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1 Introduction

Dendrimers hail from a distinctive family of macromolecules, tailored with a motif to encompass superior branching, three dimensional, high monodispersity and multivalent functional residue, all in one exquisite architecture.¹ The aforementioned attributes of dendrimers have enabled them to have innumerable applications in various fields including drug delivery, gene delivery, photodynamic therapy, biosensors, drugs for cardiovascular diseases, anti-cancer vaccines, anti-microbial vaccines, *etc.*^{2–7} However, the field of dendrimers have been widely explored and this provide an origin to a fascinating dendrimer analogue which expands divergently in a $1 \rightarrow 3$ branching fashion, namely dentromer.⁸ A significant advantage of dentromers over dendrimers corresponds to its densely distributed peripheral groups for the same generation and

An expeditious click approach towards the synthesis of galactose coated novel glycodendrimers and dentromers utilizing a double stage convergent method[†][‡]

Anand K. Agrahari, Anoop S. Singh., Rishav Mukherjee and Vinod K. Tiwari 吵 *

The primary motive behind this article is to bring to the forefront a unique kind of dendrimer which has remained a dark horse since its discovery, namely dentromer. We herein report the synthesis of glycodendrimers and glycodentromers crowned with galactose units by harnessing an expeditious synthesis of dendrimer core 18 and dentromer core 19, divergently with branching directionality $(1 \rightarrow 2)$ and $(1 \rightarrow 3)$, respectively. A competent, double stage convergent synthetic path was chosen to facilitate ease of refining and spectroscopic elucidations. By exploiting a Cu(i)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction strategy, we successfully developed a new series of galactosylated dendrimers 20, 21, 22, and 24 containing 6, 12, 18, and 18 peripheral galactose units, respectively. We are first to report the practical synthesis of 9-peripheral galactose coated glycodentromer 23 (0th generation) and 27-peripheral galactose coated glycodentromer 25 (1st generation). These synthesized scaffolds were characterized by spectral studies such as ¹H, ¹³C NMR, FT-IR, MALDI-TOF MS, HRMS and SEC analysis. Additionally, gel permeation chromatography depicted the regular progression in size from 6 to 27-peripheral galactose coated glycodendrimers along with glycodentromers, with their high monodispersity. Also, the glyco-dendrimers and dentromers synthesized from two different hypercore units i.e. dendrimers core (18) and dentromer core (19), have been supported by their UV-visible absorbance and emission spectroscopy.

> when conjoined to carbohydrate units, glycodentromers or sugar-linked dentromers undergo an enhanced hypercluster effect which prompts an enhancement in biological activity in comparison to a conventional glycodendrimer.⁹ Carbohydrates are essential scaffolds owing to their diverse role in biological processes, like functioning of the immune system, enhancing inflammatory response, malignancy, metastasis, apoptosis, *etc.*¹⁰⁻¹²

> This unique and effective feature of carbohydrates results from carbohydrate–lectin interactions playing a cardinal role in various biological systems such as biological recognition, protein folding, cell growth, cell-agglutination, cell signalling and interaction with bacteria/viruses.^{10,13} This mesmerizing unison of carbohydrates and dendrimers have drawn attention owing to its multivalency effect.¹⁴ Incorporating sugar units in a scaffold increases its biological activity as glycan–protein interaction plays a major role in various biological phenomena.¹⁵ Dendrimer chemistry is quiet useful in order to develop monodisperse multivalent glycoconjugates.¹⁶ and it has been excavated from literature that polyester dendrimers are compatible to biological system with an added advantage of easy preparation techniques. In addition, whenever ester linked dendrimers have been tested, they have been found to be non-

Department of Chemistry, Centre of Advanced Study, Institute of Science, Banaras Hindu University, Varanasi-221005, India. E-mail: Tiwari_chem@yahoo.co.in; Vinod.tiwari@bhu.ac.in

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toxic in comparison to other dendrimers.¹⁷ It has been well established, that double stage convergent method is a combination of convergent and divergent methods and in this strategy, the core unit is synthesized divergently followed by a subsequent attachment of a dendritic wedge in a convergent fashion, thereby generating the hypercore (*i.e.* dendrimer or dentromer core in present manuscript) containing dendrimer.^{8,18}

The CuAAC 1,3-dipolar cycloaddition reaction has propagated extensively ever since its finding by Sharpless^{19a} and Meldal.^{19b} The atom economy and versatility of these reactions make them a powerful tool for a diverse spectrum of organic synthesis.^{2,20} Particularly, click chemistry involving Cu(1)-catalyzed azide-alkyne cycloaddition (CuAAC), has been profusely explored during the last two decades due to an easy synthesis of diverse two or three dimensional motifs, having a plethora of applications ranging from chemical biology to material science.21 In addition, tailored 1,2,3-triazoles, bioisostere of amides, esters and other heterocycles, are frequently used as pharmacophores in several drugs, exhibiting diverse pharmacological properties. Thus, these moieties play an intriguing role as building blocks of dendrimers and impart to them sufficient biological activity, thereby making them medically important.22

The triply branched glycodendrimer construction is less facile than the doubly branched analogue due to steric reasons.²³ So, in present manuscript, we have successfully synthesized a dendrimer core (hexa-alkynylated) as well as a dentromer core (nona-alkynylated) to develop a series of glycodendrimers along with the first ever 0th '9-peripheral' and 1st generation '27-peripheral' galactose coated glycodentromers.

2 Results and discussion

The first generation azide functionalized dendrons were synthesized from methyl 3,5-dihydroxybenzoic acid (1) and methyl 3,4,5-tris-hydroxybenzoic acid (2). The crafted first generation dendritic azide was coupled with the alkyne functionalized core unit 18 and 19 to generate a series of six (20–25)



Scheme 2 Synthesis of acid functionalized dentritic scaffolds.

peripheral galactosylated glycodendrimers and glycodentromers. In this regard, methyl 3,5-dihydroxybenzoate was derived from esterification of 3,5-dihydroxybenzoic acid using methanol and sulphuric acid as catalyst. Similarly with the same strategy, methyl 3,4,5-tris-hydroxybenzoate was also prepared. Moreover, esterified dendron initiators 3, 4 were propargylated by reacting propargyl bromide, K₂CO₃, 18-crown-6 ether (co-catalyst) in dry acetone. Furthermore, the propargylated scaffolds 5 and 6 were reduced with LAH in THF followed by bromination using PBr₃ in DCM, which furnished 3,5bis(propargyloxy)benzyl bromide 9 and 3,4,5-tris(propargyloxy) benzyl bromide 10. Owing to their π - π stacking interaction, aromatic 'aglycones' have been of substantial interest for dendron synthesis.²⁴ To this end, clickable 2,3,4,6-tetra-O-acetyl-β-Dgalactopyranosyl azide 11 was selected as surface group functionality and this was stitched with aromatic scaffolds 9 and 10 to afford the bromine functionalized first generation 12 and 13 dendrons. The single triazolyl peak at 7.91 ppm in ¹H NMR, for compound 12, whereas, for 13, two distinct signals at δ 8.14 and 8.05 ppm were observed with ratio 2:1, which displayed the two chemically non-equivalent triazolyl galactosides. In ¹³C NMR, the peaks appeared at δ 144.4 and 121.2 ppm for compound 12, and δ 144.9, 144.2 & 123.0, 122.0 ppm for compound 13, confirmed the presence of triazolyl carbons. In continuation, the azidation of the compounds 12 and 13 were executed using NaN3 in DMF, which resulted in azide



Scheme 1 Synthesis of azide functionalized AB_2 and AB_3 type dendritic structure.



