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Tetrahedron
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Tetrahedron 61 (2005) 10048–10060

Synthesis of some oligopyridine–galactose conjugates and their metal complexes: a simple entry to multivalent sugar ligands

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Received 9 May 2005; revised 20 July 2005; accepted 4 August 2005

Available online 25 August 2005

Abstract—Some galactose–oligopyridine conjugates were readily assembled by combining differently functionalized oligopyridines with peracetylated galactose derivatives. Variation in the structure of the components and of the linkers employed for their connection afforded adducts of different size, shape, and conformational mobility. Complexation of the bipyridine ligands with CuOTf and of the terpyridine ligand with $Zn(OTf)_2$ afforded the corresponding peracetylated 2:1 and 1:1 complexes, respectively, as single species. Their structures were determined to be tetrahedral (Cu complexes) and trigonal-bipyramidal (Zn complex), on the basis of spectroscopic evidence. Removal of the acetyl protecting groups from the ligands afforded the corresponding polyols. The terpyridine–Zn(II) complex, unlike the bipyridine–Cu(I) complexes maintained their structures upon removal of the acetyl protecting groups.

1. Introduction

Protein–carbohydrate interactions control a variety of fundamental biological processes.[1] In many instances several carbohydrate units are involved in the binding event,[2] to take advantage of the so-called 'glycoside cluster effect'.[3,4] Artificial multivalent glycoside ligands have been synthesized with the aim of better understanding the protein–carbohydrate interaction processes and of developing inhibitors of these phenomena when they are involved in infectious cycles.

The vast majority of the multivalent sugar ligands reported so far have been assembled around dendritic or polymeric frameworks to exploit the high number of functional groups presented by these scaffolds.[3] Among the studied systems falling outside these classes of compounds, examples of metal saccharide–ligand conjugates have been particularly scarce.[5–7] This is surprising, because the metal-assisted association of carbohydrate components modified with a metal-binding ligand can open a straightforward access to carbohydrate clusters in which the number and the relative orientation of the carbohydrate residues can be modulated almost at will by changing the structure of the ligand and the nature of the metal.

As a part of a project devoted to explore the potential of metal saccharide–ligand conjugates in the field of multivalent sugar presentation, we wish to report some preliminary results on the synthesis of galactose-containing oligopyridine derivatives and their complexes with metal ions.

2. Results and discussion

Synthesis of the modified galactose residues. On the basis of its ubiquitous involvement in protein–carbohydrate interactions,[1–3] galactose was selected as the sugar component of the designed oligopyridine–carbohydrate conjugates. Derivatives **2**–**4**, featuring different spacers and handles for the connection to the oligopyridine ligands, were synthesized starting from *O*-(2,3,4,6-*O*-tetracetyl-D-galactopyranosyl) trichloroacetimidate **1**[8] and using trimethylsilyl triflate promoted glycosidation reactions (Scheme 1). In particular, amine **2** was obtained as a single β-isomer in 50% overall yield by reaction with benzyl *N*-(2-hydroxyethyl)carbamate followed by reductive cleavage of the nitrogen-protecting group; phenol **3** was prepared in 33% overall yield by β-selective glycosidation with

Keywords: Carbohydrates; *N*-ligand; Metal complexes.
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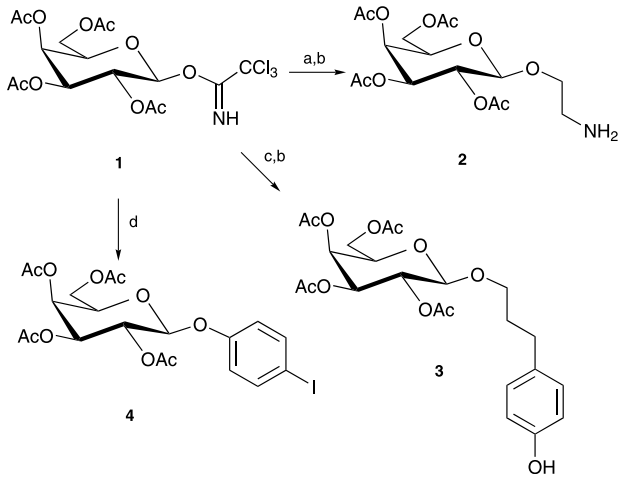
doi:10.1016/j.tet.2005.08.018



Scheme 1. Synthesis of galactose derivatives **2**–**4**. Reagents and conditions: (a) TMSOTf, $HOCH_2CH_2NHCOBn$, DCM, 0 °C, 2 h; (b) 10% Pd/C, 1 atm H_2, EtOH, rt, 2 h; (c) TMSOTf, 4-BnO–C_6H_4–$(CH_2)_3OH$, DCM, 0 °C, 2 h; (d) TMSOTf, 4-I-C_6H_4OH, DCM, 0 °C, 2 h.

3-(4-benzyloxyphenyl)-1-propanol,[9] followed by hydrogenolysis of the benzyl group; reaction of **1** with 4-iodophenol afforded (85% yield) a 78:22 mixture of anomers, from which the pure β-isomer **4** was readily obtained by chromatography in 66% yield.

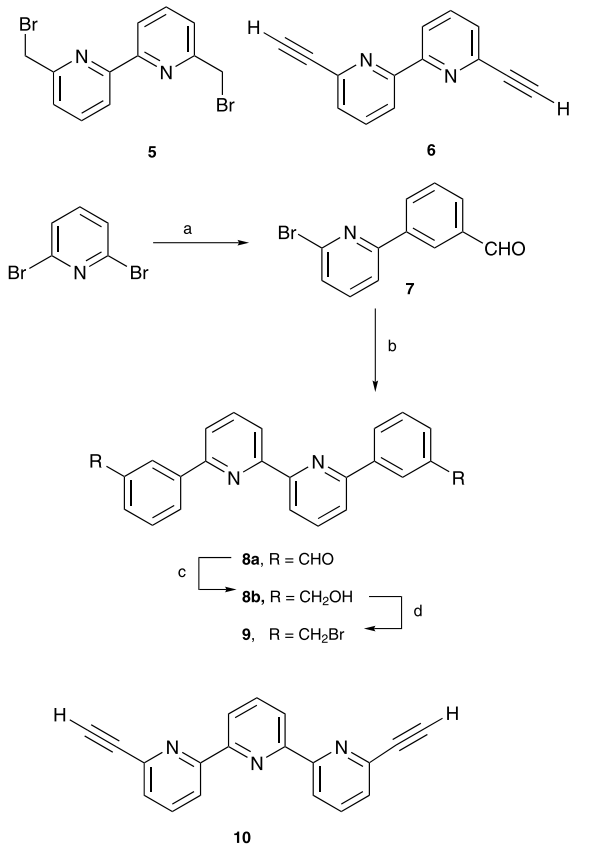
Synthesis of the oligopyridines. Oligopyridines **5**, **6**, **8**, **9**, and **10** carrying functional groups of different size and conformational mobility were selected for this study (Scheme 2). Compounds **5**,[10] **6**,[11] and **10**[12] were prepared according to literature procedures. Bis-aldehyde **8a** was obtained in two steps involving first Suzuki-type coupling of 2,6-dibromopyridine with 3-formylphenylboronic acid to afford compound **7** (56% yield),[13] and then nickel promoted homocoupling of the latter (47% yield).[14] From **8a**, dibromide **9** was readily prepared by reduction to the corresponding diol **8b** with $NaBH_4$ (96% yield) and bromination with PBr_3 (82% yield).

Synthesis of the oligopyridine–galactose conjugates and their metal complexes. By combining bipyridines **5**, **6**, **8a**, and **9** with functionalized galactose derivatives **2**-**4**, acetates **11**–**14** were obtained (Scheme 3).

Reaction of phenol **3** with dibromides **5** and **9**, carried out in the presence of cesium carbonate, afforded adducts **11** and **13** in 55 and 30% yields, respectively. The bis-acetylene derivative **12** was obtained in 33% yield by coupling bipyridine **6** with aryliodide **4** under standard Sonogashira conditions.

Imine **14** was synthesized in 90% yield by adding 6 equiv of amine **2** to a 5 mM solution of bis-aldehyde **8a** in 80:20 CH_2Cl_2/MeOH. Terpyridine **15** was obtained in 60% yield by combining galactose derivative **4** with 2″,6-diethynyl-2,2′:6′,6″-terpyridine **10** following the procedure employed for the preparation of conjugate **12**.

Formation of complexes **Cu(11)$_2$**–**Cu(14)$_2$** was performed in 92–98% yields by addition of 1 mol equiv of $CuOTf \cdot 0.5C_6H_6$ to 2 mol equiv of ligands **11**–**14** in 50:50

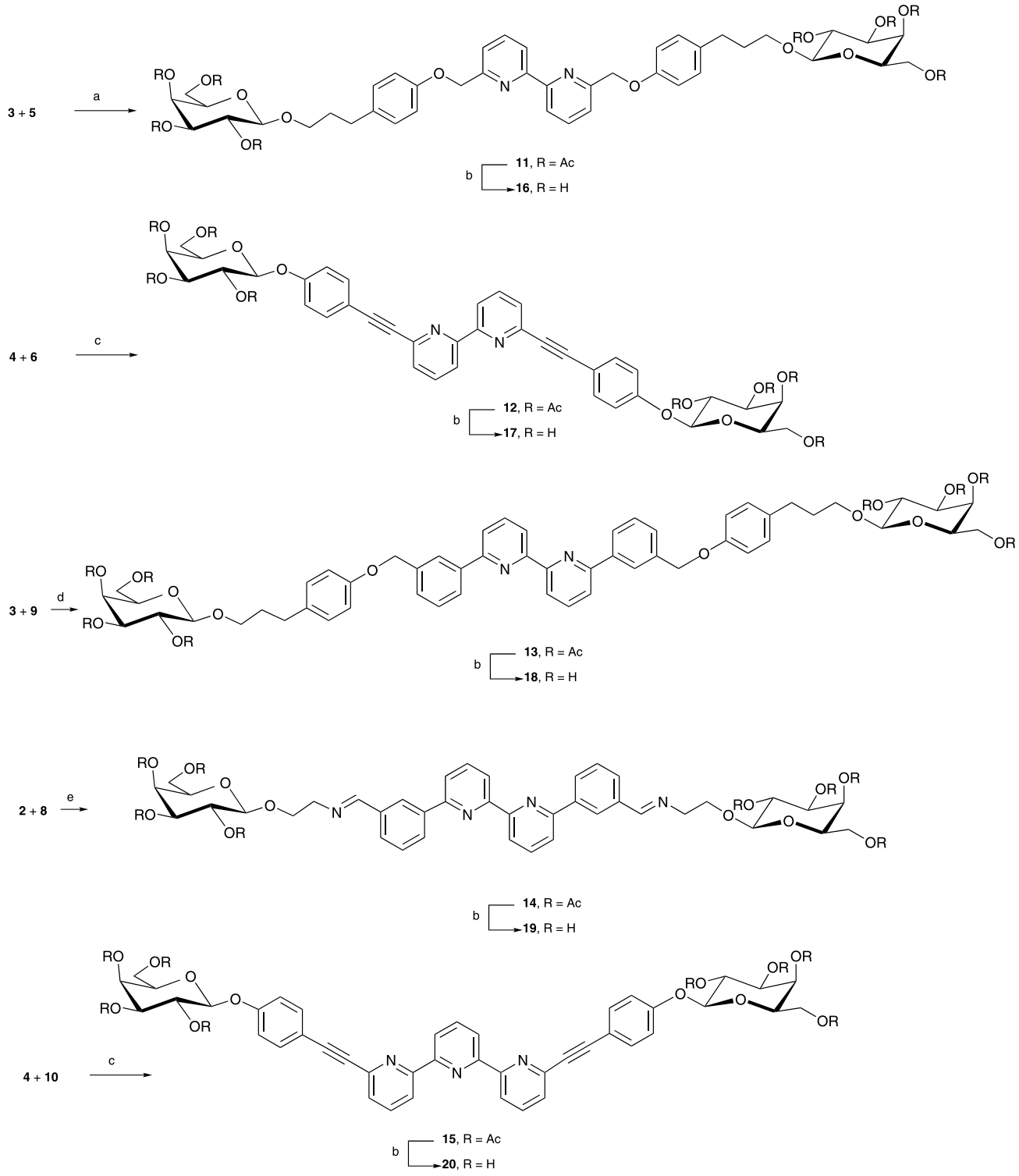


Scheme 2. Structure of oligopyridines **5**, **6**, and **10** and synthesis of bipyridines **8** and **9**. Reagents and conditions: (a), 3-formylphenyboronic acid, $Pd(OAc)_2$, PPh_3, DME, $NaHCO_3$, reflux, 22 h; (b), $NiCl_2$ hexahydrate, PPh_3, Zn, DMF, 50 °C, 22 h; (c), $NaBH_4$, EtOH, 0 °C, 5 h; (d), PBr_3, DCM, 0 °C to rt, 16 h.

acetonitrile/$CHCl_3$ to afford, after solvent evaporation, dark red solids. **Cu(11)$_2$**–**Cu(13)$_2$** were purified by filtration through a short silica gel column. Mass spectroscopy (MS-FAB) indicated the formation of adducts containing two ligands for each copper cation.

