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Application of click chemistry towards an efficient synthesis of 1,2,3-1*H*-triazolyl glycohybrids as enzyme inhibitors

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ABSTRACT

An efficient synthesis of novel 1,2,3-1*H*-triazolyl glycohybrids with two or more than two sugar units or a chromenone moiety via copper-catalysed azide–alkyne cycloaddition (CuAAC), a 1,3-dipolar cycloaddition of glycosyl azides to 2,3-unsaturated alkynyl glycosides or propargyloxy coumarins is described. The synthesised glycohybrids were screened for their α-glucosidase, glycogen phosphorylase and glucose-6-phosphatase inhibitory activities. A few of the glycohybrids showed promising inhibitory activities against these enzymes.

1. Introduction

Carbohydrates, a group of prominent biomolecules from renewable resources that have great structural diversity are crucial components at the interface of chemistry and biology. They are intricately involved in molecular recognition and act as signalling molecules.[1] Most of the intra- and intercellular events are mediated by different glycoconjugates in all living organisms.[2] Therefore, they are implicated in different ways in the aetiology and pathogenesis of metabolic disorders, parasitic and other infectious diseases.[3–6] Consequently, multivalent glycohybrids with heterocyclic appendages are of great significance in drug design and development.[7,8] The multivalent nature of these molecules is frequently used to increase the affinities[9,10] to the targets in different biological processes, such as the binding of bacteria,[11–13] bacterial toxins,[14,15] galectins[16,17] and other lectins.[18,19] Since the introduction of 'click chemistry' by K. Barry Sharpless and Morten Meldal's group, tremendous work on improvements of the Huisgen cycloaddition has been reported in the literature under different reaction conditions to access 1,2,3-1*H*-triazoles.[20–23] This reaction has extensively been utilised in drug discovery and the development of several bioconjugates. The medicinal importance of these triazoles is due to their bioisosterism with peptide bonds,[24,25] as they can actively participate in hydrogen bonding, and due to their strong dipole moments, the triazoles are extremely stable to hydrolysis and oxidative/reductive conditions.[26,27] The hydrogen bonding in these compounds can be favourable in the binding of biomolecular targets and in enhancing their solubilities.[28] The triazole unit is an important pharmacophore in several antiviral,[29,30] antifungal,[31] antibacterial,[32,33] antiparasitic[34] and antitubercular[35] agents. Very recently, glycosyl 1,2,3-1*H*-triazoles have been reported to posses α-glucosidase inhibitory activity,[36–38] which is important in development of new antidiabetic agents. The glycosyl triazoles also act as inhibitors of galectins-1 and -3, which are important in the development of anti-HIV and anticancer agents.[39] In our continued efforts[40,41] to develop new chemotherapeutics from triazoles we were interested to synthesise glycosyl triazoles with two different sugar moieties (pyranose/furanose or saturated/unsaturated) or other oxygen heterocycles and study their biological activities. Herein, we have reported the synthesis of glycohybrids consisting of a 1,2,3-1*H*-triazole unit, one or two sugar unit(s) and coumarins, using a well-known copper-catalysed azide–alkyne cycloaddition (CuAAC) reaction of two sugar azides and different alkynes. The compounds prepared were also screened for their α-glucosidase, glucose-6-phosphatase and glycogen phosphorylase inhibitory activities in vitro.

2. Results and discussion

2.1. Syntheses

2.1.1. Synthesis of 2,3-unsaturated alkynyl glycosides

The starting alkynyl glycosides **7–11** were prepared by reaction of 3,4,6-tri-*O*-acetyl-D-glucal (**1**) with different alkynyl alcohols **2–6** (Scheme 1) as nucleophiles in the presence of a catalytic amount

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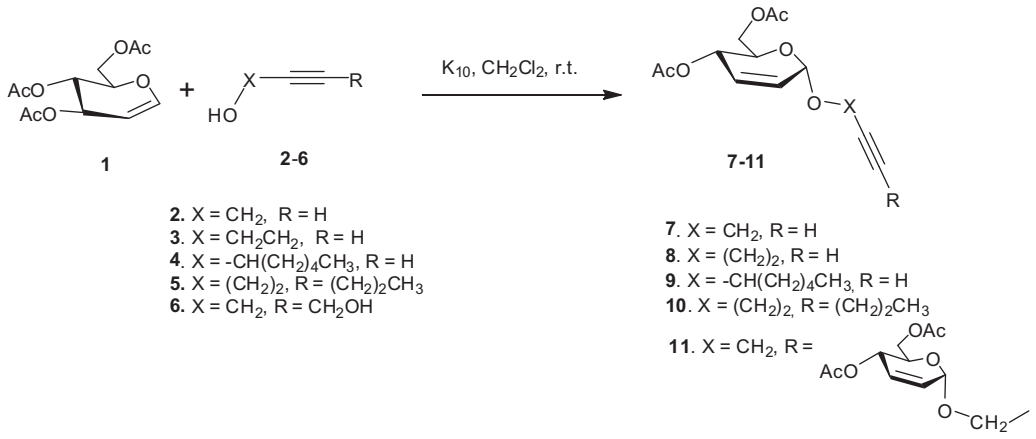


Scheme 1. Synthesis of 2,3-unsaturated alkynyl glycosides.

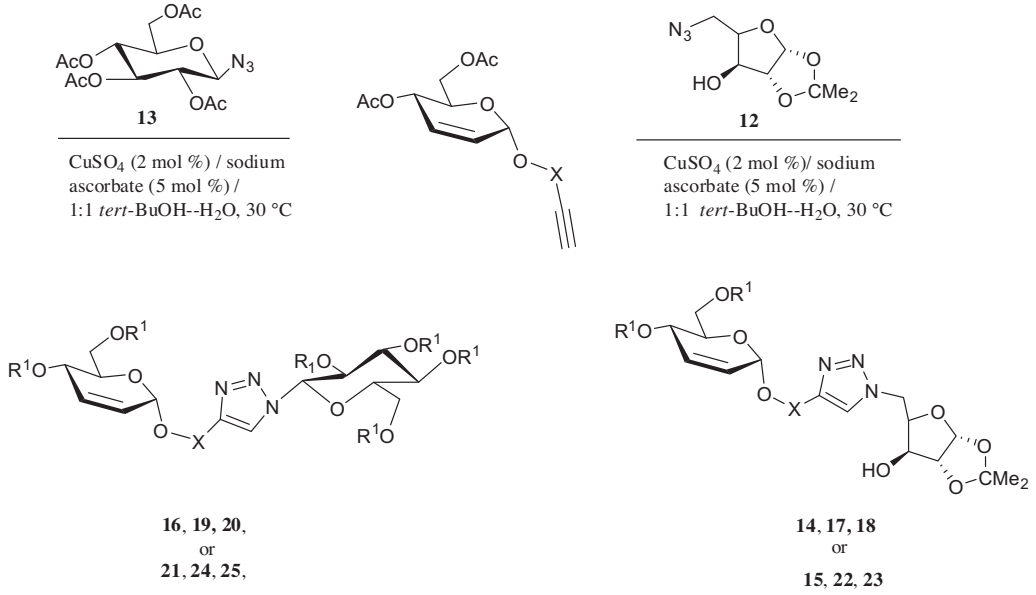
of a solid Lewis acid (Montmorillonite K-10, 30 mol %).[42] The structures of these alkynyl glycosides **7** and **8** were established on the basis of their spectroscopic data as reported in the literature. However, alkynyl glycosides **9**, **10** and **11** were prepared and characterised by us for the first time. The structures were in accordance with their spectroscopic data and microanalysis. It is important to mention here that all the alkynyl glycosides obtained above were predominantly in the α-anomeric form accompanied by minute quantity of β anomers. However, only the pure α anomers, isolated by column chromatography, were used in subsequent cycloaddition reactions.

2.1.2. Synthesis of α-D-xylofuranosyl and β-D-glucopyranosyl azides

5-Azido-5-deoxy-D-xylofuranose (**12**)[35] and 3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**13**)[43,44] were prepared from D-xylose and D-glucose as reported earlier.

2.1.3. Reaction of α-D-xylofuranosyl and β-D-glucopyranosyl azides with alkynyl glycosides

Reaction of the propynyl glycoside **7** with 5-azido-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**12**) in a mixture of 1:1 *t*-BuOH–H_2O in presence of $CuSO_4$ and sodium ascorbate at ambient temperature led to the formation of only one product, 1-(5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-1,2,3-1*H*-triazole (**14**) regioselectively in 75% yield (Scheme 2). The regioisomeric nature of the compound **14** was established on the basis of earlier reports[35] and its spectroscopic data. The ESIMS of compound **14** displayed *m/z* 484 corresponding to $[M+H]^+$. In the ^1H spectrum the anomeric proton of the furanose sugar (H-1) appeared at δ 5.95 (d, *J* 3.6 Hz, 1H), while that of the unsaturated pyranose sugar (H-1′) was seen as singlet at δ 5.13. A multiplet at δ 4.89–4.66 accounted for H-2 and H-4 of the furanose sugar. Three protons, H-5 and H-3 of the xylofuranosyl sugar, were observed as a multiplet in the range of δ 4.01–4.29. The olefinic protons (H-2′ and H-3′) of the pyranose sugar were visible as a multiplet in the range of δ 5.83–5.86, while H-4′ was observed at δ 5.33 as a multiplet. The two methylene protons (H-6′) of the unsaturated pyranose sugar, two protons of the OCH_2 linker and two protons (H-2 and H-4) of the xylofuranose sugar moiety were visible as two multiplets at δ 4.38–4.60 and δ 4.65–4.90, respectively. The triazolyl ring proton was visible as a singlet at δ 7.72. In the ^{13}C NMR spectrum the carbonyl carbons of the sugar acetyl groups were seen at δ 170.64



Scheme 2. Preparation of glycohybrid triazoles with terminal alkynyl glycosides and glycosyl azides.

and 169.94, while the anomeric C-1 and C-1′ of the furanose and pyranose sugars were observed at δ 105.15 and 93.78, respectively. The olefinic carbons (C-2′ and C-3′) of the pyranose sugar were visible at δ 127.41 and 124.20, respectively, besides the other usual signals of both the sugars. The 1,4-regioisomeric nature of the substituents in the triazole ring was evidenced by chemical shifts of C-4 and C-5 at δ 144.34 and 129.59 in accordance with the earlier reports.[35] Deacetylation of the acetyl group in compound **14** with NaOMe–MeOH at ambient temperature led to the formation of the respective deacetylated compound **15** in good yield. The structure of compound **15** was in full agreement with its spectroscopic data and microanalysis.

