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Synthesis of a *C*-disaccharide glycosyl donor as a key building block for the preparation of new biologically active heparin pentasaccharide mimetics☆

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Summary — The synthesis of the *C*-disaccharide imidate **34**, a key synthon for the synthesis of heparin pentasaccharide mimetics, is described. The *C*-interglycosidic bond was established through 9-*endo-trig* radical cyclization from two tethered monosaccharides. It was followed by conversion of the reducing end glucose unit into the required glucuronic acid derivative.

heparin / silicon tether / radical cyclization / C-disaccharide / carbohydrate mimetics

Résumé — Synthèse d'un donneur de glycosyle *C*-disaccharidique : un intermédiaire clé pour la préparation de nouveaux mimes biologiquement actifs du pentasaccharide de l'héparine. Nous décrivons la synthèse de l'imidate *C*-disaccharide **34**, un intermédiaire clé pour la préparation des mimes du pentasaccharide de l'héparine. La liaison *C*-interglycosidique est établie grâce à une cyclisation radicalaire 9-*endo-trig* à partir de deux monosaccharides temporairement connectés. Cette cyclisation est suivie d'une transformation de l'unité réductrice glucose en unité acide glucuronique.

héparine / agrafe au silicium / cyclisation radicalaire / C-disaccharide / mime de sucre

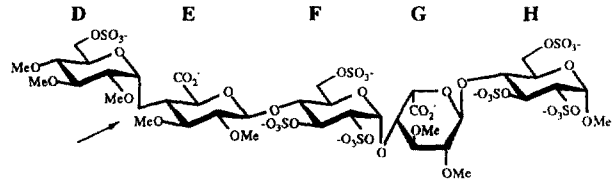
Introduction

Nature has selected to connect two monosaccharide units through an acetal linkage in order to build up a disaccharide; such a chemical function is both easily elaborated and also hydrolyzed. It is critically important that biological polymers such as nucleic acids, proteins, and polysaccharides can both be biosynthesized and biodegraded through enzymatic processes. In fact, there are not many ways to connect two six-membered rings while respecting this reversibility rule. As a consequence of this logic, a stereoelectronic effect, known as the anomeric effect, emerges. It could very well be that such an effect – which has often been claimed as critical for the conformation around the *exo*-anomeric glycosidic bond, and, as a consequence, for biological properties – is just a non-planified consequence of the logical selection of the reversible trick selected to join two sugar residues together. In order then to evaluate the contribution of such an effect, it is an attractive challenge to construct a close analog – a mimetic – of a biologically well-established oligosaccharide, in which one or several interglycosidic oxygen atoms have been replaced by a methylene group. Rather than using subtle and questionnable conformational analyses to probe the consequences of the removal of the anomeric effect [1], we indeed decided to directly examine the corresponding biological consequences of such a modification. In this way, two additional goals are also pursued:

(1) To build a molecular object which is fully resistant to glycosidases, a feature which could be of importance for the development of an oligosaccharide-based drug.

(2) To get information on the potential direct intervention and importance of an interglycosidic oxygen atom on the hydrogen bonding network with a receptor protein.

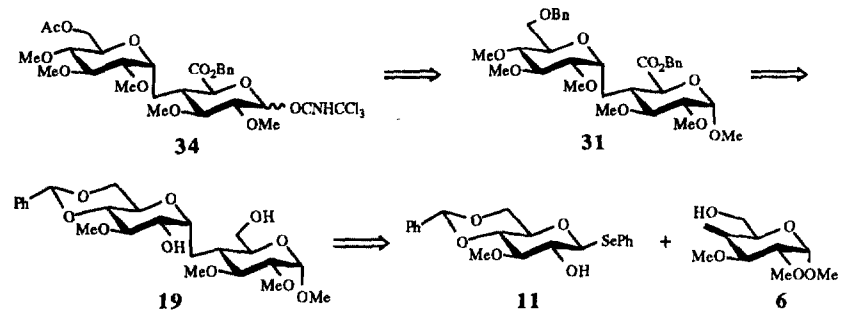
The availability of a well-established series of biologically active heparin pentasaccharides [2] allows us to investigate how the introduction of a *C*-disaccharide bond in some of them would influence the interaction with their target protein receptor, antithrombin. In this article we describe the preparation of the key disaccharide synthon **34** which is needed for the preparation of the pentasaccharide mimetic **1**.



1 (the arrow indicates the C-disaccharidic bond introduced)

☆ This article is dedicated to Professor Roger W Jeanloz on the occassion of his 80th birthday.

* Correspondence and reprints



Scheme 1. Retrosynthesis of the key compound **34**.

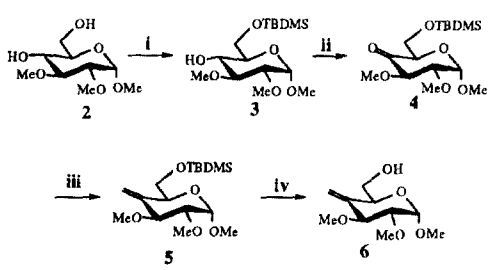
The key feature of this work is a recently developed strategy for the synthesis of *C*-disaccharides [3]; it is based on a 9-*endo-trig* radical cyclization process between two tethered monosaccharides.

Results and discussion

The structure of the pentasaccharide **1** as an ultimate goal dictated the structure of the target synthon **34**. The selected retrosynthesis of **34** is outlined in scheme 1. Compound **19** was prepared by addition of the anomeric radical generated from **11** onto the exocyclic double bond of **6**. We have shown [3] that such a reaction was possible when the radical donor was connected to the acceptor, thus making the reaction intramolecular. Subsequent manipulations of **19** include selective oxidation at position 6 of the 'reducing end' unit, acetolysis of the methyl glycoside, and introduction of the required imidate function.

Preparation of the radical acceptor **6** *(scheme 2)*

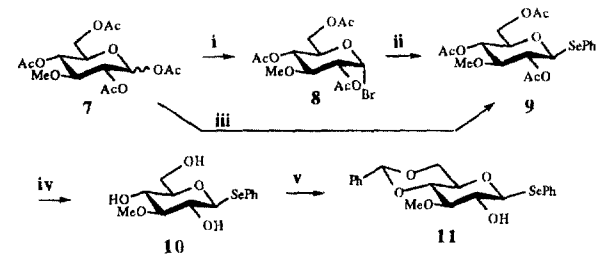
Known methyl 2,3-di-*O*-methyl-α-D-glucopyranoside **2** [4] was prepared in three steps from commercially available methyl α-D-glucopyranoside in an overall yield of 70%. The more reactive primary hydroxyl group of **2** was selectively protected as a *tert*-butyldimethylsilyl ether (95% yield). Swern oxidation [5] of the free hydroxyl function in **3** gave the ketone **4** in 93% yield. Wittig reaction then gave **5** in 60% yield. Deprotection of the primary hydroxyl function was achieved (95%) in dichloromethane/methanol (5:1, v:v), in the presence of camphorsulfonic acid.



Scheme 2. Reagents: (i) TBDMSCl, Et_3N, DMAP, CH_2Cl_2, 95%; (ii) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, 93%; (iii) $(Ph_3PMe)Br$, BuLi, THF, 60%; (iv) CSA, MeOH, CH_2Cl_2, 95%.

Preparation of the radical precursors **11** *and* **14**

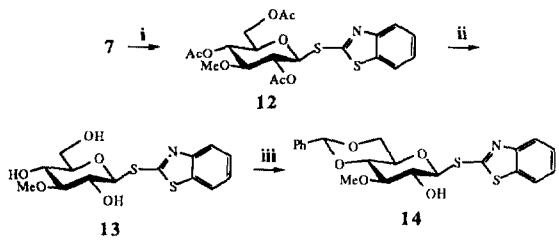
Two radical precursors have been prepared: a phenyl selenoglycoside **11**, as shown in scheme 3, and the 2-benzothiazolyl thioglycoside **14**. The 2-benzothiazolylthio group has been successfully used for radical deoxygenation of secondary alcohols [6].



Scheme 3. Reagents: (i) HBr, AcOH; (ii) $(PhSe)_2$, $NaBH_4$, EtOH, CH_2Cl_2, 86%; (iii) PhSeH, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 68%; (iv) MeONa, MeOH, 94%; (v) $PhCH(OMe)_2$, PTSA, CH_3CN, 88%.

