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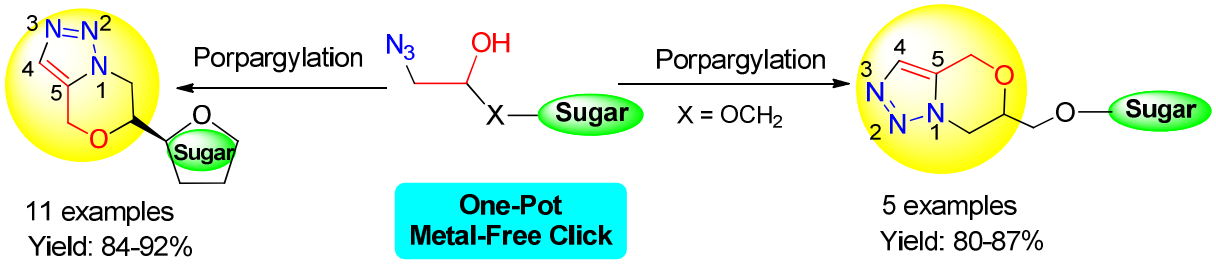
Kunj B. Mishra, Shomesh Shashi and Vinod K. Tiwari*

Graphical Abstract:



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COMMINICATION

Metal Free Synthesis of Morpholine Fused [5,1-*c*] Triazolyl Glycoconjugates *via* Glycosyl *Azido* alcohols

Cite this: DOI: 10.1039/x0xx00000x

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Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

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A series of diverse glycosyl 1,2-azido alcohols, obtained from readily available carbohydrates, were converted to structurally varied rare and novel sugar derived morpholine fused [5,1-*c*] triazoles via one-pot strategy. After incorporating propargyl functionality at hydroxyl group of sugar derived 1,2-azido alcohols, the resulted *in situ* generated azido-alkyne affords numerous *C*- and *O*-glycosyl bicyclic ring system of the medicine values *via* metal free cycloaddition reaction. Structure of all the developed molecules has been elucidated using ^{1}H NMR, ^{13}C NMR, IR and MS spectroscopy.

Introduction

Design and development of medium-sized organic scaffolds and fused heterocyclic systems 'found in numerous pharmaceutical molecules' attract always to chemists for the synthesis of novel mechanism based drugs and to improve the therapeutic efficacy of clinical medicines by adjoining these scaffolds.[1] 1,2-Azido alcohols having both functional groups at vicinal carbons are always considered as an important precursor for the synthesis of such medium sized heterocylic systems which represents excelent biological activities.[2] 1,2 azido alcohols in cojugation of carbohydrates disclose the way for maturity of large number of fused bicyclic molecules linked with biocopatible sugar and responsible for enhancement in bio action of such systems. Hence the synthesis of glycoconjugate azido alcohols and their application in organic chemistry is an increasing demand and advancement in modern drug discovery. The morpholine 'an important biologically active moiety' has been found as an excellent pharmacophore in medicinal chemistry. A number of drugs including morpholine as a constituent are available in market.[3] Therefore, many new approaches toward the synthesis of morpholine derivatives have been reported in the literature.[4]

The 1,2,3-triazole core having a significant class of biologically active nitrogen compounds exhibits a number of important biological properties such as antibacterial, anticancer, antivirus, antituberculosis, anti-HIV, antitumor, and glycosidase inhibition.[5-8] Moreover, 1,2,3-triazoles have found wide industrial applications as dyes, agrochemicals, corrosion inhibitors, and photostabilizers.[9] Hence, the synthesis of a 1,2,3-triazole nucleus or conjugation with crucial part of medicines invokes of ever growing synthetic efforts.

Huisgen dipolar cycloaddition of alkynes with organic azides is a conventional path for the synthesis of 1,2,3-triazoles but limited due to formation of its regioisomeric mixture in form of 1,4- and 1,5-isomers as products.[10] CuAAC reaction represents an extremely powerful tool for the rapid coupling of an organic azides and terminal alkynes and produces 1,4-disubstituted 1,2,3-triazoles solely .[11] Likewise, ruthenium catalyzed azide-alkyne cycloaddition (RuAAC) gives frequently opposite 1,5-regioisomer of 1,2,3-triazole; Although the expensive ruthenium complexes are required as catalysts.[12] Yet, it is realized that the metal free intramolecular azide-alkyne cycloaddition is found to be economically favourable and easy going reaction to give 1,5 regioisomer of 1,2,3-triaoles fused with hetero and carbocyclic systems for the medicinal values. Molecules having such scaffolds exhibit efficient and precious biological response including α-glucosidase enzyme (**I**), α-galactosidase (**II**), and active against alzimer disease (**IV**) (Fig. 1) .[2] It would thus be interesting to synthesize molecules possessing these moieties in conjugation of carbohydrates in fused form and evaluate their biological properties. Presently the world drug index contains numerous drugs having this structural feature in different forms including scaffold, side-chain, fused-ring, etc.[13]

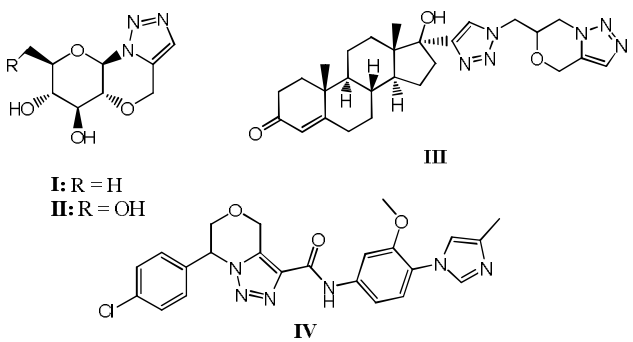

Fig. 1: Biologically active morpholine-fused triazoles

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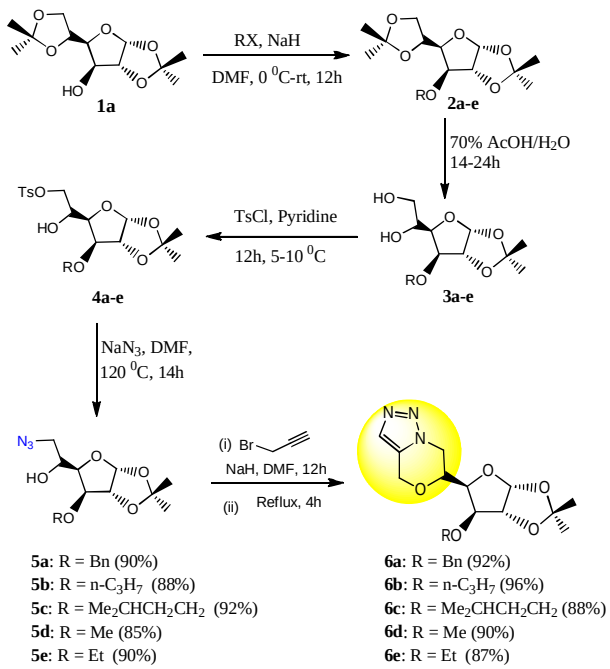
†**Electronic Supplementary Information (ESI) available:** Copies of ^{1}H and ^{13}C NMR for all the novel compounds has been provided. See DOI: DOI:10.1039/b.

Herein, we report the synthesis of novel *C*- and *O*-glycosylated morpholine fused 1,5-triazoles from diverse glycosyl azido alcohols using metal-free intramolecular thermal azide-alkyne cycloaddition reaction.

