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Synthesis of a small library of bivalent α-D-mannopyranosides for lectin cross-linking

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ABSTRACT

A small library of bivalent α-D-mannopyranosides having rigid linkers was constructed in order to evaluate the effects of inter-saccharide distances upon multivalent binding interactions with plant and bacterial lectins. To this end, iodoaryl and propargyl α-D-mannopyranosides were synthesized and the former treated with TMS-acetylene under palladium chemistry to provide their corresponding ethynylaryl derivatives. A library of 15 dimeric members was then obtained using Lewis acid catalyzed glycosidation, aryl–aryl homocoupling, transition metal catalyzed Sonogashira cross-coupling reactions, and oxidative Glaser homocoupling.

1. Introduction

Carbohydrate–protein interactions are ubiquitous in biological systems,[1] and nature uses multivalent binding strategies to compensate for the commonly low affinity and poor selectivity of carbohydrate ligands.[2–10] This phenomenon has been particularly well documented for soluble proteins (lectins) possessing multiple and often homologous carbohydrate recognition domains (CRDs). For instance, this is mainly the case for the family of galectins, mannose binding proteins, and sialoadhesins that bind to their respective carbohydrate ligands with more or less similar affinity. Toward decoding promiscuous receptor's CRDs against the given families of carbohydrate ligands, it has been observed that combining multivalency together with glycomimetic design could further enhance discrimination and selectivity.[11–15]

Moreover, Sharon has previously demonstrated that bacterial lectins at the tip of fimbriated *Escherichia coli* (FimH) possess subtle but superior affinities for aromatic α-D-mannopyranoside residues, thus illustrating the effect of what was coined 'subsite-assisted aglycone binding'.[16,17] For example, *para*-nitrophenyl and umbelliferyl α-D-mannopyranosides showed 69- to 1015-fold increased inhibitory properties in comparison to methyl α-D-mannopyranoside (MeαMan).[16–18] Additionally, discrete differences can be observed between the inhibitory properties of a given mannoside derivative against different strains of bacteria, thus illustrating again that selectivity is achievable. Using galactoside clusters having similar aromatic aglycones to those described herein for the mannosides, it was also found that a trimeric structure had the highest affinity for galectin-3 while a tetramer was more selective for galectins-1 and -5.[19] These results point toward combining the above strategies for the syntheses of more potent and selective carbohydrate ligands.

Consequently, if one next merges the intrinsic capacities of small mannoside clusters to form discrete macroscopic architectures with paucivalent lectins following variable cross-linking processes, it appears further possible to modulate both thermodynamic and kinetic parameters.[20–29] This report describes various strategies aiming at the synthesis of a small library of mannopyranoside dimers toward their relative lectin cross-linking abilities. The systematic design of a family of divalent mannosylated architectures built around more rigid scaffolds is thus proposed. This small chemical glycolibrary will be useful in pursuing our systematic investigations regarding the functions played by the subtle but critical modulations of structural parameters responsible for high avidity, with specific and tailored presentation of peripheral recognition moieties. By virtue of their flexible scaffolds and linkers, previous glycodendrimers showed negative cooperativity upon binding to lectins as shown by their increasingly contributing entropic loss.[21] Hence, by designing rigidified scaffolds with less flexible conformational and translational mobilities, we aimed at counterbalancing the negative effects observed with flexible scaffolds such as PAMAM, PPI, and polyesters.

2. Results and discussion

In our continued efforts to prepare potent ligands of improved binding selectivity against mannose binding proteins,[30–33] we

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describe herein the syntheses of mannoside dimers having intersaccharidic rigid linkers that were built using palladium(0)-catalyzed cross-coupling Sonogashira reactions[34] and oxidative copper-catalyzed alkyne homocoupling (Glaser reaction).[35]

The initial methodology followed for the synthesis of the dimer library was based on the Lewis-acid promoted O-glycosidation of **1** using various diols (Scheme 1). Giovenzena et al.[36] reported the synthesis of 2-butyne-1,4-di-yl glucoside from 2-butyne-1,4-diol promoted by trimethylsilyltriflate. A yield of 34% was reported for the β-anomer. Reacting peracetylated mannose and bisphenol A gave the α-anomer **3** in 49% yield. Mannoside **6** was obtained in 59% yield using 2-butyne-1,4-diol, accompanied by 35% of the O-peracetylated starting material.[25,32,33] Given the moderate yields obtained with the Lewis acid-catalyzed reactions, we next turned our attention to alternative procedures.

In order to produce suitable building blocks, mannose pentaacetate (**1**) was first treated with the corresponding iodophenols and boron trifluoride etherate in methylene chloride to provide key monomeric building blocks *para*- (**8**),[30] *ortho*- (**9**), and *meta*- (**10**) iodophenyl α-D-mannopyranosides in 76–96%,[37] 36%, and 63% yield, respectively (Scheme 2). Propargyl α-D-mannopyranoside **11** was also prepared in 76–95% yield by a Lewis acid-catalyzed reaction between mannose pentaacetate (**1**) and propargyl alcohol.[30–33,38]

To further expand the family of building blocks required for a versatile library construction, the synthesis of symmetrical dimers was initiated. Thus, cross-coupling of **8** with (trimethylsilyl)acetylene using palladium(0) catalysis, followed by the removal of the silyl-protecting group with TBAF under buffered conditions (HOAc) in THF afforded *para*-ethynylphenyl α-D-mannopyranoside **12** in 58% overall yield (Scheme 2). Analogous handling on *ortho*-iodide **9** and *meta*-iodide **10** gave **13** in only 10% yield and **14** in 55% yield. An improved preparation of the more hindered *ortho* isomer **13** was achieved using dichlorobis (triphenylphosphine) palladium(II) ($PdCl_2(PPh_3)_2$) in the presence of triphenylphosphine, copper(I) iodide, and acetylene gas bubbled into the reaction mixture (DMF, Et_3N, 60 °C) and the isomer **13** was obtained in an improved yield of 44%.

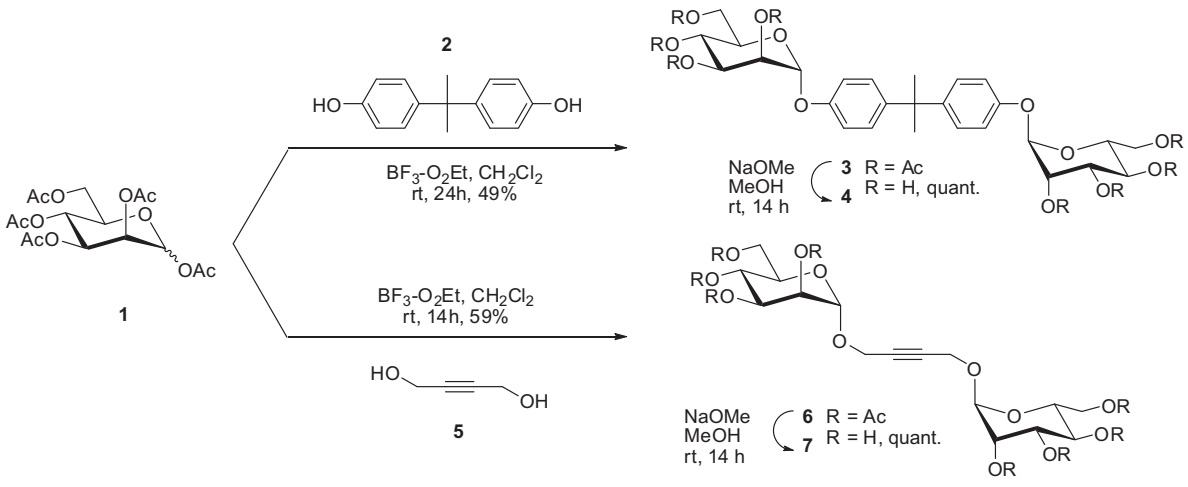
First an Ullmann type palladium-catalyzed aryl–aryl homocoupling was attempted.[39,40] The homocoupling of **8** was performed using $Pd(OAc)_2$, potassium acetate (KOAc), and tetrabutyl ammonium bromide in DMF at 130 °C for 4 h to give dimer **15** in 64% yield (Scheme 3). De-O-acetylation under Zemplén conditions (NaOMe, MeOH) afforded dimer **16** in quantitative yield. Sonogashira coupling conditions were used for the following set of dimers. Thus, double Pd(0)-catalyzed treatment of **11** onto 1,4-diiodobenzene **17** afforded dimer **18** in 88% yield (Scheme 3).[31] Analogously, *ortho* and *meta*-substituted dimers **21** and **24**, tethered on a single benzene core provided by diiodobenzenes **20** and **23**, were obtained using optimized conditions with palladium tetrakistriphenylphosphine as catalyst (Et_3N, DMF, 60 °C, 4 h) in 82% and 88% yield, respectively.

To this end, aryl iodides **8–10** were treated with their ethynylbenzene partners **12–14**, to provide symmetrical dimannosides **26**,[31] **28**, and **30**, tethered with an acetylene bridge, in essentially quantitative yields using the same above-mentioned conditions ($Pd(PPh_3)_4$, Et_3N, DMF, 60 °C, 4 h) (Scheme 4). Zemplén deprotections of **26**, **28**, and **30** were uneventful and provided unprotected compounds **27**,[31] **29**, and **31** in quantitative yields. In order to further develop the possibility offered by these intermediates, cross-coupling of 4-iodophenyl mannoside **8** with propargyl mannoside **11** was achieved using the same conditions to provide unsymmetrical dimer **32** in 98% yield.[31] Quantitative de-O-acetylation under Zemplén conditions afforded dimer **33**. Since it was anticipated that the cross-coupling of **11** with compounds **9** and **10** would provide spatially too closed mannopyranosides, the experiments were not attempted.[29]

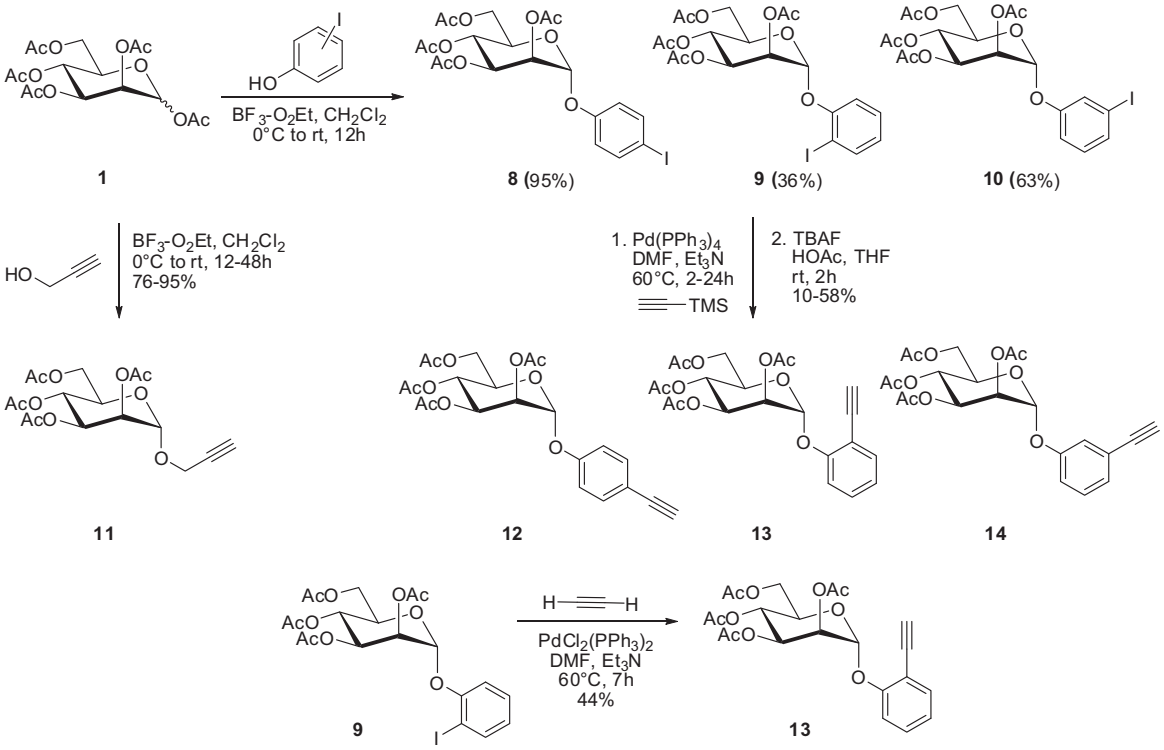
To expand the potential of this family of versatile building blocks, we further planned increasing the intersaccharidic distances by intercalating two diacetylene bridges between the aromatic residues. This was readily achieved using Glaser oxidative homocoupling under Hay's conditions.[35,41] Dimers **34**, **36**, and **38** were thus conveniently prepared in 47–68% yields using copper(II) acetate in refluxing pyridine for 48 h (Scheme 5). After standard de-O-acetylation under Zemplén conditions, the corresponding unprotected dimers **35**, **37**, and **39** were obtained. For comparison purpose, diacetylenic dimer **40** was similarly prepared and hydrogenated under Pd–C to provide **41**.[29]

In conclusion, a panel of symmetrical and unsymmetrical mannopyranoside dimers were efficiently synthesized using versatile building blocks bearing alkynyl as well as iodoaryl functionalities in the aglycone moieties. Varied palladium-catalyzed homo- and cross-coupling reactions were shown to be generally superior toward their syntheses in comparison to more classical Lewis-acid catalyzed glycosidations of diols. The best yields were obtained during either homo- or cross-coupling Sonogashira reaction in the presence of palladium tetrakistriphenylphosphine as catalyst ($Pd(PPh_3)_4$, Et_3N, DMF, 60 °C, 4–24 h) (Schemes 3 and 4).