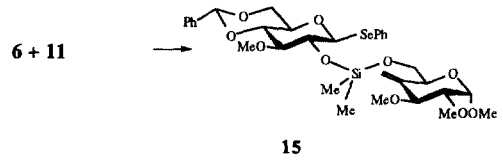
The glycoside **11** could be obtained in two different ways. An equimolar anomeric mixture of the known acetates **7** [7] (the formation of the less reactive α-anomer could not be avoided and a separation of the two anomers failed) was treated in dry dichloromethane with PhSeH (1.5 equiv) in the presence of $BF_3{\cdot}OEt_2$ to give compound **9** in 68% yield. For a large scale synthesis of **9**, it was found more efficient to use the bromide **8**, easily prepared from **7**. Reaction with sodium phenylseleno (triethoxy) borate [8] selectively gave **9** in an overall yield of 86% from the anomeric mixture **7**. Product **9** was deacetylated to give the triol **10** (94%) which, after treatment with benzaldehyde dimethylacetal in DMF under acidic conditions, yielded **11** (88%).

The second radical donor **14** was prepared in a similar way, as shown in scheme 4: acetate **7** was treated, in dry dichloromethane, with 2-benzothiazolethiol (1.5 equiv) in the presence of $BF_3{\cdot}OEt_2$ to give **12**. After deacetylation and benzylidenation as above, **14** was obtained in limited yield (24% from **7**). The phenyl selenoglycoside **11** is more easily available, furthermore preliminary experiments indicated that it is a more efficient *C*-glycosyl donor than **14**. For these reasons, it was chosen as the radical precursor in preparative experiments.

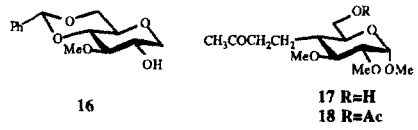


Scheme 4. Reagents: (i) 2-benzothiazolethiol, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 68%; (ii) MeONa, MeOH, 43% from **7**: (iii) $PhCH(OMe)_2$, PTSA, CH_3CN, 56%.

Synthesis of the C-disaccharide glycosyl donor

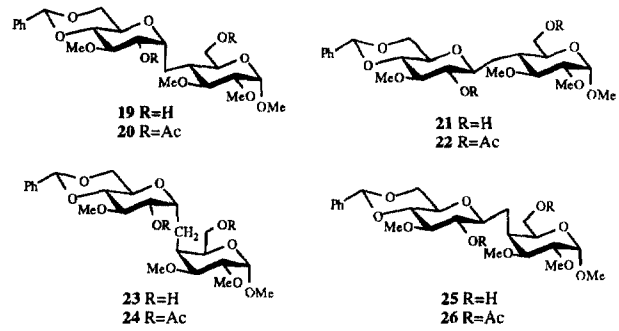


The alcohol **6** was bound to **11** through a silaketal tether to give **15**. The reaction was carried out in two steps: the secondary alcohol **11** was first treated by dichlorodimethylsilane in the presence of *n*-butyllithium in THF at −70 °C, to give the desired monochlorodimethylsilyl ether. An excess of silylating agent was used in order to minimize the formation of the symmetrical silaketal. The excess of reagent was then eliminated by evaporation before addition of a THF solution of the primary alcohol **6** in the presence of imidazole. The silaketal **15** was obtained in high yield (90%), and due to its high acid sensitivity it was in general directly used in the next reaction.



The cyclization step was achieved upon slow addition (18 h, syringe pump) of a diluted tributyltin hydride toluene solution, in the presence of AIBN, onto a refluxed toluene solution of the silaketal **15**. The silicon tether was removed by aqueous HF treatment to give a mixture of the protected *C*-disaccharides **19**, **21**, **23** and **25** (60% overall yield from **15**). The reduced product **16** (35%) and the starting material **6** (35%) were also isolated.

The homolytic cleavage of the tin–tin chemical bound in $Bu_3SnSnBu_3$ has been shown [9] to be possible via a triplet state, using a triplet sensitizer. As a possible alternative to the previously described methodology, we decided to try these conditions to a solution of the crude compound **15** in acetone, in the presence of $Bu_3SnSnBu_3$. The solution was prepared in a Pyrex tube, under argon, degassed, and irradiated for 3 h with a mercury lamp. The Pyrex container filtered out all UV radiation below 230 nm. The acetone acted as triplet sensitizer, solvent, and hydrogen donor. The mixture of

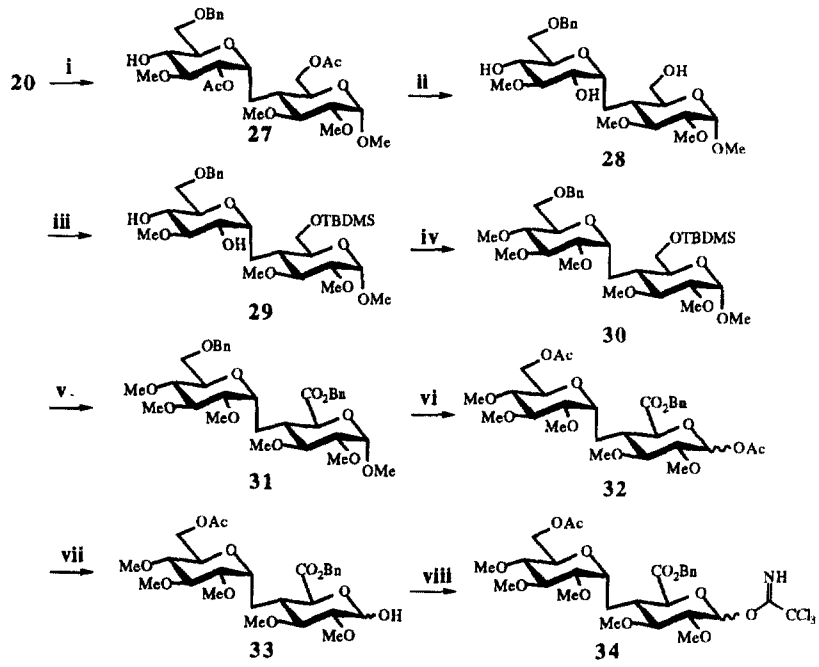


C-disaccharides was isolated in 50% yield. Among various by-products, **17** has been isolated and characterized as the acetylated derivative **18**. Its formation is due to the addition of acetone to the exocyclic double bond of **6**.

The difficult separation of the four isomeric *C*-disaccharides can only be achieved on a small fraction by reverse-phase HPLC, either on the diols (**19**, **21**, **23**, **25**) or on their diacetylated derivatives (**20**, **22**, **24**, **26**). The relative proportions of the four isomers (**19**/**21**/**23**/**25** = 70:16:14:<1) were found to be independent of the method used to generate the radical. The structure of the *C*-disaccharides was unambiguously assigned after careful ^{1}H-NMR analysis of the diacetylated compounds (see table I). The β configuration of the methylene bridge in **22** and **26** is clear from $J_{1,2}$ coupling in unit A: **22** (9.3 Hz); **26** (9.5 Hz). Compounds **20** and **24** are the two possible α anomers **20** ($J_{1,2}$ 4.9 Hz), **24** ($J_{1,2}$ 5.9 Hz). The high $J_{3,4}$ (unit B) coupling constant in **20** (10.0 Hz) and **22** (9.0 Hz) indicate the *gluco* configuration of the corresponding unit.

Table I. Proton chemical shifts and coupling constants ($CDCl_3$) in the *C*-disaccharides **20**, **22**, **24** and **26**. The unit **A** is the *C*-glycosidic unit, the unit **B** is the reducing end (methyl glycoside), H-4h refers to the hydrogen atoms of the methylene bridge.

	20		**22**		**24**		**26**	
	A	**B**	**A**	**B**	**A**	**B**	**A**	**B**
H-1	4.36	4.85	3.54	4.87	4.02	4.85	3.50	4.85
H-2	4.96	3.24	4.78	3.26	4.99	3.23	4.75	3.24
H-3	3.48	3.37	3.45	3.41	3.60	3.59	3.50	3.61
H-4	3.68	1.76	3.61	1.83	3.60	2.34	3.65	2.33
H-5	3.65	3.70	3.37	3.87	3.88	4.03	3.39	4.00
H-6a	4.29	4.32	4.22	4.30	4.22	4.09	4.34	4.15
H-6b	3.65	4.12	3.69	4.15	3.87	3.94	3.76	4.08
H-4ha	1.80		1.82		2.01		1.78	
H-4hb	1.57		1.56		1.66		1.43	
$J_{1,2}$	4.9	3.5	9.3	3.6	5.9	3.8	9.5	3.8
$J_{2,3}$	7.0	9.2	9.3	9.0	9.2	10.1	9.5	9.8
$J_{3,4}$	8.0	10.0	9.3	9.0		5.5	9.5	5.0
$J_{4,5}$			9.3	9.0		< 1	9.5	1.5
$J_{5,6a}$		2.2	5.0	2.0	4.8	8.6	5.0	3.2
$J_{5,6b}$		5.2	10.0	5.3	10.0	4.1	10.5	8.5
$J_{6a,6b}$		12.1	10.5	11.8	10.3	10.8	10.5	11.7
$J_{4,4ha}$		3.0				< 1		2.0
$J_{4,4hb}$		6.0				8.3		4.5
$J_{4ha,1}$	8.5				12.0		5.3	
$J_{4hb,1}$	3.5				2.4		10.5	
$J_{4ha,4hb}$	14.8				15.3		15.5	



Scheme 5. Reagents: (i) $NaBH_3CN$, HCl, ether, THF, 87%; (ii) MeONa, MeOH, 98%; (iii) TBDMSCl, Et_3N, DMAP, CH_2Cl_2, 86%; (iv) MeI, NaH, DMF, 93%; (v) CrO_3, H_2SO_4, acetone then BnBr, $KHCO_3$, DMF 87%; (vi) H_2SO_4, AcOH, Ac_2O, 76%; (vii) AcO^-, $NH_2NH_3^+$, DMF, 80%; (viii) CCl_3CN, DBU, CH_2Cl_2, 87% (α/β, 10:1).