The 1,4-regioisomeric nature of addition product, as recently reported by Micouin's group,[45] may be due to a six-membered polar transition state (Fig. 1) formed by the complexation of azides and alkynes with a Cu ligand. Almost similar observations of 1,4-regioisomeric products during the cycloaddition of azides with acetylenes have been reported in the literature by several other groups.[35,46,47]

Having established the reaction conditions for the regioselective cycloaddition of the above terminal alkyne **7** and the xylofuranosyl azide **12**, the scope of different substrates in such a cycloaddition was explored. Thus cycloaddition of the above alkynyl glycoside **7** with tetra-*O*-acetyl-β-D-glucopyranosyl azide (**13**) as above in the presence of $CuSO_4$ and sodium ascorbate led to the formation of the glycosylated triazole **16** in 76% yield. Similarly, the other two terminal alkynyl-2,3-unsaturated glycopyranosides **8** and **9** on CuAAC reaction[48,49] with the above glycosyl azides **12** and **13** separately led to the formation of the respective glycosylated triazoles **17**, **18**, **19** and **20**, respectively, in very good yields (Scheme 2). Deacetylation of the acetyl groups in the above compounds **16**, **17**, **18**, **19** and **20** with NaOMe–MeOH as usual gave the respective glycohybrids **21**, **22**, **23**, **24** and **25** in good yields (Scheme 2, Table 1). The structures of all the compounds were in agreement with their spectroscopic data and microanalyses.

2.1.4. Cycloaddition reaction of internal alkynyl glycosides with glycosyl azides

The cycloaddition of the internal alkynes **10** and **11** with the glycosyl azides **12** and **13** under the above-mentioned reaction conditions proved to be futile. Therefore, an alternative method of thermal cycloaddition as reported in the literature for the cycloaddition of internal alkynes with azides was employed.[50] Thus, reaction of the internal alkyne **10** with the above two glycosyl azides **12** and **13** separately in refluxing toluene led to the formation of the respective glycosyl triazoles **26** and **27** as almost 1:1 regioisomeric mixture as evidenced by the NMR spectra of the compounds. However, reaction of the alkyne **11** having similar substituents on reaction with the above glycosyl azides **12** and **13** led to the formation of respective triglycosylated triazoles **28** and **29**, respectively, in good yields (Scheme 3). Deacetylation of the acetyl groups in the compounds **28** and **29** with NaOMe–MeOH at ambient temperature gave the respective deacetylated products **30** and **31** in good yields. Structures of all the above compounds were in full agreement with their spectroscopic data and microanalyses (Scheme 3).

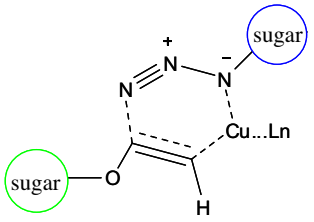


Figure 1. Proposed six-membered transition state.

2.1.5. Cycloaddition of propargyloxy coumarins 34 and 35 with sugar azides 12 and 13

The versatility of the method was further explored by the reaction of 7-*O*-propargyl-4-methyl coumarin (**34**)[51] and 4-*O*-propargyl coumarin (**35**)[52] with the above two glycosyl triazoles **12** and **13**. The propargyloxy coumarins **34** and **35** were prepared by reaction of 7-hydroxy-4-methyl coumarin (**32**) and 4-hydroxy coumarin (**33**) with propargyl bromide, respectively, in acetone in presence of anhydrous K_2CO_3 and tetrabutylammonium bromide (20 mol % as a catalyst) for 4–5 h at ambient temperature. The earlier methods[51,52] for preparation of these propargyloxy coumarins required a higher reaction temperature and a long reaction time (>12 h) with comparatively lesser yield as compared to our method. Cycloaddition of the above 7-*O*-propargyloxy coumarin **34** and the above glycosyl azides **12** and **13** separately led to the formation of the respective glycosyl triazoles **36** and **39** in very good yields, again with 1,4-regioselectivity. The deacetylation of the acetyl group in compound **36** with NaOMe–MeOH gave the respective compound **38** (Scheme 4) in good yields. Similarly, the above propargyloxy coumarin **35** on cycloaddition with the above glycosyl azides **12** and **13** led to the formation of respective glycohybrid triazoles[53] **37** and **40** in very good yields (Scheme 4). The structures of all the products were established on the basis of their spectroscopic data and microanalyses.

2.2. Biology

The above glycohybrid triazoles were screened for their enzyme inhibitory activities against α-glucosidase (EC 3.2.1.20), glycogen phosphorylase (EC 2.4.1.1) and glucose-6-phosphate (EC 3.1.3.9), enzymes that are crucial in the development of diabetes. The α-glucosidase was isolated and purified from rat intestines[54] while glycogen phosphorylase[55] and glucose-6-phosphatase[56,57] were isolated and purified from rat liver following earlier protocols. Among all the compounds screened, compounds **15**, **37, 38** and **40**, respectively showed 25.9%, 31.4%, 25.9% and 29.6% α-glucosidase inhibitory activity at 100 μmol. The standard drug, acarbose, exhibited 60% inhibition at 100 μmol concentration. On the other hand compounds **15**, **23**, **25** and **38** showed 18.5%, 47.7%, 34.1% and 20.0% inhibition of glycogen phosphorylase at 100 μM concentration. However, only two compounds **23** and **38** inhibited the glucose-6-phosphatase enzyme up to the extent of 25% at 100 μM concentration as compared to standard drug sodium-*ortho*-vandate exhibiting 36% inhibition at the same concentration. Other compounds of the series did not show any significant inhibition of any of the above three enzymes.

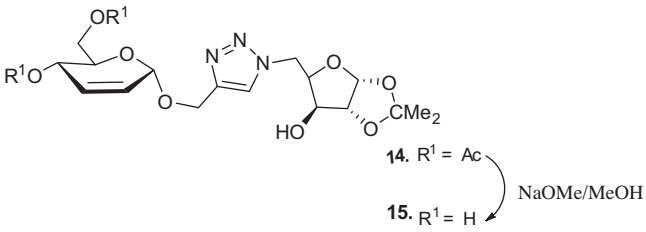
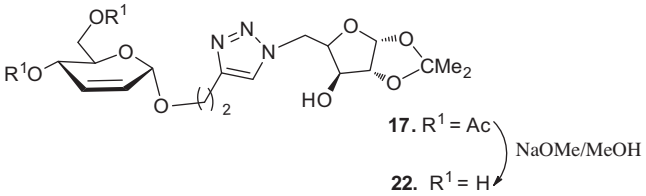
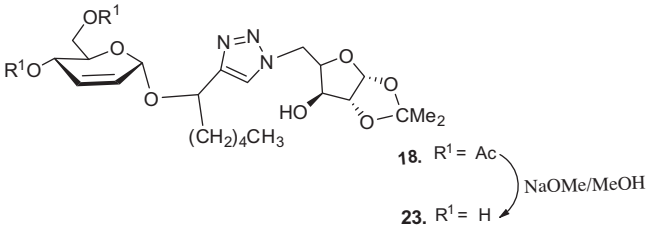
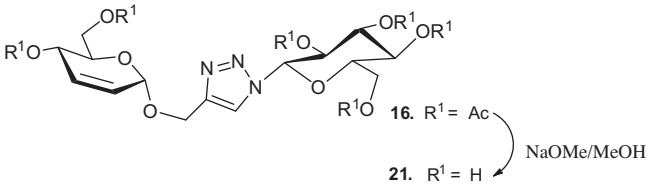
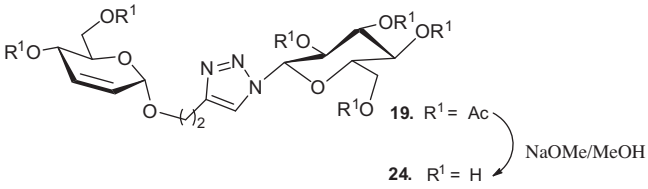
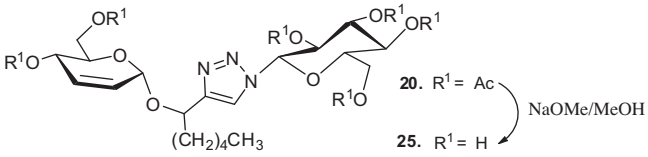
3. Conclusions

In conclusion, we have synthesised novel glycohybrid triazoles using the well-known CuAAC reaction of alkynyl glycosides and propargyloxy coumarins with sugar azides in fair to good yields. The compounds synthesised were evaluated for three enzymes, α-glucosidase, glycogen phosphorylase and glucose-6-phosphatase, showing moderate to significant inhibition. Further work in the series to get better compounds that will serve as antidiabetic agents is underway.