Results and Discussion

Our synthetic investigation begins with readily available monosaccharides (D-Glucose, D-Mannose, D-Galactose, D-Ribose, D-Xylose, etc.), which after processing a number of high yielding steps of protections and modifications afford diverse orthogonally protected sugars **1a-e**. The 1,2:5,6-di-*O*-isopropilidene-*α*-D-glucofuranose **1a** and 2,3:5,6-di-*O*-isopropilidene-D-mannofuranose **1b** were taken as starting material for the synthesis of diverse glucosidal and mannosidal furanosyl 1,2-azido alcohols. First of all, compound **1a** was subjected under substitution reaction with diverse organic halides (benzyl bromide, MeI, EtI, isopentyl bromide, and chloro propane) using basic condition in dry DMF under argon atmosphere afforded their respective *O*-substituted derivatives **2a-e**. The compounds **2a-e** were further converted to their corresponding diol's **3a-e** *via* selective 5,6-isopropylidene deprotection using mild acidic condition. Compounds **3a-e** were next reacted with tosyl chloride in dry pyridine at 5-10 ˚C for 12 hours afforded their selective tosyl derivatives **4a-e.** The subsequent azidation of all tosylated sugars with sodium azide in dry DMF at 115˚C employing anhydrous condition resulted their respective deoxy-azido sugars **5a-e** in excellent yields (Scheme 1, Table 1**)**.[14]

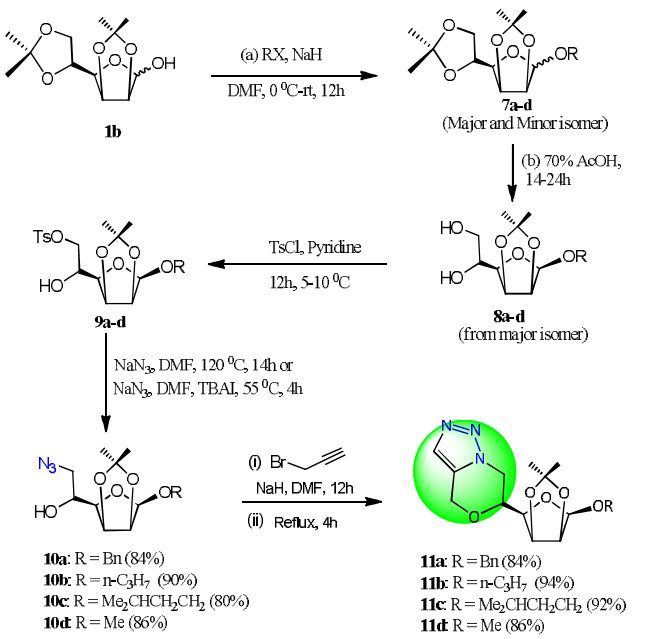


Scheme 1: Synthesis of morpholine-fused [5,1-*c*]-Triazoles (**5a-e**) from D-glucose via azido alcohol route

Once the synthesis of azido-alcohols **5a-e** was achieved, we next attempted towards the metal free azide-alkyne intramolecular cycloaddition reaction. We utilized all developed *azido* alcohols for the synthesis of desired morpholine fused [5,1-*c*] triazoles *via O*-propargylation at secondry hydroxyl group of 1,2-azido alcohols using strong base (NaH) in dry DMF at 0˚C-rt which gave azido-alkyne as intermediate. After quenching of remaining NaH adding few drops of water in reaction mixture and without isolating azido-alkyne intermediate, the reaction system subjected under thermal intramolecular azide-alkyne cyclization.

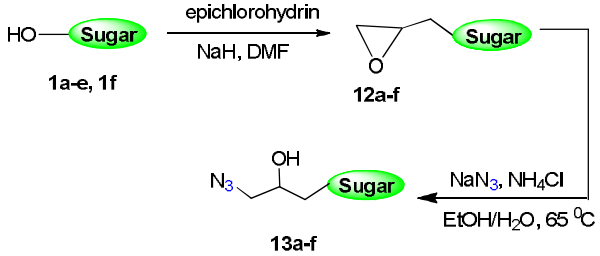
In reaction optimization study, we reacted **5a** (1.0 equiv.) with propargyl bromide (1.3 equiv) and NaH (3.0 equiv) in dry DMF (8 mL) for 12h, after quenching process, all over reaction mixture was heated at 110^{0}C for next 4 hours. Subsequent purification using column chromatography gave compound **6a** in excellent yields (92%).

The structure of compounds **6a** was deduced from their extensive spectral studies (IR, NMR, and MS). The ^{1}H NMR spectrum of compound **6a** exhibited a singlet of one proton observed at δ 7.39 assigned for the triazole-*H* proton. In addition to other signals, the appearance of one of the double doublet at δ 4.92 attributed for characteristic OCH_A proton of triazolo morpholine ring while the expected another characteristic double doublet for corresponding OCH_B proton of morpholine ring was found merged with benzylic protons which finally confirmed the precedence of thermal cyclization. A doublet at δ 5.87(3.6 Hz) confirmed the presence of anomeric proton while multiplates from δ 4.68 to δ 4.46 and δ 4.19 to 4.08 displayed the remaining carbohydrate protons. Two signals for six isopropylidene protons observed at δ 1.43 and δ 1.26. ^{13}C NMR of compound **6a** attributed two resonances at δ 129.6 and δ 127.8 corresponding to triazole-carbons. Molecular ion peak at 374 ($M+H^+$) is evidenced for the synthesis of compound **6a.**



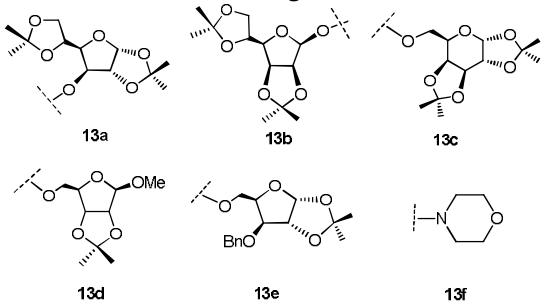
Scheme 2. Synthesis of morpholine-fused [5,1-*c*]-Triazoles (**11a-d**) from D-mannose.

Similar chemistry has been implemented with 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose**.** In this case**,** 1-*O*-substituted derivatives were obtained as a mixture of anomers where *β*-isomers **7a-d** were isolated as major constituent which were proceeded for subsequent formation of diol;s **(8a-d),** tosyl derivatives **9a-d,** azidoalcohols **10a-d** and finally morpholine-fused [5,1-*c*] triazoles **11a-d** (Scheme 2**).** We further extended our investigation for the synthesis of changed *azido* alcohols and their utilization in synthesis of morpholine fused triazoles.

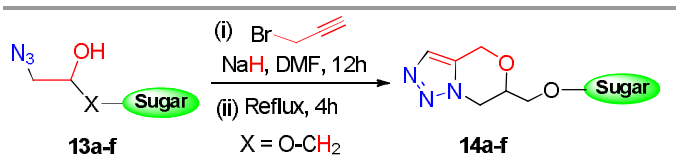


Scheme 3. Synthesis of glycosyl azido alcohols using epichlorohydrin.