The unit B of **24** and **26** has the *galacto* configuration **24** $J_{3,4}$ 5.5 Hz; **26** $J_{3,4}$ 5.0 Hz.

The major and wanted disaccharide **19** crystallized out of the mixture of *C*-disaccharides, previously enriched in this isomer by classical flash column chromatography on silica gel. This auspicious feature proved critical for the isolation of rather large amounts of **19** in pure form. X-ray analysis of **19** has been carried out and will be published elsewhere. It confirms the structure assigned from ^1H NMR analysis.

The final part of the synthesis, as depicted in scheme 5, consisted in the conversion of **20** into the glycosyl imidate **34**. To this end the benzylidene acetal was first regioselectively reduced using $NaBH_3CN$ and HCl [10] to give **27** (87%), which was then deacetylated (98%). Temporary protection of the primary alcohol function was achieved by selective introduction of the *tert*-butyldimethylsilyl ether (86%) and the resulting diol **29** was methylated (93%). Jones oxidation was performed on the silyl ether **30** to furnish the crude uronic acid which was directly benzylated (87% overall). Acetolysis of **31** using the system $H_2SO_4/AcOH/Ac_2O$ resulted in the cleavage of the anomeric methyl glycoside as well as the benzyl ether at the primary position and provided **32** (76%) as a mixture of the two anomeric acetates, which could be separated by chromatography and both fully characterized. Selective deacetylation of the anomeric position of **32** was then achieved using hydrazine in DMF (80%), and the resulting mixture of anomers **33** was finally converted to **34** by reaction with trichloroacetonitrile, in the presence of DBU [11]. A mixture of anomers (α/β, 10:1) was obtained after flash chromatography (87%). The successful conversion of the glycosyl donor **34** into the pentasaccharide **1** together with the measurement of the corresponding anti-factor Xa biological activity, has been achieved and has been reported elsewhere [12]. **34** has also been transformed into other biologically active analogues of **1** [13].

Experimental section

General

All solvents and reagents were of the best grade commercially available or were purified and dried according to standard procedures. All reactions were conducted under a dry atmosphere of argon. Reactions were monitored by TLC on silica gel 60 F_{254} (Merck) with detection by charring with H_2SO_4. Flash column chromatography was performed on silica gel 60 (E Merck 63–200 μm). HPLC experiments were performed on a Waters 600E instrument, equipped with a Waters 991 detector operating at 257 nm. The following columns were used: (1) Novapack 4 m, 60 Å, C_{18}, 150 × 3.9 mm (Waters), eluted with 80:20 H_2O–CH_3CN. (2) Lichrospher ODS-2, 4 m, C_{18}, 250 × 4.6 mm (Interchim), eluted with 75:25 H_2O-CH_3CN. Semi preparative HPLC was performed on a Porasil C_{18}, 300 × 7.8 mm eluted with 49.5:50.5 H_2O–CH_3CN. NMR spectra were recorded with Bruker AM 100, AC 250, AM 400 or AM 500 instruments for solution in $CDCl_3$ (internal Me_4Si) unless otherwise stated. MS analyses were performed on a Nermag R10-10 instrument using chemical ionisation (CI, NH_3) and detection of positive ions. Melting points were determined in capillary tubes with a Büchi 510 apparatus, and are uncorrected. Optical rotations were measured with a Perkin-Elmer Model 141 polarimeter at 23 ± 3 °C. Elemental analyses were carried out at the Service Central d'Analyses (CNRS, Vernaison, France) or at the Service d'analyse de l'Université Pierre et Marie Curie, Paris, France.

Methyl 2,3-di-O-methyl-6-O-tert-butyldimethylsilyl-α-D-glucopyranoside **3**

tert-Butyldimethylsilyl chloride (14.0 g, 92.9 mmol), Et_3N (15 mL, 108 mmol), and DMAP (260 mg, 2.13 mmol) were

added to a solution of **2** [6] (15.84 g, 71.3 mmol) in dry dichloromethane (300 mL). After 15 h stirring at room temperature, the solution was diluted with dichloromethane, washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residue was purified by flash chromatography (1.3:1 cyclohexane/ethyl acetate) to give **3** (22.79 g, 95%) as a colorless syrup. $[\alpha]_D$ +87 (*c* 1.2, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 4.83 (d, 1H, $J_{1,2}$ 3.7 Hz, H-1), 3.86 (dd, 1H, $J_{6a,6b}$ 10.5 Hz, $J_{5,6a}$ 4.8 Hz, H-6a), 3.81 (dd, 1H, $J_{5,6b}$ 4.5 Hz, H-6b), 3.65, 3.50 and 3.43 (s, 3H, OCH_3), 3.60 (ddd, 1H, $J_{4,5}$ 9.0 Hz, H-5), 3.51 (ddd, 1H, $J_{3,4}$ 9.0 Hz, $J_{4,OH}$ 1.3 Hz, H-4), 3.47 (t, 1H, $J_{2,3}$ 9.0 Hz, H-3), 3.21 (dd, 1H, H-2), 2.91 (d, 1H (C_4-O*H*), 0.91 (s, 9H, $SiC(CH_3)_3$), 0.09 (s, 6H, $Si(CH_3)_2$).

^{13}C NMR (63 MHz) δ: 97.30 (C-1), 82.70, 81.65, 71.96 and 70.41 (C-2, C-3, C-4, C-5), 63.99 (C-6), 61.16, 58.50 and 55.03 (OCH_3), 25.84 ($SiC(CH_3)_3$), 18.27 ($SiC(CH_3)_3$), −5.49 ($Si(CH_3)_2$).

MS (*m*/*z*): 354 $(M + NH_4)^+$, 337 $(M + H)^+$, 322 (M − OMe + NH_3), 305 (M − OMe).

Anal calc for $C_{15}H_{32}O_6Si$: C, 53.54; H, 9.58. Found: C, 53.69; H, 9.55.

Methyl 2,3-di-O-methyl-6-O-tert-butyldimethylsilyl-α-D-xylo-hex-4-ulopyranoside **4**

A solution of DMSO (8.7 mL, 123 mmol) in dry dichloromethane (20 mL) was added to a stirred, and cooled (−70 °C) solution of oxalyl chloride (5.4 mL, 61.9 mmol) in dry dichloromethane (120 mL). After 15 min, a solution of **3** (18.78 g, 55.8 mmol) in dry dichloromethane was slowly added. After 15 min stirring, dry triethylamine (37 mL, 265 mmol) was introduced, and after 15 min, the temperature was allowed to rise up to room temperature. Water (150 mL) was added, and the aqueous layer was extracted with dichloromethane (150 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane/ethyl acetate 9:1 then 4:1) to give **4** (17.3 g, 93%) as a colorless oil. $[\alpha]_D$ +98 (*c* 1.0, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 5.03 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.13 (dd, 1H, $J_{5,6b}$ 6.8 Hz, $J_{5,6a}$ 3.2 Hz, H-5), 4.09 (d, 1H, $J_{2,3}$ 9.9 Hz, H-3), 4.06 (dd, 1H, $J_{6a,6b}$ 11.3 Hz, H-6a), 3.81 (dd, 1H, H-6b), 3.59, 3.56 and 3.53 (s, 3H, OCH_3), 3.52 (dd, 1H, H-2), 0.89 (s, 9H, $SiC(CH_3)_3$), 0.08 (s, 6H, $Si(CH_3)_2$).

^{13}C NMR (63 MHz) δ: 202.26 (C=O), 97.42 (C-1), 84.45, 82.54 and 74.07 (C-2, C-3, C-5), 61.20 (C-6), 60.13, 59.58 and 55.75 (OCH_3), 25.76 ($SiC(CH_3)_3$), 18.24 ($SiC(CH_3)_3$), −5.41 and −5.47 ($Si(CH_3)_2$).

MS (*m*/*z*): 352 $(M + NH_4)^+$, 335 $(M + H)^+$; 320 (M − OMe + NH_3)$^+$, 303 (M − OMe)$^+$.

Anal calc for $C_{15}H_{30}O_6Si$: C, 53.86; H, 9.04. Found: C, 54.04; H, 9.17.

