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Carboxymethylglycoside lactones (CMGLs): structural variations on the carbohydrate moiety

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Abstract—New glucose and galactose based bicyclic lactones, with variations in the anomeric configuration, the protecting groups (acetyl or benzyl) and the furanosyl or pyranosyl rings were synthesized from allyl glycosides and used for the preparation of a series of new glycosylated alkyne amides.

1. Introduction

The well known biological importance of carbohydrates, especially their high affinity for several pharmacologically important receptors, has led to an increased interest in the synthesis of glycoconjugates[1,2] and their analogues, such as those based on the use of sugar amino acids (SAAs).[3] Amongst other synthons, carboxymethyl glycosides have proven to be valuable tools for the synthesis of such adducts, mostly due to the ability of the carboxylic acid group to efficiently connect the sugar moiety to another entity by amide or ester linkages. Thus, this family of compounds has been used as building blocks for the synthesis of glycoconjugate libraries for broad spectrum screening,[4–6] in combinatorial approaches to find selective inhibitors of enzymes[7,8] or for the synthesis of potentially biologically active glycoclusters.[9] Their properties have also been used in the solid-phase synthesis of oligosaccharides[10] or for the preparation of glycolipids[11] and glycodendrimers.[12–17]

Recently we have reported, that 3,4,6-tri-*O*-acetyl-α-D-glucopyranoside-2-*O*-lactone **1** (α-CMGL),[18,19] which is readily prepared from isomaltulose, reacted with amines and alcohols via selective opening of the lactone ring, giving an access to pseudodisaccharides and pseudoglucolipids (Scheme 1).[20] However, the method is limited to targets having the α-gluco configuration, that of lactone **1** arising from isomaltulose, whereas other conjugate analogues would be desired. It was therefore interesting to evaluate the possibility to enlarge the structural spectrum of the CMGLs. Herein we report the preparation of new carboxymethyl glycoside lactones, which differ in the sugar backbone, in the configuration at the anomeric centre and also in the nature of the protecting groups. The new lactones were obtained from the corresponding allyl glycosides after oxidation to the carboxymethyl glycosides. Their reactivity with respect to nucleophilic opening was illustrated by the reaction with propargyl amine, chosen for the wide spectrum of further possible transformations of the alkyne function.

2. Results and discussion

2.1. Synthesis of acetylated glycolactones

Glucose and galactose were transformed into their allyl 2,3,4,6-tetra-*O*-acetyl glycosides **2**, **3**, **7** and **8** following the literature procedure.[21] Both anomers were separated by chromatography at this stage (Scheme 2). Oxidation of the double bond with ruthenium trichloride led to peracetylated carboxymethyl derivatives,[5] which were subsequently deprotected with triethylamine in methanol and water to give **4**, **5**, **9** and **10**. These acids were then dissolved

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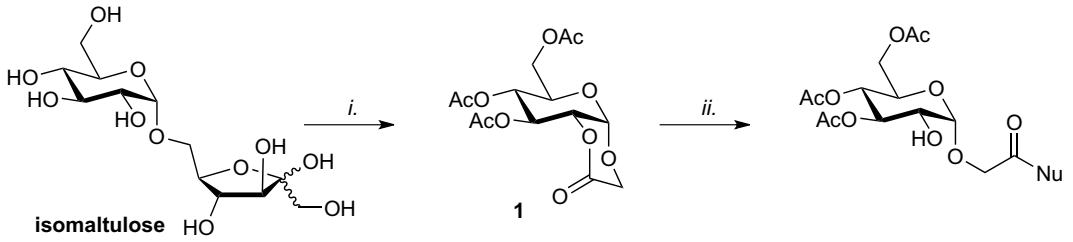
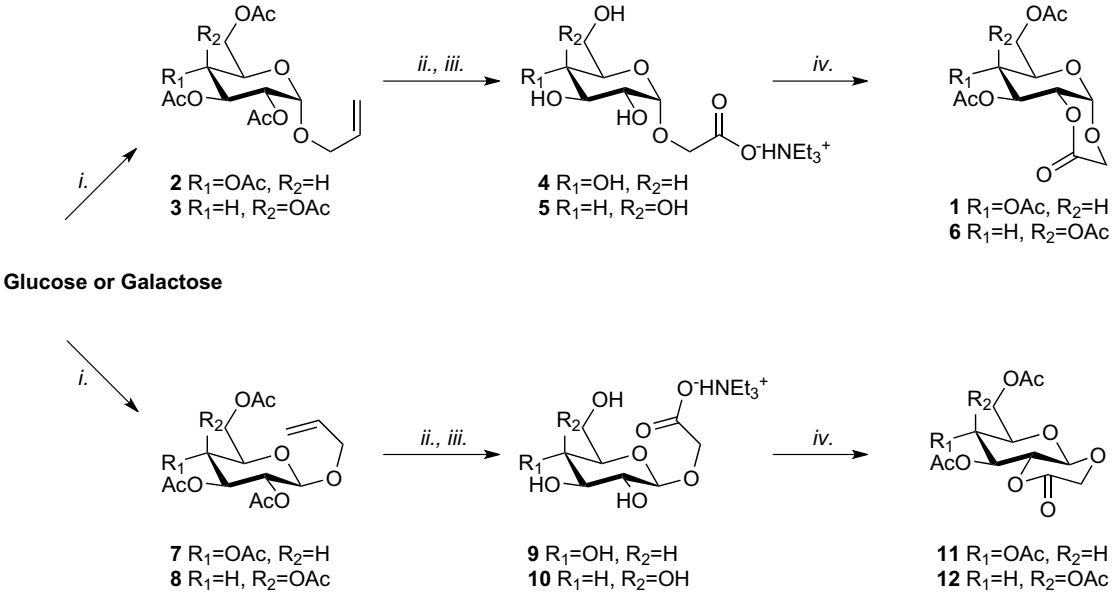
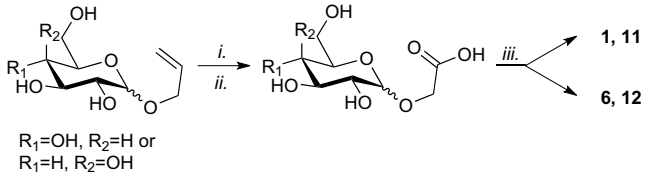


Scheme 1. Opening of the lactone ring with nucleophilic reagents. Reagents and conditions: (i) H_2O_2, H^+, then Ac_2O, pyridine; (ii) NuH (1.1 equiv), CH_2Cl_2, DMAP (cat), rt.



Scheme 2. Reagents and conditions: (i) (a) allyl alcohol, $BF_3{\cdot}Et_2O$, reflux; (b) Ac_2O, pyridine; (ii) $RuCl_3$, $NaIO_4$, $CH_2Cl_2/CH_3CN/H_2O$, 2 h, rt; (iii) TEA/MeOH/H_2O, 6h; (iv) Ac_2O, pyridine.

in a 1:1 mixture of pyridine and acetic anhydride to give the expected lactones **1**, **6**, **11** and **12** in 21–76% yield. An alternative, straightforward process, is the direct oxidation of allyl glycosides by ozonolysis, followed by reaction with $NaClO_2$ and subsequent lactonization under acetylation conditions without intermediate purification, to furnish the same lactones, as mixtures of anomers (difficult to separate at this stage) in 38–58% overall yields (Scheme 3).

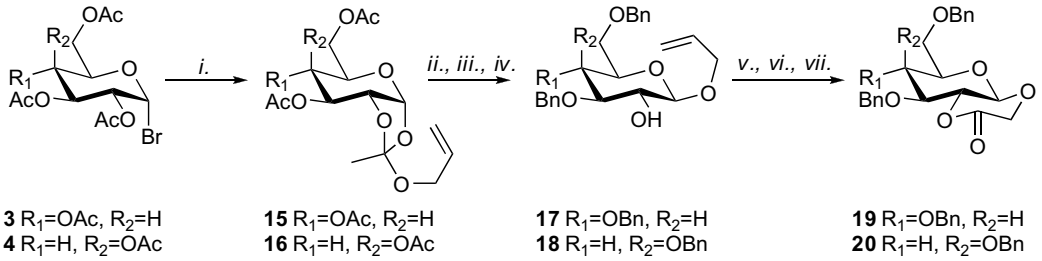


Scheme 3. Reagents and conditions: (i) O_3, MeOH, then DMS; (ii) $NaClO_2$, KH_2PO_4, H_2O, 0 °C, then rt; (iii) Ac_2O, pyridine.