Scheme 3 Synthesis of ester-linked dendrimers core and dentromer core by acid-phenol coupling using DCC/DMAP.

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functionalized dendritic architecture **14** and **15** respectively (Scheme 1). This transformation was illustrated by IR spectra, in which, peak at 2104.5 and 2103.8 cm⁻¹ confirms the formation of corresponding dendritic azides **14** and **15**. In addition, there was a down field shifting in ¹³C NMR, during conversion from $-CH_2Br$ (δ 33.2 ppm) to $-CH_2N_3$ (δ 54.6 ppm) for moiety **14** and $-CH_2Br$ (δ 33.7 ppm) to $-CH_2N_3$ (δ 54.6 ppm) for scaffold **15**, which supported the formation of respective azide.

We next, synthesized the other click counterpart of dendritic azides, as depicted in (Scheme 2 and 3). Thus, ester functionalized compound **5** and **6** were separately treated with aqueous NaOH to generate 3,5-bis(propargyloxy)benzoic acid **16** and 3,4,5-tris(propargyloxy)benzoic acid **17**, respectively (Scheme 2). The resulted compounds were further divergently condensed with phloroglucinol using DCC, DMAP to afford the hexavalent dendrimer core **18** and nonavalent alkyne dentromer core **19** (Scheme 3).

At this instant, the synthesized hypercore units were used as starting material for CuAAC coupling with dendritic wedges 14 and 15 to afford a series of glyco-dendrimers and dentromers. In this context, dendrimer core unit 18 was stitched with galactose azide 11, dendritic wedge 14 and 15 using CuSO₄- \cdot 5H₂O and sodium-L-ascorbate to prepare a series of 6, 12 and 18 peripheral galactose tethered dendrimers 20, 21 and 22, respectively (Scheme 4). In the same way, dentromer core unit 19 was clicked with galactose-azide 11, dendritic architecture 14 and 15, under similar Cu(1)-catalyzed cycloaddition condition and furnished 9 galactose coated glycodentromer 23, 18 peripheral glycodendrimer 24, and 27 galactose coated glycodentromer 25, respectively with satisfactory to good yield 60-75% (Scheme 5). Interestingly, there was no steric congestion imposed during glycodentromer synthesis. It is to noteworthy to mention that, for the synthesis of higher peripheral galactose tethered dendrimers, elevated equivalents of CuSO₄·5H₂O was



Scheme 4 Synthesis of galactosylated dendrimer (20, 21 and 22) derived from hexavalent alkyne core 18.



Scheme 5 CuAAC mediated synthesis of galactose coated dendrimers (23, 24 and 25) derived from dentromer core 19.

required for amplified yields, because the size of glycodendrimer had been increased with an increase in void number. These voids enable entrapment of the free metal ions thereby delaying the time for completion of reaction and this could be ameliorated by increasing the catalyst amount.²⁵ The symmetrical structure of developed glycodendrimers **20**, **21**, **22**, **24** and glycodentromers **23**, **25** was confirmed by their extensive spectral studies (NMR, IR, MALDI-TOF MS, HRMS and size exclusion chromatography) which led to an unequivocal structural illustration. Moreover, the synthesis of glycodendrimer **20**, **21**, **22**, **24** was evidenced by the formation for newly formed triazolyl proton peaks at the desired position (see, ESI‡).

In addition, the formation of 9 and 27 peripheral galactose tethered glycodentromer was established by ¹H and ¹³C NMR, in this regard, two triazolyl proton peaks at 8.22 and 8.11 ppm were obtained, for two different environment of the triazole with ratio 6 : 3 in the dentromer (23). In contrast to this, ¹H

NMR of glycodentromer 25 displayed the six peaks *i.e.* a–f in triazolyl region, each peak for a different environment of the triazole. If, we closely examine only outer triazolyl part of dendritic wedge (Fig. 1), it was noticed that four different triazolyl proton peaks *i.e.* a–d appeared at δ 8.09, 8.04, 8.13 and 8.11 ppm respectively with ratio a : b : c : d (4 : 2 : 2 : 1) on the periphery of glycodentromer. Next, we observed two inner triazolyl proton peak at 8.17 and 8.18 ppm for *e* and *f* with ratio 6 : 3, which established the unequivocal formation of our targeted glycodentromer 25. Further, the formation of glycodentromers was supported by MALDI-TOF MS.

There is no vibrating band of alkyne and azide in IR spectra of synthesized dendrimers which validates the absence of free alkyne or azide functionality in the developed glycodendrimers and dentromers, thereby supporting the formation of targeted glycoclusters (see, ESI, Fig. S47–S52[‡]).



Fig. 1 ¹H NMR' spectral elucidation of triazolyl region of first generation glycodentromer.

Moreover, size exclusion chromatogram (SEC) depicts the size progression from 6 peripheral glycodendrimer to 27 peripheral glycodentromer, with polydispersity index (PDI) ranging from 1.0–1.03 showing the monodispersity of the synthesized glycoclusters (Fig. 2).

Absorption and emission studies of developed glycodendrimer and dentromers were also investigated, glycodendrimer **20**, **21**, **22** have shown UV-visible absorbance at 309.90, 310.14, 311.38 nm, respectively, whereas for compound **23**, **24**, **25**, peaks were appeared at 274.25, 275.78, 274.61 nm. Thus, compound **20**, **21**, **22** were excited at the wavelength of ~309 nm



Fig. 2 SEC chromatogram of the developed glycodendrimers (20, 21, 22, 24) and glycodentromers (23, 25).

where as scaffold 23, 24, 25, at \sim 274 nm, and their emission spectra were also recorded (Fig. 3).

By observing the absorbance and emission pattern of developed glycodendrimer and dentromer, it can be inferred that, two different series of glycoclusters were formed, one with compounds 20, 21 and 22 derived from dendrimers core unit (18) whereas, the second series comprising of compounds 23, 24 and 25 were derived from dentromer core (19). Thus, we reach to a successful end where two different type of cores are involved to construct these glyco-motifs, which was also supported by UV-Vis spectroscopy.

3 Conclusions

In summary, we have fulfilled our objective to synthesize a novel class of dendrimer which was coined as dentromer by Astruc and co-workers. This has highly branched tethers and possesses an unique triple branched architecture which is guite prominent from the scaffolds that we have developed. On this aspect of hyper-branching, dentromers hold superiority over dendrimers and we have portrayed both the development of novel dentromer as well as dendrimer core scaffolds, together with the novel galactose tethered glycodentromer and dendrimers respectively by amalgamation with surface carbohydrate ligands. These hybrid architectures may serve as potential therapeutics owing to the highly biologically active carbohydrate clusters present over the periphery. It has already been disseminated that, glycodendrimers have been employed as anti-adhesives for viral and bacterial adhesion along with antibiofilms activity but the biological activity of dentromers awaits exploring.



Fig. 3 Absorbance and emission spectra of the developed glycodendrimers (20, 21, 22, 24) and glycodentromers (23, 25).

4 Experimental

4.1 General methods

All chemicals and solvent were of pure analytical grade. Thin layer chromatography (TLC) was executed on 60 F-254 silica gel, coated on aluminium plates and visualized by UV lamp, 5% H_2SO_4 methanol solution with subsequent charring by heating. In addition, alkaline KMnO₄ solution was used to locate the alkynes with subsequent heating. Flash column chromatography was performed using silica gel (230–400) mesh size. ¹H and ¹³C spectra were recorded in 500 and 125 MHz respectively. Mass spectra were recorded on Sciex-X500R QTOF, MALDI-TOF MS (with 2,5-dihydroxy benzoic acid matrix). IR was recorded in Nujol mulls in KBr pellets. The polydispersity index (M_n/M_w) of the samples was investigated in DMF at 40 °C with a flow rate of 0.5 mL min⁻¹. The calibration of columns was done against polystyrene standard samples. The absorbance and emission spectra were also recorded by using UV-visible spectroscopy.