Methyl 4-deoxy-2,3-di-O-methyl-4-C-methylene-6-O-tert-butyldimethylsilyl-α-D-xylo-hexopyranoside **5**

A 1.6 M solution of *n*-butyllithium in *n*-hexane (75 mL) was slowly added to a stirred suspension of methyltriphenylphosphonium bromide (43.3 g, 127 mmol) in dry THF (250 mL). After 30 min at room temperature, the mixture was cooled to −70 °C. A solution of **4** (13.97 g, 41.8 mmol) in THF (60 mL) was then introduced. After 30 min at −70 °C, the temperature was allowed to rise up to room temperature. One hour later a saturated aqueous solution of ammonium chloride (300 mL) was added and the aqueous layer was extracted with ether. The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 7:1 then 4:1) gave **5** (8.30 g, 60%) as a colourless oil. $[\alpha]_D$ +151 (*c* 1.3, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 5.22 (d, 1H, *J* 1 Hz, C=CH_2), 4.97 (d, 1H, *J* 1 Hz, C=CH_2), 4.88 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.11 (t, 1H, $J_{5,6a}$ 6.5 Hz, $J_{5,6b}$ 6.5, H-5), 3.96 (d, 1H, $J_{2,3}$ 10.0 Hz, H-3), 3.95 (dd, 1H, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.81 (dd, 1H, H-6b), 3.53 (s, 6H, OCH_3), 3.46 (s, 3H, OCH_3), 3.18 (dd, 1H, H-2), 0.90 (s, 9H, $SiC(CH_3)_3$), 0.09 (s, 6H, $Si(CH_3)_2$).

^{13}C NMR (63 MHz) δ: 142.47 (C-4), 106.92 (C=CH_2), 97.74 (C-1), 83.65, 81.03 and 69.47 (C-2, C-3, C-5), 63.07 (C-6), 59.34, 59.18 and 54.99 (OCH_3), 25.60 ($SiC(CH_3)_3$), 16.23 ($SiC(CH_3)_3$), −5.35 and −5.44 ($Si(CH_3)_2$).

MS (*m*/*z*): 350 $(M + NH_4)^+$, 333 $(M + H)^+$, 318 (M−OMe + NH_3)$^+$, 301 (M − OMe)$^+$.

Anal calc for $C_{16}H_{32}O_5Si$: C, 57.80; H, 9.70; Found: C, 57.89; H, 9.70.

Methyl 4-deoxy-2,3-di-O-methyl-4-C-methylene-α-D-xylo-hexopyranoside **6**

Camphorsulfonic acid was added to a solution of **5** (8.50 g, 25.6 mmol) in dichloromethane/methanol (5:1, 250 mL). After complete disappearance of the starting material (TLC cyclohexane/ethyl acetate 1:1), the solution was neutralised by addition of Et_3N. The solvent was removed under reduced pressure and the residue and purified by flash chromatography (cyclohexane/ethyl acetate 1:1 then 1:2) to yield **6** (5.32 g, 95%) as a colorless syrup. $[\alpha]_D$ +239 (*c* 1.0, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 5.24 (d, 1H, *J* 1.5 Hz, C=CH_2), 4.93 (d, 1H, *J* 1.5 Hz, C=CH_2), 4.90 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.18 (dd, 1H, $J_{5,6b}$ 7.5 Hz, $J_{5,6a}$ 3.7 Hz, H-5), 3.97 (ddd, 1H, $J_{2,3}$ 9.5 Hz, *J* 1 Hz, *J* 1 Hz, H-3), 3.91 (dd, 1H, $J_{6a,6b}$ 11.5 Hz, H-6a), 3.84 (dd, 1H, H-6b), 3.52, 3.51 and 3.45 (s, 3H, (OCH_3), 3.19 (dd, 1H, H-2).

^{13}C NMR (63 MHz) δ: 141.73 (C-4), 107.52 (C=CH_2), 97.98 (C-1), 83.31, 80.71 and 69.19 (C-2, C-3, C-5), 62.45 (C-6), 59.44, 59.26 and 55.30 (OCH_3).

MS (*m*/*z*): 236 $(M + NH_4)^+$, 219 $(M + H)^+$, 204 (M − OMe + NH_3)$^+$, 187 (M − OMe)$^+$.

Anal calc for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31; Found: C, 55.06; H, 8.37.

Phenyl 2,4,6-tri-O-acetyl-3-O-methyl-1-seleno-β-D-glucopyranoside **9**

Method 1: benzeneselenol (5.7 mL, 53.7 mmol) was added to a solution of **7** [8] (1:1 mixture of anomers; 13.05 g, 36.0 mmol) in dichloromethane (120 mL). The reaction mixture was cooled to 0 °C, and $BF_3{\cdot}OEt_2$ (8.8 mL, 71.9 mmol) was slowly added. After 3 h at room temperature, the reaction mixture was diluted with dichloromethane (100 mL), washed with saturated aqueous $NaHCO_3$ (300 mL), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. The residue **9** (8.17 g, 68% from **7**) was directly engaged in the deacetylation step.

Method 2: Sodium borohydride (510 mg, 14.6 mmol) was added at 0 °C, to a suspension of diphenyl diselenide (2.27 g, 7.27 mmol) in dry ethanol (30 mL). This solution was then transferred onto a solution of **8** (4.22 g, 11.0 mmol) in dichloromethane (25 mL) and the mixture was stirred under reflux for 3 h. The mixture was cooled to room temperature, the precipitated NaBr filtered off, and the solution concentrated under reduced pressure. The residue was dissolved

in dichloromethane (100 mL) and the organic solution was washed with 1M NaOH (50 mL) and a saturated solution of NH_4Cl (50 mL). The aqueous layers were extracted with dichloromethane (20 mL), the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane/ethyl acetate 1.7:1) to give **9** (4.35 g, 86%).

Mp 101–102 °C (ethyl acetate); $[\alpha]_D$ −20 (*c* 1.0, $CHCl_3$).

^1H NMR (400 MHz) δ: 7.71–7.66 (m, 2H, arom), 7.08–6.98 (m, 3H, arom), 5.27 (dd, 1H, $J_{1,2}$ 10.0 Hz, $J_{2,3}$ 9.4 Hz, H-2), 5.13 (t, 1H, $J_{3,4}$ 9.4 Hz, $J_{4,5}$ 9.4 Hz, H-4), 4.63 (d, 1H, H-1), 4.14 (dd, 1H, $J_{6a,6b}$ 12.2 Hz, $J_{5,6a}$ 5.3 Hz, H-6a), 4.08 (dd, 1H, $J_{5,6b}$ 2.5 Hz, H-6b), 3.28 (t, 1H, H-3), 3.16 (s, 3H, OCH_3), 3.07 (ddd, 1H, H-5), 1.77, 1.71 and 1.62 (s, 3H, $OCOCH_3$).

^{13}C NMR (63 MHz) δ: 169.99, 168.82 and 168.78 (C=O), 134.99–128.23 (C arom), 82.62 (C-3), 82.15 (C-1), 77.50 (C-5), 71.57 (C-2), 68.73 (C-4), 62.40 (C-6), 58.04 (OCH_3), 20.65, 20.32 and 20.25 ($OCOCH_3$).

MS (*m/z*): 478 $(M + NH_4)^+$, 461 $(M + H)^+$, 303 $(M - SePh)^+$.

Anal calc for $C_{19}H_{24}O_8Se$: C, 49.68; H, 5.27; Found: C, 49.85; H, 5.27.

Phenyl 3-O-methyl-1-seleno-β-D-glucopyranoside ***10***

Sodium (1.2 g) was introduced portionwise into a solution of **9** (84.3 mmol) in methanol (500 mL). After 1 h, the solution was neutralised by addition of IR-120 (H^+) resin, filtered, concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane/ethyl acetate/acetone 1.5:1:1) to give **10** as a syrup (22.7 g, 81% from **8**). $[\alpha]_D$ −58 (*c* 1.0, MeOH).

^1H NMR (250 MHz, CD_3OD) δ: 7.60–7.13 (m, 5H, arom), 4.68 (d, 1H, $J_{1,2}$ 7.2 Hz, H-1), 3.74 (dd, 1H, $J_{6a,6b}$ 12.1 Hz, $J_{5,6a}$ 1.9 Hz, H-6a), 3.54 (dd, 1H, $J_{5,6b}$ 5.2 Hz, H-6b), 3.53 (s, 3H, OCH_3), 3.27–3.14 (m, 3H, H-2, H-4, H-5), 2.99 (t, 1H, $J_{2,3}$ 8.6 Hz, $J_{3,4}$ 8.6 Hz, H-3).

^{13}C NMR (63 MHz, CD_3OD) δ: 135.40, 129.94 and 128.73 (C arom), 129.67 (C arom), 89.37, 86.04, 83.07, 74.31 and 70.96 (C-1, C-2, C-3, C-4, C-5), 62.74 (C-6), 61.34 (OCH_3).