It is now well admitted that dimeric clusters can provide insoluble complexes with tetrameric lectins, but the kinetics of formation, as well as the nature and stability of the cross-linked



Scheme 1. Synthesis of α-D-mannopyranoside dimers using Lewis acid catalyzed glycosidations of preformed diols.



Scheme 2. Syntheses of the key monomeric building blocks.

architectures vary greatly with the type of linkers.[25,29] Similarly, when the carbohydrate ligands bind too strongly (low K_ds), the speed at which the complexes are formed precludes the formations of favorable equilibrium that would provide well organized and more stable lattices.[29]

Preliminary data indicated that more rigid dimer **40** had a K_d 10 times superior than that of **MeαMan** and the flexible dimer **41** in binding to bacterial *Burkholderia cenocepacia* dimeric BC2L-A lectin.[29] These results are in contrast to those obtained from tetrameric plant lectins isolated from *Canavalia ensiformis* (ConA) and *Dioclea grandiflora* (DGL) wherein the flexible dimer **41** appeared to be superior.[25] These initial results further demonstrate the need for systematic comparisons between a wide range of oligomeric carbohydrate binding proteins and glycoclusters/glycodendrimers of varied valencies. Overall, these data point again toward the fact that increased binding and selectivity is achievable with an analogous family of similar receptors.[42] A detailed comparison of the above library with various mannopyranoside binding proteins is under investigation and will be reported in due course.

3. Experimental

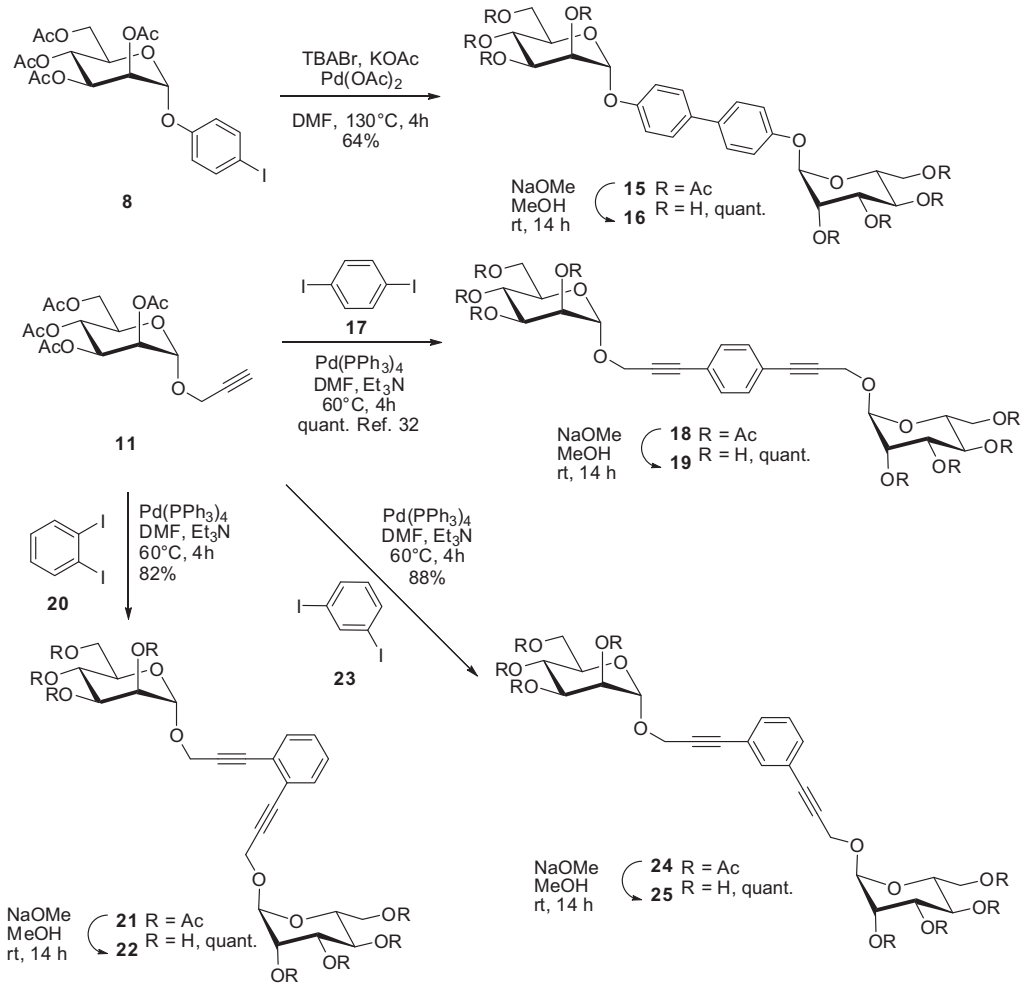
3.1. General methods

The reactions were carried out in organic media under nitrogen atmosphere using freshly distilled solvents (dichloromethane was freshly distilled under P_2O_5). Evolution of reactions was monitored by analytical thin-layer chromatography using Silica Gel 60 F_{254} precoated plates (E. Merck). Optical rotations were measured with a JASCO P-1010 polarimeter. Melting points were measured on a Fisher Jones apparatus and are uncorrected. Arabic numerals in ascending order are given to the residues from the reducing end. NMR spectra were recorded on Varian Gemini 300 and Varian Innova 600 MHz spectrometers. Proton and carbon chemical shifts (δ) are reported in ppm downfield from internal reference of residual solvents. Coupling constants (J) are reported in hertz (Hz), and the following abbreviations are used: singlet (s), doublet (d), doublet of doublets (dd), triplet (t), multiplet (m), and broad (b). Analysis and assignments were made using COSY, DEPT, and HETCOR experiments. The α-stereochemistry of the *O*-glycosidic linkages was ascertained by comparison of experimental $^1J_{C\text{-}1,H\text{-}1}$ coupling constants, determined by a coupled HSQC experiment, with known data for α-glycosides (ca. 170 Hz). High-resolution mass spectra (HRMS) were carried out by the University's analytical laboratory on a HPLC Agilent Technologies 1200 Series + Agilent Technologies 6210 MS TOF (Université du Québec à Montréal, Canada).

3.2. Procedures

3.2.1. 4,4′-Bis-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)-diphenylisopropane (3)

Boron trifluoride diethyl etherate (0.95 mL, 7.5 mmol, 1.70 equiv) was added via a syringe to a solution of mannose pentaacetate **1** (1.72 g, 4.4 mmol, 1.00 equiv) and bisphenol A (**2**) (0.49 g, 2.2 mmol, 0.50 equiv) in dry CH_2Cl_2 (70 mL) cooled to 0 °C and under N_2. The solution was allowed to warm up to room temperature and was further stirred under a stream of N_2 for 24 h, during which time reaction was judged complete by TLC (hexane/EtOAc 1:1). The reaction mixture was washed with satd $NaHCO_3$ (2 × 80 mL), 2 M HCl (2 × 80 mL), and H_2O (2 × 80 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The concentrate was purified by silica gel chromatography with hexane/EtOAc 1:1 as eluent. The titled compound **3** was obtained as a white crystalline solid (0.8 g, 49% yield); mp 79–81 °C; $[\alpha]_D^{23}$ +62.7 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz): δ 7.10 (d, $^3J_{H,H}$ 8.8 Hz, 4H, H_{ar}), 6.90 (d, $^3J_{H,H}$ 8.8 Hz, 4H, H_{ar}), 5.52 (dd, $^3J_{3,2}$ 3.4 Hz, $^3J_{3,4}$ 10.0 Hz, 2H, 2 × *H*-3), 5.46 (s, 2H, 2 × *H*-1), 5.39 (dd, $^3J_{1,2}$ 1.8 Hz, $^3J_{2,3}$ 3.3 Hz,



Scheme 3. Palladium(0)-catalyzed syntheses of dimeric mannopyranosides using aryl–aryl homocoupling and a double Sonogashira cross-coupling reaction.

2H, 2 × *H*-2), 5.33 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.0 Hz, 2H, 2 × *H*-4), 4.25 (dd, $^3J_{5,6a}$ 4.9 Hz, $^2J_{6a,6b}$ 12.1 Hz, 2H, 2 × *H*-6a), 4.11–4.03 (m, 4H, 2 × *H*-5 and *H*-6b), 2.12, 2.02, 2.00, 1.99 (4 × s, 4 × 6H, $COCH_3$), 1.60 (s, 6H, Ph-C(CH_3)$_2$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.1, 170.45, 169.9, 169.9, 169.7 (*C*=O), 153.6, 145.2, 127.8, 127.7 (C_6H_4), 95.9 (*C*-1), 69.4 (*C*-5), 69.0 (*C*-2), 68.9 (*C*-3), 62.5 (*C*-4), 62.1 (*C*-6), 41.9 (Ph-*C*(CH_3)$_2$), 30.9 (Ph-C(*C*H_3)$_2$), 21.0, 20.8, 20.6 ($COCH_3$); FAB-HRMS *m/z* calcd for $C_{43}H_{52}O_{20}$ $[M+K]^+$ 927.2689, found, 927.2997; Anal. Calcd for $C_{43}H_{52}O_{20}$: C, 58.10; H, 5.90. Found, C, 57.75; H, 5.92.