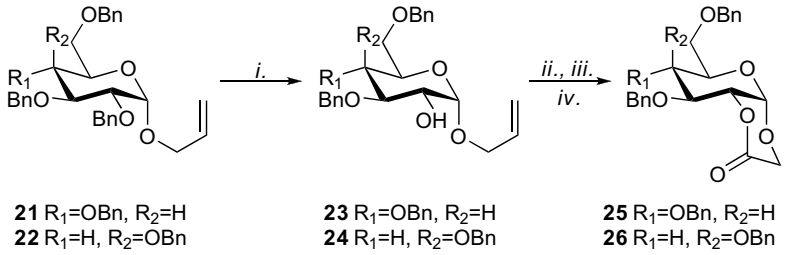
2.2. Synthesis of benzylated glycolactones

The benzylated analogues of CMGLs were then prepared. Such compounds would allow easier further manipulations on adducts when compared to the acetylated ones, which are sensitive to both basic and acidic conditions. To prepare the benzylated lactone, we had to obtain the proper allyl glycosides having the 2-OH function free. In the case of the β-anomers, we used the orthoester strategy[22] to obtain allyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside **17**[23] and allyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside **18**[23] (Scheme 4). These compounds were transformed into the expected lactones **19** and **20** via ozonolysis, oxidation of the resulting aldehydes with $NaClO_2$ and, finally, lactonization under acetylation conditions in 50% and 43% overall yield, respectively. The intermediate products were not isolated.

For the synthesis of α-anomers (Scheme 5), we used the de-O-alkylation strategy mediated by triisobutylaluminium (TIBAL) developed by Sinaÿ et al., which has been shown to selectively deprotect the 2-position of α-glucosides or galactosides.[24] Thus, after treatment of allyl-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside **21** with 5 equiv of TIBAL, the expected product **23** was isolated in 59% yield. The same method applied to allyl-2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranoside **22**, provided exclusively **24** in 56% yield. This result confirms the previous observations, showing



Scheme 4. Reagents and conditions: (i) allyl alcohol, 2,6-lutidine (2 equiv), Bu_4NBr (1.2 equiv), 4 h; (ii) MeONa/MeOH; (iii) NaH (1.25 equiv/OH), BnBr (1.25 equiv/OH), DMF; (iv) allyl alcohol, $BF_3{\cdot}OEt_2$; (v) O_3, MeOH, then DMS; (vi) $NaClO_2$, KH_2PO_4, H_2O, 0 °C, then rt; (vii) Ac_2O, pyridine.



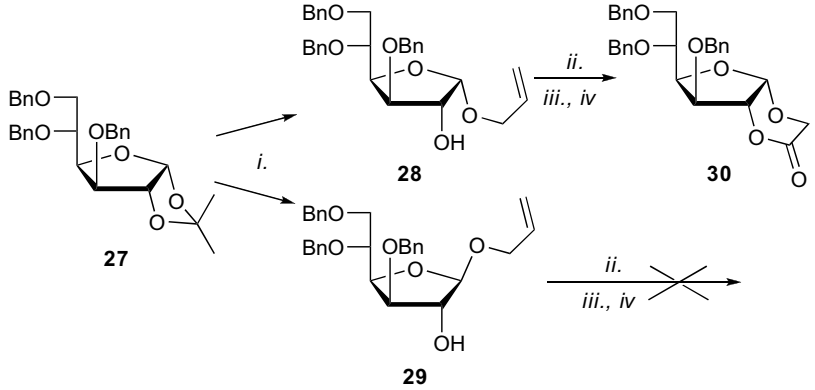
Scheme 5. Reagents and conditions: (i) TIBAL (5 equiv), toluene, 50 °C, overnight; (ii) O_3, MeOH, then DMS; (iii) $NaClO_2$, KH_2PO_4, H_2O, 0 °C, then rt; (iv) Ac_2O, pyridine.

that a benzyloxy group at the C-3 position in galactose derivatives is not sensitive to debenzylation under such conditions, in spite of its proper *cis*-orientation in respect to the alkoxy group at position C-2 and C-4.[25,26] Lactones **25** and **26** were then prepared from the allyl glycosides following the previously mentioned oxidation–acetylation sequence in 52% and 36% yield.

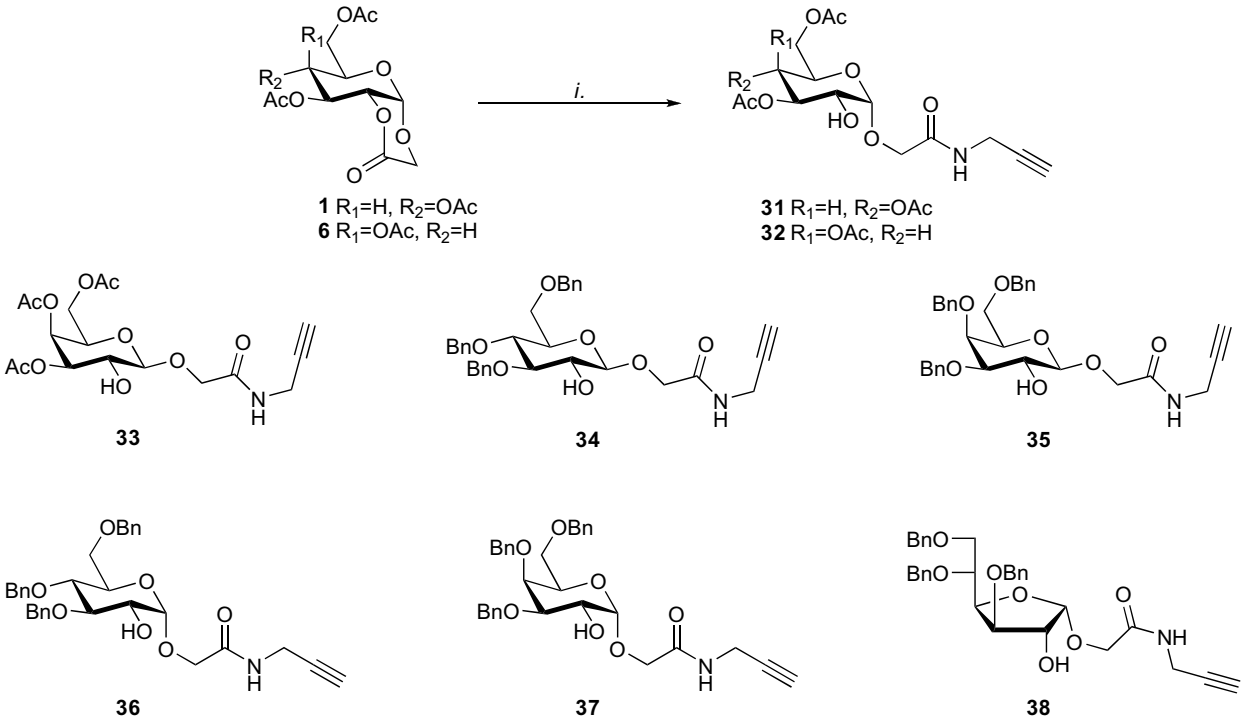
A lactone having a furanosyl ring was also prepared in this benzylated lactone series. Reaction of 1,2-*O*-isopropylidene-3,5,6-tri-*O*-benzyl-α-D-glucofuranose **27** with allyl alcohol (used also as solvent) containing BF_3 etherate as catalyst led to allyl glucofuranosides **28** and **29** in 59% and 27% yield, respectively, easily separated from each other by chromatography (Scheme 6). The typical procedure was applied to allyl glycoside **28** and afforded lactone **30** in 24% yield. An alternative method, based on heating in toluene in the presence of a catalytic amount of *p*-toluenesulfonic acid at reflux with azeotropic removal of water resulted in the expected product, although in a slower and less effective manner according to TLC. None of these conditions allowed us to obtain the β-lactone from **29**. This might be due to the observed lower stability of these benzylated lactones as compared to the acetylated ones, or, in this case, to a less favourable cycle strain in a 6–5 *trans* system. Indeed, all benzylated CMGLs, **30** in particular, had to be stored under a neutral atmosphere at low temperature, in order to prevent their spontaneous opening by a trace amount of water, especially when the compound is not a solid.

2.3. GMGLs opening reactions

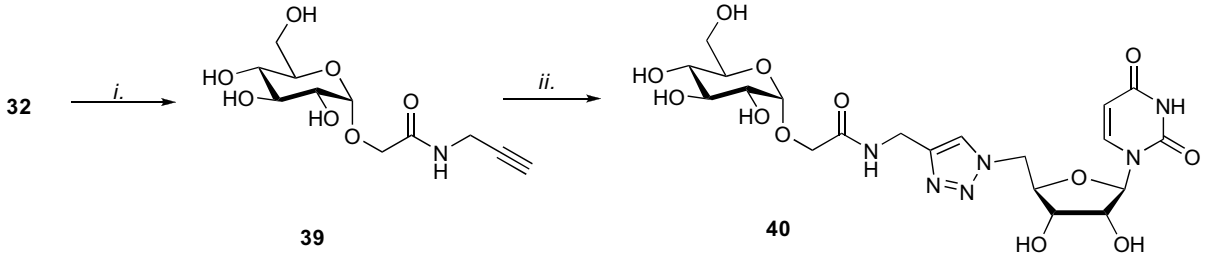
Having in hand this series of lactones, we used them for preparing new carbohydrate containing propargyl amides. These products can indeed be easily anchored to other



Scheme 6. Reagents and conditions: (i) $BF_3{\cdot}Et_2O$ (0.03 equiv), allyl alcohol, reflux, 1.5 h; (ii) O_3, MeOH, then DMS; (iii) $NaClO_2$, KH_2PO_4, H_2O, 0 °C, then rt; (iv) Ac_2O, pyridine.