Azido alcohols used in our investigation:

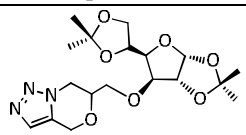
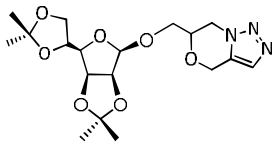
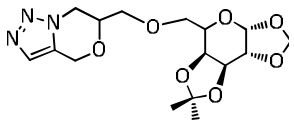
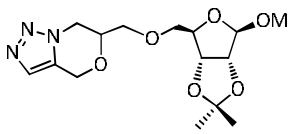
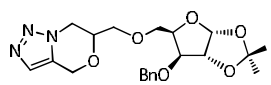
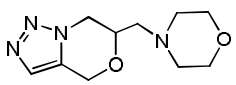


Therefore, the analogues **1a-f** treated with epichlorohydrin under basic medium in dry DMF which afforded excellent yield of glycosyl epoxides **12a-e** along with non sugar derivative **12f**. These glycosyl epoxides underwent regioselective azidation using NaN_3 in $EtOH/H_2O$ system at 65 ^{0}C in presence of ammonium chloride afforded O-glycosylated azido alcohols **13a-e** and *N*-azidoalcohols **13f (**Scheme 3). The *azido*alcohols **13a-f** thus obtained, on base-mediated propargylation using propargyl bromide in DMF followed by subsequent metal free azide-alkyne cycloaddition under thermal condition successfully afforded the desired morpholine fused [5,1-*c*] triazoles (**14a-f)** in good to excellent yields (Scheme 4, Table 1). Structure of all compounds was deduced from their extensive spectral studies (IR, NMR, and MS).



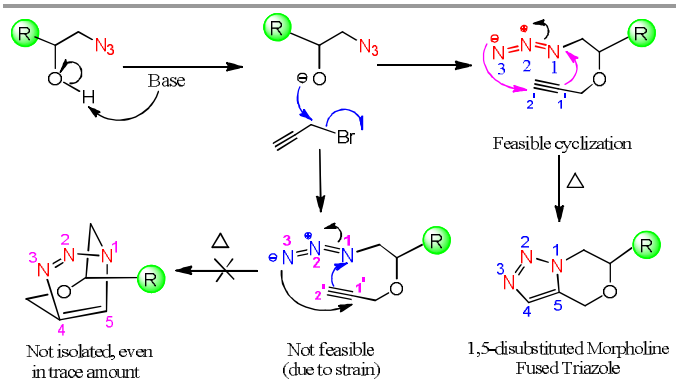
Scheme 4. Metal free synthesis of morpholine-fused [5,1-*c*] Triazoles

Table 1: Synthesis of morpholine fused triazoles (**14a-f**)

Entry[a]	Substrate	product[b]	time[c] (h)
1	**13a**	 **14a** (87 %)	16
2	**13b**	 **14b** (80 %)	13
3	**13c**	 **14c** (84 %)	16
4	**13d**	 **14d** (85 %)	14
5	**13e**	 **14e** (88 %)	14
6	**13f**	 **14f** (80 %)	13

[a]Molar ratios: Carbohydrate and other azidohydroxy triazoles (1.0 equiv.), Propargyl Bromide (1.3 equiv.), NaH (3 equiv.), [b]Morpholine-fused triazoles. [C]Reaction time in hrs.

Although a detailed investigation is required to confirm the mechanism, however we envisaged that the reaction may first involve base-prompted propargylation of azido alcohols (**5**, **10**, and **13**) followed by the metal-free thermal cycloaddition of intermediate azido-alkyne. The intramolecular cycloaddition to afford morpholine-fused 1,2,3-triazole is although possible via two different route. Because of strain free environment, the cyclization *via* path-I is more feasible which results to regioselective formation of desired morpholine-fused 1,5-triazoles (**6**, **11**, and **14**). Alternatively, in case of cyclization *via* path **II,** attack of C_2 of terminal aklyne on N_1-atom of azide, simultaneously the N_3 of azide on C_1 of alkyne is not feasible, possibly due to highly steric and strained environment in the small cavity of 1,4-disubstituted triazolyl macrocycle (Scheme 5).[15]



Scheme 5: Proposed reaction mechanism

In summary, we have developed diverse novel morpholine-fused [5,1,-*c*] triazolyl glycoconjugates using efficient and high yielding practical methodology. Three different series of novel glycosyl azido alcohols has been developed which utilized as starting material for synthesis of triazolo morpholine. The protocol exhibits a wide substrate scope, uses cheap and readily available reagents, easy to perform, and high yielding metal free reaction that creates rare and biologically relevant heterocyclic molecules.

3. EXPERIMENTAL

3.1. General methods

All of the reactions were executed in anhydrous solvents (where required) under an argon atmosphere in one hour oven dried glassware at 100 °C. All reagents and solvents were of pure analytical grade. Thin layer chromatography (TLC) was performed on 60 F_{254} silica gel, pre-coated on aluminum plates and revealed with either a UV lamp (λ_{max} = 254 nm) or a specific colour reagent (*Draggendorff* reagent or iodine vapours) or by spraying with methanolic-H_2SO_4 solution and subsequent charring by heating at 100 °C. ^{1}H and ^{13}C NMR were recorded at 300 and 75 MHz, respectively. Chemical shifts given in ppm downfield from internal TMS; *J* values in Hz. Mass spectra recorded using electro spray ionization mass spectrometry (ESI-MS). Infrared spectra recorded as Nujol mulls in KBr plates.

3.1.1 Procedure for synthesis of protected sugars: The compounds **1**,**2**,**3**,**7**,**8**,**12** and **13** were prepared from readily available carbohydrates (D-glucose, D-galactose, D-ribose) using standard protection and modification including substitution and ring opening reactions.[13a-c]

3.1.2 General procedure for synthesis of tosyl-sugars (4a-e, 9a-d): The stirring solutions of diol's (**3a-e**, **8a-d;** 1 equiv.) in pyridine at 0^{0}C were added with *p*-toluene sulphonyl chloride (1 equiv.) under anhydrous condition. The reactions was allowed to stirr below 10 ºC for 12 h. After completion of reaction (monitered by TLC), the reaction mixtures were *in vacuo* concentrated and the crude obtained were purified by flash column chromatography to afford tosyl-sugars **4a-e**, **9a-d** in good yields. Comound 1,2-*O*-Isopropylidene-3-*O*-propyl-6-*O*-tosyl-*α*-D-glucofuranose **4a** was obtained in good yield implementing similar chemistry.[13b]

1,2-*O*-Isopropylidene-3-*O*-propyl-6-*O*-tosyl-*α*-D-glucofuranose (4b): A stirring solution of 1,2-*O*-Isopropylidene-3-*O*-propyl-*α*-D-glucofuranose (1.34 g, 5.1 mmol) in pyridine was treated with *p*-toluene sulphonyl chloride (1.0 g, 5.1 mmol) at 0^{0}C under anhydrous condition followed by stirring for 12 h at 5-10°C afforded viscous liquid (1.3 g, 62%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 5.86 (d, *J* = 3.6 Hz, 1H), 4.53 (d, *J* = 3.6 Hz, 1H), 4.28-3.96 (m, 5H), 3.61-3.40 (m, 2H), 2.45 (s, 3H), 1.60-1.53 (m, 2H), 1.46, 1.30 (each s, 6H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.0, 132.5, 129.9, 128.1, 111.8, 105.0, 82.7, 82.0, 79.0, 72.2, 67.5, 26.6, 26.1, 22.8, 21.5, 10.4 ppm.