3.2.2. 4,4′-Bis-(α-D-mannopyranosyloxy)diphenylisopropane (4)

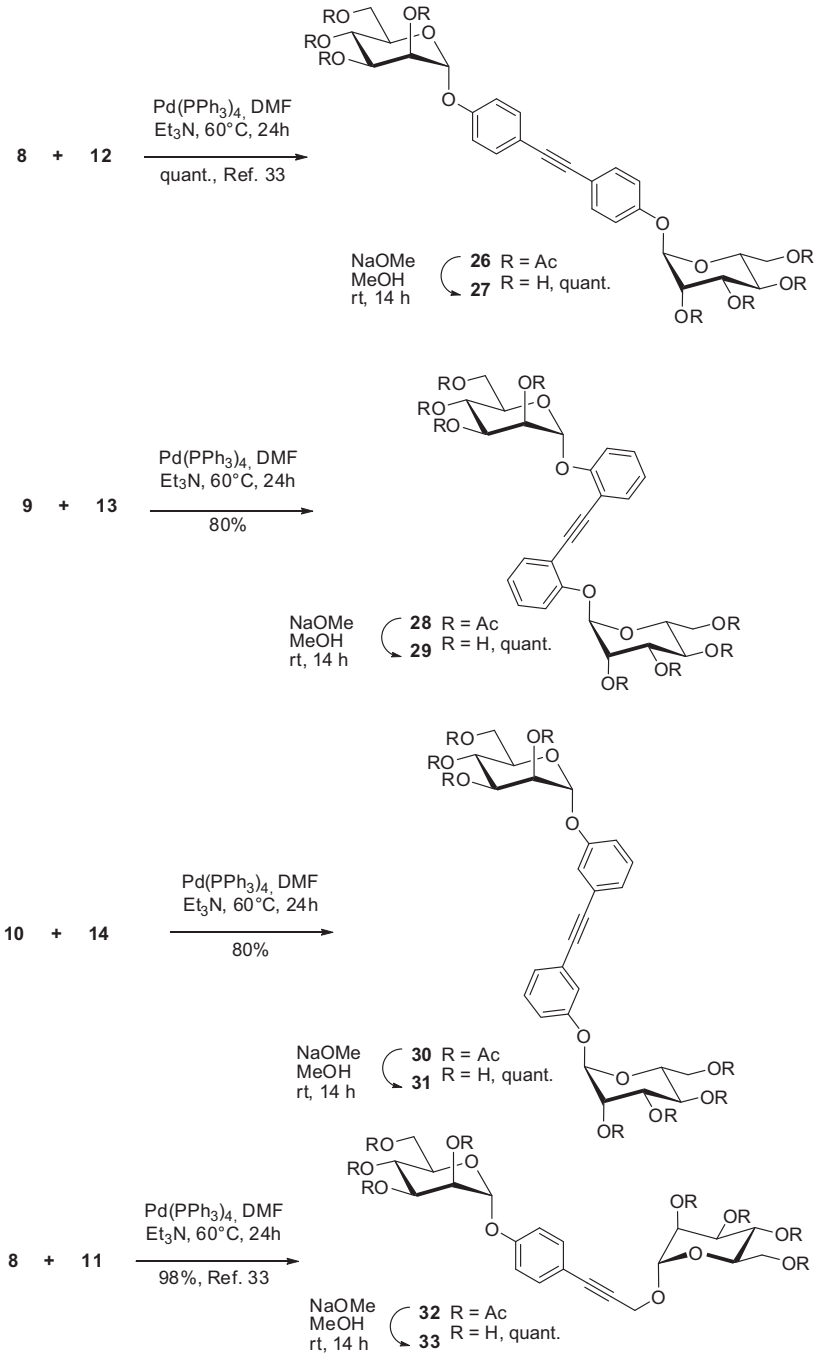
The titled compound was obtained by deacetylation of **3** (0.110 g, 0.12 mmol) using MeOH (0.9 mL) to which was added a solution of 1 M NaOMe in MeOH to set the pH at 8–9. The reaction was stirred at room temperature for 14 h and was then neutralized by the addition of acidic Amberlyst resin (IR-120). The solution was filtered, concentrated under reduced pressure and lyophilizated to afford **4** as a yellowish solid (0.065 g, 95% yield); mp 114–116 °C; $[\alpha]_D^{22}$ +107.5 (*c* 1.6, DMF); ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.11 (d, $^3J_{H,H}$ 8.8 Hz, 4H, H_{ar}), 7.00 (d, $^3J_{H,H}$ 8.8 Hz, 4H, H_{ar}), 5.30 (d, $^3J_{1,2}$ 1.6 Hz, 2H, 2 × *H*-1), 3.92 (br s, 6H, 2 × C2-O*H*, C3-O*H*, and C4-O*H*), 3.78 (t, *J* 2.9 Hz, 2H, 2 × C6-O*H*), 3.62–3.55 (m, 6H, 2 × *H*-2, *H*-3, and *H*-4), 3.47–3.16 (m, 6H, 2 × *H*-5, *H*-6a, and *H*-6b), 2.07 (s, 12H, 2 × Ph-C(*C*H_3)$_2$); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 154.4, 143.9, 127.6, 116.2 (C_6H_4), 99.1 (*C*-1), 74.9, 70.7, 70.2, 67.0, 66.8 (*C*-2, *C*-3, *C*-4, *C*-5) 61.1 (*C*-6), 30.7 [$Ph_2C(CH_3)_2$], 25.2 ($Ph_2C(CH_3)_2$); ESI$^+$-MS *m/z* calcd for $C_{27}H_{36}O_{12}$ $[M+NH_4]^+$ 570.3, found, 570.3.

3.2.3. 1,4-Bis-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)-but-2-yne (6)

To a solution of **1** (880 mg, 2.25 mmol, 2.40 equiv) in dry dichloromethane (6 mL) was added dropwise boron trifluoride diethyl etherate (537 μL, 4.27 mmol, 4.56 equiv) at 0 °C under nitrogen atmosphere. The mixture was stirred at room temperature for 3 h. Then, 2-butyne-1,4-diol (**5**) (81.5 mg, 0.937 mmol, 1.00 equiv) in acetonitrile (4 mL) was added to the solution and stirred at room temperature over night. Et_3N (606 μL, 4.27 mmol, 4.56 equiv) was added to solution at 0 °C and after evaporation of the solvent, the resulting crude product was purified by column chromatography on silica gel using gradient elution (hexane 100% to hexane/EtOAc 4:6). Compound **6** was obtained as a white crystalline solid (414 mg, 59% yield); R_f (hexane/EtOAc 4:6) 0.33; mp 52–53 °C; $[\alpha]_D^{20}$ +67.0 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.31 (dd, $^3J_{2,3}$ 3.4 Hz, $^3J_{3,4}$ 10.0 Hz, 2H, 2 × *H*-3), 5.27 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.0 Hz, 2H, 2 × *H*-4), 5.24 (dd, $^3J_{1,2}$ 1.7 Hz, $^3J_{2,3}$ 3.4, 2H, 2 × *H*-2), 4.97 (d, $^3J_{1,2}$ 1.7 Hz, 2H, 2 × *H*-1), 4.33–4.24 (m, 6H, 2 × OCH_2, and H-6a), 4.08 (dd, $^3J_{6a,6b}$ 2.5 Hz, $^3J_{5,6}$ 12.2 Hz, 2H, 2 × H-6b), 3.98 (m, 2H, *H*-5), 2.14, 2.08, 2.02, 1.96 (4 × s, 4 × 6H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.5, 169.8, 169.7, 169.6 (*C*=OCH_3), 96.0 (*C*-1), 81.5 (*C*≡*C*), 69.2 (*C*-2), 68.9 (*C*-5), 68.8 (*C*-3), 65.9 (*C*-4), 62.2 (*C*-6), 54.8 (OCH_2), 20.8, 20.6, 20.6, 20.5 (4 × $COCH_3$). FAB-HRMS *m/z* calcd for $C_{32}H_{42}O_{20}$ $[M+H]^+$ 747.2347, found, 747.2221.

3.2.4. 1,4-Bis-(α-D-mannopyranosyloxy)but-2-yne (7)

The titled compound was obtained as a white solid by deacetylation of **6** (0.170 g, 0.23 mmol) using the method described above

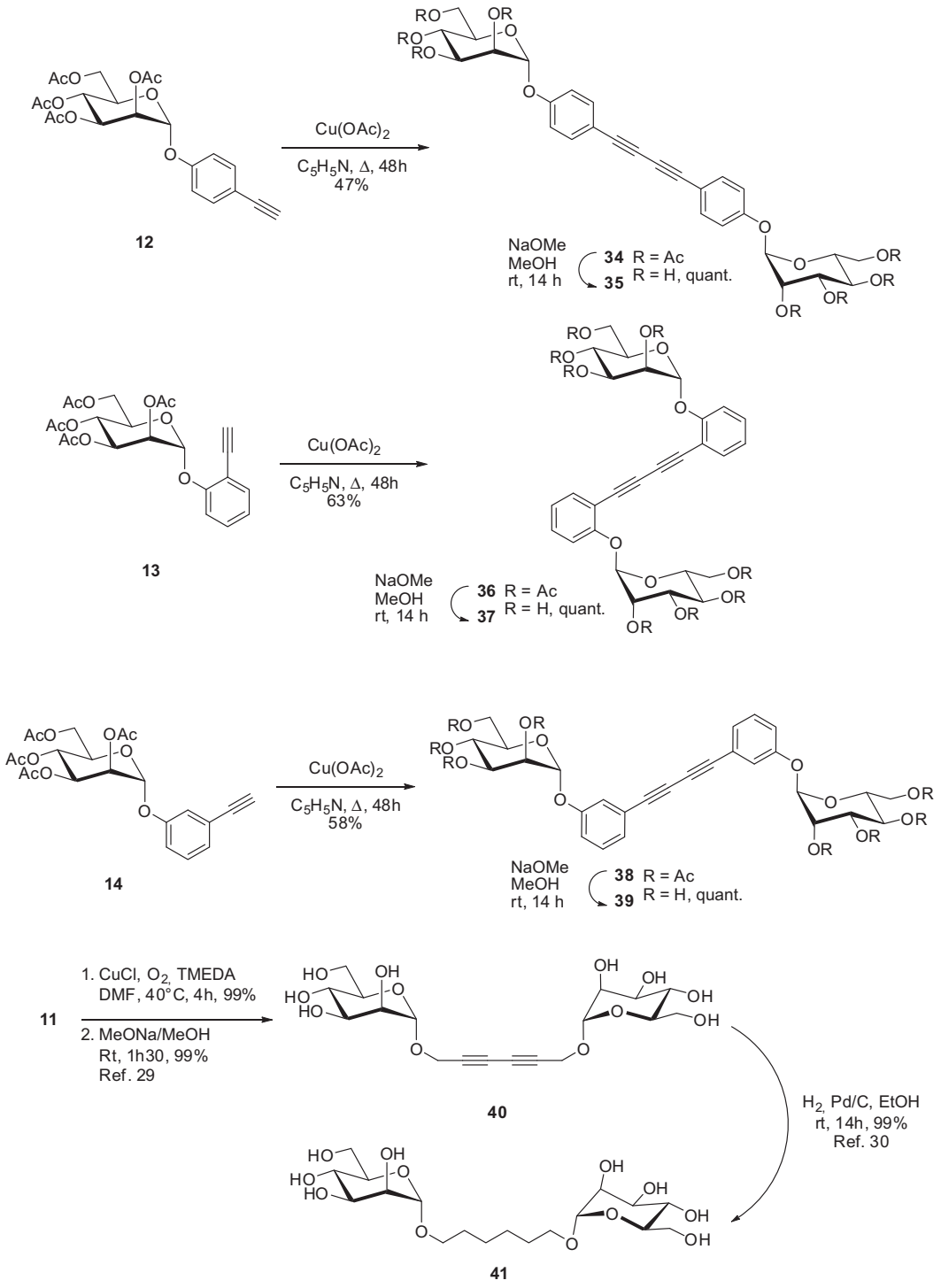


Scheme 4. Palladium(0)-catalyzed syntheses of dimeric mannopyranosides using Sonogashira cross-coupling reaction.

for **4** (0.093 g, quant. yield); R_f (EtOAC/MeOH/H_2O 6:3:1); mp 127–128 °C 0.46; $[\alpha]_D^{22}$ +122.1 (*c* 1, MeOH); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.04 (d, $^3J_{1,2}$ 1.3 Hz, 2H, 2 × *H*-1), 4.42–4.31 (m, 4H, 2 × O*CH*$_2$C≡C), 3.97 (dd, $^3J_{2,3}$ 3.1 Hz, 2H, 2 × *H*-2), 3.90–3.67 (m, 10H, 2 × *H*-4, *H*-3, *H*-6a, *H*-6b, and *H*-5); ^{13}C NMR (150 MHz, $CDCl_3$) δ 98.9 (*C*-1), 82.2 (*C*≡*C*), 73.2 (*C*-2), 70.6 (*C*-5), 70.0 (*C*-3), 66.7 (*C*-4), 60.9 (*C*-6), 54.8 ppm (O*C*H$_2$). ESI$^+$-HRMS *m/z* calcd for $C_{16}H_{26}O_{12}$ $[M+Na]^+$ 433.1316, found, 433.1312.