Scheme 7. Reagents and conditions: (i) propargyl amine (1.0 equiv, or 1.5 equiv), CH_2Cl_2, rt, 10 h.



Scheme 8. Reagents and conditions: (i) MeONa/MeOH (1 M); (ii) 5′-azido-5′-deoxyuridine (1 equiv), CuI (catalytic amount), Et_3N (catalytic amount), CH_3CN:H_2O, rt, 24 h.

compounds possessing an azido moiety using Huisgen cycloaddition ('click' chemistry).[27] Thus the glucose and galactose based lactones **1** and **6** were treated with 1 equiv of propargyl amine in anhydrous CH_2Cl_2 to give the expected amides **31** and **32**, which were isolated by column chromatography in 94% and 84% yield, respectively (Scheme 7). The same sequence provided acetylated β-galactose lactone **33** and the perbenzylated lactones **34**–**38** in 54–94% yield. An illustration of the interest of such alkynyl synthons is given with the formation of triazole **40** by reaction of the deacetylated amide **39** with 5′-azido-5′-deoxyuridine[28] (Scheme 8) under Cu(I) catalysis in CH_3CN–H_2O (1:1).

3. Conclusion

A series of new carboxymethyl-D-glycoside-2-*O*-lactones, including variations on the protecting groups and on the sugar backbone, were obtained by the oxidation of 1-*O*-allyl sugars and subsequent formation of the lactone ring. The benzylated carboxymethyl lactones proved to be more sensitive to opening by water, therefore necessitating strictly anhydrous storage conditions. All new lactones exhibited similar reactivities towards nucleophilic species as the parent α-gluco CMGL, as illustrated by the preparation of a series of propargyl amides. One of the latter could be used, as an example, in a Huisgen cycloaddition with azidodeoxyuridine, en route towards potential analogues of nucleotide sugars.

4. Experimental

4.1. General

All chemicals were purchased from Aldrich. Organic solutions were dried over anhydrous sodium sulfate. The

reactions were monitored by thin-layer chromatography on Silica Gel 60 F254 (Merck); detection was carried out by charring with a 5% H_2SO_4 solution in ethanol. Silica gel (Kieselgel 60, 70–230 mesh ASTM, Merck) was used for flash chromatography. NMR spectra were recorded with a Bruker ALS300, DRX300 or DRX500 spectrometer in $CDCl_3$. The signal of the residual protonated solvent was taken as reference. Chemical shift (δ) and coupling constants (J) are reported in ppm and Hz, respectively. The ^{13}C aromatic resonances occurring at the typical δ values were omitted for simplicity. Optical rotations were measured with a Perkin–Elmer 241 polarimeter for solutions in $CHCl_3$ at room temperature. Elemental analyses were performed by 'Service Central de Microanalyses du CNRS' 69360 Solaize (France).

4.2. General procedure for preparation of carboxymethyl-2,3,4,6-tetra-*O*-acetyl-D-glycosides 4, 5, 9 and 10

Allyl-2,3,4,6-tetra-*O*-acetyl-D-glycoside (0.1 g, 0.26 mmol) was dissolved in $CH_2Cl_2/CH_3CN/H_2O$ 2:2:3 (1.2 mL). Then $NaIO_4$ (0.420 g, 1.98 mmol) was added followed by $RuCl_3$ (1.2 mg, 0.005 mmol) and the reaction mixture was stirred vigorously for 2 h at rt. The mixture was diluted with water and extracted twice with CH_2Cl_2. The combined organic layers were dried, concentrated and purified on column chromatography (AcOEt/MeOH; 7:3), to give the expected carboxymethyl-2,3,4,6-tetra-*O*-acetyl-D-glycoside **4** (86%), **5** (95%), **9** (88%) and **10** (50%), identified by comparison of the NMR spectra with the literature data.[9,11,13,18]

4.3. General procedure for preparation of peracetylated lactones

The carboxymethyl-2,3,4,6-tetra-*O*-acetyl-D-glycoside (0.355 g, 0.874 mmol) was dissolved in $MeOH/Et_3N/H_2O$ 8:1:1 (6 mL) and after 6 h, it was coevaporated with water to its half volume about 3 times, until no triethylamine remained. Then it was concentrated to dryness, to give the proper carboxymethyl-D-glycoside, which was dissolved in pyridine (12 mL). Acetic anhydride (7 mL) was added at 0 °C, and the reaction was stirred at rt for 24 h. The solvents were then evaporated under a diminished pressure and the oily residue was purified using column chromatography.

4.4. Carboxymethyl-3,4,6-tri-*O*-acetyl-α-D-glucopyranoside-2-*O*-lactone 1

White solid, 41% (pentane/AcOEt; 3:2). All characteristics have been published previously.[18]

4.5. Carboxymethyl-3,4,6-tri-*O*-acetyl-α-D-galactopyranoside-2-*O*-lactone 6

White amorphous solid, 52% (pentane/AcOEt; 3:2); $[\alpha]_D = +113$ (c 0.9, CH_2Cl_2); MS (ESI) $m/z = 346.09$ [$C_{15}H_{18}O_{11}$ $(M+H)^+$]; ^1H NMR (300 MHz) δ 5.48 (dd, 1H, $J_{3,4} = 3.3$ Hz, $J_{4,5} = 1.2$ Hz, H-4), 5.43 (dd, 1H, $J_{2,3} = 9.9$ Hz, H-3), 5.39 (d, 1H, $J_{1,2} = 3.0$ Hz, H-1), 4.71–4.61 (m, 2H, 4.67 (d, 1H, $J_{7A,7B} = 18.0$ Hz, H-7A) and 4.65 (dd, 1H, H-2)), 4.52 (d, 1H, H-7B), 4.47–4.42 (m, 1H, H-5), 4.15–4.09 (m, 2H, H-6A and H-6B), 2.15, 2.06, 2.055 ($3\times$s, $3\times$3H, $3\times CH_3$); ^{13}C NMR (75 MHz) δ 170.8, 170.5, 170.2, ($3\times$C=O from acetyl), 164.2 (C=O), 91.5 (C-1), 76.4 (C-2), 71.9 (C-3), 70.5 (C-5), 67.3 (C-4), 64.9 (C-7), 61.7 (C-6), 21.1, 20.9, 20.8 ($3\times CH_3$). Anal. Calcd for $C_{14}H_{18}O_{10}$: C, 48.56; H, 5.24. Found: C, 48.64; H, 5.49.

4.6. Carboxymethyl-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside-2-*O*-lactone 11

White amorphous solid, 21% (pentane/AcOEt; 3:2); $[\alpha]_D = +93$ (c 1, CH_2Cl_2); HRMS (ESI) m/z calcd for $C_{14}H_{18}O_{10}Na$ $(M+H)^+$ 347.0978, found 347.0979; ^1H NMR (300 MHz) δ 5.30 (dd, 1H, $J_{3,4} = 9.1$ Hz, $J_{2,3} = 10.2$ Hz, H-3), 5.05 (dd, 1H, $J_{3,4} = 9.1$ Hz, $J_{4,5} = 10.2$ Hz, H-4), 4.75 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1), 4.50 (AB system, 2H, δ_a 4.52 δ_b 4.69, $J_{A,B} = 17.4$ Hz, H-7), 4.30 (dd, 1H, $J_{1,2} = 7.9$ Hz, $J_{2,3} = 10.2$ Hz, H-2), 4.21 (dd, 1H, $J_{5,6B} = 4.7$ Hz, $J_{6A,6B} = 12.5$ Hz, H-6B), 4.12 (dd, 1H, $J_{5,6B} = 2.3$ Hz, $J_{6A,6B} = 12.5$ Hz, H-6B), 3.91 (ddd, 1H, $J_{5,6A} = 2.3$ Hz, $J_{5,6B} = 4.7$ Hz, $J_{4,5} = 10.2$ Hz, H-5), 2.09, 2.09, 2.05 ($3\times$s, $3\times$3H, $3\times CH_3$); ^{13}C NMR (75 MHz) δ 170.6, 169.9, 169.6, 164.9 ($4\times$C=O), 95.0 (C-1), 76.5, 73.8, 71.2,68.2 (C-2, C-3, C-4, C-5), 64.5 (C-7), 61.6 (C-6), 20.8, 20.7, 20.6 ($3\times CH_3$). Anal. Calcd for $C_{14}H_{18}O_{10}$: C, 48.56; H, 5.24. Found: C, 48.46; H, 5.41.

