7.7 Hz), 4.61-4.76 (m, 2H, (H-2$_{ringB}$, H-3$_{ringB}$), 4.86 (dd, 1H, H-2$_{ringA}$, $J$ = 3.7, 5.9 Hz), 4.94 (dd, 1H, H-3$_{ringA}$, $J$ = 3.7, 5.9 Hz), 5.08 (s, 1H, H-1$_{ringB}$), 6.08 (dd, 1H, H-1$_{ringA}$, $J$ = 3.3 Hz), 7.82 (s, 1H, triazole-H). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.2, 25.7, 26.3, 26.4, 26.7, 27.1, 28.1, 28.2, 64.1, 65.9, 67.9, 68.1, 73.7, 80.3, 80.6 (double intensity), 80.7, 83.1, 83.3, 89.8, 106.6, 110.3, 113.6, 114.8, 124.4, 129.2, 132.8. APCI-MS (*m/z*) calcd: 583.27, found 584.3 (M+H). HRMS (M+Na) calcd: 606.2639, found: 606.2645. $[\alpha]_D$ = +3.5˚ (*c* 5.0, $CH_2Cl_2$).

**1,4-Disubstituted triazole (19).**

Mannofuranosyl azide (**3)** (0.25 g, 0.88 mmol), alkyne (**15**) (0.288 g, 0.96 mmol), $(PPh_3)_3$•CuBr (0.268 g, 0.29 mmol) and DBU (0.432 mL) were refluxed overnight in toluene (15 mL). After evaporation of the solvent and purification by chromatography (2:1 hexane : EtOAc) triazole (**19**) was isolated as a colorless solid (0.37 g, 72%), which was recrystallized from methanol. mp = 142-144 ˚C. $^1$H NMR[15] ($CDCl_3$): $\delta$ 1.31 (s, 6H, 2 x -$CH_3$), 1.32, 1.38, 1.41, 1.44, 1.50, 1.55 (6s, 18H total, 6 x -$CH_3$), 3.63 to 4.94 (several m, 14H, H-2 to H-6'$_{man}$, H-2 to H-6'$_{gal}$, -OC$\underline{H}_2$CNCH-), 5.52 (d, 1H, H-1$_{gal}$, $J$ = 4.8 Hz), 6.07 (d, 1H, H-1$_{man}$, $J$ = 3.3 Hz), 7.87 (s, 1H, triazole-H). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.3, 25.7, 26.2, 26.3, 26.7, 27.2, 27.3, 28.2, 65.8, 67.9, 67.9, 70.3, 71.6, 71.8, 72.3, 73.7, 80.3, 80.7, 89.8, 97.4, 109.6 (double intensity), 110.2, 110.6, 114.8, 124.5, 145.6. APCI-MS (*m/z*) calcd: 583.3, found 584.3 (M+H). HRMS (M+Na) calcd: 606.2639, found: 606.2627. $[\alpha]_D$ = -18.1˚ (*c* 5.0, $CH_2Cl_2$). Anal. Calcd for $C_{27}H_{41}N_3O_{11}$: C, 55.56; H, 7.08; N, 7.20. Found: C, 55.70; H, 7.26; N, 7.22.

**1,4-Disubstituted bis(triazole) (20).**

Mannofuranosyl azide (**3**) (0.292 g, 1.0 mmol), bis(alkyne) (**16**) (0.150 g, 0.56 mmol), $(PPh_3)_3$•CuBr (0.157 g, 0.17 mmol) and DBU (0.51 mL) were refluxed overnight in toluene (15 mL). After evaporation and purification of the residue by chromatography (2:1 hexane : EtOAc), bis(triazole) (**20**) was isolated as a colorless syrup (0.489 g, 57%). $^1$H NMR[15] ($CDCl_3$): $\delta$ 1.30, 1.34, 1.35 (3s, 9H total, 3 x -$CH_3$), 1.40, 1.47 (2s, 12H total, 4 x -$CH_3$), 1.56, 1.57, 1.64 (3s, 9H total, 3 x -$CH_3$), 3.73 to 4.96 (several m, 23H total, 2 x H-2 to H-6'$_{man}$, H-2 to H-5'$_{xyl}$, 3 x -OC$\underline{H}_2$), 5.90 (d, 1H, H-1$_{xyl}$, $J$ = 3.7 Hz), 6.07 (d, 1H, H-1$_{man}$, $J$ = 3.3 Hz), 6.09 (d, 1H, H-1$_{man}$, $J$ = 3.7 Hz), 7.87 (s, 1H, triazole-H), 7.89 (s, 1H, triazole-H). $^{13}$C NMR ($CDCl_3$): $\delta$ 24.1 (double intensity), 25.1 (double intensity), 25.5 (double intensity), 26.3, 26.8, 27.0 (double intensity), 63.6,

64.6, 66.7 (double intensity), 67.8, 72.5 (double intensity), 79.0, 79.1 (triple intensity), 79.2, 79.5 (double intensity), 82.0, 82.1, 88.6, 104.9 (double intensity), 109.4 (double intensity), 111.5, 113.6 (double intensity), 123.3, 123.4, 143.7, 144.1. APCI-MS (*m/z*) calcd: 836.38, found 837.3 (M+H). HRMS (M+Na) calcd: 859.3701, found: 859.3705. $[\alpha]_D = +11^\circ$ (*c* 5.0, $CH_2Cl_2$).

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15. The following designations are used to explain the $^{1}$H NMR spectra of **18**-**20**. For triazole (**18**), *ringA* = *N*-glycosidic mannofuranose ring, *ringB* = *O*-glycosidic mannofuranose ring. For triazole (**19**), *man* = mannofuranose ring, *gal* = galactopyranose ring. For triazole (**20**), *man* = mannofuranose ring, *xyl* = xylofuranose ring.