3.2.5. 4-Iodophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (8)

To a solution of penta-*O*-acetyl-α,β-D-mannopyranose **1** (390 mg, 1.00 mmol, 1.00 equiv) and 4-iodophenol (889 mg, 4.00 mmol, 4.00 equiv) in dry dichloromethane (10 mL) was added dropwise boron trifluoride diethyl etherate (188 μL, 1.50 mmol, 1.50 equiv) at 0 °C under nitrogen atmosphere. The mixture was stirred at room temperature overnight and the course of the reaction was monitored by TLC (hexane/EtOAc 1:1) until complete disappearance of the starting material (12–48 h). CH_2Cl_2 (50 mL) was added and the solution was washed with a 20% aqueous Na_2CO_3 solution (2 × 100 mL) and water (2 × 100 mL). The organic phase was then dried with anhydrous Na_2SO_4 and, after evaporation of the solvent, the resulting crude product was purified by flash chromatography (hexane/EtOAc 4:1) to give the titled compound **8** as a white solid (520 mg, 95% yield).[37] The titled compound was crystallized in petroleum ether with a little amount of dichloromethane; R_f (hexane/EtOAc 1:1) 0.61; mp 127–129 °C (from CH_2Cl_2/PE) (Lit. mp 127–129 °C);[31] $[\alpha]_D^{22}$ +65 (*c* 1.0, $CHCl_3$) (Lit. 65 *c* 1.0, $CHCl_3$);[18,30,31]



Scheme 5. Palladium(0)-catalyzed syntheses of dimeric mannopyranosides using Glaser homocoupling reactions.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56 (d, $^3J_{H,H}$ 8.2 Hz, 2H, H_{ar}-*meta*), 6.84 (d, $^3J_{H,H}$ 8.3 Hz, 2H, H_{ar}-*ortho*), 5.50 (dd, $^3J_{2,3}$ 3.4 Hz, $^3J_{3,4}$ 10.0 Hz, 1H, *H*-3), 5.46 (d, $^3J_{1,2}$ 1.9 Hz, 1H, *H*-1), 5.40 (dd, $^3J_{1,2}$ 1.9 Hz, $^3J_{2,3}$ 3.4 Hz, 1H, *H*-2), 5.33 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.0 Hz, 1H, *H*-4), 4.24 (dd, $^3J_{5,6a}$ 5.5 Hz, $^2J_{6a,6b}$ 12.4 Hz, 1H, *H*-6a), 4.04–4.00 (m, 2H, *H*-5, and *H*-6b), 2.16, 2.02, 2.00, 1.99 (4 × s, 4 × 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.4, 169.9, 169.8, 169.6 (*C*=O), 155.3, 138.4, 118.7 (C_6H_4), 95.7 (*C*-1, $^1J_{C\text{-}1,H\text{-}1}$ 174.4 Hz), 85.8 (C_6H_4), 69.2 (*C*-5), 69.2 (*C*-2), 68.7 (*C*-3), 65.8 (*C*-4), 62.0 (*C*-6), 20.8–20.6 ($COCH_3$); ESI$^+$-MS *m/z* calcd for $C_{20}H_{23}IO_{10}$ $[M+Na]^+$ 573.02; found, 573.06.

3.2.6. 2-Iodophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (9)

Treatment of **1** (1.0 g, 2.60 mmol, 1.00 equiv) with 2-iodophenol (1.0 g, 4.40 mmol, 1.69 equiv) and boron trifluoride diethyl etherate (0.60 mL, 4.70 mmol, 1.81 equiv) as above yielded **9** in 36% yield (0.5 g). The course of the reaction was followed by TLC (hexane/EtOAc 1:1) until complete disappearance of the starting material (17 h). CH_2Cl_2 (60 mL) was added and the solution was washed with a 20% aqueous Na_2CO_3 solution (2 × 100 mL) and water (2 × 100 mL). The organic phase was then dried with anhydrous Na_2SO_4 and, after evaporation of the solvent, the resulting crude

product was purified by flash chromatography (hexane/EtOAc 3:2) to give the titled compound **9** as a white solid (0.5 g, 36% yield); mp 143–144 °C; $[\alpha]_D^{23}$ +32.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.76 (dd, $J_{H,H}$ 1.6 Hz, $J_{H,H}$ 7.8 Hz, 1H, H_{ar}), 7.26 (m, 1H, H_{ar}), 7.05 (dd, $J_{H,H}$ 1.3 Hz, $J_{H,H}$ 8.3 Hz, 1H, H_{ar}), 6.79 (ddd, $J_{H,H}$ 1.3 Hz, $J_{H,H}$ 7.6 Hz, $J_{H,H}$ 8.9 Hz, 1H, H_{ar}), 5.68 (dd, $^3J_{2,3}$ 3.4 Hz, $^3J_{3,4}$ 10.1 Hz, 1H, *H*-3), 5.55 (d, $^3J_{1,2}$ 1.8 Hz, 1H, *H*-1), 5.51 (dd, $^3J_{1,2}$ 1.9 Hz, $^3J_{2,3}$ 3.4 Hz, 1H, *H*-2), 5.38 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.1 Hz, 1H, *H*-4), 4.25 (dd, $^3J_{5,6a}$ 5.2 Hz, $^2J_{6a,6b}$ 12.2 Hz, 1H, *H*-6a), 4.09 (m, 1H, *H*-5), 4.04 (dd, $^3J_{5,6b}$ 2.2 Hz, $^2J_{6a,6b}$ 12.2 Hz, 1H, *H*-6b), 2.17, 2.04, 2.01, 2.00 (4 × s, 4 × 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.4, 169.9, 169.7, 169.7 (*C*=O), 154.4, 139.7, 129.4, 124.7, 115.0 (C_6H_4), 95.2 (*C*-1, $^1J_{C\text{-}1,H\text{-}1}$ 174.2 Hz), 87.3 (C_6H_4), 69.8 (*C*-5), 69.3 (*C*-2), 68.9 (*C*-3), 65.8 (*C*-4), 62.0 (*C*-6), 20.8, 20.7, 20.6, 20.6 ($COCH_3$); ESI$^+$-MS *m/z* calcd for $C_{20}H_{23}IO_{10}$ $[M+H]^+$ 551.04, found, 551.13.

3.2.7. 3-Iodophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (10)

Treatment of **1** (2.0 g, 5.20 mmol, 1.00 equiv) with 3-iodophenol (2.1 g, 9.40 mmol, 1.81 equiv) and boron trifluoride diethyl etherate as above (1.1 mL, 8.7 mmol, 1.67 equiv) yielded **10** in 63% yield (1.2 g) The course of the reaction was followed by TLC (hexane/EtOAc 1:1) until complete disappearance of the starting material (22 h). CH_2Cl_2 (80 mL) was added and the solution was washed with a 20% aqueous Na_2CO_3 solution (2 × 100 mL) and water (2 × 100 mL). The organic phase was then dried with anhydrous Na_2SO_4 and, after evaporation of the solvent, the resulting crude product was purified by flash chromatography (hexane/EtOAc 2:1) to give 3-iodophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside **10** as a white solid (1.2 g, 63% yield); mp 108–109 °C; $[\alpha]_D^{23}$ +41.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.47 (dd, $J_{H,H}$ 1.7 Hz, $J_{H,H}$ 2.0 Hz, 1H, H_{ar}), 7.37 (ddd, $J_{H,H}$ 1.3 Hz, $J_{H,H}$ 2.9 Hz, $J_{H,H}$ 7.5 Hz, 1H, H_{ar}), 7.01 (m, 2H, H_{ar}), 5.49 (dd, $^3J_{3,2}$ 3.5 Hz, $^3J_{3,4}$ 10.0 Hz, 1H, *H*-3), 5.46 (d, $^3J_{1,2}$ 1.8 Hz, 1H, *H*-1), 5.38 (dd, $^3J_{1,2}$ 1.9 Hz, $^3J_{2,3}$ 3.6 Hz, 1H, *H*-2), 5.31 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.1 Hz, 1H, *H*-4), 4.24 (dd, $^3J_{5,6a}$ 6.0 Hz, $^2J_{6a,6b}$ 12.3 Hz, 1H, *H*-6a), 4.10–4.03 (m, 2H, *H*-5, *H*-6b), 2.16, 2.03, 2.02, 2.00 (4 × s, 4 × 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.4, 169.8, 169.5, 169.6 (*C*=O), 155.9, 132.2, 130.9, 125.6, 116.1 (C_6H_4), 95.8 (*C*-1, $^1J_{C\text{-}1,H\text{-}1}$ 173.8 Hz), 94.1(C_6H_4), 69.3 (*C*-5), 69.2 (*C*-2), 68.7 (*C*-3), 65.8 (*C*-4), 62.1 (*C*-6), 20.8, 20.7, 20.6 ($COCH_3$); FAB-MS *m/z* calcd for $C_{20}H_{23}IO_{10}$ $[M+H]^+$ 551.04, found, 551.13.

3.2.8. Prop-2-ynyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (11)

To a solution of **1** (250 mg, 0.64 mmol, 1.00 equiv) in dry dichloromethane (10 mL) was added boron trifluoride etherate (150 μL, 1.19 mmol, 1.90 equiv), dropwise at 0 °C under nitrogen. The mixture was allowed to warm up, and stirred at room temperature for 4 h. Propargyl alcohol (150 μL, 2.56 mmol, 4.00 equiv) was added, and the mixture was stirred at room temperature until TLC (hexane/EtOAc 1:1) showed complete disappearance of the starting material (12–48 h). After the addition of CH_2Cl_2 (20 mL), the solution was washed successively with 20% aqueous Na_2CO_3 solution (2 × 40 mL) and water (2 × 40 mL). The organic phase was dried, concentrated, and chromatography (hexane/EtOAc 2:1) gave the titled compound **11**, which crystallized after drying under vacuum (234 mg, 95% yield). Crystallization from CH_2Cl_2–petroleum ether and recrystallization from petroleum ether gave material melting at 99–100 °C, Lit. 99–100 °C;[31] $[\alpha]_D^{22}$ +56 (*c* 2.0, $CHCl_3$) [Lit. $[\alpha]_D^{22}$ +56 (*c* 2.0, $CHCl_3$)];[31] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.31 (dd, $^3J_{2,3}$ 3.4 Hz, $^3J_{3,4}$ 10.0 Hz, 1H, *H*-3), 5.26 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.0 Hz, 1H, *H*-4), 5.23 (dd, $^3J_{1,2}$ 1.7 Hz, $^3J_{2,3}$ 3.4, 1H, *H*-2), 4.99 (d, $^3J_{1,2}$ 1.7 Hz, 1H, *H*-1), 4.24 (dd, $^3J_{5,6b}$ 5.2 Hz, $^2J_{6a,6b}$ 12.2 Hz, 1H, *H*-6a), 4.24 (d, $^4J_{H,H}$ 2.4 Hz, 2H, $OCH_2C{\equiv}CH$), 4.07 (dd, $^3J_{5,6b}$ 2.5 Hz, $^2J_{6a,6b}$ 12.2 Hz, 1H, *H*-6a), 4.00 (m, 1H, *H*-5), 2.44 (t, $^4J_{H,H}$ 2.4 Hz, 1H, $OCH_2C{\equiv}CH$), 2.12, 2.07, 2.01, 1.96 (4 × s, 4 × 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.5, 169.9, 169.7, 169.6 (*C*=O), 96.1 (*C*-1, $J_{C\text{-}1,H\text{-}1}$ 173.4 Hz), 77.8 ($OCH_2C{\equiv}CH$), 75.5 ($OCH_2C{\equiv}CH$), 69.2 (*C*-5), 68.9 (*C*-3), 68.8 (*C*-2), 65.9 (*C*-4), 62.2 ($OCH_2C{\equiv}CH$), 54.9 (*C*-6), 20.8, 20.7, 20.6, 20.6 ($COCH_3$); ESI$^+$-HRMS *m/z* calcd for $C_{17}H_{22}O_{10}$ $[M+Na]^+$ 409.1105, found, 409.1100.