4.7. Carboxymethyl-3,4,6-tri-*O*-acetyl-β-D-galactopyranoside-2-*O*-lactone 12

White amorphous solid, 76% (pentane/AcOEt; 3:2 then 2:1); $[\alpha]_D = +85$ (c 1, CH_2Cl_2); HRMS (ESI) m/z calcd for $C_{14}H_{18}O_{10}Na$ $(M+Na)^+$ 369.0798, found 369.0797; ^1H NMR (500 MHz) δ 5.46 (dd, 1H, $J_{4,5} = 1.9$ Hz, $J_{3,4} = 3.5$ Hz, H-4), 5.16 (dd, 1H, $J_{2,3} = 10.5$ Hz, H-3), 4.77 (d, 1H, $J_{1,2} = 7.6$ Hz, H-1), 4.70 (d, 1H, $J_{A,B} = 17.7$ Hz, H-7A), 4.48–4.50 (m, 2H, 4.54 (d, 1H, H-7B), 4.53 (dd, 1H, H-2)), 4.20–4.16 (m, 2H, H-6A and H-6B), 4.13–4.09 (m, 1H, H-5), 2.14 (s, 3H, CH_3), 2.04 (s, 6H, $2\times CH_3$); ^{13}C NMR (75 MHz) δ 170.3 (double intensity), 169.7, 165.2 ($4\times$C=O), 95.5 (C-1), 74.6 (C-2), 72.8 (C-5), 69.5 (C-3), 66.8 (C-4), 64.5 (C-7), 61.0 (C-6), 20.6, 20.5, 20.4 ($3\times CH_3$). Anal. Calcd for $C_{14}H_{18}O_{10}$: C, 48.56; H, 5.24. Found: C, 48.64; H, 5.49.

4.8. General procedure for selective 2-O-debenzylation using TIBAL

Allyl 2,3,4,6-tetra-*O*-benzyl-α-D-pyranoside (6.0 g, 10.3 mmol) was dissolved in dry toluene (27 mL) and triisobutylaluminium (TIBAL, 51.5 mmol) as a 1.5 M toluene solution was added. The reaction mixture was stirred at 50 °C under a nitrogen atmosphere for 48 h, then cooled to 0 °C before the dropwise addition of 1 M HCl. The mixture was then portioned between water and ethyl acetate. The aqueous phase was extracted with ethyl acetate and the combined organic layers were dried, concentrated and purified on column chromatography.

4.9. Allyl 3,4,6-tri-*O*-benzyl-α-D-glucopyranoside 23

White amorphous solid, 55% (pentane/AcOEt; 6:1 then 5:1); ^{1}H NMR (300 MHz) δ 7.50–7.10 (m, 15H), 6.05–5.85 (m, 1H, –C*H*=CH$_2$), 5.36–5.28 (m, 1H, –CH=C*H*$_2$), 5.26–5.20 (m, 1H, CH=C*H*$_2$), 4.98 (d, 1H, $J_{1,2} = 3.4$ Hz, H-1), 4.96 (d, 1H, $J_{A,B} = 11.2$ Hz, from benzyl), 4.91–4.82 (m, 2H, 4.88 (d, 1H, $J_{A,B} = 11.2$ Hz), 4.86 (d, 1H, $J_{A,B} = 10.7$ Hz) from benzyl), 4.67 (d, 1H, $J_{A,B} = 12.2$ Hz, from benzyl), 4.57–4.50 (m, 2H, 4.53 (d, 1H, $J_{A,B} = 12.2$ Hz), 4.52 (d, 1H, $J_{A,B} = 10.7$ Hz) from benzyl), 4.24 (dddd, 1H, $J_{7A,9A} = 1.5$ Hz, $J_{7A,9B} = 1.5$ Hz, $J_{7A,8} = 5.3$ Hz, $J_{7A,7B} = 12.8$ Hz, H-7A), 4.07 (dddd, 1H, $J_{7B,9A} = 1.3$ Hz, $J_{7B,9B} = 1.3$ Hz, $J_{7B,8} = 6.2$ Hz, H-7B), 3.88–3.64 (m, 6H, H-2, H-3, H-4, H-5, H-6A, H-6B), 2.11 (br s, 1H, OH); ^{13}C NMR (75 MHz) δ 138.6, 138.1, 137.8 (3 × C quat.), 133.5 (–*C*H=CH$_2$), 117.9 (–CH=*C*H$_2$), 97.5 (C-1), 83.3, 77.3 and 72.9, 70.5 (C-2, C-3, C-4 and C-5), 75.3, 76.9, 73.4 (3 × CH$_2$), 68.4, 68.3 (C-6 and C-7). Other characteristics have been published elsewhere.[29]

4.10. Allyl 3,4,6-tri-*O*-benzyl-α-D-galactopyranoside 24

White amorphous solid, 62% (pentane/AcOEt; 5:1); ^{1}H NMR (500 MHz) δ 7.50–7.20 (m, 15H), 6.00–5.85 (m, 1H, –C*H*=CH$_2$), 5.14–5.08 (m, 1H, –CH=C*H*$_2$), 4.92 (d, 1H, $J_{1,2} = 3.8$ Hz, H-1), 4.83 (d, 1H, $J_{A,B} = 11.6$ Hz, from benzyl), 4.67 (d, 1H, $J_{A,B} = 11.8$ Hz, from benzyl), 4.63 (d, 1H, $J_{A,B} = 11.8$ Hz, from benzyl), 4.49 (d, 1H, $J_{A,B} = 11.6$ Hz, from benzyl), 4.43 (d, 1H, $J_{A,B} = 11.8$ Hz, from benzyl), 4.36 (d, 1H, $J_{A,B} = 11.8$ Hz, from benzyl), 4.15–4.85 (m, 2H, H-7A and H-2), 3.99–3.93 (m, 1H, $J_{7B,CH=CH_2} = 6.3$ Hz, $J_{7A,7B} = 13.0$ Hz, H-7B), 3.93–3.91 (m, 1H, H-4), 3.90–3.86 (m, 1H, H-5), 3.65 (dd, $J_{3,4} = 2.8$ Hz, $J_{2,3} = 10.1$ Hz, H-3), 3.56–3.46 (m, 2H, H-6A and H-6B), 2.16 (br s, 1H, OH); ^{13}C NMR (125 MHz) δ 138.5, 138.2, 137.9 (3 × C quat.), 133.7 (–*C*H=CH$_2$), 117.8 (–CH=*C*H$_2$), 97.7 (C-1), 79.6 (C-3), 74.6 (CH$_2$), 73.9 (C-4), 73.5, 72.4 (2 × CH$_2$), 69.7 (C-5), 69.0 (C-2), 68.8 (C-6), 68.5 (C-7). Other characteristics have been published elsewhere.[30,31]

4.11. Allyl 3,5,6-tri-*O*-benzyl-α-D-glucofuranoside 28

1,2-Isopropylidene-3,5,6-tri-*O*-benzyl-α-D-glucofuranose (1.95 g, 3.97 mmol) was dissolved in dry allyl alcohol (35 mL) containing BF_3 etherate (0.015 mL, 0.12 mmol) and the reaction mixture was stirred at reflux for 1.5 h. It was then cooled to the room temperature and the solvents were evaporated. The oily residue was purified chromatographically (pentane/ethyl acetate 6:1 then 4:1) to give **28** (1.15 g, 59%) as a major, less polar product.