The assignment of structures to these complexes was based on NMR evidence. For instance, in all cases the ^{13}C NMR signals of the bipyridine carbons in positions 5/5′ and 3/3′ were shifted downfield by 4.3–4.6 and 1.1–1.9 ppm, respectively, upon complexation. An opposite shift was experienced by the quaternary 2/2′ carbons of bipyridine, that were shifted upfield by 2.8–3.7 ppm. These trends are in agreement with those generally observed when two 6,6′-disubstituted bipyridine units complex a Cu(I) cation to afford a tetrahedral adduct.[15,16]

Further support in favor of the formation of tetrahedrally arranged complexes **Cu(11)$_2$**–**Cu(14)$_2$** also came from the variation in the chemical shift observed for the protons of the residues in the vicinity of the bipyridine nuclei. Inspection of molecular models showed that upon formation of a tetrahedral complex protons of one ligand molecule fell in the shielding cone of the bipyridine moiety of the other ligand molecule (Fig. 1). As a consequence, strong upfield shifts were expected and indeed observed. For instance, the signal of the methylene groups bound to bipyridine C-6 and C-6′ in ligand **11** were shifted by about 0.5 ppm upfield in



Scheme 3. Synthesis of oligopyridine–galactose conjugates **11**–**20**. Reagents and conditions: (a), Cs_2CO_3, MeCN, rt, 18 h; (b), 0.1 M MeONa, MeOH, rt, 15 h; (c), CuI, $PdCl_2(PPh_3)_2$, *i*-Pr_2NH, THF, reflux, 24 h; (d), Cs_2CO_3, DMF/MeCN 80:20, rt, 18 h; (e), MeOH/DCM 20:80, rt, 18 h.

complex **Cu(11)$_2$**. Similarly, the protons of the phenyl rings connected to the same bipyridine carbons in ligands **13** and **14** experienced large upfield shifts (up to more than 1 ppm) upon formation of **Cu(13)$_2$** and **Cu(14)$_2$** (see Section 4).

On the other hand, the chemical shifts of the the H and C atoms of the glactose units remained virtually unchanged upon complex formation. This showed that these residues, being isolated from the bipyridine nucleus by the spacer, were not affected by the complexation event and maintained their conformational freedom. This observation is important because it suggests that the galactose units in **Cu(11)$_2$**–**Cu(14)$_2$** were not limited by the complexation in their potential ability to interact with a biological target.

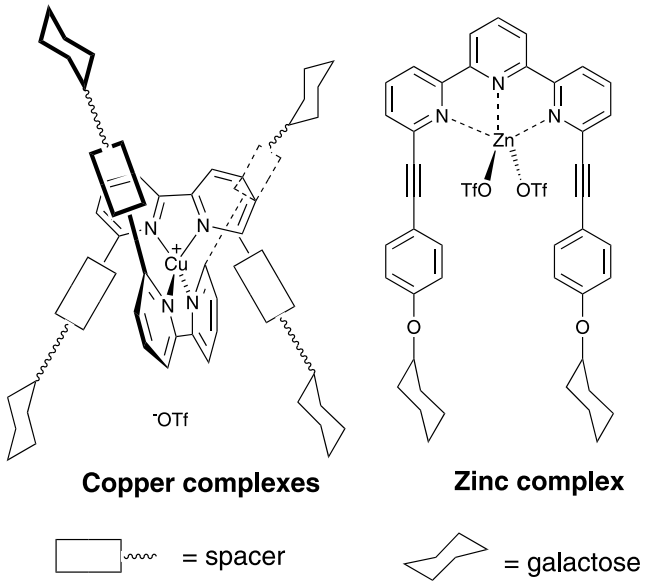


Figure 1. Schematic representation of copper(I)- and zinc(II)-complexes.

Reaction of ligand **15** with 1 mol equiv of $Zn(OTf)_2$ in chloroform afforded the corresponding 1:1 complex **Zn(15)**, to which, on the basis of literature data collected for related complexes[17] and of NMR and mass spectroscopic evidence, the trigonal bipyramidal structure reported in Figure 1 was assigned.

Having performed the synthesis of the acetylated complexes, we turned our attention to the preparation of their unprotected analogs required for biological evaluation. In principle these compounds could be obtained by two different approaches: (i) by deprotection of the acetylated complexes, and (ii) by complexation of the deacetylated ligands.

Reaction of ligands **11**–**15** with excess sodium methoxide in methanol readily gave the corresponding fully deprotected, crude polyols **16**–**20** that were isolated by simple evaporation of the reaction solvent. The extremely poor solubility of these compounds in most organic solvents[18] made their purification very difficult. Removal of sodium methoxide was only achieved by stirring a suspension of the crude polyols in water. Filtration of the mixture, however, afforded products containing large and undetermined amounts of water. These products were fully characterized by ^{1}H and ^{13}C NMR analysis and mass spectroscopy.[18]

The poor solubility of the polyhydroxylated ligands **16**–**20** made quite unpractical the synthesis of their complexes by reaction with metal triflates, requiring the use of very dilute methanol solution of the ligands.[19] However, by deacetylation of the corresponding adducts $\mathbf{Cu(11)_2}$, $\mathbf{Cu(12)_2}$, and $\mathbf{Cu(14)_2}$ (see above) unprotected complexes $\mathbf{Cu(16)_2}$, $\mathbf{Cu(17)_2}$, and $\mathbf{Cu(19)_2}$ were obtained and fully characterized.[20] The trends in the chemical shift difference between the polyhydroxylated ligands and their complexes observed in the ^{1}H and ^{13}C NMR spectra in combination with mass spectroscopy data (MS-ESI) indicated that $\mathbf{Cu(16)_2}$, $\mathbf{Cu(17)_2}$, and $\mathbf{Cu(19)_2}$ maintained the tetrahedral structure of their parent species. However, deacetylation of complex **Zn(15)** resulted in complex decomposition to afford the deprotected ligand **20**.

3. Conclusions

In conclusion, this work has demonstrated that galactose–oligopyridine conjugates could readily be assembled by combining four differently functionalized bipyridines and one terpyridine with three peracetylated galactose derivatives. Variation in the structure of the components and of the linkers employed for their connection afforded adducts of different size, shape, and conformational mobility, thus showing the generality of this approach.

Complexation of the bipyridine ligands with CuOTf and of the terpyridine ligand with $Zn(OTf)_2$ afforded the corresponding peracetylated 2:1 and 1:1 complexes, respectively, as single species. Their structures were determined to be tetrahedral (Cu complexes) and trigonal-bipyramidal (Zn complex), on the basis of NMR and mass spectroscopic evidence. Removal of the acetyl protecting groups from the ligands was possible, affording polyols that turned out to be poorly soluble in most organic solvents and in water. In contrast to the terpyridine–Zn(II) complex, the bipyridine/Cu(I) complexes survived the removal of the acetyl protecting groups and maintained their structure.

Studies dedicated to assess the binding ability[21] of these multivalent glycosylated ligands on macromolecular receptors such as lectins[22] by turbidimetric analysis[23] will be reported in due course.

4. Experimental

4.1. General methods

^{1}H NMR spectra were recorded on Bruker instruments at 300 or 500 MHz in chloroform-*d* ($CDCl_3$) unless otherwise stated, and were referenced to tetramethylsilane (TMS) at 0.00 ppm; ^{13}C NMR spectra were recorded at 75 or 125 MHz and were referenced to 77.0 ppm in $CDCl_3$. $^{13}C\{^1H\}$ NMRspectra were obtained using Waltz decoupling and were exponentially multiplied to give 0.8 Hz line broadening before Fourier transformation. All two dimensional experiments were acquired with a Bruker inverse 5 mm z-gradient probe. The 90° pulse widths were 9.2 and 13.1 μs for ^{1}H and ^{13}C, respectively. The gradient was shaped by a waveform generator and amplified by a Bruker B-AFPA-10 amplifier. A sinusoidal gradient of 1 ms length and a recovery time of 0.1 ms was used. The 2D COSY spectra were recorded with a 1024×1024 data matrix and 512 increments of 1 scan each, in magnitude mode, with a relaxation delay of 1.0 s and using a 1:1 gradient combination, then processed with zero-filling in f_1 and unshifted sine-bell apodization function. The HMQC and HMBC spectra were recorded using standard Bruker software sequences inv4gs and inv4gslplrnd, respectively. The following acquisition parameters were applied in both experiments: spectral widths in f_1 (^{13}C) and f_2 (^{1}H) dimensions 16,000 and 3000 Hz, respectively, a 1024× 1024 data matrix, 512 time increments of 200 scans each

and a 5:3:4 gradient combination. We set $\Delta_1 = 3.5$ ms in both experiments and $\Delta_2 = 60$ ms only in HMBC, as interpulse delay for the evolution of long-range coupling. The Fourier transformations were performed with shifted and unshifted sine-bell apodization functions in f_1 (^{13}C) and f_2 (^{1}H) dimension, respectively.

Optical rotations were measured at the Na-D line in a 1 dm cell at 22 °C. IR spectra were recorded on thin film or as solution in CH_2Cl_2 or as KBr pellets. 3-(4-Benzyloxyphenyl)-1-propanol,[9] and compounds **1**,[9] **5**,[10] **6**,[11] and **10** were prepared according to literature procedures. 3-(4-Benzyloxyphenyl)-1-propanol had mp 63–65 °C (lit.,[9] 64–65 °C); the β- and α-anomers of imidate **1** had mp 145–146 and 121–123 °C, respectively (lit.,[8] 146–147 and 122–123 °C); 6,6′-bis(bromomethyl)-2,2′-bipyridine had mp 180–181 °C (lit.,[10] 180–181 °C); 6,6′-diethynyl-2,2′-bipyridine had mp 190–192 °C (lit.,[11] 192–193 °C); 2″,6-diethynyl-2,2′:6′,6″-terpyridine (mp 220 °C, decomposition) had NMR data identical to those reported in the literature.[14]

4.2. Synthesis of the galactose dendrons 2–4

4.2.1. *O*-(2-Aminoethyl)-(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranose (2). *Glycosidation reaction*. To a solution of a 2:1 mixture of β and α anomers of *O*-(2,3,4,6-*O*-tetracetyl-D-galactopyranosyl) trichloroacetimidate **1** (1.40 g, 2.84 mmol) and benzyl *N*-(2-hydroxyethyl)carbamate (0.98 g, 4.76 mmol) in dry CH_2Cl_2 (30 mL) stirred under nitrogen and cooled at 0 °C, a solution of trimethylsilyl triflate (0.25 mL, 1.30 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise. After 1 h stirring at 0 °C, the reaction was quenched by the addition of triethylamine (2 mL), and the resulting mixture was concentrated under vacuum. The residue was purified by flash chromatography with a 50:50 hexane/ethyl acetate mixture as eluant. The product *O*-(2-*N*-carbobenzyloxyaminoethyl)-(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranose (0.75 g, 1.43 mmol, 50% yield) was obtained as a thick pale yellow oil. (Found: C, 55.0; H, 6.0; N, 2.5. $C_{24}H_{31}NO_{12}$ requires C, 54.8; H, 5.9; N, 2.7%); $[\alpha]_D^{22}$ +4.4 (*c* 1.2 in CH_2Cl_2); IR: ν_{max} (film)/cm^{-1} 3250, 1751, 1722, 1230; ^{1}H NMR: δ 2.00 (3H, s, Me), 2.02 (3H, s, Me), 2.05 (3H, s, Me), 2.17 (3H, s, Me), 3.35–3.50 (2H, m, CH_2NH), 3.68–3.77 (2H, m, CH_2CH_2O), 3.85–3.95 (1H, m, H-C5), 4.16 (2H, d, J=6.6 Hz, H-C6), 4.47 (1H, d, J=7.9 Hz, H-C1), 5.03 (1H, dd, J=3.4, 7.1 Hz, H-C3), 5.12 (2H, s, CH_2Ar), 5.17-5.22 (1H, m, H-C2), 5.40 (1H, d, J=3.4 Hz, H-C4), 7.32–7.40 (5H, m, aromatic H); ^{13}C NMR: δ 20.4 (2×Me), 20.5 (2×Me), 40.8 (CH$_2$–NH), 61.2 (galactose C-6), 66.7 (CH$_2$–Ar), 66.9 (galactose C-4), 68.8 (galactose C-2), 69.3 (CH$_2$ bound to anomeric O), 70.5 (galactose C-3), 70.8 (galactose C-5), 101.5 (galactose C-1), 128.0 (2 *ortho* C of aryl ring), 128.1 (*para* C of aryl ring), 128.4 (2, *meta* C of aryl ring), 136.5 (quaternary C of aryl ring), 169.5 (C=O), 170.0 (2 C=O), 170.1 (C=O), 170.2 (C=O).