3.2.9. 4-Ethynylphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (12)

Tetramethylsilylacetylene (0.500 mL, 3.50 mmol, 1.84 equiv) was added via a syringe, to a solution of 4-iodophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**8**) (1.00 g, 1.90 mmol, 1.00 equiv) and palladium tetrakistriphenyl phosphine ($Pd(PPh_3)_4$) (0.110 g, 0.09 mmol, 0.05 equiv) in a mixture of Et_3N–DMF (60–1 mL), kept under nitrogen. The reaction mixture was heated to 60 °C for 24 h at which time reaction was judged complete by TLC (hexane/EtOAc 1:1). The reaction mixture was diluted with EtOAc (60 mL) washed with 2 M HCl (3 × 100 mL), saturated $NaHCO_3$ (2 × 100 mL) and H_2O (2 × 100 mL), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the concentrate was passed through a short silica gel column with hexane/EtOAc 1:1 as eluent. The solvent was removed under reduced pressure. The concentrate was dissolved in 20 mL THF. A solution of 10 drops of tetrabutylammonium fluoride (1 M in THF) and 1 drop of acetic acid in 2 mL of THF was added dropwise. After 2 h, the solvent was removed in vacuo. The product was purified by silica gel column chromatography using hexane/EtOAc 2:1 as eluent to yield the pure compound **12** as a yellow solid (0.5 g, 58% yield); mp 93–95 °C; $[\alpha]_D^{23}$ +33.8 (*c* 1.3, $CHCl_3$); IR (neat): 3277, 2960, 2108, 1751, 1228, 1036, 837, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.41 (d, $^3J_{H,H}$ 8.9 Hz, 2H, H_{ar}), 7.01 (d, $^3J_{H,H}$ 8.8 Hz, 2H, H_{ar}), 5.48 (dd, $^3J_{2,3}$ 3.5 Hz, $^3J_{3,4}$ 10.1 Hz, 1H, *H*-3), 5.50 (d, $^3J_{1,2}$ 1.4 Hz, 1H, *H*-1), 5.40 (dd, $^3J_{1,2}$ 2.0 Hz, $^3J_{2,3}$ 3.6 Hz, 1H, *H*-2), 5.32 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.1 Hz, 1H, *H*-4), 4.23 (dd, $^3J_{5,6a}$ 5.7 Hz, $^2J_{6a,6b}$ 12.4 Hz, 1H, *H*-6a), 4.03 (m, 2H, *H*-5, *H*-6b), 3.00 (s, 1H, $C{\equiv}CH$), 2.16, 2.02, 2.00, 1.99 (4 × s, 4 × 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.4, 169.9, 169.8, 169.6 (*C*=O), 155.7, 133.6, 116.4 (C_6H_4), 95.6 (*C*-1), 82.9, 76.6 ($C{\equiv}C$), 69.3 (*C*-5), 69.2 (*C*-2), 68.7 (*C*-3), 65.8 (*C*-4), 62.0 (*C*-6), 20.8, 20.6, 20.6 ($COCH_3$); FAB-MS *m/z* calcd for $C_{22}H_{24}O_{10}$ $[M+K]^+$ 487.10; found, 486.70.

3.2.10. 2-Ethynylphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (13)

Compound **9** (0.100 g, 0.190 mmol, 1.00 equiv) in Et_3N (30 mL) was stirred under N_2 for 30 min. Dichloro-bis(triphenyl)phoshine palladium(II) ($PdCl_2(PPh_3)_2$) (1.6 mg, 0.23 μmol, 0.001 equiv) was added to the mixture. After 5 min of stirring under N_2, copper(I) iodide (CuI) (3.9 mg, 2.5 μmol, 0.01 equiv) and triphenyl phosphine (PPh_3) (3.5 mg, 0.13 μmol, 0.0007 equiv) were added to the mixture and stirred for a further 5 min. Acetylene gas was bubbled through the reaction mixture, which was then heated to 60 °C. The reaction was followed by TLC (hexane/EtOAc 2:1) and was judged to be complete after 7 h. The solvent was removed under reduced pressure and the concentrate was then passed through a column of silica gel, with hexane/EtOAc 2:1 as eluent. The purified product **13** was obtained as a white solid (0.037 g, 44% yield); mp 127–130 °C; $[\alpha]_D^{23}$ +38.3 (*c* 1.2, $CHCl_3$); IR (neat): 3271, 2907, 1742, 1240, 1137, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.45 (dd, $J_{H,H}$ 1.6 Hz, $J_{H,H}$ 7.6 Hz, 1H, H_{ar}), 7.27 (ddd, $J_{H,H}$ 1.7 Hz, $J_{H,H}$ 7.7 Hz, $J_{H,H}$ 8.5 Hz, 1H, H_{ar}), 7.08 (d, $J_{H,H}$ 8.1 Hz, 1H, H_{ar}), 7.01 (ddd, $J_{H,H}$ 0.9 Hz, $J_{H,H}$ 7.6 Hz, $J_{H,H}$ 8.5 Hz, 1H, H_{ar}), 5.63 (dd, $^3J_{2,3}$ 3.5 Hz, $^3J_{3,4}$ 10.1 Hz, 1H, *H*-3), 5.57 (d, $^3J_{1,2}$ 1.8 Hz, 1H, *H*-1), 5.3 (dd, $^3J_{1,2}$ 1.9 Hz, $^3J_{2,3}$ 3.5 Hz, 1H, *H*-2), 5.35 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.1 Hz, 1H, *H*-4), 4.24 (dd, $^3J_{5,6a}$ 5.4 Hz, $^2J_{6a,6b}$ 12.1 Hz, 1H, *H*-6a), 4.19 (m, 1H, *H*-5), 4.05 (dd, $^3J_{5,6b}$ 2.1 Hz, $^2J_{6a,6b}$ 12.1 Hz, 1H, *H*-6b), 3.32 (s, 1H, $C{\equiv}CH$), 2.17, 2.03, 2.00, 1.99 (4 × s, 4 × 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$,

150 MHz) δ 170.4, 169.9, 169.7, 169.7 (*C*=O), 156.6, 133.9, 130.0, 123.1, 115.6, 113.6 (C_6H_4), 96.4 (*C*-1), 82.4, 78.8 (*C*≡*C*), 69.6 (*C*-5), 69.5 (*C*-2), 68.8 (*C*-3), 65.9 (*C*-4), 62.1 (*C*-6), 20.8, 20.7, 20.6, 20.6 (CO*C*H$_3$); FAB-MS *m/z* calcd for $C_{22}H_{24}O_{10}$ $[M+K]^+$ 487.10, found, 487.14.

3.2.11. 3-Ethynylphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (14)

Tetramethylsilylacetylene (0.77 mL, 5.40 mmol, 2.00 equiv) was added via a syringe, to a solution of 3-iodophenyl 2,3,4,6-tetra-*O*-acetyl-mannopyranoside (**10**) (1.50 g, 2.70 mmol, 1.00 equiv) and palladium tetrakistriphenyl phosphine ($Pd(PPh_3)_4$) (0.17 g, 0.10 mmol, 0.04 equiv) in a mixture of Et_3N–DMF (30–3 mL), kept under nitrogen. The reaction mixture was heated to 60 °C for 2½ h during which time the reaction was judged complete by TLC (hexane/EtOAc 1:1). The reaction mixture diluted with EtOAc (40 mL) was washed with 2 M HCl (3 × 80 mL), saturated $NaHCO_3$ (2 × 80 mL) and H_2O (2 × 80 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the concentrate was passed through a short silica gel column using hexane/EtOAc 1:1 as eluent. The solvent was removed in vacuo. The concentrate was dissolved in 20 mL THF. A solution of 5 drops tetrabutylammonium fluoride (1 M in THF), 5 drops of acetic acid, and 5 mL THF was added dropwise. After 2 h, the solvent was removed in vacuo. The product was purified by silica gel column chromatography using hexane/EtOAc 2:1 as eluent to yield the pure compound **14** as a yellow gel (0.7 g, 55% yield); $[\alpha]_D^{23}$ +83.4 (*c* 2.6, $CHCl_3$); IR (neat): 3266, 2960, 1752, 1224, 1135, 757 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.23 (dd, $J_{H,H}$ 2.5 Hz, 1H, H_{ar}), 7.22 (d, $J_{H,H}$ 8.0 Hz, 1H, H_{ar}), 7.16 (ddd, $J_{H,H}$ 1.2 Hz, $J_{H,H}$ 2.4 Hz, $J_{H,H}$ 10.0 Hz, 1H, H_{ar}), 7.05 (ddd, $J_{H,H}$ 1.1 Hz, $J_{H,H}$ 2.6 Hz, $J_{H,H}$ 8.2 Hz, 1H, H_{ar}), 5.51 (dd, $^3J_{2,3}$ 3.5 Hz, $^3J_{3,4}$ 10.0 Hz, 1H, *H*-3), 5.48 (d, $^3J_{1,2}$ 1.8 Hz, 1H, *H*-1), 5.40 (dd, $^3J_{1,2}$ 1.9 Hz, $^3J_{2,3}$ 3.5 Hz, 1H, *H*-2), 5.31 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.0 Hz, 1H, *H*-4), 4.25 (dd, $^3J_{5,6a}$ 6.5 Hz, $^2J_{6a,6b}$ 12.4 Hz, 1H, *H*-6a), 4.06 (m, 2H, *H*-5, *H*-6b), 3.04 (s, 1H, C≡C*H*), 2.16, 2.02, 2.01, 2.01 (4 × s, 4 × 3H, COC*H*$_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.5, 169.9, 169.8, 169.7 (*C*=O), 155.3, 129.5, 126.9, 123.4, 119.9, 117.6 (C_6H_4), 95.8 (*C*-1), 82.9, 77.6 (*C*≡*C*), 69.2 (*C*-5), 69.2 (*C*-2), 68.7 (*C*-3), 65.9 (*C*-4), 62.1 (*C*-6), 21.0, 20.8, 20.6, 20.6 (CO*C*H$_3$); FAB-HRMS *m/z* calcd for $C_{22}H_{24}O_{10}$ $[M+K]^+$ 487.1007, found, 487.1785.

3.2.12. 4,4′-Bis-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)biphenyl (15)

To a solution of **8** (100 mg, 0.182 mmol, 1.00 equiv), tetrabutylammonium bromide (59 mg, 0.182 mmol, 1.00 equiv), and sodium acetate (45 mg, 0.458 mmol, 2.52 equiv), in dry DMF (1.8 mL, 0.1 M), was added palladium acetate (4 mg, 0.018 mmol, 0.10 equiv) under nitrogen. The reaction mixture was stirred at 130 °C until complete disappearance of the starting product (4 h). The reaction mixture was allowed to cool down to room temperature, then EtOAc (10 mL) was added and the organic layer was washed with water (3 × 10 mL), brine (10 mL), and dried over $MgSO_4$. After concentration under reduced pressure, the brown crude product was purified by column chromatography (hexane/EtOAc 1:1) to afford **15** as a yellowish solid (49 mg, 64%); R_f (hexane/EtOAc 55:45) 0.19; mp 164–165 °C; $[\alpha]_D^{23}$ +108.7 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.48 (d, $^3J_{H,H}$ 8.8 Hz, 4H, H_{ar}), 7.15 (d, $^3J_{H,H}$ 8.8 Hz, 4H, H_{ar}), 5.57 (dd, $^3J_{2,3}$ 3.3 Hz, $^3J_{3,4}$ 10.2 Hz, 2H, 2 × *H*-3), 5.56 (d, $^3J_{1,2}$ 1.6 Hz, 2H, 2 × *H*-1), 5.48 (dd, $^3J_{1,2}$ 1.6 Hz, $^3J_{2,3}$ 3.3 Hz, 2H, 2 × *H*-2), 5.39 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.2 Hz, 2H, 2 × *H*-4), 4.30 (dd, $^3J_{5,6a}$ 5.8 Hz, $^2J_{6a,6b}$ 12.6 Hz, 2H, 2 × *H*-6a), 4.15–4.07 (m, 4H, 2 × *H*-5, and *H*-6b), 2.22, 2.07, 2.05, 2.04 (4 × s, 4 × 6H, COC*H*$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.5, 170.0, 169.9, 169.7 (*C*=O), 154.9, 135.3, 127.9, 116.8 (C_6H_4), 95.8 (*C*-1), 69.3, 69.1, 68.8, 65.9, 62.1 (*C*-2, *C*-3, *C*-4, *C*-5, and *C*-6), 20.9, 20.7 (CO*C*H$_3$); ESI$^+$-HRMS *m/z* calcd for $C_{40}H_{46}O_{20}$ $[M+K]^+$ 885.2214, found, 885.2198.