^{1}H NMR (300 MHz) δ 7.40–7.20 (m, 15H), 5.99–5.82 (m, 1H, –C*H*=CH$_2$), 5.30–5.14 (m, 3H, –CH=C*H*$_2$ and 5.16 (d, 1H, $J_{1,2} = 4.5$ Hz, H-1)), 4.78 (d, 1H, $J_{A,B} = 11.4$ Hz, from benzyl), 4.69 (d, 1H, $J_{A,B} = 11.7$ Hz, from benzyl), 4.62–4.48 (m, 4H, from benzyl), 4.38–4.20 (m, 3H, H-2, H-4 and H7A), 4.12–3.98 (m, 3H, H-3, H-5 and H-7B), 3.85 (dd, 1H, $J_{5,6A} = 2.0$ Hz, $J_{6A,6B} = 10.7$ Hz, H-6A), 3.68 (dd, 1H, $J_{5,6B} = 5.9$ Hz, H-6B), 2.93 (d, 1H, $J_{2,OH} = 5.4$ Hz, OH); ^{13}C NMR (75 MHz) δ 138.9, 138.6, 137.9 (3 × C quat.), 133.7 (–*C*H=CH$_2$), 117.7 (–CH=*C*H$_2$), 100.4 (C-1), 83.9 (C-3), 77.9 (C-4), 76.1 (double intensity, C-2 and C-5), 73.4, 72.6, 71.7 (3 × CH$_2$), 71.2 (C-6), 69.2 (C-7). Other characteristics have been published elsewhere.[31] From the same reaction allyl-3,5,6-tri-*O*-benzyl-β-D-glucofuranoside **29** was isolated as a minor, more polar product (0.52 g, 27%). ^{1}H NMR (300 MHz) δ 7.30–7.10 (m, 15H), 5.95–5.80 (m, 1H, –C*H*=CH$_2$), 5.35–5.20 (m, 1H, –CH=C*H*$_2$), 5.20–5.17 (m, 1H, –CH=C*H*$_2$), 4.92 (br s, 1H, H-1), 4.73 (d, 1H, $J_{A,B} = 11.4$ Hz, from benzyl), 4.64–4.44 (m, 5H, from benzyls), 4.38 (dd, 1H, $J_{3,4} = 5.0$ Hz, $J_{4,5} = 8.7$ Hz, H-4), 4.26–4.14 (m, 2H, H-2 and H-7A), 4.06 (ddd, 1H, $J_{5,6A} = 2.1$ Hz, $J_{5,6B} = 5.4$ Hz, H-5), 4.00–3.90 (m, 2H, H-3 and H-7B), 3.87 (dd, 1H, $J_{6A,6B} = 10.7$ Hz, H-6A), 3.70 (dd, 1H, H-6B), 2.07 (br d, 1H, $J_{2,OH} = 3.0$ Hz, OH); ^{13}C NMR (75 MHz) δ 138.8, 138.6, 138.0 (3 × C quat.), 134.2 (–CH=*C*H$_2$), 117.0 (–*C*H=CH$_2$), 107.8 (C-1), 82.9 (C-3), 79.9 (C-4), 78.4 (C-2), 76.6 (C-5), 73.3, 72.5, 71.9 (3 × CH$_2$), 70.8 (C-6), 68.8 (C-7). Other characteristics have been published elsewhere.[32]

4.12. General procedure for the preparation of perbenzylated lactones

The starting allyl glycoside (4.1 mmol) was dissolved in MeOH (50 mL), cooled to −78 °C and ozone was bubbled through a reaction mixture until TLC indicated a lack of starting material (about 20 min). Excess ozone was removed by passing O_2 through the solution, then dimethyl sulfide (3.0 mL) was added and the mixture was stirred at rt overnight. Solvents were evaporated under reduced pressure and the oily residue was dissolved in MeOH (100 mL), cooled to about 0 °C and $NaClO_2$ (3.0 g, 33.2 mmol) in 10% KH_2PO_4 water solution (36 mL) was added dropwise. The reaction mixture was stirred at rt. overnight, then pH was decreased to about 5 with glacial acetic acid and solvents were removed under vacuum. The residue was suspended in pyridine and acetic anhydride (120 mL, 1:1 mixture) and stirred at rt overnight. Then it was concentrated and extracted with water and ethyl acetate. Organic layer was dried, concentrated and purified on column chromatography to give the expected product.

4.13. Carboxymethyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside-2-*O*-lactone 19

Pale yellow oil, 50% (pentane/acetone/toluene; 5:1:1 then 4.5:1:1); $[\alpha]_D = -21$ (*c* 1, CH_2Cl_2); HRMS (ECI) *m*/*z* calcd for $C_{29}H_{31}O_7$ $(M+H)^+$ 491.2070, found 491.2070; ^{1}H NMR (300 MHz) δ 7.40–7.10 (m, 15H), 5.03 (d, 1H, $J_{A,B} = 11.2$ Hz, from benzyl), 4.84 (d, 1H, $J_{A,B} = 10.7$ Hz, from benzyl), 4.81–4.93 (d, 1H, $J_{A,B} = 11.2$ Hz, from benzyl), 4.63–4.47 (m, 3H, 4.59 (d, 1H, $J_{A,B} = 12.2$ Hz), 4.51 (d, 1H, $J_{A,B} = 12.2$ Hz), 4.50 (d, 1H, $J_{A,B} = 10.7$ Hz) 3times from benzyls), 4.43 (d, 1H, $J_{7A,7B} = 17.0$ Hz, H-7A), 4.35–4.24 (m, 2H), 4.33 (d, 1H, $J_{1,2} = 7.7$ Hz, H-1), 4.28 (d, 1H, H-7B), 3.75–3.43 (m, 6H, H-2, H-3, H-4, H-5, H-6A and H-6B); ^{13}C NMR (75 MHz) δ 171.2 (C=O), 138.7, 138.0, 137.9 (3 times C quat.), 103.2 (C-1), 84.5, 76.9, 75.2 and 74.6 (C-2, C-3, C-4, C-5), 75.1, 75.0 and 73.4 (3 × CH$_2$), 68.7 (C-6), 65.6 (C-7). Anal. Calcd for

$C_{29}H_{30}O_7 \cdot 1.8H_2O$: C, 66.60; H, 6.49. Found: C, 66.69; H, 6.24.

4.14. Carboxymethyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside-2-*O*-lactone 20

White solid, 43% (pentane/AcOEt, 5:1 then 4:1); $[\alpha]_D = +51$ (*c* 0.2, CH_2Cl_2); HRMS (ESI) *m/z* calcd for $C_{29}H_{30}O_7Na$ $(M+Na)^+$ 513.1889, found 513.1888; ^1H NMR (500 MHz) δ 7.50–7.20 (m, 15H), 4.94 (d, 1H, $J_{A,B} = 11.2$ Hz, from benzyl), 4.85 (d, 1H, $J_{A,B} = 12.0$ Hz, from benzyl), 4.79–4.69 (m, 2H, H-2 and 1H from benzyl), 4.65 (d, 1H, $J_{7A,7B} = 17.2$ Hz, H-7), 4.61 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1), 4.58 (d, 1H, $J_{A,B} = 11.2$ Hz, from benzyl), 4.51–4.41 (m, 3H), 4.43 (d, 1H, $J_{A,B} = 11.2$ Hz, from benzyl), 4.46 (d, 1H, H-7) and 4.49 (d, 1H, $J_{A,B} = 11.2$ Hz, from benzyl), 4.99–4.96 (m, 1H, H-4), 3.77–3.71 (m, 1H, H-5), 3.69 (dd, 1H, $J_{3,4} = 3.2$ Hz, $J_{2,3} = 10.1$ Hz, H-3), 3.67–3.63 (m, 2H, H-6A and H-6B); ^{13}C NMR (125 MHz) δ 166.6 (C=O), 137.9, 137.45, 137.40 (3 × C quat.), 95.7 (C-1), 78.6 (C-3), 77.7 (C-2), 75.2 (C-5), 75.1 (CH_2), 73.7 (C-4), 73.5, 73.0 (2 × CH_2), 67.8 (C-6), 64.2 (C-7). Anal. Calcd for $C_{29}H_{30}O_7 \cdot 2H_2O$: C, 66.15; H, 6.51. Found: C, 66.58; H, 6.08.

4.15. Carboxymethyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside-2-*O*-lactone 25

White crystals (ether), 56% (pentane/acetone/toluene 8:1:1); mp = 103–104 °C; $[\alpha]_D = +88$ (*c* 0.8, CH_2Cl_2); HRMS (ESI) *m/z* calcd for $C_{29}H_{31}O_7$ $(M+H)^+$ 491.2070, found 491.2070; ^1H NMR (300 MHz) δ 7.40–7.10 (m, 15H), 5.27 (d, 1H, $J_{1,2} = 3.1$ Hz, H-1), 4.93 (d, 1H, $J_{A,B} = 10.9$ Hz, from benzyl), 4.84 (d, 1H, $J_{A,B} = 10.8$ Hz, from benzyl), 4.78 (d, 1H, $J_{A,B} = 10.9$ Hz, from benzyl), 4.63–4.42 (m, 6H, 3 × H from benzyl and 4.58 (d, 1H, $J_{7A,7B} = 17.9$ Hz, H-7A), 4.46 (d, 1H, H-7B), 4.45 (dd, 1H, $J_{2,3} = 9.1$ Hz, H-2)), 4.06–3.98 (m, 2H, H-5 and 4.02 (dd, 1H, $J_{3,4} = 8.9$ Hz, H-3)), 3.77–3.56 (m, 3H, H-4, H-6A, H-6B); ^{13}C NMR (75 MHz) δ 164.5 (C=O), 137.7, 137.6, 137.5 (3 × C quat.), 91.7 (C-1), 81.7 (C-3), 79.6 (C-2), 76.0 (C-4), 75.6, 75.2, 73.5 (3 × CH_2), 72.7 (C-5), 67.8 (C-6), 64.5 (C-7). Anal. Calcd for $C_{29}H_{30}O_7 \cdot 1/3H_2O$: C, 70.15; H, 6.22. Found: C, 70.20; H, 6.07.