3-*O*-Isopentyl-1,2-*O*-isopropylidene-6-*O*-tosyl-*α*-D-glucofuranose (4c). A stirring solution of 3-*O*-isopentyl-1,2-*O*-isopropylidene-*α*-D-glucofuranose (1.6 g, 5.7 mmol) in pyridine was treated with *p*-toluene sulphonyl chloride (1.08 g, 5.7 mmol) at 0^{0}C under anhydrous condition followed by stirring for 12 h at 10°C. Viscous liquid (1.5 g, 60%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.1 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 5.85 (d, *J* = 3.6 Hz, 1H), 4.52 (d, *J* = 3.6 Hz, 1H), 4.25 (dd, *J* = 2.7 Hz, 9.9Hz, 1H), 4.17-4.15 (m, 1H), 4.11-4.06 (m, 2H), 4.04 (d, *J* = 3.0 Hz, 1H), 3.68-3.45 (m, 2H), 2.88 (d, *J* = 5.7 Hz, 1H), 2.45 (s, 3H), 1.67-1.60 (m, 2H), 1.46-1.43 (m, 4H), 1.31 (s, 3H), 0.89 (d, *J* = 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.1, 132.6, 130.0, 128.1, 111.9, 105.0, 82.8, 81.9, 79.0, 72.2, 68.9, 67.5, 38.4, 26.7, 26.1, 24.8, 22.5, 22.3, 21.5 ppm.

1,2-*O*-Isopropylidene-3-*O*-methyl-6-*O*-tosyl-*α*-D-glucofuranose (4d): A stirring solution of 1,2-*O*-isopropylidene-3-*O*-methyl-*α*-D-glucofuranose (2.0 g, 8.5 mmol) in pyridine was treated with *p*-toluene sulphonyl chloride (1.62 g, 8.5 mmol) at 0^{0}C under anhydrous condition followed by stirring for 12 h at 10°C afforded viscous liquid (1.97 g, 60%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.1 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 5.90 (d, *J* = 3.3 Hz, 1H), 4.60 (d, *J* = 3.6 Hz, 1H), 4.38 (dd, *J* = 4.8 Hz, 13.5 Hz, 1H), 4.17-4.10 (m, 4H), 3.90 (d, *J* = 1.8 Hz, 1H), 3.46 (s, 3H), 2.44 (s, 3H), 1.48, 1.32 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.9, 132.3, 129.8, 127.8, 111.6, 105.0, 84.0, 81.1, 79.1, 67.4, 67.4, 57.6, 26.5, 26.0, 21.3 ppm.

3-*O*-Ethyl-1,2-*O*-isopropylidene-6-*O*-tosyl-*α*-D-glucofuranose (4e): A stirring solution of 1,2-*O*-isopropylidene-3-*O*-ethyl-*α*-D-glucofuranose (0.80 g, 3.2 mmol) in pyridine was treated with *p*-toluene sulphonyl chloride (0.61 g, 3.2 mmol) at 0^{0}C under anhydrous condition followed by stirring for 12 h at 5-10°C afforded viscous liquid (1.00 g, 78%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 5.87 (d, *J* = 3.6 Hz, 1H), 4.53 (d, *J* = 3.6 Hz, 1H), 4.26 (dd, *J* = 2.7 Hz, 9.6 Hz, 1H), 4.18 (m, 1H), 4.12-4.06 (m, 2H), 4.00-3.97 (m, 1H), 3.74-3.51 (m, 2H), 2.94 (s, 1H), 2.45 (s, 3H), 1.46, 1.30 (each s, 6H), 1.19 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.1, 132.9, 130.0, 128.1, 111.8, 105.8, 82.6, 78.9, 78.4, 72.2,

67.5, 65.9, 26.7, 26.6, 21.5, 15.1 ppm.

Benzyl-2,3-*O*-isopropylidene-6-*O*-tosyl-*β*-D-mannofuranose (9a): A stirring solution of benzyl-2,3-*O*-isopropylidene-*β*-D-mannofuranose (2.70 g, 8.4 mmol) in pyridine was treated with *p*-toluene sulphonyl chloride (1.90 g, 8.4 mmol) at 0^0C under anhydrous condition followed by stirring for 12 h at 10°C afforded white solid (1.96 g, 50%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, J = 8.1 Hz, 1H), 7.35-7.26 (m, 7H), 5.05 (s, 1H), 4.82 (dd, J = 4.2 Hz, 5.7 Hz, 1H), 4.64-4.56 (m, 2H), 4.41 (d, J = 11.7 Hz, 1H), 4.28-4.24 (m, 1H), 4.16-4.13 (m, 2H), 3.94 (dd, J = 3.6 Hz, 7.2 Hz, 1H), 2.68 (s, 1H), 2.43 (s, 3H), 1.42, 1.30 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.0, 132.8, 129.9, 128.5, 128.0, 112.8, 105.2, 84.7, 79.6, 78.2, 71.5, 69.0, 68.0, 25.7, 24.4, 21.5 ppm.

Propyl-2,3-*O*-isopropylidene-6-*O*-tosyl-*β*-D-mannofuranose (9b): A stirring solution of propyl-2,3-*O*-isopropylidene-*β*-D-mannofuranose (2.68 g, 10.2 mmol) in pyridine was treated with *p*-toluene sulphonyl chloride (1.9 g, 10.2 mmol) at 0^0C under anhydrous condition followed by stirring for 12 h at 10°C afforded viscous liquid (2.6 g, 62%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, J = 8.1 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 4.96 (s, 1H), 4.81 (dd, J = 3.9 Hz, 5.7 Hz, 1H), 4.57 (d, J = 6.0 Hz, 1H), 4.32-4.16 (m, 3H), 3.91 (dd, J = 3.6 Hz, 7.5 Hz, 1H), 3.51(d, J = 6.6 Hz, 15.6 Hz, 3H), 3.33-3.26 (m, 1H), 2.70 (s, 1H), 2.45 (s, 3H), 1.57-1.48 (m, 2H), 1.43, 1.30 (each s, 6H), 0.89 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.0, 132.8, 129.9, 128.0, 112.7, 105.9, 84.7, 79.7, 78.0, 71.5, 69.0, 68.1, 25.7, 24.4, 22.5, 21.5, 10.4 ppm.

Isopentyl-2,3-*O*-isopropylidene-6-*O*-tosyl-*β*-D-mannofuranose (9c): A stirring solution of isopentyl-2,3-*O*-isopropylidene-*β*-D-mannofuranose (3.28 g, 11.3 mmol) in pyridine was treated with *p*-toluene sulphonyl chloride (2.14 g, 11.3 mmol) at 0^0C under anhydrous condition followed by stirring for 12 h at 5-10°C afforded white solid (2.75 g, 55%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, J = 8.1 Hz, 1H), 7.34 (d, J = 8.1 Hz, 1H), 4.96 (s, 1H), 4.82-4.78 (m, 1H), 4.55 (d, J = 6.0 Hz, 1H), 4.31 (d, J = 7.5 Hz, 1H), 4.17-4.15 (m, 2H), 3.89 (dd, J = 3.6 Hz, 7.2Hz, 1H), 3.60 (dd, J = 6.9 Hz, 16.5 Hz, 1H), 3.36 (dd, J = 6.3 Hz, 16.2 Hz, 1H), 2.67 (d, J = 5.4 Hz, 1H), 2.45 (s, 3H), 1.69-1.58 (m, 2H), 1.48 (m, 1H), 1.43, 1.30 (each s, 6H), 0.88 (d, J = 4.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.0, 132.6, 129.9, 128.0, 112.7, 106.0, 84.7, 79.7, 78.1, 71.6, 68.2, 65.8, 38.0, 25.7, 24.8, 24.4, 22.4, 22.3, 21.5 ppm.

Methyl-2,3-*O*-isopropylidene-6-*O*-tosyl-*β*-D-mannofuranose (9d): A stirring solution of methyl-2,3-*O*-isopropylidene-*β*-D-mannofuranose (1.96 g, 8.3 mmol) in pyridine was treated with *p*-toluene sulphonyl chloride (1.5 g, 8.3 mmol) at 0^0C under anhydrous condition followed by stirring for 12 h at 10°C afforded viscous liquid (2.0 g, 65%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, J = 7.5 Hz, 1H), 7.35 (d, J = 7.5 Hz, 1H), 4.86-4.80 (m, 2H), 4.54 (d, J = 5.7 Hz, 1H), 4.31 (d, J = 7.5 Hz, 1H), 4.19-4.17 (m, 2H), 3.91 (s, 1H), 3.26 (s, 3H), 2.68 (s, 1H), 2.44 (s, 3H), 1.49, 1.30 (each s, 6H).