MS (*m/z*): 352 $(M + NH_4)^+$, 335 $(M + H)^+$.

Anal calc for $C_{13}H_{18}O_5Se$ (333.242): C, 46.86; H, 5.44; Found: C, 47.14; H, 5.56.

Phenyl 4,6-O-benzylidene-3-O-methyl-1-seleno-β-D-glucopyranoside ***11***

p-Toluenesulfonic acid (45 mg) and benzaldehyde dimethylacetal (5.4 mL, 36.0 mmol) were added to a solution of **10** (7.65 g, 23.0 mmol) in dry acetonitrile (150 mL). After stirring for 2 h at room temperature, dry K_2CO_3 (1.5 g) was added. After 30 min the solution was filtered, concentrated and the residue was purified by flash chromatography (cyclohexane/ethyl acetate 3.5:1) to give **11** (8.55 g, 88%). Mp 123–124 °C (cyclohexane/ethyl acetate); $[\alpha]_D$ −38 (*c* 1.0, $CHCl_3$).

^1H NMR (250 MHz) δ: 7.68–7.64 (m, 2H, arom), 7.50–7.30 (m, 8H, arom), 5.55 (s, 1H, C*H*Ph), 4.86 (d, 1H, $J_{1,2}$ 9.5 Hz, H-1), 4.40 (dd, 1H, $J_{6a,6b}$ 10.4 Hz, $J_{5,6a}$ 4.5 Hz, H-6a), 3.78 (dd, 1H, $J_{5,6b}$ 9.6 Hz, H-6b), 3.67 (s, 3H, OCH_3), 3.61–3.43 (m, 4H, H-2, H-3, H-4, H-5), 2.63 (s, OH).

^{13}C NMR (63 MHz, C_6D_6) δ: 138.27–126.58 (C arom), 101.35 (*C*HPh), 85.21 (C-1), 84.10, 81.32, 73.68 and 71.64 (C-2, C-3, C-4, C-5), 66.58 (C-6), 60.76 (OCH_3).

MS (*m/z*): 440 $(M + NH_4)^+$, 423 $(M + H)^+$, 265 $(M - SePh)^+$.

Anal calc for $C_{20}H_{22}O_5Se$: C, 57.01; H, 5.26; Found: C, 57.04; H, 5.24.

2-Benzothiazolyl 2,4,6-tri-O-acetyl-3-O-methyl-1-thio-β-D-glucopyranoside ***12***

2-Benzothiazolethiol (1.45 g, 8.67 mmol) was added, to a solution of **7** [8] (1:1 mixture of anomers; 2.1 g, 5.8 mmol) in dichloromethane (50 mL). The solution was cooled to 0 °C, and $BF_3{\cdot}OEt_2$ (1.8 mL, 14.7 mmol) was slowly added. After 3 h at room temperature, the reaction mixture was diluted with dichloromethane (50 mL), washed with saturated aqueous $NaHCO_3$ (100 mL), brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude residue **13** was directly engaged in the next step without further characterisation.

MS (*m/z*): 470 $(M + H)^+$.

2-Benzothiazolyl 3-O-methyl-1-thio-β-D-glucopyranoside ***13***

Sodium (205 mg) was added portionwise to a solution of **12** in dry methanol (50 mL). After 2 h at room temperature, the mixture was neutralised by addition of IR-120 (H^+) resin, filtered, concentrated under reduced pressure, and the residue was purified by flash chromatography (CH_2Cl_2/MeOH 25:1) to give **13** (0.85 g, 43% from **7**). $[\alpha]_D$ −29 (*c* 0.5, $CHCl_3$).

^1H NMR (200 MHz) δ: 7.99–7.36 (m, 4H, arom), 5.14 (d, 1H, $J_{1,2}$ 9.6 Hz, H-1), 3.97–3.52 (m, 5H, H-2, H-4, H-5, H-6a, H-6b), 3.73 (s, 3H, OCH_3), 3.32 (t, 1H, $J_{2,3}$ 8.7 Hz, $J_{3,4}$ 8.7 Hz, H-3).

MS (*m/z*): 344 $(M + H)^+$.

No correct elemental analysis has been obtained from this hydroscopic compound.

2-Benzothiazolyl 4,6-O-benzylidene-3-O-methyl-1-thio-β-D-glucopyranoside ***14***

p-Toluenesulfonic acid (15 mg) and benzaldehyde dimethylacetal (0.6 mL, 4.0 mmol) were added to a solution of **13** (790 mg, 2.30 mmol) in dry acetonitrile (20 mL). After stirring for 2 h at room temperature, dry K_2CO_3 (130 mg) was added. After 30 min the solution was filtered, concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane/ethyl acetate 3:1) to give **14** (560 mg, 56%). Mp 147 °C (cyclohexane/ethyl acetate), $[\alpha]_D$ −37 (*c* 1.0, $CHCl_3$).

^1H NMR (250 MHz) δ: 7.99–7.36 (m, 9H, arom), 5.59 (s, 1H, C*H*Ph), 5.33 (d, 1H, $J_{1,2}$ 9.8 Hz, H-1), 4.44 (dd, 1H, $J_{6a,6b}$ 10.5 Hz, $J_{5,6a}$ 4.1 Hz, H-6a), 3.83 (t, 1H, $J_{5,6b}$ 10.5 Hz, H-6b), 3.80–3.65 (m, 3H, H-2, H-4, H-5), 3.71 (s, 3H, OCH_3), 3.55 (dd, 1H, $J_{2,3}$ 8.6 Hz, $J_{3,4}$ 8.6 Hz, H-3), 3.23 (d, 1H, $J_{2,OH}$ 2.8 Hz, C_2-OH).

MS (*m/z*): 432 $(M + H)^+$.

Anal calc for $C_{21}H_{21}NO_5S_2$: C, 58.45; H, 4.90; N, 3.25; Found: C, 58.26; H, 4.95; N, 3.12.

Methyl 6-O-[(4,6-O-benzylidene-3-O-methyl-1-Se-phenyl-β-D-glucopyranos-2-O-yl)dimethylsilyl]-4-deoxy-2,3-di-O-methyl-4-C-methylene-α-D-xylo-hexopyranoside ***15***

A 1.6 M solution of *n*-butyllithium in *n*-hexane (7.0 mL, 11.2 mmol) was added to a cooled (−70 °C) solution of **11** (4.30 g, 10.2 mmol) in dry THF (30 mL) placed in a Schlenck apparatus. After 10 min, dichlorodimethylsilane (5.0 mL, 41.2 mmol) was added, and the reaction mixture was allowed

to warm up to room temperature. After 3 h, the solution was concentrated under reduced pressure and a solution of **6** (2.10 g, 9.62 mmol) and imidazole (985 mg, 14.4 mmol) in dry THF (20 mL) was added. After 30 min at room temperature, the solution was concentrated under reduced pressure, water (50 mL) was added, and the product was extracted with dichloromethane. The organic solution was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was directly engaged in the next step. For characterisation purposes, **15** was purified by flash chromatography (25:1 toluene/acetone containing 0.5% of triethylamine) to give a colourless syrup (90%).

^{1}H NMR (400 MHz, C_6D_6) δ: 7.77–6.99 (m, 10H, arom), 5.51 (m, 1H, C=CH_2), 5.24 (m, 1H, C=CH_2), 5.16 (s, 1H, CHPh), 4.85 (d, 1H, $J_{1,2}$ 3.7 Hz, H-1), 4.81 (d, 1H, $J_{1',2'}$ 9.8 Hz, H-1'), 4.45 (m, 1H, H-5), 4.38 (dd, 1H, $J_{6a,6b}$ 10.8 Hz, $J_{5,6a}$ 4.8 Hz, H-6a), 4.33 (dd, 1H, $J_{5,6b}$ 6.2 Hz, H-6b), 4.20 (m, 1H, $J_{2,3}$ 9.2 Hz, H-3), 4.05 (dd, 1H, $J_{6a',6b'}$ 10.3 Hz, $J_{5',6a'}$ 4.9 Hz, H-6a'), 3.87 (dd, 1H, $J_{2',3'}$ 8.1 Hz, H-2'), 3.52, 3.38, 3.31 and 3.27 (s, 3H, OCH_3), 3.37 (t, 1H, $J_{5',6b'}$ 10.3 Hz, H-6b'), 3.35 (t, 1H, H-4'), 3.32 (dd, 1H, H-2), 3.22 (dd, 1H, $J_{3',4'}$ 9.3 Hz, H-3'), 3.05 (ddd, 1H, $J_{4',5'}$ 9.3 Hz, H-5'), 0.38 and 0.37 (s, 3H, Si(CH_3)$_2$).

MS (m/z): 714 $(M + NH_4)^+$.