4. Experimental

Commercially available reagent grade chemicals were purchased from Sigma–Aldrich Chemical Co. or Spectrochem Pvt. Ltd

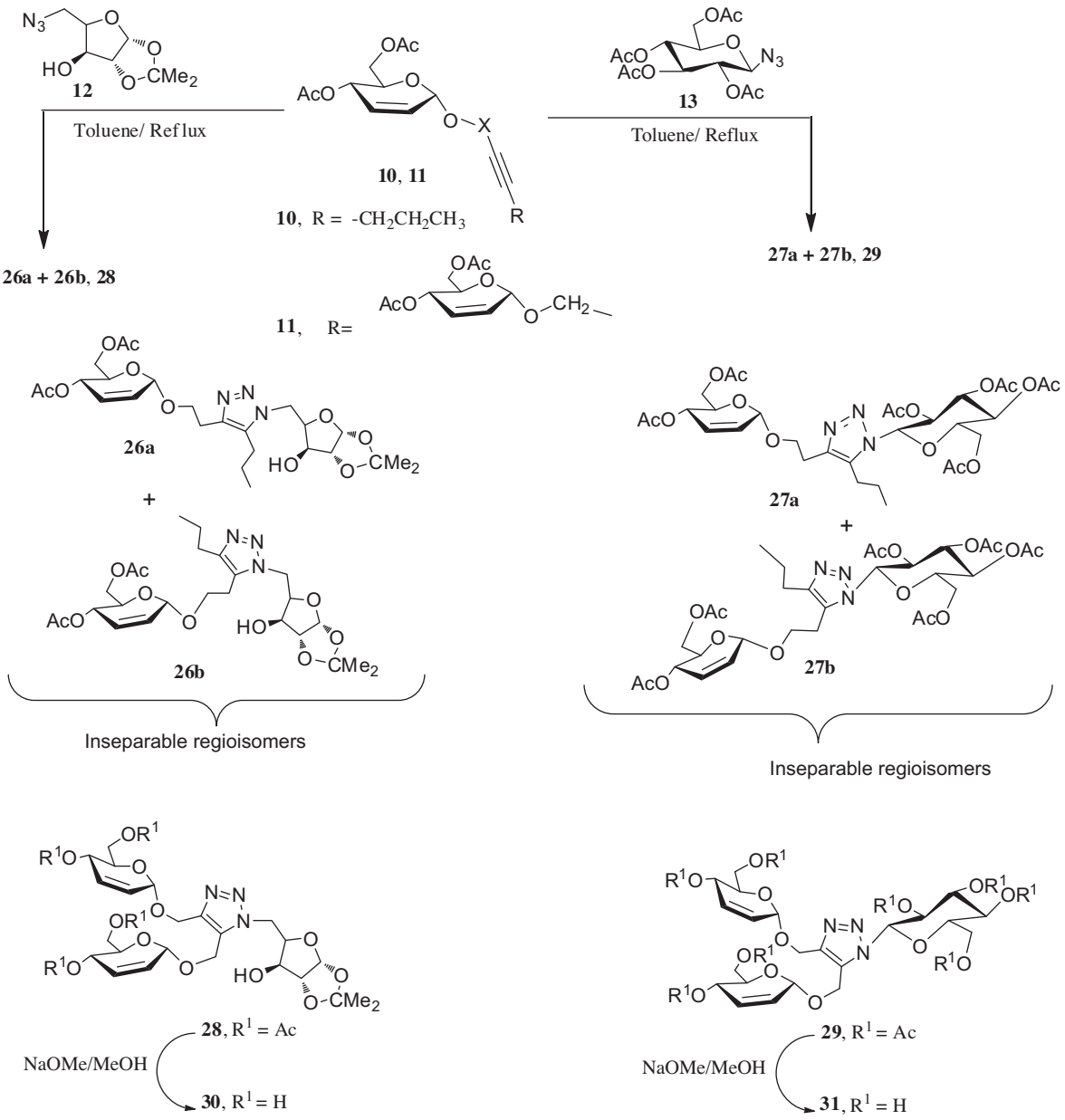
Table 1
Preparation of glycohybrid triazoles based on furanose and pyranose sugars

Entry	Substrate		Products
	Alkynyl glycosides	Sugar azides	
1	**7**	**12**	 **14.** R^1 = Ac; **15.** R^1 = H; NaOMe/MeOH
2	**8**	**12**	 **17.** R^1 = Ac; **22.** R^1 = H; NaOMe/MeOH
3	**9**	**12**	 **18.** R^1 = Ac; **23.** R^1 = H; NaOMe/MeOH
4	**7**	**13**	 **16.** R^1 = Ac; **21.** R^1 = H; NaOMe/MeOH
5	**8**	**13**	 **19.** R^1 = Ac; **24.** R^1 = H; NaOMe/MeOH
6	**9**	**13**	 **20.** R^1 = Ac; **25.** R^1 = H; NaOMe/MeOH

and were used as received. All reactions were followed by TLC on E. Merck Kieselgel 60 F254, with detection by UV light and/or spraying a 5% H_2SO_4 in EtOH followed by heating. Column chromatography was performed on Silica Gel 60 (60–120 mesh, E. Merck). IR spectra were recorded as thin films or in chloroform with a Perkin–Elmer Spectrum RX-1 (4000–450 cm^{-1}) spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Brucker DRX-300 in $CDCl_3$. Chemical shift values are reported in ppm relative to $SiMe_4$ as internal reference, *J* in Hertz. MS were performed using a Jeol SX-102 mass spectrometer and ESIMS were performed using a Quattro II (Micromass) instrument. Elemental analyses were performed on a Perkin–Elmer 2400 II elemental analyzer. Optical rotations were measured in a 1.0-dm tube with a Rudolf Autopol III polarimeter in $CHCl_3$.

4.1. 3-*O*-(4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yl)-oct-1-yne (9)

A solution of tri-*O*-acetyl-D-glucal (**1**, 1.0 g, 3.676 mmol) and octyne-3-ol (0.46 g, 3.676 mmol) in CH_2Cl_2 (10 mL) was magnetically stirred in the presence of Montmorillonite K-10 (30 mol %) at ambient temperature for 1 h. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure to give a crude mass. The latter was chromatographed over a SiO_2 column using 1:1 hexane–EtOAc as eluent to give compound **9** as a colourless oil. yield (0.98 g, 81%); R_f 0.5 (10:3 hexane–EtOAc); $[\alpha]_D$ +145 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3278, 2934, 1745, 1372, 1026; ^1H NMR (200 MHz, $CDCl_3$ + CCl_4): δ 0.93 (t, *J* 6.5 Hz, 3H, $-CH_2CH_3$), 1.31–1.52 (m, 6H, 3 × $-CH_2$), 1.75–1.80 (m, 2H, $-CH_2$), 2.12 (s,



Scheme 3. Preparation of glycohybrid triazoles with internal alkynyl glycosides and glycosyl azides.