Removal of the Cbz group. To a solution of *O*-(2-*N*-carbobenzyloxyaminoethyl)-(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranose (0.26 g, 0.50 mmol) in absolute EtOH (20 mL), 10% Pd/C (0.03 g) was added. The resulting slurry was shaken under a hydrogen atmosphere for 2 h. The mixture was then filtered through a Celite cake and the filtrate was concentrated under vacuum to afford the pure product **2** (0.195 g, 0.5 mmol, 99% yield) as a thick oil. (Found: C, 48.9; H, 6.2; N, 3.8. $C_{16}H_{25}NO_{10}$ requires C, 49.1; H, 6.4; N, 3.6%); $[\alpha]_D^{22}$ +13.1 (*c* 0.6 in CH_2Cl_2); IR: ν_{max}(film)/cm^{-1} 3320, 1751; ^{1}H NMR: δ 1.75 (2H, bs, NH_2), 1.92 (3H, s, Me), 1.98 (3H, s, Me), 2.00 (3H, s, Me), 2.09 (3H, s, Me), 2.70–2.85 (2H, m, CH_2N), 3.53–3.60 (1H, m, one H of CH_2CH_2O), 3.80–3.90 (2H, m, H-C5 and one H of CH_2CH_2O), 4.06–4.14 (2H, m, H-C6), 4.46 (1H, d, J=7.9 Hz, H-C1), 4.97 (1H, dd, J=3.2, 7.1 Hz, H-C3), 5.14 (1H, dd, J=8.1, 8.3 Hz, H-C2), 5.33 (1H, d, J=3.2 Hz, H-C4); ^{13}C NMR: δ 20.4 (Me), 20.5 (2 Me), 20.6 (Me), 41.6 (CH_2–N), 61.2 (galactose C-6), 67.0 (galactose C-4), 68.9 (galactose C-2), 69.3 (CH$_2$ bound to anomeric O), 70.6 (galactose C-5), 70.8 (galactose C-3), 101.4 (galactose C-1), 169.3 (C=O), 169.9 (C=O), 170.0 (C=O), 170.2 (C=O); MS-ESI$^+$: m/z 392 $[M+H]^+$.

4.2.2. *O*-[3-(4-Hydroxyphenyl)-1-propyl)]-(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranose (3). *Glycosidation reaction*. To a solution of a 2:1 mixture of β and α anomers of *O*-(2,3,4,6-*O*-tetracetyl-D-galactopyranosyl) trichloroacetimidate **1** (0.49 g, 1.0 mmol) and 3-(4-benzyloxy-phenyl)-1-propanol (0.36 g, 1.5 mmol) in dry CH_2Cl_2 (8 mL) stirred under nitrogen and cooled at 0 °C, a solution of trimethylsilyl triflate (0.08 mL, 0.46 mmol) in dry CH_2Cl_2 (1 mL) was added dropwise. After 2 h stirring at 0 °C, the reaction was quenched by the addition of triethylamine (0.5 mL), and the resulting mixture was concentrated under vacuum. The residue was purified by flash chromatography with a 70:30 hexane/ethyl acetate mixture as eluant. The product *O*-[3-(4-phenylmethoxyphenyl)-1-propyl)]-(2,3,4,6-*O*-tetracetyl)-β-D-galacto-pyranose (0.19 g, 0.33 mmol, 33% yield) was obtained as a thick oil. (Found: C, 63.2; H, 6.5. $C_{30}H_{36}O_{11}$ requires C, 62.9; H, 6.3%); $[\alpha]_D^{22}$ −4.4 (*c* 0.6 in CH_2Cl_2); IR: ν_{max} (film)/cm^{-1} 1752, 1224; ^{1}H NMR: δ 1.80–2.00 (2H, m, $CH_2CH_2CH_2$), 2.02 (3H, s, Me), 2.05 (3H, s, Me), 2.08 (3H, s, Me), 2.17 (3H, s, Me), 2.57–2.70 (2H, m, CH_2CH_2Ar), 3.45–3.60 (1H, m, one H of CH_2 bound to anomeric O), 3.87–3.99 (2H, m, H-C5 and one H of CH_2 bound to anomeric O), 4.10–4.25 (2H, m, H-C6), 4.48 (1H, d, J=7.9 Hz, H-C1), 5.00–5.10 (3H, m, H-C3 and OCH_2Ar), 5.26 (1H, dd, J=7.9, 9.3 Hz, H-C2), 5.41 (1H, d, J=3.4 Hz, H-C4), 6.92 (2H, A part of AB system, J=8.5 Hz, aromatic H *ortho* to O), 7.10 (2H, B part of AB system, J=8.5 Hz, aromatic H *meta* to O); 7.25–7.40 (5H, m, aromatic H of benzyloxy group); ^{13}C NMR: δ 20.4 (2×Me), 20.5 (2 Me), 30.9 (CH_2–C–CH_2), 31.2 (Ar–C–CH_2), 61.2 (galactose C-6), 67.0 (d, galactose C-4), 68.9 (d, galactose C-2), 69.0 (CH$_2$ bound to anomeric O), 70.0 (O–C–Ar), 70.6 (galactose C-3), 70.9 (galactose C-5), 101.3 (galactose C-1), 114.8 (2×aromatic C *ortho* to O), 127.4 (*para* C of benzyloxy ring), 127.8 (2×*meta* C of benzyloxy ring), 128.5 (2×*ortho* C of benzyloxy ring), 129.3 (2×C of aryl ring *meta* to O), 133.9 (quaternary aromatic C *para* to O), 137.0 (quaternary C of benzyloxy ring), 158.0 (quaternary aromatic C bound to O), 169.0 (C=O), 170.2 (2×C=O), 170.5 (C=O).

Removal of the benzyl group. To a solution of *O*-[3-(4-phenylmethoxyphenyl)-1-propyl)]-(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranose (0.30 g, 0.52 mmol) in absolute EtOH (20 mL), 10% Pd/C (0.02 g) was added. The resulting slurry

was shaken under a hydrogen atmosphere for 2 h. The mixture was then filtered through a Celite cake and the filtrate was concentrated under vacuum to afford the pure product **3** (0.25 g, 0.52 mmol, 99% yield) as a gum-like material. (Found: C, 57.0; H, 6.1. $C_{23}H_{30}O_{11}$ requires C, 57.2; H, 6.3%); $[\alpha]_D^{22}$ 0.0, $[\alpha]_{436}^{22}$ +0.8 (*c* 1 in CH_2Cl_2); IR: ν_{max}(film)/cm^{-1} 3436, 1751, 1225; ^{1}H NMR: δ 1.83–1.96 (2H, m, $CH_2CH_2CH_2$), 2.00 (3H, s, Me), 2.04 (3H, s, Me), 2.07 (3H, s, Me), 2.16 (3H, s, Me), 2.55–2.70 (2H, m, CH_2CH_2Ar), 3.41–3.55 (1H, m, one H of CH_2 bound to anomeric C), 3.80–3.95 (2H, m, H-C5 and one H of CH_2 bound to anomeric O), 4.10–4.25 (2H, m, H-C6), 4.47 (1H, d, *J*=7.8 Hz, H-C1), 5.04 (1H, dd, *J*=3.4, 10.5 Hz, H-C3), 5.25 (1H, dd, *J*=7.8, 8.3 Hz, H-C2), 5.40 (1H, d, *J*=3.4 Hz, H-C4), 5.70 (1H, b s, OH), 6.77 (2H, A part of AB system, *J*=8.5 Hz, aromatic H *ortho* to O), 7.03 (2H, B part of AB system, *J*=8.5 Hz, aromatic H *meta* to O); ^{13}C NMR: δ 20.4 (2×Me), 20.7 (2×Me), 30.8 (CH_2–*C*–CH_2), 31.2 (t, Ar–*C*–CH_2), 61.2 (galactose C-6), 67.1 (galactose C-4), 68.9 (methylene bound to anomeric O), 69.0 (galactose C-2), 70.6 (galactose C-3), 70.9 (galactose C-5), 101.3 (galactose C-1), 115.2 (2×C of aryl ring *ortho* to O), 129.4 (2×C of aryl ring *meta* to O), 132.0 (quaternary aromatic C *para* to O), 154.0 (quaternary aromatic C bound to O), 170.1 (2×C═O), 170.2 (2×C═O). MS-ESI$^+$: *m*/*z* 505.6 [M+Na]$^+$.

4.2.3. *O*-(4-Iodophenyl)-(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranose (4). To a solution of a 2:1 mixture of β and α anomers of *O*-(2,3,4,6-*O*-tetracetyl-D-galactopyranosyl) trichloroacetimidate **1** (0.49 g, 1.0 mmol) and 4-iodophenol (0.22 g, 1.0 mmol) in dry CH_2Cl_2 (8 mL) stirred under nitrogen and cooled at 0 °C, a solution of trimethylsilyl triflate (0.08 ml, 0.46 mmol) in dry CH_2Cl_2 (1 mL) was added dropwise. After 2 h stirring at 0 °C, the reaction was quenched by the addition of triethylamine (0.5 mL), and the resulting mixture was concentrated under vacuum. The residue was purified by flash chromatography with a 70:30 hexane/ethyl acetate mixture as eluant. The first eluted product (0.104 g, 0.19 mmol, 19% yield) was a pale yellow solid with mp 88–90 °C, $[\alpha]_D^{22}$ +23.0 (*c* 1 in CH_2Cl_2). On the basis of the H–C1/H–C2 coupling constant value (*J*=3.4 Hz) the α-anomeric configuration was assigned to this compound. The second eluted product (0.363 g, 0.66 mmol, 66% yield) was the β-anomer. It was obtained as a white solid with mp 44–45 °C. (Found: C, 43.3; H, 4.5. $C_{20}H_{23}IO_{10}$ requires C, 43.6; H, 4.2%); $[\alpha]_D^{22}$ +8.7 (*c* 0.7 in CH_2Cl_2); IR: ν_{max}(KBr)/cm^{-1} 1752, 1227, 1087; ^{1}H NMR: δ 2.00 (3H, s, Me), 2.05 (6H, s, 2 Me), 2.17 (3H, s, Me), 4.02–4.10 (1H, m, H-C5), 4.15–4.25 (2H, m, H-C6), 5.02 (1H, d, *J*=7.9 Hz, H–C1), 5.13 (1H, dd, *J*=3.5, 10.5 Hz, H–C3), 5.43–5.51 (2H, m, H–C4 and H–C2), 6.80 (2H, A part of AB system, *J*=8.8 Hz, aromatic H *ortho* to O), 7.60 (2H, B part of AB system, *J*=8.8 Hz, aromatic H *meta* to O); ^{13}C NMR: δ 20.4 (2×Me), 20.5 (2×Me), 61.3 (galactose C-6), 66.8 (galactose C-4), 68.5 (galactose C-2), 70.7 (galactose C-3), 71.1 (galactose C-5), 86.0 (quaternary aromatic C bound to iodine) 99.5 (galactose C-1), 119.2 (2×C of aryl ring *ortho* to O),138.4 (2×C of aryl ring *meta* to O), 156.7 (quateranry aromatic C bound to O), 170.1 (2×C═O), 170.2 (2×C═O). MS-ESI$^+$: *m*/*z* 573.2 [M+Na]$^+$.

4.3. Synthesis of oligopyridines

4.3.1. 2-Bromo-6-(3-formylphenyl)pyridine (7). To a solution of 2,6-dibromopyridine (2.00 g, 8.44 mmol), triphenylphosphine (0.44 g, 1.67 mmol), and palladium acetate (0.19 g, 0.83 mmol) in dry DME (100 mL) stirred under nitrogen at room temperature, 3-formylphenylboronic acid (1.37 g, 9.17 mmol) was added followed by a 2 M aqueous solution of sodium carbonate (25 mL, 40.8 mmol). The resulting mixture was refluxed for 22 h, and the solvent was evaporated under vacuum. The remaining aqueous phase was extracted with CH_2Cl_2 (3×50 mL), and the combined organic phases were washed with water and dried over sodium sulfate. Filtration and evaporation of the solvent under vacuum afforded the crude product that was purified by flash chromatography with a 80:20 hexane/ethyl acetate mixture as eluant. The product **7** (1.24 g, 4.72 mmol, 56% yield) was a white solid, mp 90–91 °C. (Found: C, 55.3; H, 2.9; N, 5.5. $C_{12}H_8BrNO$ requires C, 55.0; H, 3.1; N, 5.3%); IR: ν_{max}(KBr)/cm^{-1} 1688, 1552, 1430, 1188, 1125; ^{1}H NMR: δ 7.50 (1H, d, *J*=7.8 Hz, pyridine H–C3), 7.64–7.70 (2H, m, pyridine H–C4 and H *meta* to CHO), 7.79 (1H, d, *J*=7.8 Hz, pyridine H–C5), 7.98 (1H, dt, *J*=1.4, 7.8 Hz, H *para* to CHO), 8.31 (1H, dd, *J*=1.4, 7.9 Hz, H *ortho* to CHO), 8.52 (1H, t, *J*=1.4 Hz, H between pyridine and CHO), 10.15 (1H, s, CHO); ^{13}C NMR: δ 119.1 (pyridine C-5), 127.1 (pyridine C-3), 128.2 (C between pyridine ring and CHO), 129.6 (C *meta* to pyridine ring), 130.6 (C *para* to CHO), 132.7 (C *ortho* to CHO and *para* to pyridine ring), 137.0 (quaternary C bound to pyridine ring), 138.6 (quaternary carbon bound to CHO), 139.2 (pyridine C-4), 142.2 (pyridine C-2), 157.0 (pyridine C-6) 191.9 (CHO). MS-ESI$^+$: *m*/*z* 263.9 [M+H]$^+$.