3.1.3 General procedure for synthesis of C-glycosylated azido alcohols (5a-e, 10a-d): The stirring solutions of compounds **4a-e** or **9a-d** in dry DMF were treated with NaN_3. The reaction mixtures were further heated at 115 -120ºC under anhydrous condition followed by constant stirring for 12-16 hours. After completion of reaction (monitored by TLC), the reaction mixtures were *in vacuo* concentrated followed by silica gel column chromatography to afford compounds **5a-e** and **10a-d** in good yields. Comound **5a** was also achieved in good yield implementing similar chemistry.[13b]

6-*Azido*-6-deoxy-1,2-*O*-isopropylidene-3-*O*-propyl-*α*-D-glucofuranose (5b): Reaction of compound **4b** (1.34 g, 3.2 mmol) with NaN_3 (0.624 g, 9.6 mmol) in DMF at 115^0C afforded compound **5b**. Oily liquid (0.81 g, 88 % yield); IR (KBr) cm^{-1}: 3453, 2964, 2935, 2878, 2103, 1633, 1455, 1080; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.91 (d, J = 3.6 Hz, 1H), 4.57 (d, J = 3.6 Hz, 1H), 4.10-4.00 (m, 3H), 3.66-3.42 (m, 4H), 2.74 (s, 1H), 1.65-1.58 (m, 2H), 1.49, 1.32 (each s, 6H), 0.94 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 111.8, 105.1, 82.8, 81.9, 79.7, 71.9, 68.9, 54.5, 26.7, 26.1, 22.8, 10.4 ppm.

6-*Azido*-6-deoxy-3-*O*-*iso*pentyl-1,2-*O*-isopropylidene-*α*-D-glucofuranose (5c): Reaction of compound **4c** (1.5 g, 3.3 mmol) with NaN_3 (0.658 g, 10.0 mmol) in DMF at 115^0C afforded compound **5c**. Oily liquid (0.98 g, 92% yield); IR (KBr) cm^{-1}: 3472, 2958, 2872, 2104, 1711, 1633, 1466, 1081; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.90 (d, J = 3.6 Hz, 1H), 4.57 (d, J = 3.6 Hz, 1H), 4.10-3.98 (m, 3H), 3.73-3.42 (m, 4H), 2.64 (s, 1H), 1.72-1.63 (m, 2H), 1.49 (m, 4H), 1.32 (s, 3H), 0.91 (d, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 111.9, 105.1, 82.9, 81.9, 79.8, 68.9, 68.7, 54.5, 38.4, 26.7, 26.2, 24.9, 22.5, 22.3 ppm.

6-*Azido*-6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-*α*-D-glucofuranose (5d): Reaction of compound **4d** (2.0 g, 5.1 mmol) with NaN_3 (1.0 g, 15.4 mmol) in DMF at 115^0C afforded compound **5d**. Oily liquid (1.13 g, 85% yield); IR (KBr) cm^{-1}: 3460, 2955, 2867, 2103, 1718, 1633, 1460, 1070; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.89 (d, J = 3.6 Hz, 1H), 4.60 (d, J = 3.6 Hz, 1H), 4.09 (s, 2H), 3.90 (s, 1H), 3.61-3.46 (m, 5H), 2.61 (s, 1H), 1.49, 1.33 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 111.9, 105.1, 84.3, 81.3, 79.7, 68.7, 57.7, 54.4, 26.7, 26.1 ppm.

6-*Azido*-6-deoxy-1,2-*O*-isopropylidene-3-*O*-ethyl-*α*-D-glucofuranose (5e): Reaction of compound **4e** (1.0 g, 2.4 mmol) with NaN_3 (0.48 g, 7.2 mmol) in DMF at 115^0C afforded compound **5e**. Viscous liquid (0.6 g, 90% yield); IR (KBr) cm^{-1}: 3466, 2944, 2857, 2103, 1710, 1633, 1470, 1080; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.91 (d, J = 3.6 Hz, 1H), 4.57 (d, J = 3.6 Hz, 1H), 4.10-4.01 (m, 3H), 3.76-3.42 (m, 4H), 2.73 (s, 1H), 1.49, 1.32 (each s, 6H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 111.8, 105.0, 82.7, 81.9, 79.6, 68.8, 65.7, 54.5, 26.7, 26.1, 15.0 ppm.

Benzyl-6-*azido*-6-deoxy-2,3-*O*-isopropylidene-*β*-D-mannofuranose (10a): Reaction of compound **9a** (1.96 g, 4.2 mmol) with NaN_3 (0.82 g, 12.6 mmol) in DMF at 115^{0}C afforded compound **10a**. Oily liquid (1.18 g, 84% yield); IR (KBr) cm^{-1}: 3457, 3032, 2988, 2937, 2103, 1638, 1497, 1086; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.24 (m, 5H), 5.06-5.02 (m, 1H), 4.78 (m, 1H), 4.59-4.38 (m, 3H), 4.03-3.88 (m, 2H), 3.46-3.36 (m, 2H), 2.60 (s, 1H), 1.38, 1.24 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.2, 130.2, 128.5, 128.1, 112.8, 105.4, 84.8, 79.8, 79.4, 69.5, 69.1, 54.3, 25.8, 24.5 ppm.

Propyl-6-*azido*-6-deoxy-2,3-*O*-isopropylidene-*β*-D-mannofuranose (10b): Reaction of compound **9b** (2.6 g, 6.2 mmol) with NaN_3 (1.21 g, 18.7 mmol) in DMF at 115^{0}C afforded compound **10b**. White solid (1.6 g, 90% yield); IR (KBr) cm^{-1}: 3478, 2989, 2964, 2939, 2883, 2106, 1754, 1633, 1469, 1084; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.93 (s, 1H), 4.77 (dd, J = 3.9 Hz, 5.7 Hz, 1H), 4.53 (d, J = 5.7 Hz, 1H), 4.04-3.99 (m, 1H), 3.86-3.83 (m, 1H), 3.52-3.48 (m, 2H), 3.45-3.36 (m, 1H), 3.31-3.24 (m, 1H), 2.57 (s, 1H), 1.53-1.46 (m, 2H), 1.40, 1.26 (each s, 6H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 112.7, 106.0, 84.8, 79.8, 79.2, 69.5, 69.1, 54.3, 25.8, 24.4, 25.5, 10.4 ppm.

Isopentyl-6-*azido*-6-deoxy-2,3-*O*-isopropylidene-*β*-D-mannofuranose (10c): Reaction of compound **9c** (2.75 g, 6.1 mmol) with NaN_3 (1.2 g, 18.5 mmol) in DMF at 115^{0}C afforded compound **10c**. White semi solid (1.53 g, 80% yield); IR (KBr) cm^{-1}: 3453, 2922, 2871, 2101, 1744, 1633, 1465, 1088; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.99 (s, 1H), 4.86-4.82 (m, 1H), 4.58 (d, J = 5.7 Hz, 1H), 4.12-4.07 (m, 1H), 3.91 (dd, J = 4.2 Hz, 7.5 Hz, 1H), 3.68-3.36 (m, 4H), 1.68-1.62 (m, 1H), 1.47-1.39 (m, 5H), 1.33 (s, 3H), 0.89 (d, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 112.7, 106.0, 84.8, 79.8, 79.2, 69.6, 65.8, 54.3, 38.0, 25.8, 24.8, 24.5, 22.5, 22.2 ppm.