4.1.1 Experimental procedure (1) for Cu(I) azide-alkyne cycloaddition reaction. The synthesized polypropargylated alkynes and azido functionalized scaffolds were taken in round bottom flask, already having THF/water (1:1), using CuSO₄-·5H₂O (0.3 equiv. per propargyl group) and sodium ascorbate (0.3 equiv. per propargyl), stirred for 12 h at 55 °C, while for glyco-dentromer and dendrimer synthesis (0.8 equiv. of $CuSO_4 \cdot 5H_2O$, NaASc for per propargyl) were used. After completion of reaction (monitored by TLC), it was passed through cellite followed by extraction with ethyl acetate. The organic layer was washed with saturated aq. $NH_4Cl (2 \times 10 mL)$, water (10 mL) and finally, aq. Brine solution (10 mL). The ethyl acetate layer was collected and dried over anhydrous sodium sulphate followed by evaporation to obtain the crude mass. Moreover, the crude mass was subjected to flash column chromatography (SiO₂) to afford the targeted glyco-conjugate with good yield.

4.1.2 Synthesis of methyl 3,5-bis(hydroxyl) benzoate (3). The compound 1 (5.0 g, 32.4 mmol) was dissolved in dry methanol (80 mL), then after catalytic amount of conc. H₂SO₄ (1.0 mL) was added drop wise in cold condition. Further, the reaction was refluxed for 4 hour with constant stirring, after completion of reaction (monitored by TLC), and evaporated to obtain the crude mass. Further, solid was extracted with ethyl acetate (2 × 200 mL) and washed with saturated NaHCO₃ solution (2 × 50 mL), after then, organic layer was dried over anhydrous Na₂SO₄ followed by evaporation to afford targeted benzoate 3. Yield (5.06 g, 95%); $R_{\rm f} = 0.4$ (40% ethyl acetate/hexane); ¹H NMR (500 MHz, DMSO-D₆): δ 6.80 (d, J = 2 Hz, 2H), 6.43 (d, J = 1.5 Hz, 1H), 3.79–3.70 (m, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 167.0, 158.9, 131.9, 107.8, 107.7, and 52.5 ppm.²⁵

4.1.3 Synthesis of methyl 3,4, 5-tris(hydroxyl) benzoate (4). Compound 2 (5.0 g, 29.39 mmol) was reacted with methanol (80 mL), and catalytic amount of conc. H_2SO_4 (1 mL) according to the procedure involved in the formation of compound 3. Yield (5.08 g, 94%); $R_f = 0.4$ (40% EtOAc/*n*-hexane); ¹H NMR (500 MHz, DMSO-D₆): δ 9.27 (s, 2H), 8.93 (s, 1H), 6.93 (s, 2H), 3.73 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 166.2, 145.4, 138.3, 119.2, 108.4, and 51.4 ppm.²⁷

4.1.4 Synthetic procedure for methyl 3,5-bis(propargyloxy) benzoate (5). The compound 3 (4.0 g, 23.7 mmol) was dissolved in dry acetone followed by addition of K_2CO_3 (26.3 g, 190 mmol, 8 equiv.) as a base, 18-crown-6-ether (200 µL) as co-catalyst and at the end propargyl bromide (14.32 mL, 190 mmol, 8 equiv.). The said set up was refluxed for overnight, and after that the solvent was evaporated to obtain the crude mass. Moreover, the crude mass was subjected to chromatography to afford the desired compound 5 as white powder. Yield (4.23 g, 73%); $R_f = 0.5$ (15% EtOAc/*n*-hexane); ¹H NMR (500 MHz, CDCl₃): δ 7.29 (d, J = 2.0 Hz, 2H), 6.81 (s, 1H), 4.71 (d, J = 2.0 Hz, 4H), 3.90 (s, 3H), 2.54 (s, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 166.4, 158.4, 132.1, 108.8, 107.5, 77.9, 75.9, 56.1, and 52.3 ppm.²⁶

4.1.5 Synthesis of methyl 3,4,5-tris (propargyloxy)benzoate (6). The compound 4 (4.0 g, 21.7 mmol, 1.0 equiv.) was reacted with propargyl bromide (13.1 mL, 173.7 mmol, 8.0 equiv.), potassium carbonate (24.03 g, 173.7 mmol, 8.0 equiv.) and 18-

crown-6-ether (200 µL) in the presence of dry acetone (50.0 mL) according to the procedure of compound 5. Yield (4.40 g, 68%); $R_{\rm f} = 0.4$ (15% ethyl acetate/hexane); ¹H NMR (500 MHz, CDCl₃): δ 7.46 (s, 2H), 4.81–4.79 (m, 6H), 3.90 (s, 3H), 2.53 (t, J = 2.4 Hz, 2H), 2.45 (t, J = 2.4 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 166.2, 151.2, 141.0, 125.7, 109.8, 78.6, 77.9, 76.1, 75.5, 60.2, 57.0, and 52.3 ppm.²⁷

4.1.6 3,5-Bis (propargyloxy)phenyl methanol (7). To a stirred solution of methyl 3,5-bis(propargyloxy)benzoate (3.0 g, 12.28 mmol) in anhydrous THF (30.0 mL), LiAlH₄ (0.56 g, 14.7 mmol, 1.2 equiv.) was added portion wise in cold condition then after it was stirred for 4 h at room temperature till completion of reaction. The reaction was quenched by 5% aq. NaOH solution with continuous stirring which resulted in the fine precipitate. Further, the precipitate was filtered using sintered funnel; the obtained filtrate was extracted with ethylacetate and washed with water (2 × 20.0 mL) followed by brine solution. The extracted part was evaporated to get the crude mass which was subjected to column chromatography to obtain the targeted compound 7 with excellent yield. Yield (2.36 g, 89%); $R_{\rm f} = 0.4$ (25% EtOAc/*n*-hexane). NMR data was in close agreement with the available literature data.²⁶

4.1.7 Synthesis of 3,4,5-tris (propargyloxy)phenyl methanol (8). Methyl 3,4,5-tris (propargyloxy)benzoate (3.0 g, 10.1 mmol, 1.0 equiv.) was reacted with LiAlH₄ (0.46 g, 12.1 mmol, 1.2 equiv.) in the presence of dry THF (30.0 mL) according to the procedure of compound 7. Yield (2.28 g, 84%); $R_{\rm f} = 0.5$ (25% EtOAc/*n*-hexane); ¹H NMR (500 MHz, CDCl₃): δ 6.77 (s, 2H), 4.758-4.753 (m, 4H), 4.72 (d, J = 2.0 Hz, 2H), 4.64 (s, 2H), 2.51-2.50 (m, 2H), 2.45 (t, J = 2.4 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 151.6, 137.2, 136.3, 106.9, 79.1, 78.4, 75.8, 75.1, 65.1, 60.2 and 56.9 ppm.²⁷

4.1.8 3,5-Bis (propargyloxy)phenyl bromide (9). To a stirred solution of compound 7 (2.2 g, 10.1 mmol) in anhydrous dichloromethane PBr₃ (1.06 mL, 11.1 mmol, 1.1 equiv.) was added drop-wise in cold condition, after this, it was stirred for overnight. The reaction progress was (monitored by TLC) after completion of reaction, it was quenched with saturated sodium bicarbonate solution and extracted with ethyl acetate (2 × 100 mL) to produce the crude mass. The obtained residue was subjected to column chromatography (SiO₂) to afford compound **9.** Yield (2.49 g, 88%); $R_{\rm f} = 0.6$ (10% EtOAc/*n*-hexane); ¹H NMR (500 MHz, CDCl₃): δ 6.64 (d, J = 2.0 Hz, 2H), 6.55–6.54 (m, 1H), 4.67 (d, J = 2.0 Hz, 4H), 4.41 (s, 2H), 2.55 (t, J = 2.4 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃): 158.6, 139.8, 108.5, 102.2, 78.1, 75.8, 55.8, and 33.2 ppm.