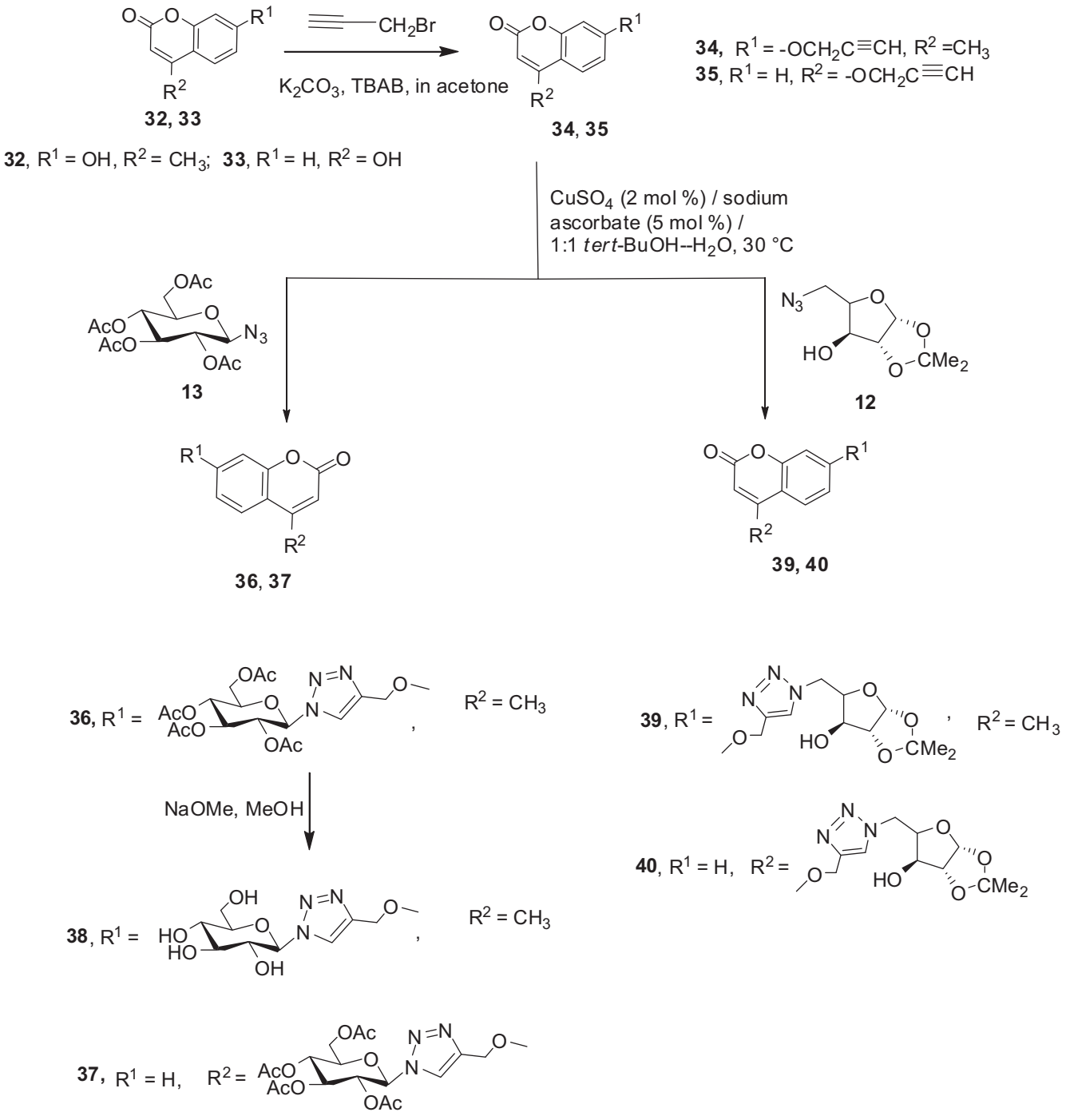
6H, 2 × –OAc), 2.43 (s, 1H, –C≡C*H*), 4.18 (m, 1H, H-5), 4.19–4.22 (m, 2H, H-6a, –OC*H*), 4.45 (m, 1H, H-6b), 5.33 (dd, 1H, $J_{3,4}$ 1.5 Hz, $J_{4,5}$ 8.2 Hz, H-4), 5.39 (s, 1H, H-1), 5.86–5.89 (m, 2H, H-2, H-3); ^{13}C (50 MHz, $CDCl_3$ + CCl_4) δ 14.08, 20.71, 20.91, 22.5. 25.1, 31.4, 35.5, 62.9, 65.2, 66.09, 67.30, 73.98, 82.31, 91.40, 127.80, 129.28, 169.86, 170.32; ESIMS: *m/z* 339 $(M+H)^+$; Anal. Calcd for $C_{18}H_{26}O_6$: C, 63.89; H, 7.74. Found: C, 63.81; H, 7.79.

4.2. 7-*O*-(4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxy)hept-3-yne (10)

Colourless oil: yield (1.0 g, 86%); R_f 0.4 (10:3 hexane–EtOAc); $[\alpha]_D$ +212 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3020, 2931, 1743, 1373, 1043; ^{1}H NMR (200 MHz, $CDCl_3$ + CCl_4): δ 0.99 (t, *J* 7.42 Hz, 3H, $-CH_3$), 1.53 (sixtet, *J* 7.1 Hz, 2H, $-CH_2$), 2.10–2.17 (m, 8H, $-CH_2C\equiv CH$, 2 × –OAc), 2.50 (m, 2H, $-CH_2$), 3.56–3.69 (m, 1H, H-5), 3.79–3.92 (m, 1H, H-6a), 4.10–4.30 (m, 3H, H-6b, $-OCH_2$), 5.07 (s, 1H, H-1), 5.33 (dd, $J_{3,4}$ 1.1 Hz, $J_{4,5}$ 9.5 Hz, H-4), 5.85–5.97 (m, 2H, H-2, H-3); ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4): δ 13.49, 20.20, 20.38, 20.74, 20.86, 22.3, 62.84, 65.24, 66.84, 67.49, 72.75, 94.87, 129.20, 127.69, 169.85, 170.32; ESIMS: *m/z* 325 $(M+H)^+$; Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 62.71; H, 7.59.

4.3. 1,4-*O*-Bis(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxy)-but-2-yne (11)

Colourless oil: yield (1 g, 87%); R_f 0.4 (10:4 hexane–EtOAc); $[\alpha]_D$ +311 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3020, 2931, 1743, 1373, 1043; ^{1}H NMR (200 MHz, $CDCl_3$ + CCl_4): δ 2.12, 2.13, (s, 6H, 2 × OAc), 4.09 (m, 1H, H-5), 4.22–4.49 (m, 4H, H-6 and OCH_2), 5.23 (s, 1H, H-1), 5.30–5.40 (m, 1H, H-4), 5.80–6.00 (m, 2H, H-2, H-3); ^{13}C NMR (300 MHz, $CDCl_3$ + CCl_4): δ 20.75, 20.90, 50.88, 55.35, 62.70, 63.85, 65.24, 92.68, 127.29, 129.75, 169.97, 170.59; ESIMS: *m/z*



Scheme 4. Preparation of glycohybrid triazoles with sugar and coumarin skeletons.

533 $(M+Na)^+$; Anal. Calcd for $C_{24}H_{32}O_{12}$: C, 56.24; H, 6.92. Found: C, 56.18; H, 6.98.

4.4. 1-(5-Deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-1,2,3-1*H*-triazole (14)

5-Azido-5-deoxy-1,2-*O*-isopropylidne-α-D-xylofuranose (**12**) (1.0 g, 4.651 mmol) and propynyl glycoside **7** (1.2 g, 4.651 mmol) were suspended in a mixture of 1:1 *t*-BuOH–water (20 mL) and stirred magnetically. A freshly prepared solution (500 μL) of sodium ascorbate (0.05 g, 0.2 mmol) in water was added, followed by addition of a freshly prepared aqueous solution (200 μL) of $CuSO_4{\cdot}5H_2O$ (0.02 g, 0.09 mmol). This heterogeneous mixture was stirred vigorously for 6 h at room temperature after which time the reaction mixture was extracted with EtOAc and water. The EtOAc layer was dried (anhyd Na_2SO_4) and evaporated under reduced pressure to give a crude product. The latter was purified by silica gel (60–120 mesh) column chromatography using 1:1 hexane–EtOAc as eluent to give compound **9** as a white solid: mp 167–168 °C; yield (1.57 g, 75%); R_f 0.5 (3:2 hexane–EtOAc); $[\alpha]_D$ +127.5 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3386, 2926, 1739,

1375, 766; ^{1}H NMR (200 MHz, $CDCl_3$ + CCl_4): δ 1.29, 1.43 (s, 6H, CMe_2), 2.07, 2.10 (s, 6H, 2 × OAc), 3.60 (br s, 1H, –OH), 4.01–4.23 (m, 3H, H-3, H-5), 4.38–4.60 and 4.65–4.90 (m, 6H, OCH_2, H-6′, H-2, H-4), 5.14 (s, 1H, H-1′), 5.33 (d, *J* 8.5 Hz, 1H, H-4′), 5.83–5.86 (m, 2H, H-2′, H-3′), 5.95 (d, *J* 3.6 Hz, 1H, H-1), 7.72 (s, 1H, triazolyl-H); ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4): δ 20.77, 20.88, 26.23, 26.87, 49.5, 61.25, 62.80, 65.27, 67.09, 74.44, 79.30, 85.40, 93.78, 105.15, 111.85, 124.20, 127.41, 129.59, 144.34, 169.94, 170.64; ESIMS: *m/z* 484 $(M+H)^+$; Anal. Calcd for $C_{21}H_{29}N_3O_{11}$: C, 52.17; H, 6.05; N, 8.69. Found: C, 52.01; H, 6.18; N, 8.49.

4.5. 1-(5-Deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4-(2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-1,2,3-1*H*-triazole (15)

Compound **14** (0.50 g, 1.0 mmol) was dissolved in NaOMe solution in MeOH (3 mL, 1 M) and was kept at room temperature for 30 min. The reaction mixture was neutralised with aq 3 N HCl, and the solvent was evaporated under reduced pressure. The residue thus obtained was dissolved in MeOH and filtered off. The filtrate was concentrated to give compound **15** as a viscous liquid: yield (0.360 g, 88%); R_f 0.5 (4:1 $CHCl_3$–MeOH); $[\alpha]_D$ +16 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3423, 2369, 1637, 1220, 771; ^{1}H NMR (300 MHz, CD_3OD): δ 1.30, 1.42 (s, 6H, CMe_2), 3.65–3.90 (m, 3H, H-3, H-6), 4.07–4.20 (m, 2H, H-5), 4.40–4.90 (m, 6H, H-2, H-4, H-4, $–OCH_2$, H-4′), 5.10 (s, 1H, H-1′), 5.72 (m, 1H, H-2′), 5.98 (m, 2H, H-1, H-3′), 7.94 (s, 1H, triazolyl-H), ^{13}C NMR (50 MHz, CD_3OH): δ 26.30, 26.97, 56.24, 61.32, 62.48, 63.97, 73.30, 75.12, 80.20, 86.35, 94.41, 105.99, 112.66, 125.58, 126.32, 134.89, 145.4; ESIMS: *m/z* 422 $(M+Na)^+$; Anal. Calcd for $C_{17}H_{25}N_3O_8$: C, 51.12; H, 6.31; N, 10.52. Found: C, 50.97; H, 6.52; N, 10.47.