4.3.2. 6,6′-Bis(3-formylphenyl)-2,2′-bipyridine (8a). A suspension of nickel dichloride hexahydrate (1.06 g, 3.87 mmol), triphenylphosphine (4.06 g, 15.47 mmol), and zinc powder (0.38 g, 5.8 mmol) in dry DMF (30 mL) was stirred at 60 °C under nitrogen for 1 h. A DMF (10 mL) solution of 2-bromo-6-(3-formylphenyl)pyridine (1.01 g, 3.86 mmol) was then added and the mixture was stirred at 60 °C for 23 h. After addition of diluted aqueous ammonia (50 mL) to the cooled mixture, this was extracted with CH_2Cl_2 (3×20 mL). The combined organic phases were washed twice with brine and dried over sodium sulfate. Filtration and evaporation of the solvent under vacuum, afforded the crude product as a cream-colored solid. This was purified by several washings with a 90:10 hexane/ethyl acetate mixture to remove the unreacted aldehyde, excess triphenylphosphine, and some triphenylphosphineoxide. The resulting solid **8a** (0.70 g, 1.9 mmol, 47% yield), mp 197–198 °C, was pure enough for analysis and subsequent manipulation. (Found: C, 78.9; H, 4.2; N, 7.9. $C_{24}H_{16}N_2O_2$ requires C, 79.1; H, 4.4; N, 7.7%); IR: ν_{max}(KBr)/cm^{-1} 1680, 1589, 1437, 1199; ^{1}H NMR: δ 7.73 (2H, t, *J*=8.5 Hz, H *meta* to CHO), 7.91 (2H, d, *J*=7.8 Hz, pyridine H-5), 8.00–8.05 (4H, m, H *para* to CHO and pyridine H-4), 8.50 (2H, d, *J*=8.5 Hz, H *ortho* to CHO and *para* to pyridine ring), 8.67 (2H, d, *J*=7.8 Hz, pyridine H-3), 8.72 (2H, s, H between CHO and pyridine ring), 10.20 (2H, s, CHO); ^{13}C NMR: δ 121.0 (2×pyridine C-3), 121.5 (2×pyridine C-5), 128.2 (2×C between CHO and pyridine ring), 129.8 (2×C *meta* to CHO and to pyridine ring), 130.8 (2×C *ortho* to

CHO and *para* to pyridine ring), 132.8 (2×C *para* to CHO), 137.1 (2×pyridine C-4), 139.0 (2×quaternary C bound to CHO), 139.1 (2×quaternary C *meta* to CHO), 154.8 (2×pyridine C-6), 155.7 (2×pyridine C-2), 192.1 (2×C of CHO). MS-ESI$^+$: *m/z* 387.1 $[M+Na]^+$.

4.3.3. 6,6′-Bis(3-hydroxymethylphenyl)-2,2′-bipyridine (8b). To a sirred suspension of dialdehyde **8a** (0.365 g, 1 mmol) in absolute EtOH (10 mL) cooled at 0 °C, $NaBH_4$ (0.08 g, 2 mmol) was added in one portion. The reaction mixture was warmed up to room temperature and stirring was continued until a clear solution was obtained (about 3 h). A few drops of water were then added and the solvent was evaporated under vacuum. The residue was dissolved in water (10 mL) and the aqueous phase was extracted with CH_2Cl_2 (2×20 mL). The combined organic phases were dried over sodium sulfate. Filtration and evaporation of the solvent under vacuum, afforded the crude product as a cream-colored solid that was purified by flash chromatography with a 98:2 CH_2Cl_2:MeOH mixture as eluant to give the product **8b** (0.353 g, 0.96 mmol, 96% yield), as a white solid, mp 142 °C. (Found: C, 78.0; H, 5.6; N, 7.9. $C_{24}H_{20}N_2O_2$ requires C, 78.2; H, 5.5; N, 7.6%); IR: ν_{max}(KBr)/cm^{-1} 3270, 1568, 1437, 1039; ^{1}H NMR: δ 3.60 (2H, bs, OH), 4.26 (4H, s, CH_2O), 7.48 (2H, d, J=8.5 Hz, H *ortho* to CH_2OH and *para* to pyridine ring), 7.55 (2H, t, J=8.4 Hz, H *meta* to CH_2OH), 7.83 (2H, d, J=8.5 Hz, pyridine H-C5), 7.95 (2H, t, J=8.5 Hz, pyridine H-C4), 8.11 (2H, d, J=8.5 Hz, H *para* to CH_2OH), 8.23 (2H, s, H between CH_2OH and pyridine ring), 8.63 (2H, d, J=8.5 Hz, pyridine H–C3); ^{13}C NMR: δ 65.1 (2×CH_2–O), 119.8 (2×pyridine C-3), 120.5 (2×d, pyridine C-5), 125.6 (2×C *para* to CH_2OH), 126.3 (2×C between CH_2OH and pyridine ring), 127.6 (2×C *meta* to CH_2OH), 129.0 (2×C *ortho* to CH_2OH and *para* to pyridine ring), 137.7 (2×pyridine C-4 and 2×quaternary C *meta* to CH_2OH), 141.8 (2×quaternary C bound to CH_2OH), 155.7 (2×pyridine C-6), 156.0 (2×pyridine C-2). MS-ESI$^+$: *m/z* 391.1 $[M+Na]^+$.

4.3.4. 6,6′-Bis(3-bromomethylphenyl)-2,2′-bipyridine (9). To a stirred solution of the diol **8b** (0.30 g, 0.81 mmol) in dry CH_2Cl_2 (10 mL) cooled at 0 °C, a solution of PBr_3 (0.46 mL) in dry CH_2Cl_2 (2 mL) was slowly added. After 30 min stirring at 0 °C the reaction mixture was warmed up to room temperature, and stirring was continued for 16 h. The reaction was quenched by the addition of a 0.1 M solution of sodium hydroxide until neutrality of the aqueous phase was obtained. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2×10 mL). The combined organic phases were dried over sodium sulfate. Filtration and evaporation of the solvent under vacuum, afforded the crude product that was purified by flash chromatography with CH_2Cl_2 as eluant to give the product **9** (0.33 g, 0.66 mmol, 82% yield), as a white solid, mp 209–211 °C. (Found: C, 58.1; H, 3.6; N, 5.4. $C_{24}H_{18}Br_2N_2$ requires C, 58.3; H, 3.7; N, 5.7%); IR: ν_{max}(KBr)/cm^{-1} 1568, 1437, 1218; ^{1}H NMR: δ 4.66 (4H, s, CH_2Br), 7.45–7.60 (4H, m, H *ortho* to CH_2Br and *para* to pyridine ring, and H *meta* to CH_2Br and *meta* to pyridine ring), 7.84 (2H, d, J=8.5 Hz, pyridine H-C5), 7.98 (2H, t, J=8.5 Hz, pyridine H-C4), 8.11 (2H, d, J=8.5 Hz, H *para* to CH_2Br), 8.24 (2H, s, H between pyridine ring and CH_2Br), 8.65 (2H, d, J=8.5 Hz, pyridine H–C3); ^{13}C NMR: δ 33.6 (2×CH_2Br), 120.5 (2×pyridine C-3), 120.8 (2×pyridine C-5), 127.2 (2×C *ortho* to CH_2Br and *para* to pyridine ring), 127.9 (2×C between CH_2Br and pyridine ring), 129.3 (2×C *meta* to CH_2Br and *meta* to pyridine ring), 129.7 (2×C *para* to CH_2Br), 138.2 (2×pyridine C-4, and 2×quaternary C *meta* to CH_2Br), 139.8 (2×quaternary C bound to CH_2Br), 155.7 (4×pyridine C-2 and C-6). MS-ESI$^+$: *m/z* 495.1 $[M+H]^+$.

4.4. Synthesis of oligopyridine–galactose conjugates

4.4.1. 6,6′-Bis-[4-[3-[(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranosyl]-prop-1-yl]-phenyloxy-methyl]-2,2′-bipyridine (11). To a stirred solution of bipyridine **5** (51 mg, 0.15 mmol) and phenol **3** (166 mg, 0.34 mmol) in dry acetonitrile (4 mL), cesium carbonate (0.3 g, 0.84 mmol) was added. The mixture was stirred at room temperature for 18 h. The solvent was then evaporated under vacuum and the residue was purified by flash chromatography with a 50:50 hexane/ethyl acetate mixture as eluant to give **11** as a light brown, gum-like material (95 mg, 0.083 mmol, 55% yield). (Found: C, 60.5; H, 5.7; N, 2.7. $C_{58}H_{68}N_2O_{22}$ requires C, 60.8; H, 6.0; N, 2.4%); $[\alpha]_D^{22}$ −2.5 (*c* 0.8 in CH_2Cl_2); IR: ν_{max}(film)/cm^{-1} 2932, 1746, 1510, 1223, 1048; ^{1}H NMR (CD_3OD): δ 1.83–1.95 (4H, m, CH_2CH_2-CH_2O), 2.00 (6H, s, Me), 2.04 (6H, s, Me), 2.07 (6H, s, Me), 2.17 (6H, s, Me), 2.56–2.72 (4H, m, $CH_2CH_2CH_2O$), 3.50 (2H, A part of an AB system, J=6.0, 10.0 Hz, one H of $CH_2CH_2CH_2O$), 3.86–3.95 (4H, m, one H of $CH_2CH_2CH_2O$ and galactose H-5), 4.17 (4H, AB system, J=6.2 Hz, galactose H-6), 4.48 (2H, d, J=8.0 Hz, galactose H-1), 5.04 (2H, dd, J=3.4, 10.4 Hz, galactose H-3), 5.23 (2H, dd, J=8.0, 10.4 Hz, galactose H-2), 5.30 (4H, s, PyCH_2O), 5.41 (2H, d, J=3.4 Hz, galactose H-4), 6.97 (4H, A part of an AB system, J=8.5 Hz, H *ortho* to O), 7.11 (4H, B part of an AB system, J=8.5 Hz, H *meta* to O), 7.57 (2H, d, J=7.6 Hz, pyridine H-5), 7.87 (2H, t, J=7.6 Hz, pyridine H-4), 8.37 (2H, d, J=7.6 Hz, pyridine H-3); ^{13}C NMR (CD_3OD): δ 20.5 (4×Me), 20.6 (2×Me), 20.8 (2×Me), 30.9 (2×CH_2–*C*–CH_2), 31.2 (2×Ar–*C*–CH_2), 61.3 (2×galactose C-6), 67.1 (2×galactose C-4), 69.0 (2×galactose C-2, and 2×CH_2 bound to anomeric O), 70.6 (2×galactose C-5), 71.0 (2×galactose C-3), 77.0 (2×CH_2 bound to pyridine), 101.3 (2×galactose C-1), 114.8 (4×aromatic C *ortho* to O), 120.3 (2×pyridine C-3), 121.4 (2×pyridine C-5), 129.4 (4×aromatic C *meta* to O), 134.1 (2×quaternary aromatic C of phenyl ring bound to CH_2), 137.9 (2×pyridine C-4), 155.0 (2×pyridine C-2), 156.8 (2×quaternary aromatic C of phenyl ring bound to O), 157.0 (2×pyridine C-6), 170.1 (8×C=O); MS-ESI$^+$: *m/z* 1145 $[M+H]^+$, 1167 $[M+Na]^+$.

4.4.2. 6,6′-Bis-[2-[4-[(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranosyl]-phenyl]-ethynyl]-2,2′-bipyridine (12). In a stirred mixture of dry THF (4.4 mL) and diisopropylamine (3.1 mL) kept under a nitrogen atmosphere, bipyridine **6** (47 mg, 0.23 mmol) and iodide **4** (251 mg, 0.46 mmol) were added. After 10 min stirring at room temperature, $PdCl_2(PPh_3)_2$ (5 mg, 0.007 mmol) and CuI (4 mg, 0.02 mmol) were added in this order. The mixture was refluxed for 24 h. Evaporation of the solvent under vacuum afforded a residue that was purified by flash chromatography

with a 50:50 hexane/ethyl acetate mixture as eluant to give **12** as a light brown, gum-like material (80 mg, 0.076 mmol, 33% yield). (Found: C, 62.0; H, 5.3; N, 2.4. $C_{54}H_{52}N_2O_{20}$ requires C, 61.8; H, 5.0; N, 2.7%); $[\alpha]_D^{22}$ +18.6 (*c* 0.2 in CH_2Cl_2); IR: ν_{max}(film)/cm^{-1} 2925, 2217, 1747, 1260, 1043; ^1H NMR (CD_3OD): δ 1.97 (6H, s, Me), 2.04 (6H, s, Me), 2.06 (6H, s, Me), 2.17 (6H, s, Me), 4.13 (4H, d, J= 6.2 Hz, galactose H-6), 4.49 (2H, t, J=6.2 Hz, galactose H-5), 5.26 (2H, A part of an AB system, J=8.0, 10.0 Hz, galactose H-2), 5.31 (2H, B part of an AB system, J=3.0, 10.0 Hz, galactose H-3), 5.38 (2H, d, J=3.0 Hz, galactose H-4), 5.61 (2H, d, J=8.0 Hz, galactose H-1), 7.10 (4H, A part of an AB system, J=8.6 Hz, H *ortho* to O), 7.68 (4H, B part of an AB system, J=8.6 Hz, H *meta* to O), 7.74 (2H, d, J=7.7 Hz, pyridine H-3), 8.04 (2H, t, J=7.7 Hz, pyridine H-4) and 8.39 (2H, d, J=7.7 Hz, pyridine H-5); ^{13}C NMR (CD_3OD): 19.0 (8×Me), 61.1 (2×galactose C-6), 67.3 (2×galactose C-4), 68.7 (2×galactose C-2), 70.8 (2× galactose C-3, and 2×galactose C-5), 87.6 (2×s, one acetylenic C), 88.3 (2×s, other acetylenic C), 98.2 (2× galactose C-1), 116.5 (4×aromatic C *ortho* to O, and 2× quaternary phenyl *C* bound to acetylenic C), 120.4 (2×pyridine C-3), 127.1 (2×pyridine C-5), 133.2 (4× aromatic C *meta* to O), 137.4 (2×pyridine C-4), 142.6 (2× pyridine C-6), 155.7 (2×pyridine C-2), 157.4 (2×aromatic C bound to O), 169.9 (4×C=O), 170.5 (4×C=O); MS-ESI$^+$: *m*/*z* 1049 $[M+H]^+$, 1071 $[M+Na]^+$.