Methyl-6-*azido*-6-deoxy-2,3-*O*-isopropylidene-*β*-D-mannofuranose (10d): Reaction of compound **9d** (2.0 g, 5.1 mmol) with NaN_3 (1.00 g, 15.4 mmol) in DMF at 115^{0}C afforded compound **10d**. Oily liquid (1.13 g, 86% yield); IR (KBr) cm^{-1}: 3452, 2991, 2937, 2836, 2099, 1628, 1443, 1089; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.90-4.82 (m, 2H), 4.58 (d, J = 5.7 Hz, 1H), 4.12-4.07 (m, 1H), 3.90 (dd, J = 3.6 Hz, 8.1 Hz, 1H), 3.60-3.44 (m, 2H), 3.31 (s, 3H), 2.62 (s, 1H), 1.47, 1.33 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 112.8, 107.0, 84.7, 79.7, 79.2, 69.6, 54.5, 54.2, 25.8, 24.5 ppm.

3.1.4.General procedure for the synthesis of glycosyl epoxides (12a-f):[13c] A solution of orthogonally protected sugar including morpholine heterocycle having OH- and NH- reaction site (1 equiv.) in anhydrous DMF was cooled to 0ºC and sodium hydride (2.0 equiv.) was added portion wise. The reaction mixture was stirred at 0ºC under argon atmosphere for 20 minutes. Epichlorohydrin (1.2 mmol) was added at 0ºC and allowed to stir for 12 hour at room temperature. Upon completion of the reaction, remaining sodium hydride was quenched by water; the solvent was removed under reduced pressure followed by extraction with ethyl acetate. The combined organic layer was washed with brine solution, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to get the crude product. Purification using flash chromatography (ethyl acetate: hexane) afforded desired epoxides **12a-f**.[13c]

3.1.5. General procedure for the synthesis of glycosyl azido alcohols 13a-f:[13c] A solution of the compounds **12a-f** in EtOH/H_2O (1:1) was treated with NaN_3 and NH_4Cl at 65ºC for 8 h. Upon completion of the reaction, the solvent was removed under reduced pressure, extracted with ethyl acetate and water. The organic layer was dried over anhydrous Na_2SO_4, filtered, concentrated under vacuum, followed by flash chromatography (ethyl acetate: hexane) afforded desired glycosyl azido alcohols **13a-f** in good yields.[13c]

3.1.6. General procedure for the synthesis of 1,2,3-triazolo[5,1-*c*]morpholine (6a-e, 11a-d and **14a-f)**
A solution of azido alcohol (**5**, 1.0 mmol) in anhydrous DMF (8 ml) was cooled to 0 ºC and NaH (3 mmol) was added portion wise. The reaction mixture was stirred at 0 ºC under argon atmosphere for 20 minutes. Then at same temperature, propargyl bromide (1.3 mmol) was added and reaction mixture was further stirred for 12 hour at room temperature. After disappearance of starting materials (monitored by TLC), reaction was quenched by water and whole reaction mixture was allowed to heat at 110 ºC with constant stirring for 3-4 hour. Upon completion of the reaction, the solvent was removed in vacuum; the residue was mixed with water (10 mL) and then extracted with ethyl acetate (3 × 15 mL). The combined organic extracts were washed with brine solution (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was subjected to flash chromatography (silica gel 234-400 mesh, $CHCl_3$/CH_3OH as eluent) to give title compound **6, 11** and **14**.

6-(3-*O*-benzyl-1,2-*O*-isopropilidene-*α*-D-glucofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 6a: Compound **5a** (100 mg, 0.3 mmol), sodium hydride (21 mg, 0.9 mmol) and propargyl bromide (0.034 ml, 4 mmol) were reacted in DMF (8 ml) using procedure described above to give **6a** (102 mg, 92%) as white solid; R_f = 0.40 (60% ethyl acetate/*n*-hexane); MS: *m/z* 374 $[M+H]^+$; IR (KBr) cm^{-1} 2963, 2927, 2856, 1628, 1455, 1375, 1261, 1094, 1023, 801: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (s, 1H), 7.26-7.24 (m, 5H), 5.87 (d, J = 3.6 Hz, 1H), 4.92 (d, J = 15.0 Hz, 1H), 4.68-4.46 (m, 5H), 4.19-4.08 (m, 4H), 1.43, 1.26 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.1, 130.2, 128.5, 128.1, 127.7, 112.0, 105.1, 81.8, 81.0, 80.2, 72.2, 70.3, 61.7, 48.1, 26.5, 25.9 ppm.

6-(1,2-*O*-isopropilidene-3-*O*-propyl-*α*-D-glucofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 6b: 5b (150 mg, 0.52 mmol), sodium hydride (37 mg, 1.5 mmol) and propargyl bromide (0.06 ml, 0.6 mmol) were reacted in DMF (8 ml) using procedure described above to give **6b** (162 mg, 96%) as yellowish viscous liquid; R_f = 0.25 (40% ethyl acetate/*n*-hexane); MS: *m/z* 326 $[M+H]^+$; IR (KBr) cm^{-1} 3142, 2965, 2936, 1636,

1455, 1375, 1217, 1081, 1022: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (s, 1H), 5.91 (d, J = 3.3 Hz, 1H), 5.09 (d, J = 14.7 Hz, 1H), 4.82-4.59 (m, 3H), 4.25-4.21 (m, 3H), 3.99 (d, J = 2.1 Hz, 1H), 3.64 (dd, J = 6.3 Hz, 15.3 Hz, 1H), 3.45 (dd, J = 6.6 Hz, 15.3 Hz, 1H), 1.64-1.57 (m, 2H), 1.50, 1.33 (each s, 6H), 0.93 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.1, 127.7, 111.8, 105.0, 81.8, 81.5, 80.2, 72.0, 70.3, 61.6, 48.0, 26.5, 25.9, 22.6, 10.3 ppm.

6-(3-*O*-isopentyl-1,2-*O*-isopropilidene-*α*-D-glucofuranose)-6,7-dihydro-4*H* [1,2,3]triazolo[5,1-*c*][1,4]oxazine, 6c: 5c (150 mg**,** 0.47 mmol), sodium hydride (34 mg, 1.42 mmol) and propargyl bromide (0.054 ml, 0.61 mmol) were reacted in DMF (8 ml) using procedure described above to give **6c** (146 mg, 88%) as white solid; R_f = 0.25 (40%) ethyl acetate/*n*-hexane); MS: *m/z* 354 $[M+H]^+$;IR (KBr) cm^{-1} 3429, 2963, 2924, 2936, 1622, 1453, 1374, 1217, 1126, 1082, 1020: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (s, 1H), 5.82 (d, J = 3.6 Hz, 1H), 5.2-4.97 (m, 1H), 4.71-4.49 (m, 3H), 4.15-4.10 (m, 3H), 3.89 (d, J = 2.7 Hz, 1H), 3.62-3.57 (m, 1H), 3.44-3.37 (m, 1H), 1.61-1.53 (m, 1H), 1.41-1.37 (m, 5H), 1.24 (s, 3H), 0.81 (d, J = 6.3 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.1, 127.8, 111.8, 105.1, 81.7, 81.6, 80.2, 70.3, 68.7, 61.6, 48.0, 38.2, 26.5, 25.9, 24.6, 22.3, 22.0 ppm.