4.16. Carboxymethyl-3,4,6-tri-*O*-benzyl-α-D-galactopyranoside-2-*O*-lactone 26

White amorphous solid, 36%, (pentane/acetone/toluene 8:1:1), $[\alpha]_D = +71$ (*c* 0.8, CH_2Cl_2); HRMS (ESI) *m/z* calcd for $C_{29}H_{31}O_7$ $(M+H)^+$ 491.2070, found 491.2071; ^1H NMR (300 MHz) δ 7.4–7.2 (m, 15H), 5.27 (d, 1H, $J_{1,2} = 3.0$ Hz, H-1), 4.89 (d, 1H, $J_{A,B} = 11.4$ Hz, from benzyl), 4.80 (dd, 1H, $J_{2,3} = 9.2$ Hz, H-2), 4.74 (d, 1H, $J_{A,B} = 11.9$ Hz, from benzyl), 4.71 (d, 1H, $J_{A,B} = 11.9$ Hz, from benzyl), 4.57 (d, 1H, $J_{A,B} = 11.4$ Hz, from benzyl), 4.53–4.33 (m, 4H, AB systems from benzyl and H-7), 4.15 (ddd, 1H, $J_{5,6A} = 6.2$ Hz, $J_{5,6B} = 6.6$ Hz, H-5), 4.00 (dd, 1H, $J_{4,5} = 1.7$ Hz, H-4), 3.92 (dd, 1H, $J_{3,4} = 2.8$ Hz, H-3), 3.65–3.50 (m, 2H), 3.59 (dd, 1H, $J_{6A,6B} = 10.9$ Hz, H-6A), 3.56 (dd, 1H, H-6B); ^{13}C NMR (75 MHz) δ 164.9 (C=O), 137.8, 137.6, 137.4 (3 × C quat.), 91.5 (C-1), 77.7 (C-3), 77.0 (C-2), 74.7 (CH_2), 73.7 (C-4), 73.4, 72.8 (2 × CH_2), 72.3 (C-5), 67.8 (C-6), 64.1 (C-7). Anal. Calcd for $C_{29}H_{30}O_72/3H_2O$: C, 69.31; H, 6.28. Found: C, 69.09; H, 6.26.

4.17. Carboxymethyl-3,5,6-tri-*O*-benzyl-α-D-glucofuranoside-2-*O*-lactone 30

Pale yellow oil, 24% (pentane/acetone/toluene; 7:1:1 then 5:1:1); $[\alpha]_D = +19$ (*c* 0.7, CH_2Cl_2); HRMS (ESI) *m/z* calcd for $C_{29}H_{31}O_7$ $(M+H)^+$ 491.2070, found 491.2068; ^1H NMR (300 MHz) δ 7.40–7.20 (m, 15H), 5.61 (d, 1H, $J_{1,2} = 4.0$ Hz, H-1), 4.82–4.74 (m, 2H, 4.78 (dd, 1H, $J_{2,3} = 1.4$ Hz, H-2) and 4.77 (d, 1H, $J_{A,B} = 11.7$ Hz, from benzyl), 4.62–4.44 (m, 5 × H from benzyls)), 4.43–4.33 (m, 2H), 4.40 (dd, 1H, $J_{3,4} = 3.7$ Hz, $J_{4,5} = 8.6$ Hz, H-4) and 4.37 (d, 1H, $J_{7A,7B} = 17.3$ Hz, H-7A), 4.26 (dd, 1H, H-3), 4.18 (d, H-7B), 3.98 (ddd, 1H, $J_{5,6A} = 2.3$ Hz, $J_{5,6B} = 4.9$ Hz, H-5), 3.87 (dd, 1H, $J_{6A,6B} = 10.7$ Hz, H-6A), 3.69 (dd, 1H, H-6B); ^{13}C NMR (75 MHz) δ 165.4 (C=O), 138.3, 138.2, 136.8 (3 × C quat.), 95.8 (C-1), 81.9 (C-3), 80.2 (C-2), 79.7 (C-4), 75.8 (C-5), 73.3, 72.7, 72.2 (3 × CH_2), 69.9 (C-6), 58.3 (C-7). Anal. Calcd for $C_{29}H_{30}O_7 \cdot H_2O$: C, 68.49; H, 6.34. Found: C, 68.53; H, 6.06.

4.18. General procedure for the reaction of the lactones with propargyl amine

The starting lactone (0.51 mmol, 0.177 g for peracetylated lactones, 0.250 g for perbenzylated lactones) was dissolved in anhydrous CH_2C_2 (2 mL) followed by the addition of propargyl amine (0.035 mL, 0.51 mmol for peracetylated lactones, 0.052 mL, 0.767 mmol for perbenzylated lactones) and the reaction mixture was stirred overnight under a nitrogen atmosphere at rt. It was then concentrated and the product was isolated by column chromatography.

4.19. (*N*-Propargylcarbamoyl)methyl-3,4,6-tri-*O*-acetyl-α-D-glucopyranoside 31

Pale yellow oil, 94% (CH_2Cl_2/MeOH; 450:15). All characteristics have been published previously.[19]

4.20. (*N*-Propargylcarbamoyl)methyl-3,4,6-tri-*O*-acetyl-α-D-galactopyranoside 32

White amorphous solid, 84% (CH_2Cl_2/MeOH; 400:15); $[\alpha]_D = +122$ (*c* 0.6, CH_2Cl_2); HRMS (ESI) *m/z* calcd for $C_{17}H_{23}O_{10}NNa$ $(M+Na)^+$ 424.1220, found 424.1213; ^1H NMR (300 MHz) δ 7.78 (t, 1H, $J_{NH,CH_2} = 5.4$ Hz, NH), 5.34 (dd, 1H, $J_{4,5} = 1.1$ Hz, $J_{3,4} = 3.4$ Hz, H-4), 5.13 (dd, 1H, $J_{2,3} = 10.5$ Hz, H-3), 4.94 (d, 1H, $J_{1,2} = 3.8$ Hz, H-1), 4.21 (d, 1H, $J_{7A,7B} = 16.0$ Hz, H-7A), 4.18–4.11 (m, 1H, H-5), 4.09–3.97 (m, 6H, H-2, H-6A, H-6B, H-7B, and 2 × NH–CH_2–), 3.89 (d, 1H, $J_{2,OH} = 5.8$ Hz, OH), 2.23 (t, 1H, $J_{CH_2-CCH} = 4.3$ Hz, CCH), 2.08, 1.994, 1.990 (3 × s, 3 × 3H, 3 × CH_3); NMR (75 MHz) δ 170.9, 170.5, 170.1, 169.2 (4 × C=O), 99.6 (C-1), 79.1 (*C*CH), 71.6 (C*C*H), 70.3 (C-3), 67.8 (C-4), 67.3 (C-7 or C-6) 67.1, 66.5 (C-2 and C-5), 61.6 (C-6 or C-7), 28.5 5 (NH–*C*H_2–), 20.8,

20.6, 20.5 ($3\times CH_3$). Anal. Calcd for $C_{17}H_{23}O_{10}N$: C, 50.87; H, 5.78; N, 3.49. Found: C, 50.95; H, 5.89; N, 3.23.

4.21. (*N*-Propargylcarbamoyl)methyl-3,4,6-tri-*O*-acetyl-β-D-galactopyranoside 33

Pale yellow oil, 83% (CH_2Cl_2/MeOH; 30:1); $[\alpha]_D = -2$ (*c* 0.6, CH_2Cl_2); HRMS (ESI) *m*/*z* calcd for $C_{17}H_{23}O_{10}NNa$ $(M+Na)^+$ 424.1220, found 424.1219; ^1H NMR (300 MHz) δ 7.45 (br t, 1H, $J_{NH,CH_2} = 5.1$ Hz, NH), 5.35 (br dd, 1H, $J_{4,5} = 2.8$ Hz, $J_{3,4} = 3.1$ Hz, H-4), 4.90 (dd, 1H, $J_{2,3} = 10.2$ Hz, H-3), 4.40 (d, 1H, $J_{1,2} = 7.7$ Hz, H-1), 4.34 (d, 1H, $J_{7A,7B} = 16.0$ Hz, H-7A), 4.22–4 (d, 1H, H-7B), 4.14–4.02 (m, 4H, H-6A, and $2\times$ NH–CH_2–), 3.95–3.88 (m, 1H, H-5), 3.84 (dd, 1H, H-2), 3.50 (br s, 1H, OH), 2.27 (t, 1H, $J_{CH_2-CCH} = 2.5$ Hz, CCH), 2.12, 2.032, 2.028 ($3\times$ s, 3×3H, $3\times CH_3$); NMR (75 MHz) δ 170.55, 170.48, 170.1, 169.3 ($4\times$ C=O), 103.4 (C-1), 79.0 (C*C*H), 72.8 (C-3), 71.8 (*C*CH), 71.0 (C-5), 68.81 (C-7), 68.79 (C-2), 67.0 (C-4), 61.4 (C-6), 28.6 (NH–*C*H_2–), 20.7, 20.63, 20.57 ($3\times CH_3$). Anal. Calcd for $C_{17}H_{23}O_{10}N$: C, 50.87; H, 5.78; N, 3.49. Found: C, 50.44; H, 5.74; N, 3.41.