No elemental analysis has been attempted on this unstable intermediate.

*Radical cyclization reaction and cleavage of the tether (formation of **19**, **21**, **23** and **25**)*

A solution of tributyltin hydride (6.1 mL, 22.7 mmol), and AIBN (200 mg, 1.22 mmol), in dry and degassed toluene (14 mL) was added over a period of 8 h to a toluene solution (850 mL) of previously obtained **15**.

For the photochemical cyclizations, crude **15** was dissolved (0.5–0.9 M solution containing 0.7–0.8 equivalents of Bu_6Sn_2) in acetone (99%, ACROS) in a Pyrex Schlenk apparatus. The solution was degassed and placed under argon. It was irradiated with a Hg-lamp for 3 h under vigorous stirring at room temperature.

After radical cyclization, the solvents were evaporated under reduced pressure and the residue was dissolved in THF. A 20-fold excess of HF (40% aqueous solution) was added. After complete desilylation (TLC, toluene/acetone 4:1) the solution was neutralised by addition of solid $NaHCO_3$, filtered and concentrated under reduced pressure. A first chromatography (cyclohexane/ethyl acetate 3:1 then 1:2) allowed the separation of the reduced alcohol **16**, unreacted **6** and a C-disaccharide fraction. The C-disaccharide fraction could be further fractionated (cyclohexane/ethyl acetate/acetone 2:1:1 then 0.5:1:1). The total yield in C-disaccharides was 60% from **15** over three steps (tethering, radical cyclization, cleavage of the connector) using the Bu_3SnH technique, and 50% after photochemical cyclization. In preparative experiments, the major C-disaccharide **19** could be crystallized out of the mixture resulting from preliminary enrichment by flash chromatography.

*1,5-Anhydro-4,6-O-benzylidene-3-O-methyl-D-glucitol **16***

Mp 120 °C (cyclohexane/ethyl acetate); $[\alpha]_D$ −3 (c 1.0, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 7.52–7.36 (m, 5H, arom), 5.56 (s, 1H, CHPh), 4.34 (dd, 1H, $J_{6a,6b}$ 10.5 Hz, $J_{5,6a}$ 4.9 Hz, H-6a), 4.08 (dd, 1H, $J_{1a,1b}$ 11.2 Hz, $J_{1a,2}$ 5.5 Hz, H-1a), 3.74 (dddd, 1H, H-2), 3.72 (t, 1H, $J_{5,6b}$ 10.5 Hz, H-6b), 3.70 (s, 3H, OCH_3), 3.58 (t, 1H, $J_{3,4}$ 9.0 Hz, $J_{4,5}$ 9.0 Hz, H-4), 3.42 (ddd, 1H, H-5), 3.38 (t, 1H, $J_{1b,2}$ 11.2 Hz, H-1b), 3.36 (t, 1H, $J_{2,3}$ 9.0 Hz, H-3), 2.58 (d, 1H, $J_{2,OH}$, 2.5 Hz, C_2-OH).

^{13}C NMR (63 MHz) δ: 137.28 (C arom), 128.93–125.96 (C arom), 101.10 (CHPh), 84.62 (C-3), 82.06 (C-4), 71.42 (C-5), 69.88 (C-1), 69.76 (C-2), 68.81 (C-6), 60.96 (OCH_3).

MS (m/z): 284 $(M + NH_4)^+$, 267 $(M + H)^+$.

Anal calc for $C_{14}H_{18}O_5$ (266.293): C, 63.15; H, 6.81; Found: C, 63.26; H, 6.81.

*Methyl 6-O-acetyl-4-C-(3-oxobutyl)-4-deoxy-2,3-di-O-methyl-α-D-glucopyranoside **18***

Compound **17** (see results and discussion) was quantitatively acetylated in Ac_2O/pyridine (1:1) in the presence of a catalytic amount of DMAP. The product was isolated after evaporation and flash chromatography.

^{1}H NMR (250 MHz) δ: 4.86 (d, 1H, $J_{1,2}$ 3.3 Hz, H-1), 4.30 (dd, 1H, $J_{6a,6b}$ 12.2 Hz, $J_{5,6a}$ 2.2 Hz, H-6a), 4.16 (dd, 1H, $J_{5,6b}$ 5.4 Hz, H-6b), 3.68 (ddd, 1H, $J_{4,5}$ 10.4 Hz, H-5), 3.56, 3.50 and 3.42 (s, 3H, OCH_3), 3.34 (dd, 1H, $J_{3,4}$ 9.6 Hz, H-3), 3.23 (dd, 1H, $J_{2,3}$ 9.3 Hz, H-2), 2.59–2.51 (m, 2H, $CH_3COCH_2CH_2C$-4), 2.15 and 2.11 (s, 3H, $OCOCH_3$ and $CH_3COCH_2CH_2C$-4), 1.85–1.76 (m, 1H, $CH_3COCH_2CH_2C$-4), 1.69–1.55 (m, 2H, H-4 and $CH_3COCH_2CH_2C$-4).

^{13}C NMR (63 MHz) δ: 207.91 ($CH_3COCH_2CH_2C$-4), 170.80 ($OCOCH_3$), 97.51 (C-1), 83.19, 80.43 and 68.86 (C-2, C-3, C-5), 64.26 (C-6), 60.76, 58.33 and 55.13 (OCH_3), 41.45 (C-4), 40.59 ($CH_3COCH_2CH_2C$-4), 29.83 ($CH_3COCH_2CH_2C$-4), 21.54 ($CH_3COCH_2CH_2C$-4), 20.77 ($OCOCH_3$).

MS (m/z): 336 $(M + NH_4)^+$, 319 $(M + H)^+$, 304 $(M - OMe + NH_3)^+$, 287 $(M - OMe)^+$.

No further characterisation of this by-product has been carried out.

*Methyl 4-C-(4,6-O-benzylidene-3-O-methyl-α-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-α-D-glucopyranoside **19***

This compound could be crystallized (see above); Mp 105 °C (cyclohexane/ethyl acetate). $[\alpha]_D$ +119 (c 1.1, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 7.50–7.35 (m, 5H, arom), 5.54 (s, 1H, CHPh), 4.88 (d, 1H, $J_{1,2}$ 3.4 Hz, H-1), 4.27 (dd, 1H, $J_{6a',6b'}$ 9.5 Hz, $J_{5',6a'}$ 3.7 Hz, H-6a'), 4.26 (ddd, 1H, H-1'), 3.85–3.79 (m, 2H, H-6a, H-2'), 3.72–3.54 (m, 5H, H-5, H-6b, H-4', H-5', H-6b'), 3.67, 3.64, 3.50 and 3.42 (s, 3H, OCH_3), 3.44 (t, 1H, $J_{2',3'}$ 9.5 Hz, $J_{3',4'}$ 9.5 Hz, H-3'), 3.41 (t, 1H, $J_{3,4}$ 9.2 Hz, H-3), 3.26 (d, 1H, $J_{2',OH}$, 5.4 Hz, C_2'-OH), 3.25 (dd, 1H, $J_{2,3}$ 9.2 Hz, H-2), 2.14 (t, 1H, J 6.4 Hz, C_6-OH), 1.93 (ddd, 1H, $J_{4,4ha}$ 5.5 Hz, $J_{4ha,1'}$ 5.5 Hz, H-4ha), 1.93–1.85 (m, 1H, H-4), 1.65 (ddd, 1H, $J_{4ha,4hb}$ 14.7 Hz, $J_{4,4hb}$ 7.3 Hz, $J_{4hb,1'}$ 3.2 Hz, H-4hb).

^{13}C NMR (63 MHz) δ: 137.29 (C arom), 128.88–125.96 (C arom), 101.11 (CHPh), 97.64 (C-1), 83.52 (C-2), 82.76, 81.95, 80.84, 72.01, 71.92 and 64.31 (C-3, C-5, C-2', C-3', C-4', C-5'), 75.19 (C-1'), 69.41 (C-6'), 62.69 (C-6), 60.93, 60.70, 58.31 and 55.20 (OCH_3), 38.80 (C-4), 25.58 (C methylene).

MS (m/z): 502 $(M + NH_4)^+$, 485 $(M + H)^+$, 470 $(M - OMe + NH_3)^+$, 453 $(M - OMe)^+$.

Anal calc for $C_{24}H_{36}O_{10}\cdot H_2O$ (502.558): C, 57.36; H, 7.62; Found: C, 57.31; H, 7.54.

Methyl 6-O-acetyl-4-C-(2-O-acetyl-4,6-O-benzylidene-3-O-methyl-α-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-α-D-glucopyranoside **20**

Compound **19** was quantitatively acetylated in Ac_2O/pyridine (1:1) in the presence of a catalytic amount of DMAP. The product was isolated after evaporation under reduced pressure and flash chromatography. $[\alpha]_D$ +87 (*c* 1.0, $CHCl_3$).