4.6. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranos-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-1,2,3-1*H*-triazole (16)

White solid: mp 90–100 °C; yield (1.3 g, 76%); R_f 0.5 (49:1 $CHCl_3$–MeOH); $[\alpha]_D$ −28 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3465, 2365, 1749, 1656, 1373, 768; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 1.84, 2.00 (s, 6H, 2 × –OAc), 2.07–2.05 (s, 12H, 4 × –OAc), 4.10–4.04 (m, 3H, H-6, H-5′), 4.19 (m, 1H, H-5), 4.32 (m, 2H, H-6′), 4.71 (s, 2H, $–OCH_2$), 5.05 (s, 1H, H-1′), 5.29 (m, 2H, H-4, H-3), 5.45 (m, 2H, H-4′, H-2), 5.95–5.90 (m, 3H, H-1, H-2′,H-3′), 7.91 (s, 1H, triazolyl-H); ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4): δ 20.01, 20.41, 20.51, 20.67, 20.80, 56.18, 57.88, 61.41, 62.70, 65.22, 67.65, 70.42, 72.65, 75.02, 85.61, 94.50, 121.24, 127.44, 129.55, 145.43, 148.6, 168.75, 169.02, 169.50, 169.73, 170.02, 170.32; ESIMS: *m/z* 642 $(M+H)^+$, 664.2 $(M+Na)^+$; Anal. Calcd for $C_{27}H_{35}N_3O_{15}$: C, 50.55; H, 5.50; N, 6.55. Found: C, 50.51; H, 5.62; N, 6.48.

4.7. 1-(5-Deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranos-1-yloxyethyl)-1,2,3-1*H*-triazole (17)

White solid: mp 140–145 °C, yield (1.08 g, 78%); R_f 0.5 (4:6 hexane–EtOAc); $[\alpha]_D$ +62 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3424, 2924, 1657, 1051, 673; ^{1}H NMR (200 MHz, $CDCl_3$ + CCl_4): δ 1.29, 1.47 (s, 6H, CMe_2), 2.07, 2.12 (s, 6H, 2 × –OAc), 3.06 (t, *J* 6.2 Hz, 2H, –triazolyl-CH_2–), 3.83 (m, 1H, H-3), 3.95–4.31 (m, 5H, H-5,-OCH_2CH_2, H-5′), 4.40–4.61 (m, 3H, H-4, H-6′), 4.85 (m, 1H, H-2), 5.05 (s,1H, H-1′), 5.29 (dd, $J_{3,4}$ 1.1, $J_{2,3}$ 9.6 Hz, 1H, H-4′), 5.87–5.84 (m, 2H, H-2′, H-3′), 5.99 (d, *J* 3.5 Hz, 1H, H-1), 7.61 (s, 1H, triazolyl-H); ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4): δ 20.75, 20.91, 26.23, 26.52, 48.69, 62.97, 65.35, 67.02, 67.45, 74.44, 77.60, 79.38, 85.37, 94.52, 105.16, 111.83, 123.17, 127.62, 129.27, 144.94, 169.94, 170.63; ESIMS: *m/z* 498 $(M+H)^+$, 520 $(M+Na)^+$; Anal. Calcd for $C_{22}H_{31}N_3O_{11}$: C, 53.11; H, 6.28; N, 8.45. Found: C, 52.98; H, 6.39; N, 8.34.

4.8. 1-(5-Deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxyhexyl)-1,2,3-1*H*-triazole (18)

Colourless solid: mp 120–122 °C, yield (0.98 g, 76%); R_f 0.4 (49:1 $CHCl_3$–MeOH); $[\alpha]_D$ +250 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3220, 2940, 1750, 1377, 856; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 0.80 (m, 3H, CH_3), 1.26, 1.44 (s, 6H, CMe_2), 1.30–151 (m, 6H, 3 × $–CH_2$), 1.78–1.98 (m, 2H, $–CHCH_2$), 2.16, 2.06 (s, 6H, 2 × OAc), 4.12–4.30 (m, 5H, H-5, $–OCH_2CH_2$, H-5′), 4.40–4.65 (m, 3H, H-4, H-6), 4.80 (m, 1H, H-2), 4.90 (m, 1H, –triazolyl-C*H*–O–), 4.98 (s, 1H, H-1′), 5.30 (d, $J_{4,5}$ 9.5 Hz, 1H, H-4′), 5.70 (d, $J_{3,2}$ 10.2 Hz, 1H, H-3′), 5.88 (d, 1H, $J_{2,3}$ 10.2 Hz, H-2′), 5.95 (d, *J* 3.2 Hz, 1H, H-1), 7.65 (s, 1H, triazolyl H); ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4): δ 14.09, 20.75, 20.91, 22.56, 26.23, 26.91, 31.59, 35.89, 49.06, 62.99, 65.30, 67.35, 71.17, 74.43, 77.60, 79.31, 85.39, 91.72, 105.17, 111.85, 122.97, 127.84, 129.13, 148.55, 169.90, 170.46; ESIMS: *m/z* 576 $(M+Na)^+$; Anal. Calcd for $C_{26}H_{39}N_3O_{11}$: C, 56.41; H, 7.10; N, 7.59. Found: C, 56.38; H, 7.22; N, 7.48.

4.9. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranose-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxyethyl)-1,2,3-1*H*-triazole (19)

Colourless solid: mp 140–145 °C; yield (1.35 g, 80%); R_f 0.5 (49:2 $CHCl_3$–MeOH); $[\alpha]_D$ +78 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3465, 2365, 1749, 1656, 1373, 768; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 1.84, 2.00, 2.09, 2.05, 2.06, 2.07 (s, 18H, 6 × OAc), 3.03 (m, 2H, $–OCH_2CH_2$-triazolyl), 3.75 (m, 1H, H-5), 3.92–4.38 (m, 7H, H-5′, H-6, $–OCH_2$, H-6′), 4.98 (s, 1H, H-1′), 5.12–5.42 (m, 4H, H-2, H-3, H-4, H-4′), 5.80–5.93 (m, 3H, H-1, H-2′, H-3′), 7.61 (s, 1H, triazolyl-H); ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4): δ 20.04, 20.43, 20.56, 20.68, 20.86, 26.50, 61.44, 62.80, 67.01, 67.41, 67.67, 70.20, 72.63, 75.10, 76.32, 76.96, 85.64, 94.57, 119.74, 127.67, 129.22, 145.63, 168.55, 169.07, 169.49, 169.84, 170.04, 170.37; ESIMS *m/z* 678.1 $(M+Na)^+$; Anal. Calcd for $C_{28}H_{37}N_3O_{15}$: C, 51.30; H, 5.69; N, 6.41. Found: C, 51.26; H, 5.74; N, 6.37.

4.10. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranos-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxyhexyl)-1,2,3-1*H*-triazole (20)

Colourless solid: mp 130 °C; yield (1.48 g, 77.8%); R_f 0.4 (49: 1 $CHCl_3$–MeOH); $[\alpha]_D$ +119 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3479, 2938, 1753, 1642, 1220, 660; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 0.86 (m, 3H, –alkyl-CH_3), 1.28 (m, 6H, 3 × $–CH_2$), 1.84 (m, 5H, $–CHCH_2$. OAc), 1.99, 2.03, 2.07 (s, 15H, 5 × OAc), 3.80–4.40 (m, 7H, H-5, H-5′, H-6, $–OCH_2$, H-6′), 4.80 (s, 1H, H-1′), 4.90 (m, 1H, –triazolyl-C*H*–O–) 5.12–5.42 (m, 4H, H-2, H-3, H-4, H-4′), 5.80–5.93 (m, 3H, H-1, H-2′, H-3′), 7.61 (s, 1H, triazolyl-H); δ ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4): δ 14.04, 19.88, 20.31, 20.37, 20.52, 20.61, 20.81, 22.50, 25.44, 31.60, 36.40, 61.31, 62.95, 65.28, 67.32, 67.66, 70.52, 71.60, 72.31, 75.14, 85.69, 91.61, 119.49, 128.00, 128.83, 150.16, 168.92, 169.22, 169.60, 169.81, 170.04, 170.17; ESIMS: *m/z* 678.1 $(M+Na)^+$; Anal. Calcd for $C_{32}H_{45}N_3O_{15}$: C, 54.00; H, 6.37; N, 5.90. Found: C, 53.94: H, 6.43; N, 5.86.

4.11. 1-(β-D-Glucopyranos-5-yl)-4-(2,3-dideoxy-β-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-1,2,3-1*H*-triazole (21)

Viscous oil: yield (0.25 g, 83%); R_f 0.4 (7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +9.6 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3417, 2927, 2366, 1588, 1219, 772; ^{1}H NMR (300 MHz, $CDCl_3$ + CD_3OD): δ 3.52–4.09 (m,

9H, H-3, H-4, H-4′, H-5, H-5′, H-6, H-6′), 4.70 (s, 2H, –OCH_2), 5.10 (s, 1H, H-1′), 5.60 (d, 1H, *J* 9.1 Hz, H-3′), 5.70 (d, 1H, *J* 9.1 Hz, H-2′), 5.93 (d, *J* 10.2 Hz, 1H, H-1), 8.03 (s, 1H, triazolyl-H); ^{13}C NMR (50 MHz, CD_3OD) δ 61.6, 62.6, 64.2, 70.7, 73.4, 77.1, 78.1, 79.7, 80.9, 89.4, 94.0, 123.2, 124.5, 126.3, 148.9; ESIMS: *m/z* 391.3 $(M+H)^+$; Anal. Calcd for $C_{15}H_{23}N_3O_9$: C, 46.20; H, 5.95; N, 10.79. Found: C, 46.11; H, 6.01; N, 10.71.