4.1.9 Synthesis of 3,4,5-tris (propargyloxy)phenyl bromide (10). Compound 8 (2.0 g, 6.0 mmol) was reacted with PBr₃ (0.63 mL, 6.60 mmol, 1.1 equiv.) in the presence of dichloromethane according to the procedure of compound 9. Yield (1.84 g, 75%); $R_{\rm f} = 0.5$ (15% EtOAc/*n*-hexane); ¹H NMR (500 MHz, CDCl₃): δ 6.79 (s, 2H), 4.76 (d, J = 2.5 Hz, 4H), 4.72 (d, J = 3.0 Hz, 2H), 4.45 (s, 2H), 2.53 (t, J = 2.4 Hz, 2H), 2.47 (t, J = 2.9 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 151.5, 137.1, 133.6, 109.4, 78.9, 78.1, 76.0, 75.3, 60.3, 57.0, and 33.6 ppm. Mass data HRMS: m/z $C_{16}H_{14}BrO_{3}^+$; calculated = 333.0121; found = 333.0115 (M + H)⁺.

4.1.10 Synthesis of compound (11). This compound was synthesized by the previous available standard reaction protocol and well elucidated by our previous synthetic work.²⁰

4.1.11 Glycoconjugate dendron (12). 3,5-Bis (propargyloxy) phenyl bromide 9 (2.0 g, 7.16 mmol, 1.0 equiv.) was clicked with galactose azide 11 (6.4 g, 17.1 mmol, 2.4 equiv.) using CuSO₄· 5 H₂O (1.1 g, 4.29 mmol, 0.6 equiv.) and NaASc (0.86 g, 0.29 mmol, 0.6 equiv.) in the presence of THF/H₂O (1 : 1) according to the procedure 1. Yield (6.02 g, 82%); $R_{\rm f} = 0.4$ (60% EtOAc/*n*-hexane); ¹H NMR (500 MHz, CDCl₃): δ 7.91 (s, 2H), 6.63 (s, 2H), 6.55 (1H), 5.84 (d, J = 9.0 Hz, 2H), 5.54–5.51 (m, 4H), 5.23 (dd, J = 7.0, 3.0 Hz, 2H), 5.18–5.15 (m, 4H), 4.39 (s, 2H), 4.22 (t, J = 6.0 Hz, 2H), 4.17–4.06 (m, 5H), 2.18 (s, 6H), 2.00 (s, 6H), 1.97 (s, 6H), 1.84 (s, 6H); ¹³C NMR (125 MHz, CDCl₃): δ 170.2, 169.8, 169.7, 168.9, 153.3, 144.4, 139.9, 121.2, 108.4, 101.9, 86.1, 73.9, 70.6, 67.8, 66.7, 61.9, 61.1, 60.2, 33.2, 20.57, 20.56, 20.4, and 20.1 ppm.

4.1.12 Synthesis of glycoconjugate dendron (13). 3,4,5-Tris (propargyloxy)phenyl bromide **10** (1 g, 3.0 mmol, 1.0 equiv.) was clicked with galactose azide **11** (4.03 g, 10.8 mmol, 3.6 equiv.) using CuSO₄·5H₂O (0.67 g, 2.70 mmol, 0.9 equiv.) and NaASc (0.54 g, 2.70 mmol, 0.9 equiv.) in the presence of THF/H₂O (1 : 1) according to the procedure **1**. Yield (0.3.44 g, 79%); $R_f = 0.4$ (80% EtOAc/*n*-hexane); ¹H NMR (500 MHz, CDCl₃): δ 8.14 (s, 1H), 8.06 (s, 2H), 6.74 (s, 2H), 5.94–5.88 (m, 3H), 5.69 (t, J = 10.0 Hz, 1H), 5.59–5.42 (m, 5H), 5.31–5.20 (m, 8H), 4.43 (d, J = 4.5 Hz, 2H), 4.30–4.10 (m, 10H), 2.21 (s, 9H), 2.02–1.99 (m, 18H), 1.83 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 170.3, 170.2, 170.1, 170.0, 169.9, 169.8, 168.9, 168.7, 151.9, 144.9, 144.2, 137.7, 133.6, 123.0, 122.0, 108.8, 86.2, 85.7, 73.9, 73.5, 71.0, 70.7, 67.9, 66.7, 66.88, 66.80, 66.4, 62.8, 61.1, 60.9, 60.3, 33.7, 20.6, 20.5, 20.4, and 20.1 ppm.

4.1.13 Glycoconjugate dendron (14). To a stirred solution of glycoconjugate dendron 12 (1.5 g, 1.46 mmol) in DMF (5.0 mL), sodium azide (0.38 g, 5.84 mmol, 4.0 equiv.) was added. Further, the reaction was stirred for 12 h at 80 °C, the reaction mixture was diluted with ethyl acetate and washed with chilled saturated brine solution (3 \times 10 mL). The organic layer was collected and dried over anhydrous sodium sulphate followed by evaporation to produce the crude mass, further which was subjected to column chromatography to afford dendritic azide 13 as white solid. Yield (1.35 g, 94%); $R_{\rm f} = 0.4$ (60% EtOAc/ hexane); ¹H NMR (500 MHz, CDCl₃): δ 7.93 (s, 2H), 6.62 (s, 1H), 6.59 (s, 2H), 5.85 (d, J = 9.5 Hz, 2H), 5.55–5.54 (m, 4H), 5.25 (dd, J = 7.5, 3.0 Hz, 2H), 5.20 (s, 4H), 4.28 (s, 2H), 4.23–4.14 (m, 6H), 2.21 (s, 6H), 2.04 (s, 6H), 2.00 (s, 6H), 1.87 (s, 6H); ¹³C NMR (125 MHz, CDCl₃): δ 170.3, 169.9, 169.7, 169.0, 159.6, 144.5, 137.8, 121.2, 107.5, 101.6, 86.2, 74.0, 70.7, 67.8, 66.7, 62.0, 61.1, 54.6, 20.6, 20.4, and 20.1 ppm. IR (KBr): v_{max} 3471.75, 2936.37, 2104.55, 1755.31, 1671.90, 1598.72 and 1372.00 cm⁻¹. HRMS: $m/z C_{41}H_{50}N_9O_{20}^+$; calculated = 988.3167; found = 988.3083 (M $+ H)^{+}$.