3.2.13. 4,4′-Bis-(α-D-mannopyranosyloxy)biphenyl (16)

The titled compound was obtained as a yellowish solid by deacetylation of **15** (0.077 g, 0.09 mmol) using the method described above for **4** (0.046 g, quant. yield); decomposed at 220–225 °C; $[\alpha]_D^{23}$ +129.6 (*c* 1, DMSO); ^1H NMR (DMSO-d_6 and D_2O exchange, 300 MHz) δ 7.50 (d, $^3J_{H,H}$ 6.9 Hz, 4H, H_{ar}), 7.10 (d, $^3J_{H,H}$ 6.9 Hz, 4H, H_{ar}), 5.38 (s, 2H, 2 × *H*-1), 3.86–3.40 (m, 12H, 2 × *H*-2, *H*-3, *H*-4, *H*-5, *H*-6a, and *H*-6b); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 155.7, 133.5, 127.4, 117.2 (C_6H_4), 99.0 (*C*-1), 75.1, 70.7, 70.1, 66.7, 61.1 (*C*-2, *C*-3, *C*-4, *C*-5, and *C*-6); ESI$^+$-HRMS *m/z* calcd for $C_{24}H_{30}O_{12}$ $[M+Na]^+$ 533.1629, found, 533.1625.

3.2.14. 1,2-Bis-[1,1′(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)prop-2,2′-ynyl]benzene (21)

Nitrogen gas was bubbled through a solution of 2-propynyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**11**) (0.400 g, 1.03 mmol, 1.00 equiv) and 1,2-diiodobenzene (**20**) (0.170 g, 0.51 mmol, 0.50 equiv) in DMF–Et_3N (10–10 mL) for 25 min $Pd(PPh_3)_4$ (0.054 mg, 0.047 mmol, 0.05 equiv) was added and the mixture was stirred under N_2 for 5 min. The reaction mixture was heated to 60 °C and stirred under a stream of N_2 for 4 h after which time the reaction was judged complete by TLC (hexane/EtOAc 1:1). The reaction mixture was cooled and dissolved in diethylether/toluene (100 mL/50 mL), then washed with 2 M HCl (2 × 150 mL), with saturated $NaHCO_3$ soln (1 × 150 mL), and then H_2O (1 × 150 mL). The crude extract was then purified by column chromatography in silica gel with hexane/EtOAc 1:1 as eluent. The titled compound **21** was obtained as a yellow crystalline solid (0.3532 g, 82% yield); mp 80–84 °C; $[\alpha]_D^{23}$ +51.3 (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.38 (d, $J_{H,H}$ 5.8 Hz, 1H, H_{ar}), 7.37 (d, $J_{H,H}$ 5.8 Hz, 1H, H_{ar}), 7.22 (d, $J_{H,H}$ 5.8 Hz, 1H, H_{ar}), 7.21 (d, $J_{H,H}$ 5.8 Hz, 1H, H_{ar}), 5.30 (dd, $^3J_{3,2}$ 3.3 Hz, $^3J_{3,4}$ 6.9 Hz, 2H, 2 × *H*-3), 5.28 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.5 Hz, 2H, 2 × *H*-4), 5.24 (dd, $^3J_{1,2}$ 1.8 Hz, $^3J_{2,3}$ 3.3 Hz, 2H, 2 × *H*-2), 5.08 (d, $^3J_{1,2}$ 1.5 Hz, 2H, 2 × *H*-1), 4.49 (s, 4H, H_2CC≡C), 4.23 (dd, $^3J_{5,6a}$ 4.9 Hz, $^2J_{6a,6b}$ 12.3 Hz, 2H, 2 × *H*-6a), 4.05–4.01 (m, 4H, 2 × *H*-5, and *H*-6b), 2.09, 2.00, 1.97, 1.91 (4 × s, 4 × 6H, COC*H*$_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.4, 169.7, 169.6, 169.5 (*C*=O), 132.0, 128.3, 124.6 (C_6H_4), 96.2 (*C*-1), 87.3, 85.4 (*C*≡*C*), 69.3 (*C*-5), 68.9 (*C*-2), 68.9 (*C*-3), 65.9 (*C*-4), 62.1 (*C*-6), 55.6 (H_2*C*C≡C), 20.8, 20.7, 20.5, 20.4 (CO*C*H$_3$); FAB-MS *m/z* calcd for $C_{40}H_{46}O_{20}$ $[M+K]^+$ 885.22, found, 885.38.

3.2.15. 1,2-Bis-[1,1′(α-D-mannopyranosyloxy)-prop-2,2′-ynyl]benzene (22)

The titled compound was obtained as a yellowish solid by deacetylation of **21** (0.150 g, 0.018 mmol) using the method described above for **4** (0.087 g, quant. yield); mp 92–93 °C; $[\alpha]_D^{23}$ +129.3 (*c* 1.2, MeOH); ^1H NMR (DMSO-d_6, 300 MHz) δ 7.51 (d, $J_{H,H}$ 6.4 Hz, 1H, H_{ar}), 7.50 (d, $J_{H,H}$ 5.6 Hz, 1H, H_{ar}), 7.40 (d, $J_{H,H}$ 5.6 Hz, 1H, H_{ar}), 7.38 (d, $J_{H,H}$ 5.5 Hz, 1H, H_{ar}), 4.93 (br s, 2H, 2 × H-1), 4.86 (d, *J* 4.4 Hz, 2H, 2 × C-O*H*), 4.78 (d, *J* 4.4 Hz, 2H, 2 × C-OH), 4.65 (d, *J* 5.5 Hz, 2H, 2 × C-O*H*), 4.55 (t, *J* 4.2 Hz, 2H, 2 × C-O*H*), 4.51, 4.49 (2 × s, 4H, 2 × H_2CC≡C), 3.64–3.46 (m, 10H, 2 × *H*-2, *H*-3, *H*-4, *H*-5, *H*-6a, and *H*-6b); ^1H NMR (D_2O exchange in DMSO-d_6, 300 MHz) δ 7.51 (d, $J_{H,H}$ 5.2 Hz, 1H, H_{ar}), 7.49 (d, $J_{H,H}$ 5.67 Hz, 1H, H_{ar}), 7.39 (d, $J_{H,H}$ 5.7 Hz, 1H, H_{ar}), 7.38 (d, $J_{H,H}$ 5.3 Hz, 1H, H_{ar}), 4.92 (d, $^3J_{1,2}$ 1.2 Hz, 2H, 2 × *H*-1), 4.50, 4.48 (2 × s, 4H, 2 × H_2CC≡C), 3.70–3.35 (m, 10H, 2 × *H*-2, *H*-3, *H*-4, *H*-5, *H*-6a, and *H*-6b); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 132.0, 128.9, 124.3 (C_6H_4), 98.2 (*C*-1), 89.7, 84.2 (*C*≡*C*), 74.4, 70.9, 70.2, 70.1, 66.7 (*C*-2, *C*-3, *C*-4, *C*-5), 61.1, 61.0 (*C*-6, *C*-6′), 53.6 (CH_2); ESI$^+$-MS *m/z* calcd for $C_{24}H_{30}O_{12}$ $[M-8(OH)]^+$ 346.1, found, 346.8.

3.2.16. 1,3-Bis-[1,1′(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)prop-2,2′-ynyl]benzene (24)

Nitrogen gas was bubbled through a solution of 2-propynyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**11**) (1.30 g, 3.30 mmol, 1.00 equiv) and 1,3-diiodobenzene (0.51 g, 1.50 mmol, 0.45 equiv) in DMF–Et_3N (13–13 mL) for 25 min. Palladium tetrakis triphenylphosphine ($Pd(PPh_3)_4$) (0.17 g, 0.14 mmol, 0.04 equiv) was added and the mixture was stirred under N_2 for 5 min. The reaction mixture was heated to 60 °C and stirred under a stream of N_2 for 4 h after which time the reaction was judged complete by TLC (hexane/EtOAc 1:1). The reaction mixture was cooled and dissolved in diethylether/toluene (100 mL/50 mL), then washed with 2 M HCl (2 × 150 mL), with saturated $NaHCO_3$ soln (1 × 150 mL) and then with H_2O (1 × 150 mL). The crude extract was then purified by column chromatography in silica gel with hexane/EtOAc 2:3 as eluent. The title product **24** was obtained as a yellow crystalline solid (1.20 g, 88% yield); mp 74–77 °C; $[\alpha]_D^{23}$ +34 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.50 (s, 1H, H_{ar}), 7.38 (dd, $J_{H,H}$ 1.43 Hz, $J_{H,H}$ 7.8 Hz, 2H, H_{ar}), 7.36 (d, $J_{H,H}$ 7.9 Hz, 1H, H_{ar}), 5.35 (dd, $^3J_{3,2}$ 3.4 Hz, $^3J_{3,4}$ 10.0 Hz, 2H, 2 × *H*-3), 5.28 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.0 Hz, 2H, 2 × *H*-4), 5.28 (dd, $^3J_{1,2}$ 2.5 Hz, $^3J_{2,3}$ 4.3 Hz, 2H, 2 × *H*-2), 5.06 (d, $^3J_{1,2}$ 1.5 Hz, 2H, 2 × *H*-1), 4.46 (d, $^4J_{H,H}$ 5.1 Hz, 4H, 2 × $H_2CC{\equiv}C$), 4.27 (dd, $^3J_{5,6a}$ 5.2 Hz, $^2J_{6a,6b}$ 12.3 Hz, 2H, 2 × *H*-6a), 4.11–4.06 (m, 2H, 2 × *H*-6b), 4.04–4.01 (m, 2H, 2 × *H*-5), 2.13, 2.06, 2.01, 1.96 (4 × s, 4 × 6H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.5, 169.8, 169.8, 169.6 (*C*=O), 134.9, 132.0, 128.5, 122.4 (C_6H_4), 96.2 (*C*-1), 86.1, 83.9 (*C*≡*C*), 69.4 (*C*-2, *C*-4), 69.0, 68.9 (*C*-3, *C*-5), 66.0 (*C*-2, *C*-4), 62.3 (*C*-6), 55.5 ($H_2CC{\equiv}C$), 20.8, 20.6, 20.6, 20.6 ($COCH_3$); FAB-HRMS *m/z* calcd for $C_{40}H_{46}O_{20}$ $[M+K]^+$ 885.2220, found, 885.2211.

3.2.17. 1,3-Bis-[1,1′(α-D-mannopyranosyloxy)-prop-2,2′-ynyl]benzene (25)

The titled compound was obtained as a yellowish solid by deacetylation of **24** (0.35 g, 0.42 mmol) using the method described above for **4** (0.20 g, quant. yield); mp 65–69 °C; $[\alpha]_D^{23}$ +137.7 (*c* 1.3, MeOH); ^1H NMR (DMSO-d_6, 600 MHz) δ 7.49 (d, $J_{H,H}$ 6.5 Hz, 2H, H_{ar}), 7.47 (br s, 1H, H_{ar}), 7.41 (dd, $J_{H,H}$ 7.1 Hz, $J_{H,H}$ 8.3 Hz, 1H, H_{ar}), 4.85 (s, 2H, 2 × *H*-1), 4.83 (d, *J* 4.3 Hz, 2H, 2 × C2-O*H*), 4.74 (d, *J* 5.4 Hz, 2H, 2 × C4-O*H*), 4.59 (d, *J* 6.0 Hz, 2H, 2 × C3-O*H*), 4.50 (t, *J* 6.1 Hz, 2H, 2 × C6-O*H*), 4.46 (s, 2H, 2 × $H_2CC{\equiv}C$), 3.66 (m, 4H, 2 × *H*-2, and *H*-6a), 3.45 (m, 4H, 2 × *H*-3, and *H*-6b), 3.34 (m, 2H, 2 × *H*-5), 3.31–3.22 (m, 2H, 2 × *H*-4); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 134.0, 131.8, 129.3, 122.4 (C_6H_4), 98.4 (*C*-1), 85.6, 84.5 (*C*≡*C*), 74.5 (*C*-4), 70.9 (*C*-3), 70.1 (*C*-2), 66.9 (*C*-5), 61.2 (*C*-6), 53.6 ($H_2CC{\equiv}C$); FAB-HRMS *m/z* calcd for $C_{24}H_{30}O_{12}$ $[M+K]^+$ 549.1374, found, 549.1404.