4.12. 1-(5-Deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4-(2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxyethyl)-1,2,3-1*H*-triazole (22)

Colourless solid: mp 50–55 °C; yield (0.19 g, 82%); R_f 0.5 (4:1 $CHCl_3$–MeOH); $[\alpha]_D$ +11 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3379, 2926, 2368, 1658, 1055; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.21, 1.33 (s, 6H, CMe_2), 2.89 (t, 3H, *J* 6.6 Hz, –CH_2-triazolyl), 3.51 (m, 4H, –OCH_2, H-6′), 3.90 (m, 2H, H-5), 4.09 (s, 1H, H-3), 4.32–4.60 (m, 4H, H-2, H-4, H-4′, H-5′), 5.10 (s, 1H, H-1′), 5.63 (d, *J* 9.9 Hz, 1H, H-3′), 5.82 (d, *J* 9.9 Hz, 1H, H-2′), 5.86 (d, 1H, *J* 3.4 Hz, H-1), 7.89 (s, 1H, triazolyl H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 26.45, 26.52, 27.06, 49.17, 61.25, 62.66, 67.04, 73.26, 73.94, 79.66, 85.44, 94.06, 104.94, 111.17, 123.44, 125.75, 134.97, 144.57; ESIMS: *m/z* 414 $(M+H)^+$, 436 $(M+Na)^+$; Anal. Calcd for $C_{18}H_{27}N_3O_8$: C, 52.29; H, 6.58; N, 10.16. Found: C, 52.21; H, 6.63; N, 10.05.

4.13. 1-(5-Deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4-(2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxyhexyl)-1,2,3-1*H*-triazole (23)

Colourless solid: mp 60–65 °C; yield (0.20 g, 84%); R_f 0.6 (4:1 $CHCl_3$–MeOH); $[\alpha]_D$ +28 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3420, 2940, 1658, 1377, 856; ^{1}H NMR (300 MHz, $CDCl_3$ + CD_3OD): δ 0.89 (m, 3H, –CH_3), 1.42 (s, 3H, CH_3), 1.31, 1.43 (s, 6H, CMe_2), 1.19–1.50 (m, 6H, 3 × alkyl CH_2), 1.77, 1.92 (m, 2H, –$CHCH_2$), 3.65–3.85 (m, 3H, H-5′, H-6′), 4.02–4.20 (m, 2H, H-5), 4.40–4.78 (m, 4H, H-3, H-4, H-4′, and –O–C*H*-alkyl), 4.85 (s, 1H, H-1′), 5.00 (m, 1H, H-2), 5.61 (d, *J* 10.7 Hz, 1H, H-2′), 5.93 (m, 2H, H-1, H-3′), 7.83 (s, 1H, triazolyl-H); ^{13}C NMR (50 MHz, $CDCl_3$ + CD_3OD): δ 17.59, 26.32, 29.24, 29.68, 30.34, 35.37, 39.69, 53.55, 65.44, 65.85, 74.06, 76.26, 78.08, 83.19, 89.31, 95.06, 109.00, 115.69, 127.21, 129.58, 137.69, 152.48. ESIMS *m/z* 492.2 $(M+Na)^+$; Anal. Calcd for $C_{22}H_{35}N_3O_8$: C, 56.28; H, 7.51; N, 8.95. Found: C, 56.19; H, 7.62; N, 8.89.

4.14. 1-(β-D-Glucopyranose-5-yl)-4-(2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxyethyl)-1,2,3-1*H*-triazole (24)

Colourless gum: yield (0.20 g, 85%); R_f 0.5 (7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +15.6 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3430, 2362, 1588, 765; ^{1}H NMR (300 MHz, $CDCl_3$+ DMSO-d_6): δ 2.99 (t, 2H, *J* 6.1 Hz, triazolyl-CH_2CH_2), 3.20 (br s, 4 × OH), 3.40–3.62 (m, 8H, H-3, H-4, H-6, H-5, H-5′, 2 × OH), 3.70–3.90 (m, 5H, H-2, –OCH_2, H-6′) 4.06 (m, 1H, H-4′), 4.95 (s, 1H, H-1′), 5.48 (d, *J* 9.2 Hz, 1H, H-3′), 5.63 (m, 1H, H-2′), 5.86 (d, *J* 10.1 Hz, 1H, H-1), 7.93 (s, 1H, triazolyl-H), ^{13}C NMR (50 MHz, $CDCl_3$ + DMSO-d_6): δ 29.75, 31.35, 66.09, 67.55, 71.71, 74.65, 77.27, 77.92, 82.11, 85.10, 92.69, 92.86, 126.54, 130.41, 139.73, 149.17; ESIMS: *m/z* 426 $(M+Na)^+$; Anal. Calcd for $C_{16}H_{25}N_3O_9$: C, 47.64; H, 6.25; N, 10.42. Found: C, 47.59; H, 6.32; N, 10.36.

4.15. 1-(β-D-Glucopyranos-5-yl)-4-(2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxyhexyl)-1,2,3-1*H*-triazole (25)

Colourless gum: yield (0.14 g, 83%); R_f 0.6 (7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +101 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3430, 2925, 2366, 1584, 771; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 0.88 (m, 3H, –alkyl-CH_3), 1.30 (m, 6H, 3 × –CH_2), 1.78 (m, 2H, –O–(CH)CH_2), 3.30–4.15 (m, 12H, H-2, H-3, H-4, H-5, H-6, H-6′, 4 × –OH), 4.81–4.91 (m, 2H, –O–(*CH*)–CH_2–, H-1′), 5.49 (d, 1H, *J* 9.0 Hz, H-2′), 5.60 (m, 1H, H-3′), 5.86 (d, *J* 9.7 Hz, 1H, H-1), 7.98 (s, 1H, triazolyl H); ^{13}C NMR (50 MHz, $CDCl_3$ + DMSO-d_6): δ 19.06, 27.29, 30.15, 36.27, 36.46, 40.72, 65.86, 67.28, 74.49, 75.01, 77.19, 77.75, 81.9, 84.99, 92.81, 96.01, 126.32, 130.39, 139.60; 153.19; ESIMS: *m/z* 482 $(M+Na)^+$; Anal. Calcd for $C_{20}H_{33}N_3O_9$: C, 52.28; H, 7.24; N, 9.14. Found: C, 52.19; H, 7.29; N, 9.09.

4.16. 1-(5-Deoxy-2,3-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxyethyl)-5-propyl-1,2,3-1*H*-triazole (26a) and 1-(5-deoxy-2,3-*O*-isopropylidene-α-D-xylofuranos-5-yl)-5-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxyethyl)-4-propyl-1,2,3-1*H*-triazole (26b) as inseparable regioisomers

Brown viscous: yield (1.15 g, 72% yield); R_f 0.6 (49:1 $CHCl_3$–MeOH); $[\alpha]_D$ +42.7 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3423, 2927, 2363, 1735, 1219, 672; ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): because of the regioisomeric nature duplicity of almost all the signals were observed. δ 0.98, 1.24 (two t merged with each other, *J* 7.12 Hz, 6H, regioisomeric $CH_3CH_2CH_2$–), 1.26 (s, 6H, CH_3 of CMe_2), 1.44 (s, 6H, CH_3 of CMe_2), 1.74–1.67 (m, 2H, –CH_2), 1.62, 1.72 (m, each 2H, CH_3CH_2–), 2.08, 2.09, 2.13, 2.16 (s, 12H, 2 × –OAc), 2.63 (m, 4H, 2 × triazolyl-$CH_2CH_2CH_3$), 2.93–2.89 (m, 4H, triazolyl-CH_2CH_2O–), 3.70, 3.90 (m, 4H, H-5), 4.00–4.25 (m, 8H, 2 × –OCH_2CH_2–, H-5′, H-3), 4.38–4.27 (m, 4H, 2 × H-6′), 4.50–4.68 (m, 4H, regioisomeric H-2, H-4), 4.94, 5.00 (s, 1H, 2 × H-1′), 5.23–5.94 (m, 2H, regioisomeric H-4′), 5.93–5.78 (m, 6H, regioisomeric H-2′, H-3′, H-1); ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4): δ 13.90, 14.00, 22.44, 22.72, 23.20, 24.14 (–CH_3 of acetate), 26.17, 26.82, 26.86, 27.04 (CMe_2) regioisomeric mix, 29.66, 30.55 (–CH_2), 45.84, 46.21 (C-5), 62.60, 62.81 (regioisomeric mix C-6′), 65.20, 65.36 (regioisomeric mix C-4′), 66.76, 66.86 (–OCH_2), 66.98, 67.66 (C-5′), 74.22, 74.30 (C-2), 79.62, 79.71 (C-3), 85.23, 94.2, 94.3 (C-1′), 105.0 (C-1), 111.65, 111.61 (CMe_2) 127.07, 128.76, (regioisomeric C-2′), 129.00, 129.50 (regioisomeric C-3′), 132.33, 134.9, (regioisomeric triazolyl C-4), 141.42, 145.0 (regioisomeric triazolyl C-4), 167.41, 169.92, 170.39, 170.60, (regioisomeric –OAc); ESIMS: *m/z* 562 $(M+Na)^+$; Anal. Calcd for $C_{25}H_{37}N_3O_{10}$: C, 55.65; H, 6.91; N, 7.79. Found: C, 55.59; H, 6.98; N, 7.66.