4.1.14 Synthesis of glycoconjugate dendron (15). Glycoconjugate 13 (1.5 g, 1.03 mmol) was reacted with sodium azide (0.27 g, 4.12 mmol, 4.0 equiv.) in anhydrous DMF (10.0 mL) according to the procedure of compound 14 as white solid. Yield (1.36 g, 93%); $R_{\rm f} = 0.4$ (80% EtOAc/*n*-hexane); ¹H NMR (500 MHz, CDCl₃): δ 8.12 (s, 1H), 8.04 (s, 2H), 6.65 (s, 2H), 5.59–5.87 (m, 3H), 5.69–5.65 (m, 1H), 5.61–5.59–5.52 (m, 5H), 5.29–5.18 (m, 8H), 4.30–4.08 (m, 12H), 2.20 (s, 9H), 2.028–2.024 (m, 18H), 1.83 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 170.3, 170.2, 170.1, 170.0, 169.9, 169.8, 168.9, 168.7, 152.2, 144.9, 144.3, 137.4, 131.5, 122.9, 121.9, 107.9, 86.2, 85.8, 77.2, 77.0, 76.7, 73.9, 73.5, 71.0, 70.7, 67.9, 66.7, 66.8, 66.7, 66.3, 62.9, 61.9, 60.9, 54.6, 20.5, 20.48, 20.45, and 20.1 ppm. IR (KBr): $\nu_{\rm max}$ 3453.88, 2932.34, 2103.88, 1755.03, 1669.15, 1371.83 and 1223.35 cm⁻¹. HRMS: $m/z C_{58}H_{71}N_{15}O_{30}^{-+}$; calculated = 1415.4393; found = 1415.4313 (M + H)⁺.

4.1.15 Synthesis of 3,5-bis (propargyloxy)benzoic acid (16). To a stirred solution of 3,5-bis (propargyloxy)methyl benzoate (1.0 g, 4.1 mmol) in methanol (10 mL), NaOH (1.63 g, 40.9 mmol, 10 equiv.) in water (2.0 mL) was added drop-wise at room temperature. The reaction mixture was stirred for 12 h at 80 °C, then, the hydrochloric acid (4 M, 4 mL) was poured in reaction mixture with continuous stirring below 5 °C. Further, the reaction mixture was extracted with dichloromethane (3 × 20 mL), followed by evaporation to obtain the crude mass, which was purified by column chromatography (SiO₂) to afford white floppy solid with yield (0.895 g, 95%); $R_f = 0.5$ (40% EtOAc/*n*-hexane); ¹H NMR (500 MHz, DMSO-D₆) δ 13.14 (s, 1H), 7.16 (d, J = 2.5 Hz, 2H), 6.84–6.83 (1H), 4.84 (d, J = 2.0 Hz, 4H), 3.59–3.58 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 166.7, 158.1, 132.9, 108.3, 106.9, 78.8, 78.5, and 55.7 ppm.²⁸

4.1.16 Synthesis of 3,4,5-tris (propargyloxy)benzoic acid (17). 3,4,5-Tris (propargyloxy)methyl benzoate (1.0 g, 3.35 mmol) was reacted with aqueous sodium hydroxide (1.34 g, 33.5 mmol, 10.0 equiv.) in methanol according to the procedure of compound **16**, as white solid. Yield (0.886 g, 93%); $R_{\rm f} = 0.4$ (40% EtOAc/*n*-hexane); ¹H NMR (500 MHz, CDCl₃): δ 7.55 (s, 2H), 4.85 (d, J = 1.5 Hz, 2H), 4.83 (d, J = 2.0 Hz, 4H), 2.55 (s, 2H), 2.47–2.46 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 166.0, 146.6, 137.1, 119.9, 105.8, 73.9, 73.1, 71.6, 70.9, 55.6, and 52.4 ppm.²⁹

4.1.17 Synthesis of dendrimers core unit 1 (18). Phloroglucinol (0.1 g, 0.793 mmol, 1.0 equiv.), 3,5-bis (propargyloxy) benzoic acid (0.730 g, 3.17 mmol, 4.0 equiv.), N,N'-dicyclohexylcarbodiimide 'DCC' (0.817 g, 3.96 mmol, 5.0 equiv.), 4-dimethylaminopyridine 'DMAP' (0.213 g, 1.74 mmol, 2.2 equiv.) in anhydrous dichloromethane were stirred at room temperature for 95 h. After completion of reaction (monitored by TLC), the reaction mixture was concentrated and subjected to column chromatography using DCM as the eluent to afford the desired dendrimers core unit with good yield. Yield (0.429 g, 71%); $R_{\rm f} =$ 0.6 (DCM); ¹H NMR (500 MHz, CDCl₃): δ 7.44 (d, *J* = 2.4 Hz, 6H), 7.15 (s, 3H), 6.90 (t, J = 2.4 Hz, 3H), 4.75 (d, J = 2.4 Hz, 12H), 2.569-2.560 (m, 6H); ¹³C NMR (125 MHz, CDCl₃): δ 163.8, 158.6, 151.4, 130.8, 113.3, 109.4, 108.4, 77.7, 76.1, and 56.2 ppm. IR (KBr): *v*_{max} 3280.88, 2924.37, 2853.95, 2119.54, 1738.95, 1608.82, 1447.51 and 1295.84 cm⁻¹. HRMS: $m/z C_{45}H_{31}O_{12}^+$; calculated = 763.1811; found = 763.1794 $(M + H)^+$.

4.1.18 Synthesis of dentromer core unit 2 (19). Pholroglucinol (0.1 g, 0.892 mmol, 1.0 equiv.) was reacted with 3,4,5-tris (propargyloxy)methyl benzoic (0.901 g, 3.17 mmol, 4.0 equiv.), DCC (0.817 g, 3.96 mmol, 5.0 equiv.), and DMAP (0.213 g,

1.74 mmol, 2.2 equiv.) in anhydrous CH_2Cl_2 according to the procedure of compound **18** as white solid yield (0.44 g, 60%); $R_f = 0.4$ (DCM); ¹H NMR (500 MHz, CDCl₃): δ 7.62 (s, 6H), 7.14 (s, 3H), 4.87 (d, J = 2.0 Hz, 6H), 4.84 (d, J = 2.0 Hz, 12H), 2.55 (s, 6H), 2.48 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): 163.7, 151.5, 142.0, 124.3, 113.4, 110.5, 78.5, 77.7, 76.4, 75.7, 60.4, and 57.1 ppm. IR (KBr): ν_{max} 3285.31, 2923.70, 2853.39, 2119.13, 1738.21, 1733.17, 1591.29, 1500.55, 1434.53 and 1317.32 cm⁻¹. HRMS: $m/z = C_{54}H_{36}O_{15}^{++}$; calculated = 947.1946; found = 947.1947 (M + H)⁺.

4.1.19 Synthetic procedure for 6 peripheral galactosylated glycodendrimer (20). The compound 11 (0.391 g, 1.04 mmol, 8.0 equiv.) was reacted with dendrimer core 18 (0.10 g, 0.131 mmol, 1.0 equiv.), CuSO₄·5H₂O (0.156 g, 0.628 mmol, 4.8 equiv.), and sodium-1-ascorbate (0.124 g, 6.29 mmol, 4.8 equiv.) according to procedure 1 to afford the glycodendrimer 20. Yield (0.291 g, 74%); $R_{\rm f} = 0.5$ (5% methanol/DCM); ¹H NMR (500 MHz, CDCl₃): δ 7.96 (s, 6H, triazolyl-*H*), 7.45 (d, J = 2.0 Hz, 6H, aromatic-C*H*), 7.16 (s, 3H, aromatic-CH), 6.93 (s, 3H), 5.86 (d, J = 9.5 Hz, 6H, H₄), 5.57-5.54 (m, 12H, H₂, H₃), 5.26-5.23 (m, 18H, H₁, H_{6a}, H_{6b}), 4.24–4.14 (m, 18H, H_5 , CH_2OAr), 2.21 (s, 18H, $6 \times COCH_3$), 2.03 (s, 18H, 6 \times COCH₃), 1.99 (s, 18H, 6 \times COCH₃), 1.87 (s, 18H, 6 × COCH₃); ¹³C NMR (125 MHz, CDCl₃): δ 170.3, 169.9, 169.7, 169.0, 163.8, 159.3, 151.4, 144.0, 130.9, 121.4, 113.3, 109.3, 107.7, 86.2, 74.0, 73.8, 77.7, 67.8, 66.8, 62.1, 61.1, 20.6, 20.5, 20.4, and 20.1 ppm. IR (KBr): vmax 2958.6, 2925.14, 2854.48, 1749.11, 1597.85, 1455.19, 1372.46, 1220.10 and 923.60 cm⁻¹. HRMS: m/z C₁₂₉H₁₄₆N₁₈O₆₆²⁺ calculated = 1501.9322; found = $1501.9310 (M + H)^{2+}$.