4.4.3. 6,6′-Bis-[3-[4-[3-[(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranosyl]-prop-1-yl]-phenyloxy-methyl]phenyl]-2,2′-bipyridine (13). To a stirred solution of bipyridine **9** (74 mg, 0.15 mmol) and phenol **3** (166 mg, 0.34 mmol) in a mixture of dry DMF (4 mL) and dry acetonitrile (1 mL), cesium carbonate (0.3 g, 0.84 mmol) was added. The mixture was stirred at room temperature for 18 h. Water (5 mL) was then added and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 (2×10 mL). The combined organic phases were dried over sodium sulfate. Filtration and evaporation of the solvent under vacuum, afforded the crude product that was purified by flash chromatography with a 50:50 hexane/ethyl acetate mixtures as eluant to give **13** as a light brown, gum-like solid (58 mg, 0.045 mmol, 30% yield). (Found: C, 64.5; H, 5.6; N, 2.5. $C_{70}H_{76}N_2O_{22}$ requires C, 64.8; H, 5.9; N, 2.2%); $[\alpha]_D^{22}$ −3.4 (*c* 0.15 in CH_2Cl_2); ν_{max}(CH_2Cl_2)/cm^{-1} 2948, 1747, 1510, 1223, 1050; ^1H NMR (CD_3OD): δ 1.85 (4H, quintet, J=6.5 Hz, $CH_2CH_2CH_2O$), 1.95 (6H, s, Me), 1.99 (6H, s, Me), 2.08 (6H, s, Me), 2.17 (6H, s, Me), 2.63 (4H, t, J=6.5 Hz, $CH_2CH_2CH_2O$), 3.52 (2H, A part of an AB system, J=6.5, 9.8 Hz, one H of $CH_2CH_2CH_2O$), 3.83 (2H, B part of an AB system, J=6.5, 9.8 Hz, one H of $CH_2CH_2CH_2O$), 4.04 (2H, quartet, J=6.2 Hz, galactose H-5), 4.12 (4H, AB system, J=3.6, 6.2 Hz, galactose H-6), 4.58 (2H, d, J=4.4 Hz, galactose H-1), 5.04–5.14 (4H, m, galactose H-2 and H-3), 5.23 (4H, s, $ArCH_2O$), 5.38 (2H, br s, galactose H-4), 6.99 (4H, A part of an AB system, J= 8.6 Hz, H *ortho* to OCH_2Ar), 7.14 (4H, B part of an AB system, J=8.6 Hz, H *meta* to OCH_2Ar), 7.55 (4H, d, J= 5.1 Hz, H *para* to CH_2OAr and H *para* to pyridine ring), 7.95 (2H, d, J=7.2 Hz, pyridine H-5), 8.02 (2H, t, J= 7.5 Hz, pyridine H-4), 8.16 (2H, t, J=5.1 Hz, H *meta* to pyridine ring), 8.31 (2H, br s, H between pyridine ring and OCH_2Ar), 8.54 (2H, d, J=7.5 Hz, pyridine H-3); ^{13}C NMR (CD_3OD): 19.5 (8×Me), 30.9 (2×CH_2–*C*–Ar), 31.6 (2× CH_2–*C*–CH_2), 61.6 (2×galactose C-6), 67.9 (2×galactose C-4, and 2×CH_2–*C*H_2–O–anomeric C), 69.6 (2×galactose C-2), 70.0 (2×Ar–*C*–O), 70.7 (2×galactose C-5), 71.4 (2×galactose C-3), 101.2 (2×galactose C-1), 115.1 (4× aromatic C *ortho* to O), 119.8 (2×pyridine C-3), 120.6 (2× pyridine C-5), 126.1 (2×aromatic C of phenyl ring between pyridine ring and CH_2–OAr), 126.3 (2×aromatic C *meta* to pyridine ring and CH_2–OAr), 128.2 (2×aromatic *para* to pyridine ring), 129.0 (2×aromatic C *para* to CH_2–OAr), 129.5 (4×aromatic C *meta* to O), 134.0 (2×quaternary aromatic C *para* to O), 138.2 (2×quaternary aromatic C bound to CH_2–OAr, and 2×pyridine C-4), 138.5 (2× quaternary C bound to pyridine ring), 156.8 (2×quaternary aromatic C bound to O),157.0 (4×pyridine C-2 and C-6), 170.0 (4×C=O), 171.0 (4×C=O); MS-ESI$^+$: *m*/*z* 1297 $[M+H]^+$, 1319 $[M+Na]^+$.

4.4.4. 6,6′-Bis-[3-[*N*-2-[(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranosyl]-ethyl]-imminomethyl] phenyl]-2,2′-bipyridine (14). A solution of dialdehyde **8a** (35 mg, 0.09 mmol) and amine **2** (241 mg, 0.61 mmol) in a mixture of CH_2Cl_2 (14 mL) and MeOH (3.5 mL) was stirred overnight at room temperature. The solvent was then evaporated under vacuum and water (2 mL) and Et_2O (10 mL) were then added. The organic phase was separated and the aqueous phase was extracted with Et_2O (2×10 mL). The combined organic phases were dried over sodium sulfate. Filtration and evaporation of the solvent under vacuum, afforded the product **14** as a light brown solid (87 mg, 0.081 mmol, 90% yield) that softened into a very thick oil when heated at 48 °C and remained like that up to 220 °C. (Found: C, 60.2; H, 5.5; N, 5.3. $C_{56}H_{62}N_4O_{20}$ requires C, 60.5; H, 5.6; N, 5.0%); $[\alpha]_D^{22}$ +2.3 (*c* 0.4 in CH_2Cl_2); IR: ν_{max}(CH_2Cl_2)/ cm^{-1} 2925, 1747, 1651, 1370, 1226, 1060; ^1H NMR (CD_3CN): δ 1.97 (6H, s, Me), 2.07 (12H, s, Me), 2.16 (6H, s, Me), 3.75–3.84 (2H, m, one H of NCH_2CH_2O), 3.89–3.97 (6H, m, galactose H-5, one H of NCH_2CH_2O, and one H of NCH_2CH_2O), 4.12–4.22 (6H, m, one hydrogen of NCH_2-CH_2O and galactose H-6), 4.56 (2H, d, J=8.0 Hz, galactose H-1), 5.00 (2H, dd, J=3.5, 11.5 Hz, galactose H-3), 5.20 (2H, dd, J=8.0, 11.5 Hz, galactose H-2), 5.50 (2H, br s, galactose H-4), 7.60 (2H, t, J=7.7 Hz, aromatic H *meta* to pyridine ring), 7.86 (2H, dt, J=1.1, 7.7 Hz, aromatic H *para* to pyridine ring), 7.89 (2H, dd, J=0.8, 7.2 Hz, pyridine H-5), 7.98 (2H, t, J=7.2 Hz, pyridine H-4), 8.33 (2H, dt, J=1.1, 7.7 Hz, aromatic H *para* to CH=N), 8.42 (2H, s, CH=N), 8.50 (2H, t, J=1.1 Hz, aromatic H *ortho* to CH=N and *ortho* to pyridine ring), 8.66 (2H, dd, J=0.8, 7.2 Hz, pyridine H-3); ^{13}C NMR (CD_3CN): δ 20.3 (2×Me), 20.5 (2×Me), 20.6 (4×Me), 60.5 (2×CH_2–N), 61.2 (2× galactose C-6), 67.0 (2×galactose C-4), 68.6 (2×galactose C-2), 68.9 (2×CH_2–O–galactose C-1), 70.6 (2×galactose C-5), 70.8 (2×galactose C-3), 101.3 (2×galactose C-1), 119.9 (2×pyridine C-3), 120.4 (2×pyridine C-5), 126.8 (2×aromatic C between pyridine ring and CH=N), 128.5 (2×aromatic C *para* to pyridine ring), 129.0 (2×aromatic C *meta* to pyridine ring and *meta* to CH=N), 129.3 (2× aromatic C *para* to CH=N), 136.4 (2×quaternary C bound to CH=N), 137.7 (2×pyridine C-4), 139.7 (2×aromatic C bound to pyridine ring), 155.5 (2×pyridine C-6), 155.8 (2×pyridine C-2), 163.3 (2×CH=N), 170.0 (4×C=O),

170.1 (2×C═O), 170.3 (2×C═O); MS-ESI$^+$: *m/z* 1111 $[M+H]^+$, 1133 $[M+Na]^+$.

4.4.5. 2″,6-Bis-[2-[4-[(2,3,4,6-*O*-tetracetyl)-β-D-galactopyranosyl]-phenyl]-ethynyl]-2,2′:6′,6″-terpyridine (15). In a stirred mixture of dry THF (4.6 mL) and diisopropylamine (3.1 mL) kept under a nitrogen atmosphere, terpyridine **10** (63 mg, 0.22 mmol) and iodide **4** (260 mg, 0.47 mmol) were added. After 10 min stirring at room temperature, $PdCl_2(PPh_3)_2$ (5 mg, 0.007 mmol) and CuI (4 mg, 0.02 mmol) were added in this order. The mixture was refluxed for 24 h. Evaporation of the solvent under vacuum afforded a residue that was purified by flash chromatography with a 50:50 hexane/ethyl acetate mixture as eluant to give **15** as a light brown solid (150 mg, 0.13 mmol, 60%) that softened into a very thick oil when heated at 145 °C and remained like that up to 220 °C. (Found: C, 62.6; H, 4.6; N, 4.0. $C_{59}H_{55}N_3O_{20}$ requires C, 62.9; H, 4.9; N, 3.7%); $[\alpha]_D^{22}$ +11.0 (*c* 0.4 in CH_2Cl_2); IR: $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2936, 2220, 1752, 1229, 1077; ^{1}H NMR (CD_3OD): δ 2.00 (6H, s, Me), 2.08 (6H, s, Me), 2.07 (6H, s, Me), 2.09 (6H, s, Me), 4.20 (4H, d, J=6.4 Hz, galactose H-6), 4.14 (2H, t, J=6.4 Hz, galactose H-5), 5.30 (2H, dd, J=3.2, 10.0 Hz, galactose H-3), 5.35–5.45 (4H, m, galactose H-1 and H-2), 5.50 (2H, d, J=3.2 Hz, galactose H-4), 7.10 (4H, A part of an AB system, J=8.8 Hz, aromatic H *ortho* to O), 7.55–7.65 (6H, m, terpyridine H-5 and H-3″, and aromatic H *meta* to O), 7.98 (2H, t, J=7.9 Hz, terpyridine H-4 and H-4″), 8.08 (1H, t, J=7.9 Hz, terpyridine H-4′), 8.47 (2H, d, J=7.9 Hz, terpyridine H-3′ and H-5′), 8.57 (2H, d, J=7.9 Hz, terpyridine H-3 and H-5″); ^{13}C NMR (CD_3OD): 20.5 (8×Me), 61.0 (2×galactose C-6), 66.8 (2×galactose C-4), 68.5 (2×galactose C-2), 70.7 (2×galactose C-3), 71.2 (2×galactose C-5), 88.2 (4×acetylenic C), 99.0 (2×galactose C-1), 116.8 (4×aromatic C *ortho* to O and 2×quaternary phenyl *C* bound to acetylenic C), 120.6 (2×terpyridine C-3 and C-5″), 121.8 (2×terpyridine C-3′ and C-5′), 127.4 (2×terpyridine C-5 and C-3″), 133.2 (4×aromatic C *meta* to O), 137.6 (2×terpyridine C-4 and C-4″), 138.1 (1×terpyridine C-4′), 143.0 (2×terpyridine C-6 and C-2″), 155.0 (2×terpyridine C-2′ and C-6′), 156.7 (2×terpyridine C-2 and C-6″), 158.0 (2×aromatic C bound to O), 170.5 (8×C═O); MS-ESI$^+$: *m/z* 1126 $[M+H]^+$.