^1H NMR (500 MHz): see table I.

^{13}C NMR (63 MHz) δ: 170.81, 169.80 (C=O), 137.18 (C arom), 128.92–125.95 (C arom), 101.31 (*C*HPh), 97.51 (C-1), 83.22 (C-2), 81.94, 69.25 and 63.83 (C-5, C-4′, C-5′), 81.81 (C-3), 78.78 (C-3′), 72.74 (C-2′), 71.96 (C-1′), 69.49 (C-6′), 64.17 (C-6), 60.64, 59.82, 58.30 and 55.19 (O*C*H$_3$), 39.00 (C-4), 26.47 (C methylene), 20.91, 20.76 (OCO*C*H$_3$).

MS (*m/z*): 586 $(M + NH_4)^+$, 569 $(M + H)^+$, 554 $(M - OMe + NH_3)^+$, 537 $(M - OMe)^+$.

Anal calc for $C_{28}H_{40}O_{12}\cdot H_2O$: C, 57.33; H, 7.22; Found: C, 57.28; H, 7.07.

Methyl 6-O-acetyl-4-C-(2-O-acetyl-4,6-O-benzylidene-3-O-methyl-β-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-α-D-glucopyranoside **22**

Compound **21** was quantitatively acetylated in Ac_2O/pyridine (1:1) in the presence of a catalytic amount of DMAP. The product was isolated after evaporation under reduced pressure and flash chromatography. $[\alpha]_D$ +20 (*c* 0.1, $CHCl_3$).

^1H NMR (500 MHz): see table I.

MS (*m/z*): 586 $(M + NH_4)^+$, 569 $(M + H)^+$.

The isolation of this compound has been performed on a very small scale, so that no destructive elemental analysis has been achieved on the sample and the next two other isomers.

Methyl 6-O-acetyl-4-C-(2-O-acetyl-4,6-O-benzylidene-3-O-methyl-α-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-α-D-galactopyranoside **24**

Compound **23** was quantitatively acetylated in Ac_2O/pyridine (1:1) in the presence of a catalytic amount of DMAP. The product was isolated after evaporation under reduced pressure and flash chromatography. $[\alpha]_D$ +72 (*c* 0.1, $CHCl_3$).

^1H NMR (500 MHz): see table I.

MS (*m/z*): 586 $(M + NH_4)^+$, 569 $(M + H)^+$, 554 $(M - OMe + NH_3)^+$, 537 $(M - OMe)^+$.

Methyl 6-O-acetyl-4-C-(2-O-acetyl-4,6-O-benzylidene-3-O-methyl-β-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-α-D-galactopyranoside **26**

Compound **25** was quantitatively acetylated in Ac_2O/pyridine (1:1) in the presence of a catalytic amount of DMAP. The product was isolated after evaporation under reduced pressure and flash chromatography. $[\alpha]_D$ +55 (*c* 0.31, $CHCl_3$).

^1H NMR (500 MHz): see table I.

MS (*m/z*): 586 $(M + NH_4)^+$, 569 $(M + H)^+$, 554 $(M - OMe + NH_3)^+$, 537 $(M - OMe)^+$.

Methyl 6-O-acetyl-4-C-(2-O-acetyl-6-O-benzyl-3-O-methyl-α-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-α-D-glucopyranoside **27**

A saturated solution of HCl in ether was slowly added at 0 °C to a solution of **20** (2.47 g, 4.35 mmol) and $NaBH_3CN$ (2.93 g, 46.5 mmol) in THF (80 mL) containing 4 Å molecular sieves and a few crystals of methyl orange. After 1.5 h, the solution was filtered, aqueous saturated $NaHCO_3$ (100 mL) was added, and the product was extracted with ether. The organic layer was dried ($MgSO_4$), filtered, evaporated under reduced pressure, and the residue was purified by flash chromatography (cyclohexane/ethyl acetate/acetone 5:2:2) to give **27** (2.15 g, 87%). $[\alpha]_D$ +90 (*c* 1.0, $CHCl_3$).

^1H NMR (400 MHz) δ: 7.36–7.25 (m, 5H, arom), 4.89 (dd, 1H, $J_{2',3'}$ 7.3 Hz, $J_{1',2'}$ 4.3 Hz, H-2′), 4.84 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.58 and 4.55 (d, 1H, J_{gem} 12.0 Hz, OC*H*$_2$Ph), 4.31 (dd, 1H, $J_{6a,6b}$ 12.2 Hz, $J_{5,6a}$ 2.0 Hz, H-6a), 4.25 (ddd, 1H, $J_{4ha,1'} \approx 10$ Hz, $J_{4hb,1'} \approx 3$ Hz, H-1′), 4.09 (dd, 1H, $J_{5,6b}$ 5.5 Hz, H-6b), 3.81–3.62 (m, 5H, H-5, H-4′, H-5′, H-6a′, H-6b′), 3.50, 3.49, 3.46 and 3.39 (s, 3H, OC*H*$_3$), 3.41–3.34 (m, 2H, H-3, H-3′), 3.18 (dd, 1H, $J_{2,3}$ 9.4 Hz, H-2), 2.90 (d, 1H, $J_{4',OH}$, 5.0 Hz, C′$_4$-OH), 2.12 and 2.06 (s, 3H, OCOC*H*$_3$), 1.77–1.68 (m, 2H, H-4, H-4ha), 1.51 (ddd, 1H, $J_{4ha,4hb}$ 14.5 Hz, $J_{4,4h} \approx 7$ Hz, H-4hb).

^{13}C NMR (63 MHz) δ: 170.84 and 169.84 (C=O), 137.97 (C arom), 128.42–127.66 (C arom), 97.56 (C-1), 83.20 (C-2), 81.90, 79.98, 73.45, 71.88, 69.86 and 69.56 (C-3, C-5, C-2′, C-3′, C-5′), 73.55 (O*C*H$_2$Ph), 70.10 (C-1′), 69.65 (C-6′), 64.56 (C-6), 60.61, 59.55, 58.31 and 55.16 (O*C*H$_3$), 39.46 (C-4), 26.58 (C methylene), 21.02 and 20.84 (OCO*C*H$_3$).

MS *m/z*: 588 $(M + NH_4)^+$, 539 $(M - OMe)^+$.

Anal calc for $C_{28}H_{42}O_{12}$ (570.633): C, 58.94; H, 7.42. Found: C, 59.02; H, 7.62.

Methyl 4-C-(6-O-benzyl-3-O-methyl-α-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-α-D-glucopyranoside **28**

Sodium (0.6 g) was added portionwise to a solution of **27** (2.15 g, 3.77 mmol) in anhydrous methanol (200 mL). After 30 min at room temperature, the mixture was neutralised by addition of IR-120 (H^+) resin, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane/acetone 1:1) gave **28** (1.80 g, 98%). $[\alpha]_D$ +80 (*c* 1.0, $CHCl_3$).

^1H NMR (400 MHz) δ: 7.39–7.28 (m, 5H, arom), 4.89 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.60 and 4.55 (d, 1H, J_{gem} 12.0 Hz, OC*H*$_2$Ph), 3.96–3.90 (m, 2H, H-1′, H-5′), 3.81 (dd, 1H, $J_{6a',6b'}$ 10.2 Hz, $J_{5',6a'}$ 7.0 Hz, H-6a′), 3.75–3.70 (m, 3H, H-6a, H-6b, H-4′), 3.66 (ddd, 1H, $J_{2',3'}$ 5.5 Hz, $J_{2',OH}$, 5.5 Hz, $J_{1',2'}$ 4.5 Hz, H-2′), 3.63 (s, 3H, OC*H*$_3$), 3.56 (dd, 1H, $J_{5',6b'}$ 4.9 Hz, H-6b′), 3.52–3.47 (m, 1H, H-5), 3.49 (s, 6H, 2OC*H*$_3$), 3.42 (s, 3H, OC*H*$_3$), 3.40 (t, 1H, $J_{3',4'}$ 5.5 Hz, H-3′), 3.36 (dd,1H, $J_{3,4}$ 9.8 Hz, $J_{2,3}$ 9.3 Hz, H-3), 3.23 (dd, 1H, H-2), 3.17 (d, 1H, $C_{2'}$-OH), 2.48 (t, 1H, C_6-OH), 1.80–1.67 (m, 2H, H-4, H-4ha), 1.58 (ddd, 1H, $J_{4ha,4hb}$ 14.8 Hz, *J* 7.5 Hz, *J* 4.5 Hz, H-4hb).

^{13}C NMR (63 MHz) δ: 137.89 (C arom), 128.36–127.65 (C arom), 97.65 (C-1), 83.45 (C-2), 82.21 and 80.35 (C-3, C-3′), 75.73 and 70.96 (C-1′, C-5′), 73.25 (O*C*H$_2$Ph), 72.49 (C-5), 69.65 (C-4′), 68.27 (C-6′), 68.03 (C-2′), 62.15 (C-6), 61.16, 58.84, 58.20 and 55.12 (O*C*H$_3$), 38.55 (C-4), 28.26 (C methylene).