4.17. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranos-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-5-propyl-1,2,3-1*H*-triazole (27a) and 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranos-5-yl)-5-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-4-propyl-1,2,3-1*H*-triazole (27b) as inseparable regioisomers

Brown viscous oil: yield (1.50 g, 70%); R_f 0.4 (49:1 $CHCl_3$–MeOH); $[\alpha]_D$ +25.4 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3021, 2368, 1750, 1662, 1220, 765; ^{1}H NMR (200 MHz, $CDCl_3$ + CCl_4): δ 0.98, 1.03 (two t merged with each other, *J* 7.12 Hz, 6H, regioisomeric $CH_3CH_2CH_2$–), 1.60–1.75 (m, 4H, regioisomeric $CH_3CH_2CH_2$–), 1.81, 1.82, 2.02, 2.05, 2.06, 2.07 (s, 36H, regioisomeric 6 × –OAc), 2.50–2.62 (m, 4H, regioisomeric $CH_3CH_2CH_2$–), 2.85–3.12 (m, 4H, regioisomeric –OCH_2CH_2–), 3.60–4.40 (m, 20H, regioisomeric H-3, H-4, H-5, H-5′, H-6, H-6′, OCH_2CH_2-triazolyl), 5.01 (s, 2H, regioisomeric H-1′), 5.20–5.40 (m, 4H, regioisomeric H-2, H-4′), 5.70–5.90 (m, 6H, H-1, H-2′, H-3′), ^{13}C NMR (50 MHz, $CDCl_3$ + CCl_4): δ 13.83, 14.00 (regioisomeric alkyl-CH_3), 20.09, 20.46, 20.64, 20.88 (OAc) 22.54, 25.85, 26.74 (alkyl-CH_2), 61.49 (C-6), 62.79 (C-4′), 65.14, 65.26 (regioisomeric C-2), 66.97, 67.20 (regioisomeric C-4 pyranose sugar), 67.64, 67.74 (regioisomeric –OCH_2), 69.69 (C-5′),

72.89 (C-3), 75.00 (C-5), 84.82, 85.18 (regioisomeric C-1), 94.54, 94.70 (regioisomeric C-1′), 127.75, 129.06, 129.66, (C-2′, C-3′), 142.66, 130.92 (triazolyl C-4, C-5), 168.30, 169.00, 169.86, 170.13, 170.50 (–OAc); ESIMS: 698.2 *m/z* $(M+H)^+$, 720 $(M+Na)^+$; Anal. Calcd for $C_{31}H_{43}N_3O_{15}$: C, 53.37; H, 6.21; N, 6.02. Found: C, 53.31; H, 6.28; N, 6.08.

4.18. 1-(5-Deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4,5-bis-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-1,2,3-1*H*-triazole (28)

Light brown gum: yield (0.91 g, 64%); R_f 0.5 (49: 2 $CHCl_3$–MeOH), $[\alpha]_D$ −222 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3414, 2926, 2361, 1740, 1217, 765; ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 1.27, 1.43 (s, 6H, CMe_2), 2.10, 2.13 (s, 12H, 4 × –OAc), 4.01 (m, 2H, H-5′, H-5″), 4.05–4.25 m, 5H, H-3, H-6′, H-6″), 4.51 (m, 4H, H-4, H-5, –OH), 4.67–4.73 (m, 5H, 2 × $–OCH_2$, H-2), 4.84 (s, 1H, H-1′), 4.94 (m, 1H, H-4′), 5.08 (s, 1H, H-1″), 5.28–5.32 (m, 1H, H-4″), 5.77 (d, *J* 10.2 Hz, 1H, H-3′), 5.89–5.92 (m, 1H, 2 × H-2′, H-3″), 5.94 (d, *J* 4.8 Hz, 1H, H-1); ^{13}C NMR (50 MHz, $CDCl_3 + CCl_4$): δ 14.24, 20.75, 20.83, 26.22, 26.92, 46.22, 46.50, 56.65, 56.87, 62.69, 63.17, 64.05, 65.05, 67.55, 74.14, 75.0, 79.35, 79.24, 85.18, 85.36, 93.66, 94.81, 105.07, 111.50, 111.83, 126.55, 130.23, 170.73, 169.85; ESIMS: *m/z* 748 $(M+Na)^+$; Anal. Calcd for $C_{32}H_{43}N_3O_{16}$: C, 52.96; H, 5.97; N, 5.79. Found: C, 52.89; H, 6.03; N, 5.71.

4.19. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranos-5-yl)-4-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-5-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-1,2,3-1*H*-triazole (29)

Colourless gum: yield (1.20 g, 71% yield.); R_f 0.4 (49:1 $CHCl_3$–MeOH); $[\alpha]_D$ +54 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3483, 3023, 2367, 1749, 1373, 1224, 766; ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 1.85, 2.01, 2.06, 2.07, 2.08, 2.09, 2.11 (s, 24H, 8 × –OAc), 4.02–4.13 (m, 4H, H-5′, H-5″, H-6), 4.15–4.28 (m, 5H, H-5, H-6′, H-6″), 4.75, 4.83 (s, 4H, 2 × $–OCH_2CH_2$-triazolyl), 4.98–5.06 (m, 2H, H-4, H-1), 5.17 (s, 1H, H-1″), 5.18–5.30 (m, 3H, H-4′, H-4″, H-3), 5.41 (m, 1H, H-2), 5.81–5.98 (m, 5H, H-1, H-2′, H-2″, H-3′, H-3″); ^{13}C NMR (50 MHz, $CDCl_3 + CCl_4$): δ 20.10, 20.39, 20.46, 20.50, 20.65, 20.78, 52.33, 55.55, 60.46, 61.21, 61.50, 62.75, 65.22, 67.26, 67.60, 70.00, 70.28, 72.63, 72.82, 75.09, 85.90, 92.24, 93.30, 127.08, 127.30, 129.66, 129.79, 135.65, 143.15, 148.00, 168.75, 168.87, 169.59, 169.71, 169.91, 170.01, 170.40, 170.44; ESIMS: *m/z* 884 $(M+H)^+$, 906 $(M+Na)^+$; Anal. Calcd for $C_{38}H_{49}N_3O_{21}$: C, 51.64; H, 5.59; N, 4.75. Found: C, 51.60; H, 5.63; N, 4.71.

4.20. 1-(5-Deoxy-1,2-*O*-*isopropylidene*-α-D-*xylofuranos-5-yl*)-4-(*2,3-dideoxy*-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-5-(2,3-dideoxy-α-D-*erythro*-hex-2-eno-pyranyloxymethyl)-1,2,3-1*H*-triazole (30)

Colourless gum; yield (0.25 mg, 80%); R_f 0.5 (4:1 $CHCl_3$–MeOH); $[\alpha]_D$ +20 (*c* 0.1, MeOH); IR (neat) cm^{-1}: 3409, 2138, 1638, 1413, 771; ^1H NMR (300 MHz, DMSO-d_6): δ 1.20, 1.30 (s, 6H, CMe_2), 3.50 (br s, 3H, –OH), 3. 90 (d, *J* 7.9 Hz, 2H, H-5′, H-5″), 4.09 (br s, 2H, OH), 4.35–4.45 (m, 2H, H-5), 4.46–4.49 (m, 3H, H-3, H-6′, H-6″), 4.51 (s, 4H, 2 × $–OCH_2$-triazolyl), 4.58–4.62 (m, 2H, H-2, H-4), 4.69, 4.88 (d, *J* 12.5 Hz, 2H, H-4′, H-4″), 5.03 (s, 2H, H-1′, H-1″), 5.60 (d, *J* 10.1 Hz, H-2′, H-2″), 5.83 (m, 2H, H-3″, H-3″), 5.86 (d, *J* 3.7 Hz, 1H, H-1); ^{13}C NMR (50 MHz, $CDCl_3$ + DMSO-d_6) δ 31.21, 31.86, 52.49, 59.23, 61.29, 67.21, 77.01, 78.19, 78.81, 84.53, 90.21, 98.28, 109.69, 115.89, 129.85, 136.73, 140.45, 151.08; ESIMS: *m/z* 748 $(M+Na)^+$; Anal. Calcd for $C_{24}H_{35}N_3O_{12}$: C, 51.70; H, 6.33; N, 7.54. Found: C, 51.64; H, 6.39; N, 7.51.

4.21. 1-(β-D-Glucopyranose-5-yl)-4-(2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl)-5-(2,3-dideoxy-α-D-*erythro*-hex-2-enopyranos-1-yloxymethyl) 1,2,3-1*H*-triazole (31)

Light brown gum: yield (0.30 g, 79%); R_f 0.5 (7:3 $CHCl_3$–MeOH); $[\alpha]_D$ +44.6 (*c* 0.1, MeOH); IR (Neat) cm^{-1}: 3413, 2362, 1650, 1567, 1415, 657; ^1H NMR (300 MHz, CD_3OD): δ 3.31 (br s, 1H, OH), 3.56 (m, 1H, H-4), 3.62–3.75 (m, 7H, H-3, H-5, H-5′, H-5″, H-6), 3.90, 4.09 (m, 2H, H-6′, H-6″), 4.21–4.29 (m, 2H, H-4′, H-4″), 4.74–4.79 (m, 5H, H-2, 2 × $–OCH_2$), 5.07 (s, 2H, H-1′, H-1″), 5.70–5.76 (m, 3H, H-2′, H-2″, H-3′), 5.75–5.67 (m, 2H, H-1 and H-3″);. ^{13}C NMR (50 MHz, CD_3OD): δ 52.19, 61.0, 62.44, 62.70, 64.08, 64.19, 71.0, 73.30, 73.76, 78.40, 81.14, 87.80, 87.92, 94.93, 95.16, 97.46, 126.52, 126.73, 135.51, 135.67, 138.04, 143.81; ESIMS: *m/z* 570 $(M+Na)^+$; Anal. Calcd for $C_{22}H_{33}N_3O_{13}$: C, 48.26, H, 6.08; N, 7.67. Found: C, 48.16; H, 6.13; N, 7.53.