6-(1,2-*O*-isopropilidene-3-*O*-methyl-*α*-D-glucofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 6d: 5d (130 mg**,** 0.5 mmol), sodium hydride (0.36 mg, 1.5 mmol) and propargyl bromide (0.057 ml, 0.65 mmol) were reacted in DMF (8 ml) using procedure described above to give **6d** (133 mg, 90%) as yellowish viscous liquid; R_f = 0.25 (40% ethyl acetate/*n*-hexane); MS: *m/z* 298 $[M+H]^+$;IR (KBr) cm^{-1} 3442, 2988, 2935, 1635, 1455, 1375, 1217, 1082: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (s, 1H), 5.82 (d, J = 3.9 Hz, 1H), 5.01 (d, J = 15.0 Hz, 1H), 4.75 (d, J = 15.0 Hz, 1H), 4.62-4.53 (m, 2H), 4.19-4.04 (m, 3H), 3.82 (d, J = 2.7 Hz, 1H), 3.38 (s, 3H), 1.42, 1.26 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 130.1, 127.7, 111.8, 105.0, 83.2, 81.2, 80.0, 70.3, 61.6, 57.9, 47.8, 26.5, 25.8 ppm.

6-(3-*O*-ethyl-1,2-*O*-isopropilidene-*α*-D-glucofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 6e: Compound **5e** (100 mg**,** 0.36 mmol), sodium hydride (26 mg, 1.09 mmol) and propargyl bromide (0.041 ml, 0.46 mmol) were reacted in DMF (8 ml) using procedure described above to give **6e** (97 mg, 87%) as viscous liquid; R_f = 0.25 (40% ethyl acetate/*n*-hexane); MS: *m/z* 312 $[M+H]^+$;IR (KBr) cm^{-1} 2976, 2930, 2886, 1738, 1551, 1449, 1378, 1088, 888, 474:^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (s, 1H), 5.94-5.92 (m, 1H), 5.09 (dd, J = 2.1 Hz, 15.0 Hz, 1H), 4.83-4.59 (m, 3H), 4.30-4.17 (m, 3H), 4.01 (s, 1H), 3.74 (t, J = 7.2 Hz, 1H), 3.58-3.53 (m, 1H), 1.51, 1.34 (each s, 6H), 1.22 (t, J = 6.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.2, 127.9, 111.9, 105.1, 82.1, 81.4, 80.1, 70.6, 66.0, 61.8, 48.1, 26.6, 25.9, 15.0 ppm.

6-(Benzyl-1,2-*O*-isopropilidene-3-*O*-*β*-D-mannofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 11a: Compound **10a** (130 mg**,** 0.38 mmol), sodium hydride (27 mg, 1.16 mmol) and propargyl bromide (0.043 ml, 0.5 mmol) were reacted in DMF (8 ml) using procedure described above to give **11a** (119 mg, 84%) as R_f = 0.25 (35% ethyl acetate/*n*-hexane); MS: *m/z* 374 $[M+H]^+$;white solid; IR (KBr) cm^{-1} 3421, 3090, 2988, 2941, 2913, 1743, 1682, 1447, 1380, 1255, 1106, 1083: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (s, 1H), 7.29-7.24 (m, 5H), 5.05-4.96 (m, 2H), 4.78-4.73 (m, 2H), 4.60-4.43 (m, 4H), 4.16-3.96 (m, 3H), 1.37, 1.24 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.1, 130.3, 128.3, 127.8, 127.8, 112.6, 105.6, 84.5, 79.6, 79.1, 70.7, 69.3, 61.7, 47.6, 25.7, 24.4 ppm.

6-(Propyl-1,2-*O*-isopropilidene-3-*O*-*β*-D-mannofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 11b: Compound **10b** (150 mg**,** 0.52 mmol), sodium hydride (37 mg, 1.5 mmol) and propargyl bromide (0.060 ml, 0.67 mmol) were reacted in DMF (8 ml) using procedure described above to give **11b** (158 mg, 94%) as yellowish viscous liquid; R_f = 0.25 (35% ethyl acetate/*n*-hexane); MS: *m/z* 326 $[M+H]^+$;IR (KBr) cm^{-1} 3434, 3137, 2963, 2938, 2878, 1714, 1630, 1456, 1374, 1210, 1163, 1043, 862: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41 (s, 1H), 5.05-4.95 (m, 2H), 4.82-4.77 (m, 2H), 4.70-4.60 (m, 1H), 4.54 (d, J = 5.7 Hz, 1H), 4.18-4.15 (m, 2H), 4.00 (d, J = 3.9 Hz, 1H), 3.51 (dd, J = 6.9 Hz, 13.8 Hz, 1H), 3.31 (d, J = 6.6 Hz, 15.9 Hz, 1H), 1.53-1.46 (m, 2H), 1.38, 1.25 (each s, 6H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.3, 127.7, 112.5, 106.0, 84.6, 79.4, 79.1, 70.8, 69.0, 61.6, 47.6, 25.7, 24.3, 22.3, 10.2 ppm..

6-(Isopentyl-1,2-*O*-isopropilidene-3-*O*-*β*-D-mannofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 11c: Compound **10c** (130 mg**,** 0.41 mmol), sodium hydride (29 mg, 1.2 mmol) and propargyl bromide (0.047 ml, 5.3 mmol) were reacted in DMF (8 ml) using procedure described above to give **11c** (133 mg, 92%) as yellowish viscous liquid; R_f = 0.25 (35% ethyl acetate/*n*-hexane); MS: *m/z* 354 $[M+H]^+$;IR (KBr) cm$^-$3444, 3130, 2983, 2948, 2870, 1710, 1604, 1456, 1374, 1211, 1150, 1045, 860: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43 (s, 1H), 5.05-4.53 (m, 6H), 4.17-3.98 (m, 3H), 3.63-3.56 (m, 1H), 3.37 (dd, J = 6.6 Hz, 15.9 Hz, 1H), 1.64-1.53 (m, 1H), 1.39, 1.27 (each s, 6H), 0.83 (d, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 130.4, 127.9, 112.7, 106.2, 74.7, 79.5, 79.1, 71.0, 65.9, 61.8, 47.8, 38.0, 25.8, 24.7, 24.4, 22.4, 22.1 ppm.

6-(Methyl-1,2-*O*-isopropilidene-3-*O*-*β*-D-mannofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 11d: Compound **10d** (120 mg, 0.46 mmol), NaH (33 mg, 1.3 mmol) and propargyl bromide (0.053 ml, 5.8 mmol) were reacted in DMF (8 ml) using procedure described above to give **11d** (117 mg, 86%) as white solid; R_f = 0.25 (35% ethyl acetate/*n*-hexane); MS: *m/z* 298 $[M+H]^+$; IR (KBr) cm^{-1} 3137, 2989, 2947, 2833, 1716, 1625, 1450, 1381, 1270, 1207, 1160, 1105, 1049, 860: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (s, 1H), 5.10 (dd, J = 15.9 Hz, 1H), 4.93-4.85 (m, 3H), 4.75 (d, J = 8.1 Hz, 1H), 4.60 (d, J = 5.7 Hz, 1H)4.27-4.25 (m, 2H), 4.06 (t, J = 3.0 Hz, 1H), 3.34 (s, 3H), 1.46, 1.34 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.4, 127.9, 112.8, 107.1, 84.5, 79.5, 79.1, 70.9, 61.8, 54.6, 47.7, 25.8, 24.4

6-(1,2:5,6-Di-O-isopropilidene-3-O-oxymethylene-*α*-D-

glucofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 14a: Compound **13a** (166 mg**,** 0.46 mmol), sodium hydride (33 mg, 1.3 mmol) and propargyl bromide (0.053 ml, 0.59 mmol) were reacted in DMF (8 ml) using procedure described above to give **14a** (158 mg, 87%) as yellowish viscous liquid; R_f = 0.30 (60% ethyl acetate/*n*-hexane); MS: *m/z* 398 $[M+H]^+$;IR (KBr) cm^{-1} 3447, 2987, 2935, 1713, 1634, 1456, 1374, 1216, 1073, 1020: ^1H NMR (300 MHz, $CDCl_3$): δ 7.42 (s, 1H), 5.82 (s, 1H), 5.04 (d, J = 15.0 Hz, 1H), 4.79-4.74 (m, 1H), 4.51 (m, 2H), 4.20-3.75 (m, 9H), 1.43, 1.34, 1.32, 1.25 (each s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.3, 127.9, 111.9, 109.1, 105.2, 83.2, 82.5, 81.1, 72.7, 72.1, 70.4, 67.5, 61.8, 47.0, 26.6, 26.6, 26.0, 25.1 ppm.