4.22. (*N*-Propargylcarbamoyl)methyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside 34

Pale yellow amorphous solid, 94% (CH_2Cl_2/MeOH; 300:12); $[\alpha]_D = +5$ (*c* 0.3, CH_2Cl_2); HRMS (ESI) *m*/*z* calcd for $C_{32}H_{35}O_7N$ $(M+H^+)$ 568.2311, found 568.2312; 7.46 (t, 1H, $J_{NH,CH_2} = 5.2$ Hz, NH), 7.30–7.10 (m, 15H), 4.85–4.69 (m, 3H, 4.82 (d, 1H, $J_{A,B} = 11.5$ Hz), 4.76 (d, 1H, $J_{A,B} = 11.5$ Hz) and 4.72 (d, 1H, $J_{A,B} = 11.1$ Hz) from benzyls), 4.52 (d, 1H, $J_{A,B} = 12.1$ Hz, from benzyl), 4.49–4.39 (m, 2H, 4.46 (d, 1H, $J_{A,B} = 11.1$ Hz), 4.43 (d, 1H, $J_{A,B} = 12.1$ Hz) from benzyls), 4. 4.24 (d, 1H, $J_{7A,7B} = 16.0$ Hz, H-7A), 4.18 (d, 1H, $J_{1,2} = 7.4$ Hz, H-1), 4.12 (d, 1H, H-7B), 4.04–3.87 (m, 2H, $2\times$ NH–CH_2–), 3.66–3.32 (m, 7H, H-2, H-3, H-4, H-5, H-6A, H-6B and OH), 2.12 (t, 1H, $J_{CH_2-CCH} = 2.5$ Hz, CCH); ^{13}C NMR (75 MHz) δ 169.6 (C=O), 138.3, 137.7, 137.6 ($3\times$ C quat.), 103.2 (C-1), 84.4, 79.2 (C*C*H), 77.2, 75.2 (CH_2), 75.0, 74.9 (CH_2), 73.7, 73.5 (CH_2), 71.5 (*C*CH), 68.9 (C-7), 68.2 (C-6), 28.5 (NH–*C*H_2–). Anal. Calcd for $C_{32}H_{35}O_7N$: C, 70.44; H, 6.47; N, 2.57. Found: C, 70.03; H, 7.07; N, 2.59.

4.23. (*N*-Propargylcarbamoyl)methyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside 35

Pale yellow oil, 85% (pentane/acetone/toluene; 4:1:1 then pentane/AcOEt; 1:1); $[\alpha]_D = +3$ (*c* 1, CH_2Cl_2); HRMS (ESI) *m*/*z* calcd for $C_{32}H_{35}O_7NNa$ $(M+Na)^+$ 568.2311, found 568.2311; ^1H NMR (300 MHz) δ 7.48 (t, 1H, $J_{NH,CH_2} = 5.0$ Hz, NH), 7.30–7.10 (m, 15H), 4.77 (d, 1H, $J_{A,B} = 11.5$ Hz, from benzyl), 4.63 (d, 1H, $J_{A,B} = 11.9$ Hz, from benzyl), 4.55–4.46 (m, 2H, 4.51 (d, 1H, $J_{A,B} = 11.5$ Hz), 4.77 (d, 1H, $J_{A,B} = 11.9$ Hz) from benzyl), 4.37 (d, 1H, $J_{A,B} = 11.9$ Hz, from benzyl), 4.34 (d, 1H, $J_{A,B} = 11.9$ Hz, from benzyl), 4.24–4.04 (m, 3H), 4.20 (d, 1H, $J_{A,B} = 16.2$ Hz, H-7A), 4.16 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1), 4.09 (d, 1H, H-7B), 4.97–3.84 (m, 4H, H-2, $2\times$ NH–CH_2–, and H4 or H-5), 3.57–3.44 (m, 3H, H-6A, H-6B and H-4 or H-5), 3.35–3.17 (m, 2H, 3.32 (dd, 1H, $J_{3,4} = 2.6$ Hz, $J_{2,3} = 9.8$ Hz, H-3) and OH), 2.06 (t, 1H, $J_{CH_2-CCH} = 2.5$ Hz, CCH); ^{13}C NMR (75 MHz) δ 169.5 (C=O), 138.1, 137.6, 137.5 ($3\times$ C quat.), 103.5 (C-1), 81.9 (C-3), 79.1 (C*C*H), 74.5 (CH_2), 73.7, 73.5 (CH_2), 72.1 (double intensity, CH_2 and C-2 or C-4 or C-5), 71.4 (*C*CH), 70.5, 68.7 (C-7), 68.1 (C-6), 28.5 (NH–*C*H_2–). Anal. Calcd for $C_{32}H_{35}O_7N{\cdot}1/2H_2O$: C, 68.19; H, 6.62; N, 2.49. Found: C, 68.57; H, 6.27; N, 2.46.

4.24. (*N*-Propargylcarbamoyl)methyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside 36

Colorless oil, 54% (pentane/acetone/toluene; 4:1:1 then pentane/AcOEt; 1:1); $[\alpha]_D = +88$ (*c* 0.5, CH_2Cl_2); HRMS (ESI) *m*/*z* calcd for $C_{32}H_{35}O_7NNa$ $(M+Na)^+$ 568.2311, found 568.2309; ^1H NMR (300 MHz) δ 7.70 (t, 1H, $J_{NH,CH_2} = 5.4$ Hz, NH), 7.30–7.05 (m, 15H), 4.84 (d, 1H, $J_{A,B} = 11.3$ Hz, from benzyl), 4.76–4.68 (m, 3H, $2\times$ H from benzyls and H-1), 4.54 (d, 1H, $J_{A,B} = 12.0$ Hz, from benzyl), 4.58–4.47 (m, 3H, $3\times$ H from benzyls), 4.11 (d, 1H, $J_{7A,7B} = 16.2$ Hz, from benzyl), 4.01–3.93 (m, 3H, 3.97 (d, 1H, H-7B) and $2\times$ NH–CH_2–), 3.80–3.60 (m, 5H, H-2, H-3, H-4, H-5, H-6A), 3.57 (dd, 1H, $J_{5,6A} = 1.7$ Hz, $J_{6A,6B} = 10.5$ Hz, H-6B); 3.25 (br s, 1H, OH), 2.13 (t, 1H, $J_{CH_2-CCH} = 2.5$ Hz, CCH); ^{13}C NMR (75 MHz) δ 169.6 (C=O), 138.4 (double intensity), 137.8, ($3\times$ C quat.), 99.6 (C-1), 82.1, 79.2 (C*C*H), 74.4, 75.2 (CH_2), 74.8 (CH_2), 73.5 (CH_2), 71.7, 71.4 (*C*CH), 71.3, 68.0 (C-6), 67.3 (C-7), 28.5 (NH–*C*H_2–). Anal. Calcd for $C_{32}H_{35}O_7N$: C, 70.44; H, 6.47. Found: C, 70.07; H, 6.35.

4.25. (*N*-Propargylcarbamoyl)methyl-3,4,6-tri-*O*-benzyl-α-D-galactopyranoside 37

Pale yellow oil, 64% (pentane/acetone/toluene; 4:1:1 then pentane/AcOEt; 1:1); $[\alpha]_D = +84$ (*c* 0.6, CH_2Cl_2); HRMS (ESI) *m*/*z* calcd for $C_{32}H_{35}O_7N$ $(M+H)^+$ 568.2311, found 568.2310; ^1H NMR (300 MHz) δ 7.75 (t, 1H, $J_{NH,CH_2} = 5.2$ Hz, NH), 7.35–7.15 (m, 15H), 4.81 (d, 1H, $J_{1,2} = 3.9$ Hz, H-1), 4.78 (d, 1H, $J_{A,B} = 11.4$ Hz, from benzyl), 4.69 (d, 1H, $J_{A,B} = 11.4$ Hz, from benzyl), 4.53–4.47 (m, 2H), 4.49, ($2\times$ d, $2\times J_{A,B} = 11.4$ Hz), 4.43 (d, 1H, $J_{A,B} = 11.7$ Hz, from benzyl), 4.37 (d, 1H, $J_{A,B} = 11.7$ Hz, from benzyl), 4.20–3.91 (m, 7H, H-7A, H-7B, both HNCH_2, H-4, H-5, and 4.18 (dd, 1H, $J_{2,3} = 10.0$ Hz, H-2)), 3.73 (dd, 1H, $J_{3,4} = 2.6$ Hz, H-3), 3.60–3.45 (m, 2H, H-6A and H-6B), 2.13 (t, 1H, $J_{CH_2-CCH} = 2.6$ Hz, CCH); ^{13}C NMR (75 MHz) δ 169.9 (C=O), 138.2, 137.6, 137.5, ($3\times$ C quat.), 99.8 (C-1), 79.2 (C*C*H), 78.8 (C-3), 74.6, 73.45 ($2\times CH_2$), 73.2, (C-4), 72.0 (CH_2), 71.3 (*C*CH), 70;1 (C-5), 68.3 (C-6), 68.0 (C-2), 67.4 (C-7), 28.5 (NH–*C*H_2–). Anal. Calcd for $C_{32}H_{35}O_7N{\cdot}1/2H_2O$: C, 69.30; H, 6.54; N, 2.53. Found: C, 69.63; H, 6.28; N, 2.43.