4.5. Deprotection of the acetylated ligands 11-14 to polyols 16-19

General procedure. A solution of ligand (typical amount 0.015 mmol) in 0.1 M MeONa in MeOH (2 mL, 0.2 mmol) was stirred overnight under nitrogen. The solvent was evaporated under vacuum from the resulting suspension, and the residue was shaken with water (2 mL) for 3 h. The solid was filtered and washed with water until the filtered water was neutral. All the crude products obtained by filtration were insoluble in most organic solvents and soluble in DMSO. The solubility in MeOH was enough to record NMR spectra on very diluted solutions of these compounds. ^{1}H NMR (CD_3OD) showed the presence of large but difficult to determine amount of water in the samples. Satisfactory analytical data could not be obtained.

4.5.1. 6,6′-Bis-[4-[3-(β-D-galactopyranosyl)-prop-1-yl]-phenyloxymethyl]-2,2′-bipyridine (16). White solid. ^{1}H NMR (CD_3OD): δ 1.91 (4H, quintet, J=7.0 Hz, CH_2CH_2-CH_2O), 2.68 (4H, t, J=7.0 Hz, $CH_2CH_2CH_2O$), 3.45–3.60 (6H, m, galactose H-5, H-2, and H-3), 3.57 (2H, A part of an AB system, J=6.4, 9.7 Hz, one H of $CH_2CH_2CH_2O$), 3.74 (4H, AB system, J=6.0 Hz, galactose H-6), 3.85 (2H, d, J=3.4 Hz, galactose H-4), 3.92 (2H, B part of an AB system, J=6.4, 9.7 Hz, one H of $CH_2CH_2CH_2O$), 4.22 (2H, d, J=7.4 Hz, galactose H-1), 5.27 (4H, s, $PyCH_2O$), 6.97 (4H, A part of an AB system, J=8.5 Hz, aromatic H *ortho* to O), 7.17 (4H, B part of an AB system, J=8.5 Hz, aromatic H *meta* to O), 7.60 (2H, d, J=7.6 Hz, pyridine H-5), 7.94 (2H, t, J=7.6 Hz, pyridine H-4), 8.33 (2H, d, J=7.6 Hz, pyridine H-3); ^{13}C NMR (CD_3OD): δ 31.2 (2×CH_2–*C*–Ar), 31.8 (2×CH_2–*C*–CH_2Ar), 61.4 (2×galactose C-6), 68.9 (2×CH_2 bound to anomeric O), 69.3 (2×galactose C-4), 70.8 (2×Py*C*H_2O), 71.6 (2×galactose C-2), 74.0 (2×galactose C-3), 75.5 (2×galactose C-5), 104.1 (2×galactose C-1), 114.9 (4×aromatic C of phenyl ring *ortho* to O), 120.3 (2×pyridine C-3), 121.7 (2×pyridine C-5), 129.6 (4×aromatic C of phenyl ring *meta* to O), 135.0 (2×quaternary C of phenyl ring bound to CH_2), 138.0 (2×pyrdine C-4), 156.0 (2×pyridine C-2), 156.8 (2×quaternary C of phenyl ring bound to O), 157.7 (2×pyridine C-6); MS-ESI$^+$: *m/z* 831 $[M+Na]^+$. HRMS *m/z* 808.34278.

4.5.2. 6,6′-Bis-[2-[4-(β-D-galactopyranosyl)-phenyl]-ethynyl]-2,2′-bipyridine (17). White solid ^{1}H NMR (CD_3OD): δ 3.63 (2H, dd, J=3.4, 9.8 Hz, galactose H-3), 3.71–3.79 (2H, m, galactose H-5), 3.81 (4H, AB system, J=5.0, 8.0 Hz, galactose H-6), 3.85 (2H, dd, J=7.8, 9.9 Hz, galactose H-2), 3.95 (2H, d, J=3.4 Hz, galactose H-4), 4.97 (2H, d, J=7.8 Hz, galactose H-1), 7.18 (4H, A part of an AB system, J=8.6 Hz, aromatic H *ortho* to O), 7.60 (4H, B part of an AB system, J=8.6 Hz, aromatic H *meta* to O), 7.65 (2H, d, J=7.7 Hz, pyridine H-3), 7.97 (2H, t, J=7.7 Hz, pyridine H-4), 8.35 (2H, d, J=7.7 Hz, pyridine H-5); ^{13}C NMR (CD_3OD): δ 61.0 (2×galactose C-6), 68.8 (2×galactose C-4), 70.8 (2×galactose C-2), 73.4 (2×galactose C-3), 75.7 (2×galactose C-5), 87.2 (2×acetylenic C bound to pyridine), 88.8 (2×acetylenic C bound to ArO), 101.2 (2×galactose C-1), 115. (2×quaternary aromatic C bound to acetylenic C), 116.6 (4×aromatic C *ortho* to O), 120.4 (2×pyridine C-3), 127.1 (2×pyridine C-5), 133.1 (4×aromatic C *meta* to O), 137.5 (2×pyridine C-4), 143.0 (2×pyridine C-6), 155.0 (2×pyridine C-2),158.0 (2×quaternary aromatic C bound to O); MS-ESI$^+$: *m/z* 735 $[M+Na]^+$. HRMS *m/z* 712.22595.

4.5.3. 6,6′-Bis-[3-[4-[3-(β-D-galactopyranosyl)-prop-1-yl]-phenyloxymethyl]phenyl]-2,2′-bipyridine (18). White solid. ^{1}H NMR (CD_3OD): δ 1.91 (4H, quintet, J=8.0 Hz, $CH_2CH_2CH_2O$), 2.69 (4H, t, J=8.0 Hz, $CH_2CH_2CH_2O$), 3.45–3.60 (6H, m, galactose H-3, H-5, and H-2), 3.57 (2H, A part of an AB system, J=8.0, 9.8 Hz, one H of $CH_2CH_2CH_2O$), 3.76 (4H, d, J=6.6 Hz, galactose H-6), 3.86 (2H, d, J=3.5 Hz, galactose H-4), 3.92 (2H, B part of an AB system, J=8.0, 9.8 Hz, one H of $CH_2CH_2CH_2O$), 4.22 (2H, d, J=7.6 Hz, galactose H-1), 5.20 (4H, s, $ArCH_2O$), 6.98 (4H, A part of an AB system, J=8.6 Hz, aromatic H *ortho* to O), 7.18 (4H, B part of an AB system, J=8.6 Hz, aromatic H *meta* to O), 7.55 (4H, d, J=5.1 Hz,

aromatic H *para* to CH_2OAr and aromatic H *para* to pyridine ring), 7.95 (2H, d, $J=7.8$ Hz, pyridine H-5), 8.03 (2H, t, $J=7.8$ Hz, pyridine H-4), 8.16 (2H, t, $J=5.1$ Hz, aromatic H *meta* to pyridine ring), 8.31 (2H, br s, aromatic H between pyridine ring and CH_2OAr), 8.55 (2H, d, $J=7.8$ Hz, pyridine H-3); ^{13}C NMR (CD_3OD): δ 30.9 (2× CH_2–*C*–Ar), 31.4 (2×CH_2–*C*–CH_2), 61.1 (2×galactose C-6), 68.6 (2×CH_2–CH_2–*C*), 69.0 (2×galactose C-4), 69.8 (2×Ar–*CH_2*–O), 71.3 (2×galactose C-2), 73.7 (2× galactose C-3), 75.2 (2×galactose C-5), 103.0 (2× galactose C-1), 114.7 (4×aromatic C *ortho* to O), 119.4 (2×pyridine C-3), 120.2 (2×pyridine C-5), 125.8 (2× aromatic C between pyridine ring and CH_2OAr), 126.0 (2×aromatic C *meta* to pyridine ring and CH_2OAr), 128.0 (2×aromatic C *para* to pyridine ring), 128.5 (2×aromatic C *para* to CH_2OAr), 129.1 (4×aromatic C *meta* to O), 135.0 (2×quaternary aromatic C *para* to O), 137.7 (2× pyridine C-4), 138.0 (2×s, quaternary aromatic C *meta* to pyridine ring), 156.0 (4×pyridine C-2 and C-6) and 157.5 (2×quaternary aromatic C bound to O); MS-ESI$^+$: *m/z* 983 $[M+Na]^+$. HRMS *m/z* 960.40331.

4.5.4. 6,6′-Bis-[3-[*N*-2-(β-D-galactopyranosyl)-ethyl]-imminomethyl]-phenyl]-2,2′-bipyridine (19). White solid. ^1H NMR (CD_3OD): δ 3.41–3.60 (6H, m, galactose H-2, H-3, and H-5), 3.72–3.78 (4H, m, galactose H-6), 3.85 (2H, br d, $J=3.0$ Hz, galactose H-4), 3.90–4.00 (6H, m, N*CH_2*CH_2O and one H of NCH_2*CH_2*O), 4.20–4.30 (2H, m, one H of NCH_2*CH_2*O), 4.35 (2H, d, $J=8.0$ Hz, galactose H-1), 7.63 (2H, t, $J=7.8$ Hz, aromatic H *meta* to pyridine ring and *meta* to CH=N), 7.85 (2H, d, $J=7.7$ Hz, aromatic H *para* to pyridine ring), 8.01 (2H, d, $J=7.2$ Hz, pyridine H-5), 8.06 (2H, t, $J=7.2$ Hz, pyridine H-4), 8.34 (2H, d, $J=7.8$ Hz, aromatic H *para* to CH=N), 8.57 (2H, s, *CH*=N), 8.65 (2H, br s, aromatic C between pyridine ring and CH=N), 8.76 (2H, d, $J=7.2$ Hz, pyridine H-3); ^{13}C NMR (CD_3OD): δ 60.3 (2×*CH_2*–N), 61.2 (2×galactose C-6), 68.8 (2×N–CH_2*CH_2*–O), 69.1 (2×galactose C-4), 71.2 (2×galactose C-2), 73.6 (2×galactose C-3), 75.3 (2× galactose C-5), 103.8 (2×galactose C-1), 119.7 (2× pyridine C-3), 120.2 (2×pyridine C-5), 126.3 (2×aromatic C between pyridine ring and CH=N), 128.8 (4×aromatic C *para* to pyridine ring and aromatic C *meta* to pyridine ring and *meta* to CH=N), 129.2 (2×aromatic C *para* to CH=N), 136.2 (2×quaternary aromatic C bound to CH=N), 137.9 (2×pyridine C-4), 139.7 (2×quaternary aromatic C bound to pyridine ring), 155.5 (2×pyridine C-2), 156.0 (2×pyridine C-6), 164.8 (2×CH=N); MS-ESI$^+$: *m/z* 797 $[M+Na]^+$. HRMS *m/z* 774.31085.

4.6. Synthesis of Cu(I) and Zn(II) complexes

4.6.1. Synthesis of the Cu(I) complexes. *General procedure*. To a stirred solution of ligand (typical amount 0.01 mmol) in $CHCl_3$ (0.5 mL), kept under nitrogen at room temperature, $CuOTf\cdot 0.5C_6H_6$ (0.36 mL of a 0.01 M solution in acetonitrile, 0.005 mmol) was added. The red solution was stirred at room temperature for 24 h. The solvent was then evaporated under vacuum to afford a red solid that was purified by a filtration on a short column of silica gel for flash chromatography with a 95:5 CH_2Cl_2/MeOH mixture as eluant (when attempted, this purification degraded complex **Cu(14)$_2$** that was isolated as crude product). In all cases the recovery of the complex was virtually quantitative.

Compound **Cu(11)$_2$**. Red solid. ^1H NMR (CD_3OD): δ 1.75–1.86 (8H, m, 2×CH_2*CH_2*CH_2O), 1.98 (12H, s, Me), 2.01 (12H, s, Me), 2.07 (12H, s, Me), 2.16 (12H, s, Me), 2.45–2.61 (8H, m, *CH_2*CH_2CH_2O), 3.52 (4H, A part of an AB system, $J=6.0$, 10.0 Hz, one H of CH_2CH_2*CH_2*O), 3.82 (4H, B part of an AB system, $J=6.0$, 10.0 Hz, H of CH_2CH_2*CH_2*O), 4.06–4.22 (12H, m, galactose H-5 and H-6), 4.64 (4H, d, $J=7.8$ Hz, galactose H-1), 4.82 (8H, s, 2×Ar*CH_2*O), 5.08–5.19 (8H, m, galactose H-2 and H-3), 5.41 (4H, br s, galactose H-4), 6.25 (8H, A part of an AB system, $J=8.3$ Hz, aromatic H *ortho* to O), 6.80 (8H, B part of an AB system, $J=8.3$ Hz, aromatic H *meta* to O), 7.78 (4H, d, $J=7.6$ Hz, pyridine H-5), 8.09 (4H, t, $J=7.6$ Hz, pyridine H-4), 8.20 (4H, d, $J=7.6$ Hz, pyridine H-3); ^{13}C NMR (CD_3OD): δ 19.0 (8×Me), 19.4 (8×Me), 30.3 (4× Ar–*C*–CH_2), 31.3 (4×CH_2–*C*–CH_2), 61.1 (4×galactose C-6), 67.4 (4×galactose C-4), 68.4 (4×CH_2 bound to anomeric O), 69.2 (4×galactose C-2), 70.3 (4×galactose C-5), 70.4 (4×ArO–*CH_2*), 70.9 (4×galactose C-3), 100.8 (4×galactose C-1), 113.2 (8×aromatic C *ortho* to O), 121.4 (4×pyridine C-3), 125.7 (4×pyridine C-5), 128.9 (8×aromatic C *meta* to O), 134.3 (4×quaternary aromatic C *para* to O), 138.9 (4×pyridine C-4), 151.5 (4×pyridine C-2), 155.0 (4×pyridine C-6), 155.8 (4×quaternary aromatic C bound to O), 169.9 (8×C=O), 170.5 (8× C=O); MS-FAB: *m/z* 2353 $[M-OTf]^+$; HRMS *m/z* 2351.79451 $[M-OTf]^+$.