4.22. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranose-1-yl)-4-(4-methyl-2*H*-chromen-2-one-7-yloxymethyl)-1,2,3-1*H*-triazole (36)

Colourless solid: mp >250 °C, yield (1.12 g, 73%); R_f 0.5 (49:1 $CHCl_3$–MeOH); $[\alpha]_D$ −11 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3467, 2365, 1746, 1619, 1378, 857; ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 1.81, 1.99, 2.01, 2.05 (s, 12H, 4 × –OAc), 2.41 (s, 3H, coumarinyl-CH_3), 4.07–4.30 (m, 3H, H-5 and H-6), 5.22 (m, 1H, H-4), 5.26 (s, 3H, $–OCH_2$-triazolyl), 5.48 (dd, *J* 11.7 Hz, 2.4 Hz, 2H, H-2, H-3,), 6.10 (d, *J* 11.7 Hz, 1H, H-1), 6.13 (d, *J* 2.4 Hz, 1H, coumarinyl-H-3), 6.94 (two d, *J* 7.5 Hz, 2.4 Hz, 2H, –ArH), 7.51 (d, *J* 2.4 Hz, 1H, ArH), 8.08 (s, 1H, triazolyl-H); ^{13}C NMR (50 MHz, $CDCl_3$ + DMSO-d_6) δ 23.09, 24.52, 24.98, 25.11, 66.19, 66.71, 72.39, 75.24, 77.31, 79.21, 89.82, 106.84, 116.97, 117.41, 118.66, 127.13, 130.46, 156.93, 160.07, 165.18, 166.02, 173.25, 173.87, 174.27, 174.76; ESIMS: *m/z* 610 $(M+Na)^+$; Anal. Calcd for $C_{27}H_{29}N_3O_{12}$: C, 55.20; H, 4.98; N, 7.15. Found: C, 55.18; H, 5.03; N, 7.11.

4.23. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranos-1-yl)-4-(*2H*-chromen-2-one-4-yloxymethyl) 1,2,3-1*H*-triazole (37)

Colourless solid: mp >285 °C, yield, (1.24 g, 81%) R_f 0.4 (49:1 $CHCl_3$–MeOH); $[\alpha]_D$ −32 (*c* 0.1, DMSO); IR (KBr) cm^{-1}: 3481, 3077, 2373, 1750, 1622, 1376, 927; ^1H NMR (300 MHz, $CDCl_3 + CCl_4$ + DMSO-d_6): δ 1.74, 1.93, 1.97, 1.99 (s, 12H, 4 × –OAc), 4.02–4.12 (m, 2H, H-6), 4.33 (m, 1H, H-5), 5.17 (t, *J* 9.7 Hz, 1H, H-4), 5.37 (s, 2H, $–OCH_2$), 5.51 (t, *J* 9.4 Hz, 1H, H-3), 5.61 (t, *J* 9.4 Hz, 1H, H-2), 6.00 (s, 1H, H-coumarinyl-H-3), 6.32 (d, *J* 9.0 Hz, 1H, H-1), 7.28 (m, 2H, –ArH), 7.56 (m, 1H, –ArH), 77.73 (d, *J* 7.8 Hz, 1H, –Ar H), 8.54 (s, 1H, triazolyl-H), ^{13}C NMR (50 MHz, $CDCl_3 + CCl_4$ + DMSO-d_6) δ 24.98, 25.36, 25.49, 25.61, 66.79, 67.73, 72.71, 75.42, 77.35, 78.62, 89.24, 96.53, 120.37, 121.43, 128.09, 129.04, 129.17, 137.65, 146.91, 158.03, 166.58, 169.40, 173.38, 174.21, 174.42, 174.90; ESIMS: *m/z* 574 $(M+H)^+$, 596 $(M+Na)^+$; Anal. Calcd for $C_{26}H_{27}N_3O_{12}$: C, 54.45; H, 4.75; N, 7.33. Found: C, 54.38; H, 4.83; N, 7.29.

4.24. 1-(β-D-Glucopyranos-1-yl)-4-(4-methyl-2*H*-chromen-2-one-7-yloxymethyl)-1,2,3-1*H*-triazole (38)

Colourless solid: mp >250 °C, yield, (0.32 g, 88%); R_f 0.6 (4:1 $CHCl_3$–MeOH); $[\alpha]_D$ −1 (*c* 0.1, DMSO); IR (KBr) cm^{-1}: 3405, 2364, 1692, 1398, 611; ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 2.39 (s, 3H, coumarinyl-4-CH_3), 2.74 (m, 1H, H-4), 3.20 (br s, 4 × OH), 3.51 (m, 3H, H-4, H-6), 3.70 (m, 1H, H-5), 3.81 (t, *J* 8.7 Hz, 1H, H-3), 4.02 (m, 1H, H-2), 5.23 (s, 2H, $–OCH_2$), 5.53 (d, *J* 9.3 Hz, 1H, H-1), 6.06 (s, 1H, coumarinyl-H), 6.98 (m, 2H, –ArH), 7.56 (d, *J* 8.6 Hz, 1H, –ArH), 7.86 (m, 2H, ArH), 8.26 (s, 1H, triazolyl-H); ^{13}C

NMR (50 MHz, $CDCl_3$ + DMSO-d_6): δ 23.39, 45.94, 65.78, 66.73, 74.43, 77.22, 81.98, 82.97, 84.90, 92.79, 106.62, 116.59, 117.56, 118.56, 131.16, 147.00, 159.86, 165.24, 166.17; ESIMS: *m/z* 442 $(M+Na)^+$; Anal. Calcd for $C_{19}H_{21}N_3O_8$: C, 54.41; H, 5.05; N, 10.02. Found: C, 54.38; H, 5.13; N, 9.96.

4.25. 1-(5-Deoxy-2,3-*O*-isopropylidene-α-D-xylofuranos-5-yl)-4-(4-methyl-2*H*-chromen-2-one-7-yloxymethyl)-1,2,3-1*H*-triazole (39)

Colourless solid: yield; mp 145–148 °C; (1.60 g, 80%); R_f 0.5 (49:1 $CHCl_3$–MeOH); $[\alpha]_D$ +3 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3326, 2927, 2366, 1722, 1622, 1385, 1072, 878; ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 1.29, 1.42 (s, 6H, CMe_2), 2.42 (s, 3H, $-CH_3$), 4.17 (m, 1H, H-3), 4.45–4.59 (m, 3H, H-4, H-5), 4.79 (m, 1H, H-2), 5.25 (s, 2H, $-OCH_2$), 5.95 (d, *J* 2.9 Hz, 1H, H-1), 6.11 (s, 1H, H-3 coumarin), 6.95 (m, 2H, –ArH), 7.48–7.54 (m, 1H, –ArH), 7.95 (s, 1H, triazolyl H-5); ^{13}C NMR (50 MHz, $CDCl_3$ + DMSO-d_6) δ 18.48, 26.09, 26.69, 49.29, 74.06, 79.26, 85.31, 95.94, 101.89, 104.94, 111.54, 111.90, 112.43, 113.76, 124.51, 125.60, 152.40, 154.93, 160.77, 161.11; ESIMS: *m/z* 452 $(M+Na)^+$; Anal. Calcd for $C_{21}H_{23}N_3O_7$: C, 58.74; H, 5.40; N, 9.79. Found: C, 58.65; H, 5.49; N, 9.71.

4.26. 1-(5-Deoxy-1,2-*O*-isopropyliden-α-D-xylofuranos-5-yl)-4-(2*H*-chromen-2-one-oxymethyl)-1,2,3-1*H*-triazole (40)

Light brown solid: mp 145–148 °C; yield (1.54 g, 80%); R_f 0.6 (49:1 $CHCl_3$–MeOH); $[\alpha]_D$ −20 (*c* 0.1, MeOH); IR (KBr) cm^{-1}: 3400, 2985, 2365, 1685, 1622, 1379, 766; ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 1.26, 1.39 (s, 6H, CMe_2), 3.43 (br s, 1H, OH), 4.14 (d, *J* 2.6 Hz, 1H, H-3), 4.46 (m, 1H, H-4), 4.49 (d, *J* 3.6 Hz, 1H, H-2), 4.58–4.67 (m, 2H, H-5), 5.37 (s, 2H, $-OCH_2$), 5.89 (d, *J* 3.6 Hz, 1H, H-1), 6.04 (s, 1H, coumarinyl-H-3), 7.27 (dd, *J* 8.3 Hz, 0.6 Hz, 2H, –ArH), 7.56–7.52 (m, 1H, –ArH), 7.76 (dd, *J* 8.3 Hz, 0.6 Hz, 1H, –ArH), 8.20 (s, 1H, triazolyl-H); ^{13}C NMR (50 MHz, $CDCl_3$ + DMSO-d_6): δ 26.48, 27.09, 49.57, 63.25, 74.08, 79.53, 85.49, 91.78, 104.99, 111.29; 115.54, 116.91, 123.35, 124.68, 126.26, 133.27, 141.41, 153.23, 162.02, 164.85, ESIMS: *m/z*: 416 $(M+H)^+$; Anal. Calcd for $C_{20}H_{21}N_3O_7$: C, 57.83; H, 5.10; N, 10.12. Found: C, 57.78; H, 5.18; N, 10.08.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2010.10.017.

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