4.1.20 Synthetic procedure for 12 peripheral galactosylated glycodendrimer (21). The glycoconjugate dendron 14 (0.21 g, 0.21 mmol, 8.0 equiv.) was reacted with dendrimers core 18 (20 mg, 0.026 mmol, 1.0 equiv.), CuSO₄·5H₂O (31 mg, 0.126 mmol, 4.8 equiv.), and sodium-L-ascorbate (25 mg, 0.126 mmol, 4.8 equiv.) according to procedure 1 to afford the glycodendrimer 21. Yield (0.149 g, 85%); $R_{\rm f} = 0.4$ (5% methanol/ DCM); ¹H NMR (500 MHz, CDCl₃): δ 7.92 (s, 12H), 7.69 (s, 6H), 7.39 (s, 6H), 7.11 (s, 3H), 6.90 (s, 3H), 6.60 (s, 6H), 6.53 (s, 12H), 5.87 (d, J = 9.0 Hz, 12H), 5.55–5.51 (m, 24H), 5.46 (s, 12H), 5.26– 5.13 (m, 48H), 4.26-4.24 (m, 12H), 4.17-4.09 (m, 24H), 2.17 (s, 36H), 1.98-1.96 (m, 72H), 1.80 (s, 36H); ¹³C NMR (125 MHz, CDCl₃): δ 170.2, 169.9, 169.7, 169.0, 163.8, 159.7, 159.3, 151.3, 144.1, 143.6, 136.8, 130.8, 123.1, 121.5, 113.3, 109.2, 107.5, 101.9, 86.1, 73.9, 70.6, 67.8, 66.8, 62.2, 61.8, 61.1, 53.9, 20.56, 20.54, 20.4, and 20.1 ppm. IR (KBr): vmax 3473.00, 2925.79, 2853.53, 1754.48, 1598.94, 1460.89, 1372.11, 1223.38 and 1050.88 cm^{-1} . MALDI-TOF MS: mass; exact $C_{291}H_{324}N_{54}O_{132}Na^+;$ calculated = 6709.0193; found = $6704.0401 (M + Na)^+$.

4.1.21 Synthetic procedure for 18 peripheral galactosylated glycodendrimer (22). The glycoconjugate dendron 15 (0.148 g, 0.104 mmol, 8.0 equiv.) was reacted with dendrimer core 18 (10 mg, 0.013 mmol, 1.0 equiv.), $CuSO_4 \cdot 5H_2O$ (16 mg, 0.062 mmol, 4.8 equiv.), and sodium-L-ascorbate (14 mg, 0.062 mmol, 4.8 equiv.) according to procedure 1 to afford the glycodendrimer 22. Yield (79 mg, 65%); $R_f = 0.35$ (5% methanol/DCM); ¹H NMR (500 MHz, CDCl₃): δ 8.16 (s, 6H, middle

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triazolyl-H), 8.05 (s, 12H, outer triazolyl-H), 7.76 (s, 6H, inner triazole-*H*), 7.44 (d, *J* = 1.5 Hz, 6H, -ArH), 7.14 (s, 3H, phloroglucinol H), 6.97 (s, 3H, Core ArH), 6.69 (s, 12H, dendron Ar-H), 5.93-5.90 (18H, H4), 5.69-5.65 (m, 6H, H₂), 5.56-5.52 (m, 36H, H₂, H₃, H₁), 5.45 (s, 12H, -CH₂Ar), 5.29-5.14 (m, 60H, H₁, H_{6a}, H_{6b}), 4.30-4.27 (18H, H₅), 4.21-4.17 (12H, -OCH₂ para triazole), 4.14-4.11 (m, 24H, -OCH₂ meta triazole), 2.18-2.17 $(m, 54H, 18 \times COCH_3), 1.99-1.95 (m, 108H, 36 \times COCH_3), 1.75$ (s, 54H, 18 × COCH₃) ¹³C NMR (125 MHz, CDCl₃): δ 170.3, 170.2, 170.08, 170.06, 169.8, 169.7, 168.9, 168.7, 163.9, 159.4, 152.3, 151.3, 144.4, 143.9, 143.6, 139.1, 137.8, 130.9, 130.5, 123.3, 123.0, 122.2, 113.9, 109.2, 108.0, 86.0, 85.7, 73.8, 73.5, 70.9, 70.6, 67.9, 67.7, 66.8, 66.2, 62.6, 62.2, 61.1, 60.9, 54.0, 20.5, 20.4, 20.1, and 20.0 ppm. IR (KBr): v_{max} 3470.41, 2925.65, 2853.11, 1753.98, 1596.63, 1445.34, 1372.45, 1223.83 and 1050.76 cm⁻¹. MALDI-TOF MS: exact mass: $C_{393}H_{450}N_{72}O_{192}H^+$ calculated = 9249.7735; found = $9242.5430 (M + H)^+$.

4.1.22 Synthetic procedure for 9 peripheral galactosylated glycodendrimer (23). The compound 11 (0.444 g, 1.189 mmol, 11 equiv.) was reacted with dentromer core unit 19 (0.1 g. 0.108 mmol, 1.0 equiv.), CuSO₄·5H₂O (194 mg, 0.778 mmol, 7.2 equiv.), and sodium-L-ascorbate (154 mg, 0.778 mmol, 7.2 equiv.) according to procedure 1 to afford the glycodentromer 23. Yield (0.277 g, 60%); $R_{\rm f} = 0.5$ (5% methanol/DCM); ¹H NMR (500 MHz, CDCl₃): δ 8.23 (s, 3H, triazolyl H), 8.11 (s, 6H, triazolyl-H), 7.57 (s, 6H, Ar-CH), 7.14 (s, 3H, core-Ar-CH), 5.95-5.92 (m, 9H, H₄), 5.72 (t, J = 9.5 Hz, 3H, H₂), 5.61–5.55 (m, 18H, $H_2, H_3, (6H) H_1$, 5.39–5.27 (m, 24H, H_1, H_{6a}, H_{6b}), 4.37–4.16 (m, 27H, H₅, -OCH₂Ar), 2.21 (s, 27H, 9 × COCH₃), 2.03 (s, 27H, 9 × $COCH_3$), 1.99 (s, 27H, 9 × $COCH_3$), 1.83 (s, 27H, 9 × $COCH_3$); ¹³C NMR (125 MHz, CDCl₃): δ 170.4, 170.3, 170.1, 170.0, 169.9, 169.8, 168.9, 168.6, 163.6, 151.9, 144.6, 143.8, 142.4, 124.3, 123.4, 122.2, 114.0, 109.8, 86.1, 85.7, 73.9, 73.5, 71.0, 70.7, 67.9, 67.8, 66.8, 66.4, 62.8, 61.1, 60.9, 20.6, 20.5, 20.4, and 20.1 ppm. IR (KBr): v_{max} 3454.86, 2925.58, 2854.19, 1754.96, 1433.58, 1373.10, 1224.37 and 1050.62 cm⁻¹. MALDI-TOF MS: exact mass: $C_{180}H_{207}N_{27}O_{96}Na^+$ calculated = 4305.2038; found = $4303.9077 (M + Na)^+$.