Compound **Cu(12)$_2$**. Red solid. ^1H NMR (CD_3OD): δ 2.00 (12H, s, Me), 2.06 (12H, s, Me), 2.08 (12H, s, Me), 2.21 (12H, s, Me), 4.20–4.26 (8H, m, galactose H-6), 4.34 (4H, t, $J=6.5$ Hz, galactose H-5), 5.25–5.41 (12H, m, galactose H-3, H-2, and H-1), 5.51 (4H, d, $J=3.2$ Hz, galactose H-4), 6.73 (8H, A part of an AB system, $J=8.7$ Hz, aromatic H *meta* to O), 6.85 (8H, B part of an AB system, $J=8.6$ Hz, aromatic H *meta* to O), 7.77 (4H, d, $J=7.6$ Hz, pyridine H-5), 8.00 (4H, t, $J=7.8$ Hz, pyridine H-4), 8.12 (4H, d, $J=8.0$ Hz, pyridine H-3); ^{13}C NMR (CD_3OD): δ 19.1 (8×Me), 19.3 (8×Me), 61.1 (4×galactose C-6), 67.3 (4×galactose C-4), 68.7 (4×galactose C-2), 70.7 (4×galactose C-3), 70.9 (4×galactose C-5), 86.4 (4×acetylenic C bound to pyridine), 92.0 (4×acetylenic C bound to phenyl ring), 98.0 (4×galactose C-1), 115.0 (4×quaternary aromatic C bound to acetylenic C), 116.3 (8×aromatic C *ortho* to O), 121.1 (4×pyridine C-3), 128.4 (4×pyridine C-5), 132.5 (8× aromatic C *meta* to O), 137.7 (4×pyridine C-4), 141.4 (4×pyridine C-6), 151.6 (4×pyridine C-2), 157.5 (4×aromatic C bound to O), 169.8 (4×C=O), 170.0 (4×C=O), 170.5 (4×C=O), 170.6 (2×C=O); MS-FAB: *m/z* 2161 $[M-OTf]^+$; HRMS *m/z* 2159.56450 $[M-OTf]^+$.

Compound **Cu(13)$_2$**. Red solid. ^1H NMR (CD_3OD): δ 1.71 (8H, quintet, $J=6.5$ Hz, CH_2*CH_2*CH_2O), 1.95 (12H, s, Me), 1.99 (12H, s, Me), 2.00 (12H, s, Me), 2.14 (12H, s, Me), 2.47 (8H, t, $J=6.5$ Hz, *CH_2*CH_2CH_2O), 3.43 (4H, A part of an AB system, $J=6.5$, 9.8 Hz, one H of CH_2CH_2*CH_2*O), 3.75 (4H, B part of an AB system, $J=6.5$, 9.8 Hz, one H of CH_2CH_2*CH_2*O), 4.04 (4H, q, $J=6.2$ Hz, galactose H-5), 4.12 (8H, AB system, $J=3.6$, 6.2 Hz, galactose H-6), 4.39

(8H, s, ArCH_2O), 4.53 (4H, d, J=7.8 Hz, galactose H-1), 5.02–5.13 (8H, m, galactose H-2 and H-3), 5.38 (4H, br s, galactose H-4), 6.36 (8H, A part of an AB system, J=8.6 Hz, aromatic H *ortho* to OCH_2Ar), 6.83 (8H, B part of an AB system, J=8.6 Hz, aromatic H *meta* to OCH_2Ar), 7.03–7.09 (8H, m, aromatic H of phenyl ring in *meta* and *para* position to pyridine ring), 7.24 (8H, d, J=6.7 Hz, aromatic H of phenyl ring *para* to CH_2OAr), 7.38 (8H, d, J=7.7 Hz, pyridine H-5), 7.75 (4H, t, J=7.7 Hz, pyridine H-4), 7.97 (4H, d, J=7.7 Hz, pyridine H-3), 8.06 (4H, br s, aromatic H of phenyl ring between pyridine and CH_2OAr); ^{13}C NMR (CD_3OD): δ 19.5 (12×Me), 19.8 (4×Me), 30.8 (4×Ar–*C*–CH_2), 31.6 (4×CH_2*C*–CH_2), 61.5 (4×galactose C-6), 67.8 (4×galactose C-4), 68.6 (4×Ar–*C*–O), 68.8 (4×CH_2 bound to anomeric O), 69.6 (4×galactose C-2), 70.7 (4×galactose C-5), 71.4 (4×galactose C-3), 101.2 (4×galactose C-1), 114.5 (8×aromatic C *ortho* to O), 121.3 (4×pyridine C-3), 125.2 (4×pyridine C-5), 125.6 (4×aromatic C between pyridine and CH_2OAr), 127.3 (4×aromatic C *meta* to CH_2OAr), 127.5 (4×aromatic C *para* to pyridine), 128.1 (4×aromatic C *ortho* to pyridine and *para* to CH_2OAr), 129.2 (4×aromatic C *meta* to O), 134.0 (4×quaternary aromatic C *para* to O), 137.4 (4×quaterrnary C bound to CH_2OAr), 138.2 (4×pyridine C-4), 139.0 (4×quaternary aromatic C bound to pyridine), 153.3 (4×pyridine C-2), 156.9 (4×aromatic C bound to O, and 4×pyridine C-6), 170.5 (8×C=O), 171.0 (8×C=O); MS-FAB: *m/z* 2658 $[M-OTf]^+$; HRMS *m/z* 2655.91478 $[M-OTf]^+$.

Compound **Cu(14)$_2$**. Red solid. ^{1}H NMR (CD_3CN): δ 1.80 (12H, s, Me), 1.89 (12H, s, Me), 1.98 (12H, s, Me), 1.99 (12H, s, Me), 3.46–3.57 (4H, m, one H of N*C*$H_2$$CH_2O$), 3.80–3.96 (8H, m, one H of N*C*$H_2$$CH_2O$, and one hydrogen of NCH_2*C*H_2O), 4.02–4.12 (12H, m, galactose H-6 and one hydrogen of NCH_2*C*H_2O), 4.48 (4H, d, J=7.8 Hz, galactose H-1), 4.90–5.02 (12H, m, galactose H-2, H-3, and H-5), 5.28 (4H, br s, galactose H-4), 7.14 (4H, t, J=7.5 Hz, aromatic H *meta* to pyridine), 7.36 (4H, d, J=7.5 Hz, aromatic H *para* to pyridine), 7.58 (4H, d, J=7.5 Hz, aromatic H *para* to CH=N), 7.65 (4H, d, J=7.0 Hz, pyridine H-5), 7.72 (4H, br s, CH=N), 7.95–8.04 (8H, m, pyridine H-4 and H-3), 8.21 (4H, br s, aromatic H between CH=N and pyridine ring); ^{13}C NMR (CD_3CN): δ 19.7 (8×Me), 19.8 (8×Me), 60.0 (4×NCH_2), 61.2 (4×galactose C-6), 67.3 (4×galactose C-4), 68.7 (4×galactose C-2), 69.1 (4×CH_2 bound to anomeric O), 70.5 (8×galactose C-3 and C-5), 100.8 (4×galactose C-1), 121.5 (4×pyridine C-3), 124.8 (4×pyridine C-5), 126.4 (4×aromatic C between pyridine ring and CH=N), 128.0 (4×aromatic C *meta* to pyridine ring), 128.8 (4×aromatic *para* to pyridine ring), 130.4 (4×aromatic C *para* to CH=N), 135.5 (4×quaternary aromatic C bound to CH=N), 138.2 (4×pyridine C-4), 138.7 (4×quaternary aromatic C bound to pyridine ring), 152.8 (4×pyridine C-2), 156.0 (4×pyridine C-6), 161.1 (4×CH=N), 169.7 (8×C=O), 170.0 (8×C=0); MS-FAB: *m/z* 2284 $[M\text{-}OTf]^+$; HRMS *m/z* 2283.73221 $[M-OTf]^+$.

4.6.2. Deprotection of the acetylated complexes Cu(11)$_2$, Cu(12)$_2$, and Cu(14)$_2$ to Cu(16)$_2$, Cu(17)$_2$, and Cu(19)$_2$. This was performed following the procedure described above for the deprotection of the acetylated ligands.

Compound **Cu(16)$_2$**. Red solid. ^{1}H NMR (CD_3OD): δ 1.83–190 (8H, m, CH_2*C*$H_2$$CH_2O$), 2.56 (8H, t, J=7.4 Hz, *C*$H_2$$CH_2$*C*$H_2$O), 3.47–3.60 (16H, m, galactose H-3, galactose H-5, galactose H-2, and one H of CH_2CH_2*C*H_2O), 3.77 (8H, d, J=6.0 Hz, galactose H-6), 3.88 (4H, d, J=3.3 Hz, galactose H-4), 3.90 (4H, B part of an AB system, J=6.4, 9.7 Hz, one H of CH_2CH_2*C*H_2O), 4.25 (4H, d, J=7.7 Hz, galactose H-1), 4.80 (8H, s, PyCH_2O), 6.22 (8H, A part of an AB system, J=8.5 Hz, aromatic H *ortho* to O), 6.81 (8H, B part of an AB system, J=8.5 Hz, aromatic H *meta* to O), 7.76 (4H, d, J=8.1 Hz, pyridine H-3), 8.08 (4H, t, J=8.1 Hz, pyridine H-4), 8.18 (4H, d, J=8.1 Hz, pyridine H-5); ^{13}C NMR (CD_3OD): δ 30.6 (4×CH_2–*C*–Ar), 31.5 (4×CH_2–*C*–CH_2), 61.1 (4×galactose C-6), 68.5 (4×CH_2–CH_2–*C*–O), 68.9 (4×galactose C-4), 70.5 (4×Py*C*H_2O), 71.2 (4×galactose C-2), 73.7 (4×galactose C-3), 75.3 (4×galactose C-5), 103.7 (4×galactose C-1), 113.0 (8×aromatic C *ortho* to O), 121.5 (4×pyridine C-3), 125.8 (4×pyridine C-5), 128.9 (8×aromatic H *meta* to O), 134.7 (4×quaternary aromatic C *para* to O), 139.0 (4×pyridine C-4), 151.6 (4×pyridine C-2), 155.0 (4×pyridine C-6), 155.8 (4×quaternary aromatic C bound to O); MS-ESI$^+$: *m/z* 1679 $[M-OTf]^+$; HRMS *m/z* 1679.61973 $[M-OTf]^+$.

Compound **Cu(17)$_2$**. Red solid. ^{1}H NMR (CD_3OD): δ 3.63 (4H, dd, J=3.4, 9.6 Hz, galactose H-3), 3.79–3.90 (16H, m, galactose H-5, H-6, and H-2), 3.95 (4H, d, J=3.0 Hz, galactose H-4), 4.90 (4H, d, J=7.7 Hz, galactose H-1), 6.70 (8H, A part of an AB system, J=8.6 Hz, aromatic H *ortho* to O), 6.90 (8H, B part of an AB system, J=8.6 Hz, aromatic H *meta* to O), 7.71 (4H, d, J=7.5 Hz, pyridine H-3), 7.96 (4H, t, J=7.7 Hz, pyridine H-4), 8.08 (4H, d, J=7.7 Hz, pyridine H-5); ^{13}C NMR (CD_3OD): δ 61.3 (4×galactose C-6), 68.9 (4×galactose C-4), 70.6 (4×galactose C-2), 73.4 (4×galactose C-3), 75.8 (4×galactose C-5), 86.2 (4×acetylenic C bound to pyridine ring), 92.2 (4×acetylenic C bound to phenyl ring), 100.9 (4×galactose C-1), 109.0 (4×quaternary aromatic C bound to acetylenic carbon), 116.2 (8×aromatic C *ortho* to O), 121.0 (4×pyridine C-3), 128.0 (4×pyridine C-5), 132.3 (8×aromatic C *meta* to O), 137.6 (4×pyridine C-4), 143.0 (4×pyridine C-6), 152.0 (4×pyridine C-2), 158.0 (4×quaternary aromatic C bound to O); MS-ESI$^+$: *m/z* 1487 $[M-OTf]^+$; HRMS *m/z* 1487.39145 $[M-OTf]^+$.