3.2.18. Bis-2-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)diphenylacetylene (28)

Nitrogen gas was bubbled through a solution of 2-ethynylphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**13**) (0.330 g, 0.74 mmol, 3.89 equiv) and 2-iodophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**9**) (0.100 g, 0.19 mmol, 1.00 equiv) in Et_3N–DMF (20–2 mL) for 15 min. $Pd(PPh_3)_4$ (0.012 g, 0.010 mmol, 0.05 equiv) was added and the mixture was stirred under N_2 gas for 5 min and was then stirred at 60 °C under a stream of N_2 gas for 22 h until the reaction was judged complete by TLC (hexane/EtOAc 1:1). The reaction mixture was dissolved in $CHCl_3$ (50 mL) and washed with 2 M HCl (3 × 80 mL), then with saturated $NaHCO_3$ (2 × 80 mL) and with H_2O (2 × 80 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered, and the solvent removed under reduced pressure. The concentrate was purified by column chromatography on silica gel (hexane/EtOAc 1:1). Compound **28** was obtained as a yellowish crystalline powder (0.127 g, 80% yield); mp 148–150 °C; $[\alpha]_D^{23}$ +34.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.43 (dd, $J_{H,H}$ 1.5 Hz, $J_{H,H}$ 7.6 Hz, 2H, H_{ar}), 7.25 (dd, *J* 1.6 Hz, *J* 8.5 Hz, 2H, H_{ar}), 7.13 (d, $J_{H,H}$ 8.0 Hz, 2H, H_{ar}), 7.07 (ddd, $J_{H,H}$ 0.9 Hz, $J_{H,H}$ 7.6 Hz, $J_{H,H}$ 8.3 Hz, 2H, H_{ar}), 5.67 (dd, $^3J_{2,3}$ 3.5 Hz, $^3J_{3,4}$ 10.0 Hz, 2H, 2 × *H*-3), 5.64 (d, $^3J_{1,2}$ 1.6 Hz, 2H, 2 × *H*-1), 5.59 (dd, $^3J_{1,2}$ 1.8 Hz, $^3J_{2,3}$ 3.4 Hz, 2H, 2 × *H*-2), 5.37 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.0 Hz, 2H, 2 × *H*-4), 4.29–4.23 (m, 4H, 2 × *H*-5, and *H*-6a), 4.04 (d, $^3J_{5,6b}$ 5.2 Hz, $^2J_{6a,6b}$ 10.2 Hz, 2H, 2 × *H*-6b), 2.17, 2.01, 1.96, 1.98 (4 × s, 4 × 6H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.4, 169.7, 169.5 (*C*=O), 155.6, 134.1, 129.6, 123.2, 115.3, 114.9 (C_6H_4), 96.3 (*C*-1), 89.7 (*C*≡*C*), 69.9 (*C*-3), 69.4 (*C*-5), 69.3 (*C*-2), 65.9 (*C*-4), 62.0 (*C*-6), 20.8, 20.6, 20.6, 20.6 ($COCH_3$); FAB-HRMS *m/z* calcd for $C_{42}H_{46}O_{20}$ $[M+K]^+$ 909.2220, found, 909.2176.

3.2.19. Bis-2-(α-D-mannopyranosyloxy)diphenylacetylene (29)

The titled compound was obtained as a yellowish solid by deacetylation of **28** (0.041 g, 0.048 mmol) using the method described above for **4** (0.025 g, quant. yield); mp 104–108 °C; $[\alpha]_D^{23}$ +3.8 (*c* 1.0, DMF); IR (DMF): 3545.0 cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz) δ 7.51 (dd, $J_{H,H}$ 1.4 Hz, $J_{H,H}$ 9.0 Hz, 2H, H_{ar}), 7.34–7.25 (m, 4H, H_{ar}), 7.04 (ddd, $J_{H,H}$ 1.3 Hz, $J_{H,H}$ 8.2 Hz, 2H, H_{ar}), 5.50 (s, 2H, 2 × *H*-1), 4.11 (br s, 8H, C-O*H*), 3.94 (d, *J* 1.65 Hz, 2H, 2 × *H*-2), 3.82 (m, 2H, 2 × *H*-3), 3.62, 3.43 (m, 6H, 2 × *H*-4, *H*-5, and *H*-6); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 156.6, 132.9, 130.0, 122.3, 116.5, 113.7 (C_6H_4), 99.2 (*C*-1), 88.0 (*C*≡*C*), 75.2, 70.8, 70.2, 67.0, 66.6 (*C*-2, *C*-3, *C*-4, *C*-5), 61.0 (*C*-6); ESI^+-MS *m/z* calcd for $C_{26}H_{30}O_{12}$ $[M+NH_4]^+$ 552.2, found, 552.2.

3.2.20. Bis-3a-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)diphenylacetylene (30)

Nitrogen gas was bubbled through a solution of 3-ethynylphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**14**) (0.330 g, 0.74 mmol, 4.93 equiv) and 3-iodophenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**10**) (0.082 g, 0.15 mmol, 1.00 equiv) in Et_3N–DMF (20–2 mL) for 15 min. $Pd(PPh_3)_4$ (0.086 g, 0.0074 mmol, 0.05 equiv) was added and the mixture was stirred under N_2 gas for 5 min. The reaction was continued at 60 °C under a stream of N_2 gas for 24 h. The reaction was judged complete by TLC (hexane/EtOAc 1:1). The reaction mixture was dissolved in $CHCl_3$ (30 mL) and washed with 2 M HCl (3 × 60 mL), then with saturated $NaHCO_3$ (2 × 60 mL) then with H_2O (2 × 60 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered, and the solvent removed under reduced pressure. The concentrate was purified by column chromatography on silica gel (hexane/EtOAc 1:1). Compound **30** was obtained as a yellowish crystalline powder (0.104 g, 80% yield); mp 78–79 °C; $[\alpha]_D^{23}$ +126.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.26 (m, 4H, H_{ar}), 7.19 (ddd, $J_{H,H}$ 1.1 Hz, $J_{H,H}$ 2.3 Hz, $J_{H,H}$ 7.7 Hz, 2H, H_{ar}), 7.05 (ddd, $J_{H,H}$ 1.0 Hz, $J_{H,H}$ 2.5 Hz, $J_{H,H}$ 8.3 Hz, 2H, H_{ar}), 5.53 (dd, $^3J_{2,3}$ 3.5 Hz, $^3J_{3,4}$ 10.3 Hz, 2H, 2 × *H*-3), 5.51 (d, $^3J_{1,2}$ 2.00 Hz, 2H, 2 × *H*-1), 5.42 (dd, $^3J_{1,2}$ 1.9 Hz, $^3J_{2,3}$ 3.6 Hz, 2H, 2 × *H*-2), 5.33 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.2 Hz, 2H, 2 × *H*-4), 4.26 (dd, $^3J_{5,6a}$ 6.1 Hz, $^2J_{6a,6b}$ 12.4 Hz, 2H, 2 × *H*-6a), 4.09–4.07 (m, 2H, 2 × *H*-5), 4.06–4.04 (m, 2H, 2 × *H*-6b), 2.17, 2.03, 2.01, 2.01 (4 × s, 4 × 6H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.5, 169.9, 169.8, 169.7 (*C*=O), 155.4, 129.6, 126.4, 124.3, 119.3, 117.2, (C_6H_4), 95.8 (*C*-1), 89.1 (*C*≡*C*), 69.3 (*C*-5), 69.2 (*C*-2), 68.8 (*C*-3), 66.0 (*C*-4), 62.1 (*C*-6), 20.8, 20.6, 20.6 ($COCH_3$); FAB-HRMS *m/z* calcd for $C_{42}H_{46}O_{20}$ $[M+K]^+$ 909.2220, found, 909.2027.

3.2.21. Bis-3-(α-D-mannopyranosyloxy)diphenylacetylene (31)

The titled compound was obtained as a yellowish solid by deacetylation of **30** (0.110 g, 0.12 mmol) using the method described above for **4** (0.066 g, quant. yield); mp 80–82 °C; $[\alpha]_D^{23}$ +74.0 (*c* 1.0, DMSO); IR (DMF): 3540 cm^{-1}; ^1H NMR (DMSO-d_6, 600 MHz) δ 7.33 (dd, $J_{H,H}$ 8.0 Hz, $J_{H,H}$ 7.9 Hz, 2H, H_{ar}), 7.25 (dd, $J_{H,H}$ 1.9 Hz, $J_{H,H}$ 3.6 Hz, 2H, H_{ar}), 7.19 (d, $J_{H,H}$ 7.6 Hz, 2H, H_{ar}), 7.12

(m, 2H, H_{ar}), 5.42 (d, $^3J_{1,2}$ 1.6 Hz, 2H, 2 × *H*-1), 5.01 (d, *J* 4.4 Hz, 2H, 2 × C2-O*H*), 4.81 (d, *J* 5.7 Hz, 2H, 2 × C4-O*H*), 4.73 (d, *J* 6.0 Hz, 2H, 2 × C3-O*H*), 4.46 (t, *J* 5.9 Hz, 2H, 2 × C6-O*H*), 3.82 (br s, 2H, 2 × *H*-2), 3.67 (m, 2H, 2 × *H*-3), 3.59 (ddd, $J_{OH,6a}$ 5.8 Hz, $^3J_{5,6a}$ 7.8 Hz, $^2J_{6a,6b}$ 11.8 Hz, 2H, 2 × *H*-6a), 3.52–3.43 (m, 4H, 2 × *H*-5, and *H*-6b), 3.39 (m, 2H, 2 × *H*-4); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 156.3, 130.0, 123.1, 119.3, 117.9 (C_6H_4), 98.6 (*C*-1), 89.1 (*C*≡*C*), 75.1 (*C*-4), 70.6 (*C*-3), 70.0 (*C*-2), 66.7 (*C*-5), 61.0 (*C*-6); FAB-MS *m/z* calcd for $C_{26}H_{30}O_{12}$ $[M+H]^+$ 535.17, found, 535.12.

3.2.22. Bis-4-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)diphenyl-but-1,3-diyne (34)

4-Ethynylphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**12**) (0.230 g, 0.52 mmol, 1.00 equiv) and copper(II) acetate $[Cu(OAc)_2H_2O]$ (0.011 g, 0.054 mmol, 0.10 equiv) were refluxed in pyridine (20 mL) under a stream of N_2 gas. The reaction was followed by TLC on silica gel (hexane/EtOAc 1:1) and was judged complete after 48 h. The reaction mixture was diluted in CH_2Cl_2 (40 mL) washed with 2 M HCl (3 × 80 mL), then with saturated $NaHCO_3$ (2 × 80 mL) then with H_2O (2 × 80 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The concentrate was purified by column chromatography on silica gel with hexane EtOAc 1/1 as eluent. The titled compound **34** was obtained as yellow crystalline powder (0.108 g, 47% yield); mp 88–89 °C; $[\alpha]_D^{23}$ +79.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.63 (d, $J_{H,H}$ 8.6 Hz, 4H, H_{ar}), 7.06 (d, $J_{H,H}$ 8.7 Hz, 4H, H_{ar}), 5.53 (dd, $^3J_{2,3}$ 3.5 Hz, $^3J_{3,4}$ 8.0 Hz, 2H, 2 × *H*-3), 5.43 (s, 2H, 2 × *H*-1), 5.44 (dd, $^3J_{1,2}$ 1.8 Hz, $^3J_{2,3}$ 3.5 Hz, 2H, 2 × *H*-2), 5.34 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.1 Hz, 2H, 2 × *H*-4), 4.26 (dd, $^3J_{5,6a}$ 5.2 Hz, $^2J_{6a,6b}$ 12.4 Hz, 2H, 2 × *H*-6a), 4.09–4.03 (m, 4H, 2 × *H*-5, and *H*-6b), 2.20, 2.05, 2.04, 2.02 (4 × s, 4 × 6H, COC*H*$_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.4, 169.9, 169.8, 169.6 (*C*=O), 156.0, 134.1, 116.6 (C_6H_4), 95.6 (*C*-1), 80.8, 73.5 (*C*≡*C*), 69.4 (*C*-5), 69.2 (*C*-2),68.7 (*C*-3), 65.9 (*C*-4), 62.0 (*C*-6), 20.8, 20.6, 20.6 (COCH$_3$); FAB-HRMS *m/z* calcd for $C_{44}H_{46}O_{20}$ $[M+K]^+$ 933.2220, found, 933.1648.