4.1.23 Synthetic procedure for 18 peripheral galactosylated glycodendrimer (24). The glycoconjugate dendron 14 (0.293 g, 0.297 mmol, 11.0 equiv.) was reacted with 19 (25 mg, 0.027 mmol, 1.0 equiv.), CuSO₄·5H₂O (48 mg, 0.194 mmol, 7.2 equiv.), and sodium-L-ascorbate (38 mg, 0.194 mmol, 7.2 equiv.) according to procedure 1 to afford the glycodendrimer 24. Yield (0.165 g, 63%); $R_{\rm f} = 0.6$ (10% methanol/DCM); ¹H NMR (500 MHz, CDCl₃): δ 7.96 (s, 6H, peripheral inner triazolyl-*H*), 7.94 (s, 18H, outer triazolyl-H), 7.89 (s, 3H, inner middle triazolyl-H), 7.56 (s, 6H, aromatic-CH), 7.12 (s, 3H, phloroglucinol core-CH), 6.58–6.56 (m, 27H, periphery-CH, AB₂), 5.99 (d, J = 19.5 Hz, 18H, H₄), 5.57-5.41 (m, 54H, H₂, H₃, -CH₂Ar), 5.28-5.23 (m, 36H, H₁, H_{6a}), 5.11 (s, 36H, H_{6b}, -OCH₂ triazole inner-H), 4.27-4.11 (m, 54H, H₅, $-OCH_2$ triazole outer-*H*), 2.18 (s, 54H, 18 × COCH₃), 1.99–1.97 (m, 108H, 36 \times COCH₃), 1.795–1.790 (m, 54H, 18 \times COCH₃); ¹³C NMR (125 MHz, CDCl₃): δ 170.2, 170.0, 169.8, 169.0, 163.4, 159.7, 159.6, 144.1, 143.5, 139.2, 137.1, 123.79, 123.74, 121.8, 121.7, 113.9, 107.5, 101.9, 86.0, 73.9, 70.7, 67.8, 66.8, 61.8, 61.1, 53.9, 20.6, 20.5, 20.4, and 20.1 ppm. IR (KBr):

 $\nu_{\rm max}$ 3449.82, 2924.54, 2852.77, 1754.32, 1599.95, 1462.09, 1372.17, 1223.79 and 1053.35 cm^{-1}. MALDI-TOF MS: exact mass: $C_{423}H_{477}N_{81}O_{195}H^+$, calculated = 9815.0106; found = 9817.8810 (M + H)^+.

4.1.24 Synthetic procedure for 27 peripheral galactosylated glycodentromer (25). The glycoconjugate dendron 15 (0.252 g, 0.178 mmol, 11.0 equiv.) was reacted with dentromer core unit **19** (15 mg, 0.016 mmol, 1.0 equiv.), CuSO₄·5H₂O (29.1 mg, 0.117 mmol, 7.2 equiv.), and sodium-L-ascorbate (23 mg, 0.117 mmol, 7.2 equiv.) according to procedure 1 to afford the glycodentromer 25. Yield (0.128 g, 58%); $R_{\rm f} = 0.55$ (10%) methanol/DCM); ¹H NMR (500 MHz, CDCl₃): δ 8.19 (s, 3H, triazolyl H), 8.18 (s, 6H, triazolyl-H), 8.12 (s, 6H), 8.11 (s, 3H), 8.09 (s, 12H, triazolyl-H), 8.04 (s, 6H, triazolyl-H), 7.64 (s, 6H, core Ar-H), 7.17 (s, 3H, core Ar-H), 6.85 (s, 6H, AB₃ dendron Ar-H), 6.79 (s, 12H, AB₃ dendron Ar-H), 5.95-5.92 (m, 27H, H₄), 5.72-5.67 (m, 9H, H₂), 5.61–5.46 (m, 63H, H₂, H₃, -CH₂Ar), 5.30–5.12 (m, 99H, H₁, H_{6a}, H_{6b}, -OCH₂ para triazole-H), 4.34-4.30 (m, 27H, H₅), 4.22-4.10 (m, 54H, -OCH₂, triazole outer-H), 2.18-2.17 (m, 81H, 27 \times COCH₃), 1.99–1.95 (m, 162H, 56 \times COCH₃), 1.75– 1.71 (m, 81H, 27 \times COCH₃); ¹³C NMR (125 MHz, CDCl₃): δ 170.3, 170.2, 170.1, 169.9, 169.7, 168.9, 168.7, 163.8, 152.28, 152.24, 151.3, 144.8, 144.4, 144.06, 144.02, 143.5, 142.4, 139.2, 137.7, 137.5, 131.2, 130.7, 124.5, 124.0, 123.9, 123.4, 123.2, 122.5, 122.4, 113.9, 109.9, 108.1, 85.9, 85.6, 73.7, 73.4, 71.0, 70.7, 67.9, 67.7, 66.8, 66.2, 63.2, 63.1, 62.6, 61.1, 60.9, 54.0, 20.5, 20.4, 20.1, and 20.0 ppm. IR (KBr): v_{max} 3485.35, 3147.14, 2922.89, 2851.93, 1755.09, 1595.23, 1441.07, 1372.82, 1223.87, 1103.89 1051.39 cm^{-1} . MALDI-TOF MS: and exact mass: $C_{576}H_{666}N_{108}O_{285}H^+$ calculated = 13 660.1182; found = 13 627.0547 $(M + H)^+$.

Conflicts of interest

There are no conflicts to declare.

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References

(a) D. A. Tomalia, Prog. Polym. Sci., 2005, 30, 294–324; (b)
 S. M. Grayson and J. M. J. Fréchet, Chem. Rev., 2001, 101, 3819–3867; (c) G. R. Newkome and C. Shreiner, Chem. Rev., 2010, 110, 6338–6442; (d) J.-P. Majoral and A.-M. Caminade, Chem. Rev., 1999, 99, 845–880; (e)
 D. Wang, C. Deraedt, J. Ruiz and D. Astruc, Acc. Chem. Res.,

2015, **48**, 1871–1880; (*f*) M. Sowinska and Z. Urbanczyk-Lipkowska, *New J. Chem.*, 2014, **38**, 2168–2203.