4.26. (*N*-Propargylcarbamoyl)methyl-3,4,6-tri-*O*-benzyl-α-D-glucofuranoside 38

Pale yellow oil, 85% (CH_2Cl_2/MeOH; 30:1); $[\alpha]_D = +10$ (*c* 0.9, CH_2Cl_2); HRMS (ESI) *m*/*z* calcd for $C_{32}H_{35}O_7NNa$ $(M+Na)^+$ 568.2311, found 568.2315; ^1H NMR (300 MHz) δ 7.30–7.10 (m, 16H, NH and aromatics), 5.00 (d, 1H, $J_{1,2} = 4.3$ Hz, H-1), 4.67 (d, 1H,

$J_{A,B} = 11.5$ Hz, from benzyl), 4.57 (d, 1H, $J_{A,B} = 11.7$ Hz, from benzyl), 4.48 (br s, 2H, CH_2 from benzyl), 4.47–4.39 (m, 2H), 4.44 (d, 1H, $J_{A,B} = 11.7$ Hz), 4.42 (d, 1H, $J_{A,B} = 11.5$ Hz), 4.33 (dd, 1H, $J_{3,4} = 4.5$ Hz, $J_{4,5} = 8.3$ Hz, H-4), 4.22–4.10 (m, 4H), 4.22–4.17 (H-2), 4.17 (d, 1H, $J_{7A,7B} = 15.6$ Hz, H-7A), 4.04 (d,1H, H-7B), 4.04 (dd, 1H, $J_{2,3} = 2.5$ Hz, H-3), 3.95–3.86 (m, 3H, H-5 and both HNCH_2), 3.74 (dd, 1H, $J_{5,6A} = 2.2$ Hz, $J_{6A,6B} = 10.7$ Hz, H-6A), 3.59 (dd, 1H, $J_{5,6B} = 5.5$ Hz, H-6B), 3.50 (br s, OH), 2.09 (t, 1H, $J_{CH_2-CCH} = 2.5$ Hz, CCH); ^{13}C NMR (75 MHz) δ 169.4 (C=O), 138.6, 138.3, 137.7, (3 × C quat.), 103.0 (C-1), 83.2 (C-3), 79.3 (C*C*H), 78.2 (C-4), 76.0 (C-5), 75.7 (C-2), 73.3, 72.4, 71.9 (3 × CH_2), 71.5 (*C*CH), 70.5 (C-6), 68.4 (C-7), 28.5 (NH–*C*H_2–). Anal. Calcd for $C_{32}H_{35}O_7N$: C, 70.44; H, 6.47; N, 2.57. Found: C, 70.08; H, 6.09; N, 2.54.

4.27. (*N*-Propargylcarbamoyl)methyl-α-D-glucopyranoside 39

Amide **32** (1.061 g, 0.00264 mol) was dissolved in MeOH (15 mL) and MeONa in MeOH (1 M) was added in a catalytic amount. The reaction was stirred at room temperature. After 48 h, Dowex (H+) was added and the mixture was stirred for 30 min. Then Dowex was separated by filtration, the organic solvents were evaporated and the residue was purified by column chromatography (CH_2Cl_2/MeOH; 4:1) to give 0.663 g of the desired product as a white foam in 91% yield. $[\alpha]_D = +188$ (*c* 1, H_2O); HRMS (ESI) *m*/*z* calcd for $C_{11}H_{17}O_7N$ $(M+Na)^+$ 298.0903, found 298.09054; ^{1}H NMR (500 MHz, D_2O) δ 5.06 (d, 1H, $J_{1,2} = 3.6$ Hz, H-1), 4.28 (AB system, 2H, δ_{7A} 4.36, δ_{7B} 4.21, $J_{A,B} = 15.6$ Hz, H-7), 4.13 (d, 2H, $J_{NH-CH_2} = 2.3$ Hz, NH–*C*H_2), 3.93 (dd, 1H, $J_{6A,5} = 2.2$ Hz, $J_{6A,6B} = 12.2$ Hz, H-6A), 3.86 (t, 1H, $J_{2,3} = J_{3,4} = 9.8$ Hz, H-3), 3.84 (dd, 1H, $J_{6B,5} = 12.2$ Hz, H-6B), 3.76 (ddd, 1H, $J_{4,5} = 9.8$ Hz, H-5), 3.69 (dd, 1H, H-2), 3.53 (t, 1H, H-4), 2.72 (t, 1H, CH_2C*CH*); ^{13}C NMR (125 MHz) δ 172.2 (C=O), 99.2 (C-1), 79.6 (C*C*H), 73.2 (C-4), 72.6 (C-5), 72.3 (*C*CH), 71.5 (C-2), 69.7 (C-3), 66.8 (C-7), 60.7 (C-6), 28.8 (NH*C*H_2). Anal. Calcd for $C_{11}H_{17}O_7N{\cdot}1/4H_2O$: C, 47.23; H, 6.31; N, 5.01. Found: C, 47.06; H, 6.37; N, 4.84.

4.28. *N*-Methyl[-4-[1-(5′-deoxyuridin)-1,2,3-triazole]]carbamoylmethyl-α-D-glucopyranoside 40

Amide **39** (0.604 g, 0.0022 mol) was dissolved in 11 mL CH_3CN/H_2O (1:1), (0.59 g, 0.0022 mol) of azidouridine were added, as well as a catalytic amount of CuI and of triethylamine (1 mL). After 24 h, the reaction was completed, the solvents evaporated and the residue chromatographed on a 10*g* C18 cartridge using a H_2O/MeOH gradient (9:1) to give 0.560 g of the product in 47% yield as a white solid, $[\alpha]_D = +89$ (*c* 1, H_2O); HRMS (ESI) *m*/*z* calcd for $C_{20}H_{28}O_{12}N_6Na$ $(M+Na)^+$ 567.1663, found 567.1666; ^{1}H NMR (CD_3OD, 500 MHz) δ 8.09 (s, 1H, CCHN), 7.53 (d, 1H, $J_{NCHCHCO} = 8.2$ Hz, NC*H*CHCO), 5.90 (m, 2H, CHC*H*CO, H-1′), 5.03 (d, 1H, $J_{1,2} = 3.6$ Hz, H-1), 4.99 (m, 2H, H-5′), 4.73 (s, 2H, NH*C*H_2), 4.46–4.37 (m, 3H, H-2′, H-4′, H-7A), 4.30 (t, 1H, $J_{3',4'} = 6.0$ Hz, H-3′), 4.24 (d, 1H, $J_{7A,7B} = 16.1$ Hz, H-7B), 4.00 (dd, 1H, $J_{6B,6A} = 2.2$ Hz, $J_{6B,5} = 12.0$ Hz, H-6B), 3.89–3.86 (m, 2H, H-6A, H-3), 3.77 (m, 1H, H-5), 3.66 (dd, 1H, $J_{2,3} = 9.5$ Hz, H-2), 3.49 (t, 1H, $J_{3,4} = 9.4$ Hz, H-4). ^{13}C NMR (125 MHz) δ 175.8, 159.8, 150.7 (3C=O), 148.7 (Cq), 143.2 (*CH*CHCO), 127.2 (*CH*CN), 103.1 (CH*CH*CO), 100.9 (C-1), 93.4 (C-1′), 82.7 (C-2′), 74.7 (C-3), 74.2 (C-5), 74.0 (C-4′), 73.1 (C-2), 71.7 (C-3′), 71.5 (C-4), 67.0 (C-7), 62.5 (C-6), 52.3 (C-5′), 35.2 (NH*C*H_2). Anal. Calcd for $C_{20}H_{28}O_{12}N_6{\cdot}2H_2O$: C, 41.38; H, 5.56; N, 14.48. Found: C, 41.38; H, 5.35; N, 14.18.

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