6-(2,3:4,6Ddi-O-isopropilidene-1-O-oxymethylene-*β*-D-Mannofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 14b: Compound **13b** (140 mg**,** 0.39 mmol), sodium hydride (28 mg, 1.1 mmol) and propargyl bromide (0.045 ml, 0.5 mmol) were reacted in DMF (8 ml) using procedure described above to give **14b** (123 g, 80%) as brownish solid; R_f = 0.30 (60% ethyl acetate/*n*-hexane); MS: *m/z* 398 $[M+H]^+$; IR (KBr) cm^{-1} 3456, 3140, 2995, 2946, 1644, 1466, 1375, 1210, 1078: ^1H NMR (300 MHz, $CDCl_3$): δ 7.49 (s, 1H), 5.14-5.04 (m, *2*H), 4.78 (m, 2H), 4.64 (s, 1H), 4.49-4.41 (m, 2H), 4.13-3.85 (m, 2H), 3.72 (m, 1H), 1.45, 1.43, 1.37, 1.32 (each s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.1, 127.8, 112.6, 108.9, 106.6, 84.7, 80.3, 79.2, 72.8, 72.4, 72.2, 66.9, 66.5, 61.7, 46.7, 26.6, 25.6, 24.9, 24.3 ppm.

6-(1,2:3,4-Di-O-isopropilidene-6-O-oxymethylene-*α*-D galactopyranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 14c: Compound **13c** (140 mg**,** 0.39 mmol), sodium hydride (28 mg, 1.1 mmol) and propargyl bromide (0.045 ml, 0.5 mmol) were reacted in DMF (8 ml) using procedure described above to give **14c** (130 g, 84%) as yellowish viscous liquid; R_f = 0.30 (60% ethyl acetate/*n*-hexane); MS: *m/z* 398 $[M+H]^+$;IR (KBr) cm^{-1} 3457, 3142, 2988, 2936, 1640.456, 1374, 1217, 1078: ^1H NMR (300 MHz, $CDCl_3$): δ 7.49 (s, 1H), 5.53 (d, J = 4.5 Hz, 1H), 5.11 (d, J = 15.0 Hz, 1H), 4.83 (d, J = 15.0 Hz, 1H), 4.62-4.55 (m, 2H), 4.33-4.16 (m, 3H), 4.09-4.00 (m, 1H), 3.90-3.70 (m, 4H), 1.54, 1, 1.45, 1.33 (each s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.4, 128.0, 109.3, 108.6, 96.2, 72.7, 71.1, 70.7, 70.6, 70.4, 67.1, 66.9, 61.8, 47.2, 25.9, 25.8, 24.7, 24.2 ppm.

6-(Methyl-2,3-*O*-isopropilidene-5-*O*-oxymethylene-*β*-D-ribofuranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 14d: Compound **13d** (100 mg, 0.33 mmol), sodium hydride (23 mg, 1.0 mmol) and propargyl bromide (0.038 ml, 0.42 mmol) were reacted in DMF (8 ml) using procedure described above to give **14d** (95 mg, 85%) as yellowish viscous liquid; R_f = 0.30 (60% ethyl acetate/*n*-hexane); MS: *m/z* 342 $[M+H]^+$;IR (KBr) cm^{-1} 2925, 2855, 1724, 1635, 1455, 1383, 1216, 1165, 1075, 1020, 857: ^1H NMR (300 MHz, $CDCl_3$): δ 7.48 (s, 1H), 5.11 (d, J = 15.3 Hz, 1H), 4.96 (s, 1H), 4.84 (d, J = 15.0 Hz, 1H), 4.67-4.53 (m, 3H), 4.36-4.05 (m, 3H), 3.85-3.70 (m, 2H), 3.58-3.56 (m, 2H), 3.32 (s, 3H), 1.48, 1.32 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.3, 127.8, 112.2, 109.1, 84.8, 84.6, 81.7, 72.5, 72.4, 70.8, 61.7, 54.6, 46.9, 26.1, 24.6 ppm.

6-(3-*O*-Benzyl-1,2-*O*-isopropilidene-5-*O*-oxymethylene-*α*-D-galactopyranose)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 14e: Compound **13e** (100 mg**,** 0.26 mmol), sodium hydride (19 mg, 0.79 mmol) and propargyl bromide (0.03 ml, 0.33 mmol) were reacted in DMF (8 ml) using procedure described above to give **14e** (95 mg, 88%) as yellowish liquid; R_f = 0.30 (60% ethyl acetate/*n*-hexane); MS: *m/z* 418 $[M+H]^+$;IR (KBr) cm^{-1} 3409, 2987, 2938, 1712, 1454, 1373, 1138, 869: ^1H NMR (300 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.31-7.27 (m, 5H), 5.94 (d, J = 3.6 Hz, 1H), 5.08 (dd, J = 1.8 Hz, 15.0 Hz, 1H), 4.82-4.38 (m, 7H), 4.18-3.65 (m, 6H), 1.49, 1.32 (each s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.3, 130.4, 128.5, 128.0, 127.6, 111.7, 105.1, 82.0, 81.7, 79.1, 72.7, 72.6, 71.8, 71.3, 69.4, 61.8, 46.9, 26.6, 26.1 ppm.

6-(Morpholine)-6,7-dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazine, 14f: Compound **13f** (80 mg**,** 0.43 mmol), sodium hydride (30 mg, 1.2 mmol) and propargyl bromide (0.049 ml, 0.55 mmol) were reacted in DMF (8 ml) using procedure described above to give **14f** (77 mg, 80%) as redish semi white solid; IR (KBr) cm^{-1} R_f = 0.15 (70% ethyl acetate/*n*-hexane); MS: *m/z* 225 $[M+H]^+$;3416, 2980, 2934, 1710, 1630, 1456, 1116, 1058, 868, 471: ^1H NMR (300 MHz, $CDCl_3$): δ 7.49 (s, 1H), 5.10 (d, J = 15.0 Hz, 1H), 4.81 (d, J = 15.0 Hz, 1H), 4.56 (d, J = 10.2 Hz, 1H), 4.14-4.07 (m, 2H), 3.75-3.72 (m, 4H), 2.84-2.75 (m, 1H), 2.64-2.57 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 130.4, 127.0, 71.8, 66.7, 61.8, 60.4, 54.3, 48.4 ppm.

Acknowledgement

VKT gratefully acknowledge Council of Scientific & Industrial Research (CSIR), New Delhi (Grant No. 02(0173)/13/EMR-II) for the funding and CISC, Department of Chemistry, Banaras Hindu University for providing spectroscopic data of synthesized compounds. KBM gratefully acknowledges UGC, New Delhi, for a fellowship (JRF & SRF).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/

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