- 2 V. K. Tiwari, B. B. Mishra, K. B. Mishra, N. Mishra, A. S. Singh and X. Chen, *Chem. Rev.*, 2016, **116**, 3086–3240.
- 3 (*a*) U. Boas and P. M. H. Heegaard, *Chem. Soc. Rev.*, 2004, 33, 43–63; (*b*) D. Kushwaha and V. K. Tiwari, *J. Org. Chem.*, 2013, 78, 8184–8190.
- 4 (a) D. C. R. Astruc, Acad. Sci., 1996, 322, 757-766; (b)
 A. Archut and F. Vögtle, Chem. Soc. Rev., 1998, 27, 233-240;
 (c) D. K. Smith and F. Diederich, Chem.-Eur. J., 1998, 4, 1351-1361.
- 5 (a) M. J. F. Jean and D. A. Tomalia, J. Polym. Sci., Part A: Polym. Chem., 2001, 1, 587–604; (b) C. Bottcher, B. Schade, C. Ecker, J. P. Rabe, L. J. Shu and A. D. Schlüter, Chem.– Eur. J., 2005, 11, 2923–2928.
- 6 C. Ornelas, J. Ruiz, C. Belin and D. Astruc, *J. Am. Chem. Soc.*, 2009, **131**, 590–601.
- 7 (a) C. Lee, J. A. Mac Kay, J. M. J. Fréchet and F. Szoka, *Nat. Biotechnol.*, 2005, 23, 1517–1526; (b) M. V. Walter and M. Malkoch, *Chem. Soc. Rev.*, 2012, 41, 4593–4609.
- 8 (a) D. Astruc, C. Deraedt, R. Djeda and C. Ornelas, *Molecules*, 2018, 23, 966; (b) C. Ornelas, *Macromol. Chem. Phys.*, 2016, 217, 149–174.
- 9 (a) K. L. Wooley, C. J. Hawker and J. M. J. Fréchet, Angew. Chem., Int. Ed. Engl., 1994, 33, 82–85; (b) R. S. Bagul, M. M. Hosseini, T. C. Shiao and R. Roy, Can. J. Chem., 2017, 95, 975–983.
- 10 Carbohydrates in Drug Discovery and Development, ed. V. K. Tiwari, Elsevier, 2020.
- 11 (a) H. J. Gabius, S. Andre, J. Jimenez-Barbero, A. Romero and D. Solis, *Trends Biochem. Sci.*, 2012, 36, 298–313; (b) H. Lis and N. Sharon, *Chem. Rev.*, 1998, 98, 637–674; (c) J. J. Lundquist and E. J. Toone, *Chem. Rev.*, 2002, 102, 555– 578.
- 12 (a) M. Mammen, S.-K. Choi and G. M. Whitesides, Angew. Chem., Int. Ed., 1998, 37, 2754–2794; (b) V. K. Tiwari, A. Kumar and R. R. Schmidt, Eur. J. Org. Chem., 2012, 12, 2945–2956; (c) N. Mishra, A. S. Singh, A. K. Agrahari, S. Singh, M. Singh and V. K. Tiwari, ACS Comb. Sci., 2019, 21, 389–399; (d) N. Mishra, A. K. Agrahari, P. Bose, S. K. Singh, A. S. Singh and V. K. Tiwari, Sci. Rep., 2020, 10, 3586.
- 13 N. K. Saadeh, R. Roy, R. S. Bagul, T. C. Shiao and M. Hosseini, *Polym. Chem.*, 2017, **8**, 5354–5366.
- 14 (*a*) R. Sharma, I. Zhang, L. Abbassi, R. Rej, D. Maysinger and R. Roy, *Polym. Chem.*, 2015, 33, 490–498; (*b*) J. Camponovo, C. Hadad, J. Ruiz, E. Cloutet, S. Gatard, J. Muzart, S. Bouquillon and D. Astruc, *J. Org. Chem.*, 2009, 74, 5071– 5074.
- 15 Y. M. Chabre and R. Roy, *Chem. Soc. Rev.*, 2013, **42**, 4657–4708.
- 16 J.-d' A. K. Twibanire and T. B. Grindley, *Polymers*, 2012, 4, 794–879.
- 17 Y. M. Chabre, P. P. Brisebois, L. Abbassi, S. C. Kerr, J. V. Fahy,
 I. Marcotte and R. Roy, *J. Org. Chem.*, 2011, 76, 724–727.

- 18 (a) K. L. Wooley, C. J. Hawker and J. M. J. Frechet, J. Am. Chem. Soc., 1991, 113, 4252–4261; (b) R. Sharma, K. Naresh, Y. M. Chabre, R. Rej and N. K. Saadeh, Polym. Chem., 2014, 4321–4331.
- 19 (a) V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, 41, 2596– 2599; (b) C. W. Tornoe, C. Christensen and M. Meldal, *J. Org. Chem.*, 2002, 67, 3057–3064.
- 20 A. K. Agrahari, A. S. Singh, A. K. Singh, N. Mishra, M. Singh,
 P. Prakas and V. K. Tiwari, *New J. Chem.*, 2019, 43, 12475–12482.
- 21 (a) K. B. Mishra and V. K. Tiwari, J. Org. Chem., 2014, 79, 5752-5762; (b) P. Dwivedi, K. B. Mishra, B. B. Mishra, N. Singh, R. K. Singh and V. K. Tiwari, Glycoconjugate J., 2015, 32, 127-140; (c) K. B. Mishra, R. C. Mishra and V. K. Tiwari, RSC Adv., 2015, 5, 51779-51789; (d) A. Mishra and V. K. Tiwari, ChemistrySelect, 2017, 2, 9466-9471; (e) D. Kushwaha, R. Singh and V. K. Tiwari, Tetrahedron Lett., 2014, 55, 4532-4536; (f) A. Kushwaha, A. K. Agrahari, K. Manar, C. Yadav, V. K. Tiwari, M. G. B. Drew and N. Singh, New J. Chem., 2019, 43, 8939-8949; (g) A. K. Singh, A. K. Agrahari, A. S. Singh, V. K. Tiwari and P. Prakash, Sci. Rep., 2020, DOI: 10.1038/s41598-020-70921-2.
- 22 (a) E. Bonandi, M. S. Christodoulou, G. Fumagalli,
 D. Perdicchia, G. Rastelli and D. Passarella, *Drug Discov. Today*, 2017, 22, 1572–1581; (b) B. zhang, *Eur. J. Med. Chem.*, 2019, 168, 357–372.
- 23 (a) M. Touaibia and R. Roy, *Mini-Rev. Med. Chem.*, 2007, 7, 1270–1283; (b) A. Imberty, Y. A. Chabre and R. Roy, *Chem.– Eur. J.*, 2008, 14, 7490–7499.
- 24 (a) F. Casoni, L. Dupin, G. Vergoten, A. Meyer, C. Ligeour, T. Gehin, O. Vidal, E. Souteyr, J. J. Vasseur, Y. Chevolot and F. Morvan, *Org. Biomol. Chem.*, 2014, 12, 9166–9179; (b) R. U. Kadam, M. Bergmann, M. Hurley, D. Garg, M. Cacciarini, M. A. Swiderska, C. Nativi, M. Sattler, A. R. Smyth, P. Williams, M. Camara, A. Stocker, T. Darbre and J. L. Reymond, *Angew. Chem., Int. Ed.*, 2011, 50, 10631–10635.
- 25 (a) M. Arseneault, C. Wafer and J.-F. Morin, *Molecules*, 2015,
 20, 9263–9294; (b) M. Arseneault, P. Dufour, I. Levesque and
 J.-F. Morin, *Polym. Chem.*, 2011, 2, 2293–2298; (c)
 A. Papadopoulos, T. C. Shiao and R. Roy, *Mol. Pharm.*,
 2012, 9, 394–403; (d) C.-B. Yim, I. Dijkgraaf, R. Merkx,
 C. Versluis, A. Eek, G. E. Mulder, D. T. S. Rijkers,
 O. C. Boerman and R. M. J. Liskamp, *J. Med. Chem.*, 2010,
 53, 3944–3953.
- 26 B. P. Dash, R. Satapathy, B. P. Bode, C. T. Reidl, J. W. Sawicki, A. J. Mason, J. A. Maguire and N. S. Hosmane, *Organometallics*, 2012, **31**, 2931–2935.
- 27 C. J. Ruiz, E. Cloutet and D. Astruc, *Chem.–Eur. J.*, 2009, **15**, 2990–3002.
- 28 C. Yang, J. P. Flynn and J. Niu, Angew. Chem., Int. Ed., 2018, 57, 16194–16199.
- 29 X. Liu, Q. Ling, L. Zhao, G. Qiu, Y. Wang, L. Song, Y. Zhang, J. Ruiz, D. Astruc and H. Gu, *Macromol. Rapid Commun.*, 2017, 1700448, 1–11.