Compound **Cu(19)$_2$**. Red solid. ^{1}H NMR (CD_3OD): δ 3.35–3.58 (20H, m, galactose H-3, H-5, and H-2, and N*C*$H_2$$CH_2$-O), 3.65–3.80 (12H, m, one hydrogen of NCH_2*C*H_2O and galactose H-6), 3.87 (4H, d, J=3.0 Hz, galactose H-4), 3.90–4.10 (4H, m, one hydrogen of NCH_2*C*H_2O), 4.21 (4H, d, J=7.2 Hz, galactose H-1), 7.11 (4H, t, J=7.8 Hz, aromatic H *meta* to pyridine ring and *meta* to CH=N), 7.45 (4H, d, J=7.8 Hz, aromatic H *para* to pyridine ring), 7.61 (4H, d, J=7.8 Hz, aromatic H *para* to CH=N), 7.73 (4H, d, J=7.2 Hz, pyridine H-3), 7.82 (4H, s, CH=N), 8.03–8.20 (12H, m, pyridine H-4 and H-5, and aromatic H between pyridine ring and CH=N); ^{13}C NMR (CD_3OD): δ 60.0 (4×CH_2–N), 61.1 (4×galactose C-6), 68.6 (4×CH_2*C*H_2–O), 68.8 (4×galactose C-4), 71.0 (4×galactose C-2), 73.5 (4×galactose C-3), 75.2 (4×galactose C-5), 103.7 (4×galactose C-1), 121.6 (4×pyridine C-3), 124.9 (4×pyridine C-5), 127.1 (4×aromatic C between pyridine

ring and CH=N), 127.9 (4×aromatic C *para* to pyridine ring), 128.4 (4×aromatic C *meta* to pyridine ring and *meta* to CH=N), 130.4 (4×aromatic C *para* to CH=N), 135.1 (4×aromatic C bound to CH=N), 138.6 (4×pyridine C-4), 138.9 (4×quaternary aromatic C bound to pyridine ring), 152.7 (4×pyridine C-2), 156.1 (4×pyridine C-6), 162.7 (4×CH=N); MS-ESI$^+$: *m/z* 1611 $[M-OTf]^+$; HRMS *m/z* 1611.56120 $[M-OTf]^+$.

4.6.3. Synthesis of the Zn(15) complex. To a stirred solution of ligand **15** (30 mg, 0.026 mmol) in $CHCl_3$ (0.5 mL), kept under nitrogen at room temperature, $Zn(OTf)_2$ (9.6 mg, 0.026 mmol) was added. The solution was stirred at room temperature for 15 h. The solvent was then evaporated under vacuum to afford a pale yellow solid in quantitative yield. ^{1}H NMR (CD_3OD): δ 2.02 (6H, s, Me), 2.08 (6H, s, Me), 2.09 (6H, s, Me), 2.23 (6H, s, Me), 4.25 (4H, d, $J=6.4$ Hz, galactose H-6), 4.39 (2H, t, $J=6.4$ Hz, galactose H-5), 5.32 (2H, dd, $J=3.2$, 10.0 Hz, galactose H-3), 5.46–5.58 (4H, m, galactose H-1 and H-2), 5.53 (2H, d, $J=3.2$ Hz, galactose H-4), 6.93 (4H, A part of an AB system, $J=8.7$ Hz, aromatic H *meta* to O), 7.04 (4H, B part of an AB system, $J=8.7$ Hz, aromatic H *ortho* to O), 7.56 (1H, t, $J=7.9$ Hz, terpyridine H-4′), 7.75 (2H, d, $J=7.9$ Hz, terpyridine H-5 and H-3″), 8.17 (2H, d, $J=7.9$ Hz, terpyridine H-3′ and H-5′), 8.24 (2H, t, $J=7.9$ Hz, terpyridine H-4 and H-4″), 8.55 (2H, d, $J=7.9$ Hz, pyridine H-3 and H-5″); ^{13}C NMR (CD_3OD): δ 19.1 (4×Me), 19.2 (4×Me), 61.0 (2×galactose C-6), 67.2 (2×galactose C-4), 68.6 (2×galactose C-2), 70.7 (2×galactose C-3), 71.0 (2×galactose C-5), 83.7 (2×acetylenic C bound to terpyridine), 94.9 (2×acetylenic C bound to phenyl), 98.0 (2×galactose C-1), 114.3 (2×quaternary phenyl *C* bound to acetylene), 116.6 (4×aromatic C *ortho* to O), 122.2 (2×terpyridine C-3 and C-5″), 124.1 (2×terpyridine C-3′ and C-5′), 132.3 (2×terpyridine C-5 and C-3″), 133.1 (4×aromatic C *meta* to O), 141.1 (2×pyridine C-4 and C-4″), 142.8 (2×pyridine C-6 and C-2″), 142.9 (1×pyridine C-4′), 149.7 (2×pyridine C-2′ and C-6′), 149.9 (2×pyridine C-2 and C-6″), 158.2 (2×aromatic C bound to O), 169.8 (2×C=O), 169.9 (2×C=O), 170.4 (2×C=O), 170.5 (2×C=O); MS-FAB: *m/z* 1339 $[M-OTf]^+$; HRMS *m/z* 1338.21783 $[M-OTf]^+$.

4.6.4. 2″,6-Bis-[2-[4-(β-D-galactopyranosyl)-phenyl]-ethynyl]-2,2′:6′,6″-terpyridine 20. This compound was obtained attempting the deacetylation of **Zn(15)** (see above for condition and isolation). White solid. ^{1}H NMR (DMSO-d_6): δ 3.44 (2H, dd, $J=3.2$, 9.6 Hz, galactose H-3), 3.53-3.68 (8H, m, galactose H-2, H-5, and H-6), 3.74 (2H, d, $J=3.2$ Hz, galactose H-4), 4.93 (2H, d, $J=7.6$ Hz, galactose H-1), 7.13 (4H, A part of AB system, $J=8.7$ Hz, aromatic H *ortho* to O), 7.62 (4H, B part of AB system, $J=8.7$ Hz, aromatic H *meta* to O), 7.74 (2H, d, $J=7.7$ Hz, terpyridine H-5 and H-3″), 8.07 (2H, t, $J=7.8$ Hz, terpyridine H-4 and H-4″), 8.16 (1H, t, $J=7.9$ Hz, terpyridine H-4′), 8.49 (2H, d, $J=7.8$ Hz, terpyridine H-3′ and H-5′), 8.63 (2H, d, $J=8.0$ Hz, terpyridine H-3 and H-5″); ^{13}C NMR (DMSO-d_6): δ (2×galactose C-6), 68.9 (2×galactose C-4), 70.8 (2×galactose C-2), 73.5 (2×galactose C-3), 75.7 (2×galactose C-5), 87.1 (2×acetylenic C bound to terpyridine), 89.0 (2×acetylenic C bound to phenyl), 101.3 (2×galactose C-1), 116.6 (2×quaternary carbon of phenyl ring bound to acetylenic C), 116.7 (4×aromatic C *ortho* to O), 120.3 (2×C-5 and C-3″ of terpyridine), 121.3 (2×C-3′ and C-5′ of terpyridine), 127.5 (2×C-3 and C-5″ of terpyridine), 133.0 (4×aromatic C *meta* to O), 137.4 (2×C-4 and C-4″ of terpyridine), 138.0 (terpyridine C-4′), 143.1 (2×terpyridine C-2 and C-6″), 155.0 (2×terpyridine C-2′ and C-6′), 157.0 (2×terpyridine C-6 and C-2″), 158.0 (2×aromatic C bound to O); MS-ESI$^+$: *m/z* 812 $[M+yNa]^+$.

Acknowledgements

This work was supported by UNIMI, MIUR and CNR. We want to thank professor Anna Bernardi, Universita' di Milano, for helpful suggestions and discussions.

References and notes

1. Lee, Y. C.; Lee, R. T. *Acc. Chem. Res.* **1995**, *28*, 321–327.
2. Mann, D. A.; Kiessling, L. L. The Chemistry and Biology of Multivalent Saccharide Displays. In *Glycochemistry—Principles, Synthesis, and Applications*; Wang, P. G., Bertozzi, C. R., Eds.; Marcel Dekker, 2001; pp 221–275.
3. Lundquist, J. J.; Toone, E. J. *Chem. Rev.* **2002**, *102*, 555–578.
4. For a review on polyvalent interactions in biological systems see: Mammen, M.; Choi, S.-K.; Whitesides, G. M. *Angew. Chem., Int. Ed.* **1998**, *37*, 2754–2794.
5. (a) Sakai, S.; Sasaki, T. *J. Am. Chem. Soc.* **1994**, *116*, 1587–1588. (b) Sakai, S.; Shigemasa, Y.; Sasaki, T. *Tetrahedron Lett.* **1997**, *38*, 8145–8148.
6. Roy, R.; Kim, J. M. *Tetrahedron* **2003**, *59*, 3881–3893.
7. For the synthesis of a bipyridine–desoxyribose conjugate see: Brotschi, C.; Häberli, A.; Leumann, C. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 3012–3014. For a recent paper, on building a carbohydrate cluster see: Kojima, S.; Hasegawa, T.; Yonemura, T.; Sasaki, K.; Yamamoto, K.; Makimura, Y.; Takahashi, T.; Suzuki, T.; Suzuki, Y.; Kobayashi, K. *Chem. Commun.* **2003**, 1250–1252.
8. Amvam-Zollo, P.-H.; Sinaÿ, P. *Carbohydr. Res.* **1986**, *150*, 199–212.
9. Ronald, R. C.; Wheeler, C. J. *J. Org. Chem.* **1984**, *49*, 1658–1660.
10. Rodriguez-Ubis, J. C.; Alpha, B.; Plancherel, D.; Lehn, J.-M. *Helv. Chim. Acta* **1984**, *67*, 2264–2269.
11. Butler, I. R.; Soucy-Breau, C. *Can. J. Chem.* **1991**, *69*, 1117–1123.
12. Khan, M. S.; Al-Mandhary, M. R. A.; Al-Suti, M. K.; Hisahm, A. K.; Raithby, P. R.; Ahrens, B.; Mahon, M. F.; Male, L.; Marseglia, E. A.; Tedesco, E.; Friend, R. H.; Köhler, A.; Feeder, N.; Teat, S. J. *J. Chem. Soc., Dalton Trans.* **2002**, 1358–1368.
13. Puglisi, A.; Benaglia, M.; Roncan, G. *Eur. J. Org. Chem.* **2003**, 1552–1558.
14. Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Montanucci, M. *Synthesis* **1984**, 736–738.
15. See inter alia: (a) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Woods, C. R.; Siegel, J. S. *Eur. J. Org. Chem.* **2001**, 173–180. For a detailed NMR study of the complexes described in Ref. 15a see: (b) Annunziata, R.; Benaglia, M.;

Famulari, A.; Raimondi, L. *Magn. Reson. Chem.* **2001**, *39*, 341–354.

16. It must be noted that ligand **14** contains two additional nitrogen atoms as potentially competing binding sites for Cu(I). It has been shown however, that the imine nitrogens of some imine-bridged olygobipyridine ligands were not involved in the complexation with Cu(I) cations, that occurred exclusively at the bipyridine nitrogens. On the basis of NMR evidence we believe that this is also the case for the complexation of ligand **14**. For a leading reference see: Stiller, R.; Lehn, J.-M. *Eur. J. Inorg. Chem.* **1998**, 977–982.
17. (a) Einstein, F. W. B.; Penfold, B. R. *Acta Crystallogr.* **1966**, *20*, 924–926. (b) Harrison, P. G.; Begley, M. J.; Kikabhai, T.; Killer, F. *J. Chem. Soc., Dalton Trans.* **1986**, 929–938. (c) Roberto, D.; Tessore, F.; Ugo, R.; Bruni, S.; Manfredi, A.; Quici, S. *Chem. Commun.* **2002**, 846–847.
18. Compounds **16**-**19** were scarcely soluble in MeOH and reasonably soluble in DMSO, that was the only solvent for ligand **20**. Analytically pure samples of **16**-**20** could not be obtained.
19. Attempts of running the complexation reaction of **16–20** in DMSO met with no success, probably because of the strongly coordinating nature of this solvent.
20. Complexes $\mathbf{Cu(16)_2}$, $\mathbf{Cu(17)_2}$, and $\mathbf{Cu(19)_2}$ were enough soluble in CD_3OD to obtain NMR data. $\mathbf{Cu(18)_2}$ was insoluble in CD_3OD. When the NMR spectra of these complexes were recorded in DMSO extensive complex decomposition was observed. As in the case of the polyols, from which they formally derive, isolation of analytically pure compounds was not possible. These solubility properties may represent a problem in the biological studies of such a compounds. Studies are currently underway in order to solve this problem.
21. Houseman, B. T.; Mrksich, M. *Chem. Biol.* **2002**, *9*, 443–454 and references therein.
22. Kitano, H.; Sumi, Y.; Tagawa, K. *Bioconjug. Chem.* **2001**, *12*, 56–61 and references therein.
23. For a recent example see: Sansone, F.; Chierici, E.; Casnati, A.; Ungaro, R. *Org. Biomol. Chem.* **2003**, *1*, 1802–1809.