3.2.23. Bis-4-(α-D-mannopyranosyloxy)diphenylbut-1,3-diyne (35)

The titled compound was obtained as a yellowish solid by deacetylation of **34** (0.098 g, 0.12 mmol) using the method described above for **4** (0.064 g, quant. yield); mp 163–164 °C; $[\alpha]_D^{23}$ +89.2 (*c* 1.2, DMF); IR (DMF): 3561.0 cm^{-1}; ^{1}H NMR (DMSO-d_6, 600 MHz) δ 7.52 (d, $J_{H,H}$ 8.6 Hz, 4H, H_{ar}), 7.11 (d, $J_{H,H}$ 8.7 Hz, 4H, H_{ar}), 5.44 (s, 2H, 2 × *H*-1), 5.07 (s, 2H, 2 × C2-O*H*), 4.85 (d, *J* 4.8 Hz, 2H, 2 × C4-O*H*), 4.76 (d, *J* 3.8 Hz, 2H, 2 × C3-O*H*), 4.46 (br s, 2H, 2 × C6-O*H*), 3.82 (br s, 2H, 2 × *H*-2), 3.66 (dd, $^3J_{2,3}$ 4.5, $^3J_{3,4}$ 8.3 Hz, 2H, 2 × *H*-3), 3.59–3.45 (m, 4H, 2 × *H*-4, *H*-6a), 3.41 (m, 2H, 2 × *H*-6b), 3.34 (m, 2H, 2 × *H*-5); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 157.4, 113.7, 134.0, 117.1 (C_6H_4), 98.6 (*C*-1), 81.5, 72.9 (*C*≡*C*), 75.2 (*C*-5), 70.6 (*C*-3), 69.9 (*C*-2), 66.6 (*C*-4), 61.0 (*C*-6); FAB-MS *m/z* calcd for $C_{28}H_{30}O_{12}$ $[M-4OH]^+$ 486.1, found, 486.2.

3.2.24. Bis-2-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)diphenyl-but-1,3-diyne (36)

2-Ethynylphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**13**) (0.12 g, 0.27 mmol, 1.00 equiv) and copper(II) acetate $[Cu(OAc)_2H_2O]$ (0.0029 g, 0.014 mmol, 0.05 equiv) were refluxed in pyridine (10 mL) under a stream of N_2 gas. Reaction was followed by TLC on silica gel (hexane/EtOAc 1:1) and was judged complete after 24 h. The reaction mixture was diluted in CH_2Cl_2 (30 mL) washed with 2 M HCl (3 × 60 mL), then with saturated $NaHCO_3$ (2 × 60 mL) and with H_2O (2 × 60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and the solvent was removed in vacuo. The concentrate was purified by column chromatography on silica gel using gradient elution (hexane/EtOAc 1:1 then pure EtOAc). The titled compound **36** was obtained as yellow crystalline powder (0.078 g, 63% yield); mp 74–76 °C; $[\alpha]_D^{23}$ +5.3 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.56 (dd, $J_{H,H}$ 1.8 Hz, $J_{H,H}$ 7.7 Hz, 2H, H_{ar}), 7.3 (ddd, $J_{H,H}$ 1.7 Hz, $J_{H,H}$ 8.0 Hz, $J_{H,H}$ 8.4 Hz, 2H, H_{ar}), 7.10 (d, $J_{H,H}$ 8.1 Hz, 4H, H_{ar}), 7.03 (m, 2H, H_{ar}), 5.64 (dd, $^3J_{2,3}$ 3.5 Hz, $^3J_{3,4}$ 10.0 Hz, 2H, 2 × *H*-3), 5.59 (d, $^3J_{1,2}$ 1.8 Hz, 2H, 2 × *H*-1), 5.55 (dd, $^3J_{1,2}$ 1.9 Hz, $^3J_{2,3}$ 3.5 Hz, 2H, 2 × *H*-2), 5.36 (t, $^3J_{3,4} = {}^3J_{4,5}$ 9.9 Hz, 2H, 2 × *H*-4), 4.30–4.23 (m, 4H, 2 × *H*-5, and *H*-6a), 4.11–4.05 (m, 2H, 2 × *H*-6b), 2.17, 2.01, 2.01, 1.99 (4 × s, 4 × 6H, COC*H*$_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.04, 169.8, 167.8, 169.4 (*C*=O), 157.3, 134.5, 130.3, 123.2, 116.0, 113.6 (C_6H_4), 96.8 (*C*-1), 79.5, 77.7 (*C*≡*C*), 69.5 (*C*-5), 69.4 (*C*-2), 68.7 (*C*-3), 65.9 (*C*-4), 62.1 (*C*-6), 21.0, 20.5, 20.6, 20.6 (COCH$_3$); FAB-HRMS *m/z* calcd for $C_{44}H_{46}O_{20}$ $[M+K]^+$ 933.2220, found, 933.2621.

3.2.25. Bis-2-(α-D-mannopyranosyloxy)diphenyl-but-1,3-diyne (37)

The titled compound was obtained as a white solid by deacetylation of **36** (0.070 g, 0.082 mmol) using the method described above for **4** (0.046 g, quant. yield); mp 130–132 °C; $[\alpha]_D^{23}$ −0.8 (*c* 1.3, DMF); IR (DMF): 3544.0 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 7.55 (dd, $J_{H,H}$ 1.5 Hz, $J_{H,H}$ 7.7 Hz, 2H, H_{ar}), 7.41 (ddd, $J_{H,H}$ 1.6 Hz, $J_{H,H}$ 8.3 Hz, 2H, H_{ar}), 7.30 (d, $J_{H,H}$ 8.4 Hz, 2H, H_{ar}), 7.04 (dd, $J_{H,H}$ 7.5 Hz, $J_{H,H}$ 7.4 Hz, 2H, H_{ar}), 5.48 (s, 2H, 2 × *H*-1), 5.07 (d, *J* 4.4 Hz, 2H, 2 × C2-O*H*), 4.94 (d, *J* 5.5 Hz, 2H, 2 × C3-O*H*), 4.9 (d, *J* 5.8 Hz, 2H, 2 × C4-O*H*), 4.43 (t, *J* 5.8 Hz, 2H, 2 × C6-O*H*), 3.91 (br s, 2H, 2 × *H*-2), 3.75 (m, 2H, 2 × *H*-3), 3.59 (m, 2H, 2 × *H*-6a), 3.55–3.50 (m, 2H, 2 × *H*-4), 3.48–3.36 (m, 4H, 2 × *H*-5, and *H*-6a); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 158.1, 134.1, 131.3, 122.2, 116.0 (C_6H_4), 99.1 (*C*-1), 78.7, 77.2 (*C*≡*C*), 75.2 (*C*-5), 70.6 (*C*-3), 69.9 (*C*-2), 66.6 (*C*-4), 61.0 ppm (*C*-6); ESI$^+$-MS *m/z* calcd for $C_{28}H_{30}O_{12}$ $[M+H]^+$ 558.2, found, 558.2.

3.2.26. Bis-3-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy) diphenyl-but-1,3-diyne (38)

Compound **14** (0.100 g, 0.22 mmol, 1.00 equiv) and copper(II) acetate $[Cu(OAc)_2H_2O]$ (0.0044 g, 0.022 mmol, 0.10 equiv) were refluxed in pyridine (10 mL) under a stream of N_2 gas. The reaction was followed by TLC on silica gel (hexane/EtOAc 1:1) and was judged complete after 48 h. The reaction mixture was diluted with CH_2Cl_2 (30 mL) washed with 2 M HCl (3 × 60 mL), then with saturated $NaHCO_3$ (2 × 60 mL) then with H_2O (2 × 60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The concentrate was purified by silica gel column chromatography using gradient elution (hexane/EtOAc 2:1 then 1:1). Compound **38** was obtained as yellow amorphus powder (0.058 g, 58% yield); mp 85–88 °C; $[\alpha]_D^{23}$ +73.8 (*c* 2.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.28 (m, 2H, H_{ar}), 7.25 (d, $J_{H,H}$ 8.0 Hz, 2H, H_{ar}), 7.21 (ddd, $J_{H,H}$ 1.2 Hz, $J_{H,H}$ 2.5 Hz, $J_{H,H}$ 8.0 Hz, 2H, H_{ar}), 7.08 (ddd, $J_{H,H}$ 1.2 Hz, $J_{H,H}$ 2.5 Hz, $J_{H,H}$ 8.1 Hz, 2H, H_{ar}), 5.51 (dd, $^3J_{2,3}$ 3.5 Hz, $^3J_{3,4}$ 10.0 Hz, 2H, 2 × *H*-3), 5.48 (d, $^3J_{1,2}$ 1.8 Hz, 2H, 2 × *H*-1), 5.41 (dd, $^3J_{1,2}$ 1.8 Hz, $^3J_{2,3}$ 3.5 Hz, 2H, 2 × *H*-2), 5.32 (t, $^3J_{3,4} = {}^3J_{4,5}$ 10.0 Hz, 2H, 2 × *H*-4), 4.25 (dd, $^3J_{5,6a}$ 6.465 Hz, $^2J_{6a,6b}$ 12.6 Hz, 2H, 2 × *H*-6a), 4.12–4.04 (m, 4H, 2 × *H*-5, and *H*-6b), 2.18, 2.04, 2.03, 2.01 (4 × s, 4 × 6H, COC*H*$_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.6, 169.9, 169.9, 169.715 (*C*=O), 155.4, 129.8, 127.4, 123.0, 120.2, 118.3 (C_6H_4), 95.9 (*C*-1), 81.1, 74.1 (*C*≡*C*), 69.3 (*C*-2 and *C*-5), 68.8 (*C*-3), 66.0 (*C*-4), 62.2 (*C*-6), 20.8, 20.6, 20.6 (COCH$_3$); FAB-HRMS *m/z* calcd for $C_{44}H_{46}O_{20}$ $[M+K]^+$ 933.2220, found, 933.2387.

3.2.27. Bis-3-(α-D-mannopyranosyl)diphenyl-but-1,3-diyne (39)

The titled compound was as a yellowish solid obtained by deacetylation of **38** (0.023 g, 0.027 mmol) using the method described above for **4** (0.015 g, quant. yield); mp 80–82 °C; $[\alpha]_D^{23}$ +71.0 (*c* 1.0, DMF); IR (DMF): 3540 cm^{-1}; ^{1}H NMR (DMSO-d_6,

600 MHz) δ 7.35 (dd, $J_{H,H}$ 8.0 Hz, $J_{H,H}$ 8.0 Hz, 2H, H_{ar}), 7.29 (br s, 2H, H_{ar}), 7.23 (d, $J_{H,H}$ 7.7 Hz, 2H, H_{ar}), 7.18 (ddd, $J_{H,H}$ 1.6 Hz, $J_{H,H}$ 2.4 Hz, $J_{H,H}$ 8.2 Hz, 2H, H_{ar}), 5.39 (d, $^{3}J_{1,2}$ 1.6 Hz, 2H, 2 × *H*-1), 5.09 (d, *J* 4.4 Hz, 2H, 2 × C2-O*H*), 4.87 (d, *J* 5.7 Hz, 2H, 2 × C4-O*H*), 4.71 (d, *J* 6.0 Hz, 2H, 2 × C3-O*H*), 4.53 (t, *J* 5.8 Hz, 2H, 2 × C6-O*H*), 3.81 (br s, 2H, 2 × *H*-2), 3.65 (m, 2H, 2 × *H*-3), 3.58 (m, 2H, 2 × *H*-6a), 3.41 (m, 4H, 2 × *H*-5, and *H*-6b), 3.36 (m, 2H, 2 × *H*-4); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 156.3, 130.2, 126.2, 121.4, 120.0, 119.2 (C_6H_4), 98.9 (*C*-1), 81.7 (*C*≡*C*), 75.1 (*C*-4), 73.3 (*C*≡*C*), 70.6 (*C*-3), 69.9 (*C*-2), 66.7 (*C*-5), 61.0 (*C*-6); FAB-HRMS *m/z* calcd for $C_{28}H_{30}O_{12}$ $[M+K]^+$ 597.1374, found, 597.2025.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2011.03.041.

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