MS, *m/z*: 504 $(M + NH_4)^+$, 487 $(M + H)^+$, 455 $(M - OMe)^+$.

Anal calc for $C_{24}H_{38}O_{10}$: C, 59.25; H, 7.87. Found: C, 59.13; H, 7.97.

Methyl 4-C-(6-O-benzyl-3-O-methyl-α-D-gluco-pyranosylmethyl)-4-deoxy-2,3-di-O-methyl-6-O-tert-butyldimethylsilyl-α-D-glucopyranoside ***29***

A solution of **28** (0.696 g, 1.43 mmol), Et_3N (0.3 mL, 2.16 mmol), DMAP (195 mg, 1.60 mmol), and *tert*-butyldimethylsilyl chloride (270 mg, 1.79 mmol) in dichloromethane (20 mL), was stirred overnight at room temperature. Aqueous saturated NH_4Cl (30 mL) was added and the aqueous phase was extracted three times with dichloromethane. The organic solution was dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane/ethyl acetate/acetone 3:1:1) gave **29** (0.738 g, 86%). $[\alpha]_D$ +79 (*c* 1.0, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 7.37–7.27 (m, 5H, arom), 4.85 (d, 1H, $J_{1,2}$ 3.4 Hz, H-1), 4.60 and 4.55 (d, 1H, J_{gem} 12.1 Hz, OCH_2Ph), 3.97 (d, 1H, *J* 5.4 Hz, $C_{4'}$-OH), 3.96–3.90 (m, 2H, H-1′, H-5′), 3.82–3.75 (m, 3H, H-4′, H-6a, H-6a′), 3.72–3.67 (m, 2H, H-2′, H-6b), 3.67, 3.52, 3.49 and 3.41 (s, 3H, OCH_3), 3.64 (dd, 1H, $J_{6a',6b'}$ 10.2 Hz, $J_{5',6b'}$ 5.3 Hz, H-6b′), 3.47–3.41 (m, 2H, H-5, H-3′), 3.36 (dd, 1H, $J_{3,4}$ 10.5 Hz, $J_{2,3}$ 9.3 Hz, H-3), 3.33 (d, 1H, *J* 7.2 Hz, $C_{2'}$-OH), 3.18 (dd, 1H, H-2), 1.80 (ddd, 1H, $J_{4ha,4hb}$ 15.0 Hz, $J_{4ha,1'}$ 10.0 Hz, $J_{4,4ha}$ 2.0 Hz, H-4ha), 1.71 (dddd, 1H, $J_{4,5}$ 8.5 Hz, H-4), 1.55 (ddd, 1H, $J_{4,4hb}$ 5.4 Hz, $J_{4hb,1'}$ 5.4 Hz, H-4hb), 0.91 (s, 9H, $SiC(CH_3)_3$), 0.06 (s, 6H, $Si(CH_3)_2$).

^{1}H NMR (**31** + trichloroacetyl isocyanate, 400 MHz) δ: 9.05 and 8.73 (s, 1H, NH), 7.37–7.26 (m, 5H, arom), 5.10 (t, 1H, $J_{3',4'} \approx 3$ Hz, $J_{4',5'} \approx 3$ Hz, H-4′), 5.01 (dd, 1H, $J_{2',3'} \approx 3$ Hz, $J_{1',2'} \approx 2$ Hz, H-2′), 4.82 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.58 and 4.53 (d, 1H, J_{gem} 12.0 Hz, OCH_2Ph), 4.23 (m, 1H, H-1′), 4.16 (m, 1H, $J_{5',6a'} \approx 6.5$ Hz, $J_{5',6b'} \approx 6.5$ Hz, H-5′), 3.83–3.73 (m, 3H, H-6a, H-6a′, H-6b′), 3.69 (t, 1H, H-3′), 3.66 (dd, 1H, $J_{6a,6b}$ 12.0 Hz, $J_{5,6b}$ 4.5 Hz, H-6b), 3.52, 3.48, 3.46 and 3.37 (s, 3H, OCH_3), 3.42 (ddd, 1H, $J_{4,5}$ 10.5 Hz, $J_{5,6a}$ 2.0 Hz, H-5), 3.31 (t, 1H, $J_{2,3}$ 9.3 Hz, $J_{3,4}$ 9.3 Hz, H-3), 3.13 (dd, 1H, H-2), 1.71 (ddd, 1H, $J_{4ha,4hb}$ 14.0 Hz, $J_{4ha,1'}$ 6.0 Hz, $J_{4,4ha}$ 4.7 Hz, H-4ha), 1.68–1.60 (m, 1H, H-4), 1.54 (ddd, 1H, $J_{4hb,1'}$ 6.5 Hz, $J_{4,4hb}$ 4.2 Hz, H-4hb), 0.88 (s, 9H, $SiC(CH_3)_3$), 0.56 and 0.55 (2s, 6H, $Si(CH_3)_2$).

^{13}C NMR (63 MHz) δ: 138.12 (C arom), 128.32–127.55 (C arom), 97.29 (C-1), 83.71 (C-2), 81.98 (C-3), 80.98 and 73.14 (C-5, C-3′), 75.17 and 70.14 (C-1′, C-5′), 73.27 (OCH_2Ph), 69.45 (C-4′), 69.23 (C-6′), 68.46 (C-2′), 63.01 (C-6), 61.29, 59.07, 58.05 and 54.96 (OCH_3), 37.31 (C-4), 28.04 (C methylene), 25.86 ($SiC(CH_3)_3$), 18.29 ($SiC(CH_3)_3$), −2.50 and −2.65 ($Si(CH_3)_2$).

MS, *m/z*: 618 $(M + NH_4)^+$, 601 $(M + H)^+$, 586 $(M - OMe + NH_3)^+$, 569 $(M - OMe)^+$.

Anal calc for $C_{30}H_{52}O_{10}Si$: C, 59.97; H, 8.72. Found: C, 60.12; H, 8.62.

Methyl 4-C-(6-O-benzyl-2,3,4-tri-O-methyl-α-D-gluco-pyranosylmethyl)-4-deoxy-2,3-di-O-methyl-6-O-tert-butyldimethylsilyl-α-D-glucopyranoside ***30***

A 60% suspension of NaH in oil was slowly added to a solution of MeI (0.55 mL, 8 mmol) and **29** (735 mg, 1.22 mmol) in anhydrous DMF. After 40 min, methanol (1 mL) was added and, after additionnal 10 min the solution was concentrated under reduced pressure and the reaction product was extracted with ether. The ether solution was dried ($MgSO_4$), concentrated under reduced pressure, and the residue was purified by flash chromatography (cyclohexane/ethyl acetate 2:1) to give **30** (711 mg, 93%). $[\alpha]_D$ +103 (*c* 0.97, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 7.36–7.26 (m, 5H, arom), 4.82 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.66 and 4.51 (d, 1H, J_{gem} 12.2 Hz, OCH_2Ph), 4.36 (ddd, 1H, $J_{4ha,1'}$ 10.5 Hz, $J_{1',2'}$ 5.2 Hz, $J_{4hb,1'}$ 2.6 Hz, H-1′), 3.76 (dd, 1H, $J_{6a,6b}$ 11.3 Hz, $J_{5,6a}$ 2.8 Hz, H-6a), 3.69–3.65 (m, 2H, H-6b, H-6a′), 3.63 (dd, 1H, $J_{6a',6b'}$ 10.4 Hz, $J_{5',6b'}$ 2.3 Hz, H-6b′), 3.59, 3.53, 3.48, 3.46, 3.45 and 3.39 (s, 3H, OCH_3), 3.57–3.44 (m, 3H, H-3, H-5, H-5′), 3.30–3.22 (m, 3H, H-2′, H-3′, H-4′), 3.20 (dd, 1H, $J_{2,3}$ 9.3 Hz, H-2), 1.83 (ddd, 1H, $J_{4ha,4hb}$ 15.2 Hz, $J_{4,4ha}$ 2.4 Hz, H-4ha), 1.81–1.73 (m, 1H, H-4), 1.60 (ddd, 1H, $J_{4,4hb}$ 6.5 Hz, H-4hb), 0.89 (s, 9H, $Si-C(CH_3)_3$), 0.052 and 0.046 (2s, 6H, $Si-(CH_3)_2$).

^{13}C NMR (63 MHz) δ: 138.23 (C arom), 128.21–127.45 (C arom), 97.22 (C-1), 83.35, 83.31, 81.94, 81.50, 79.37, 71.98 and 71.48 (C-2, C-3, C-5, C-2′, C-3′, C-4′, C-5′), 73.44 (OCH_2Ph), 72.24 (C-1′), 68.96 (C-6′), 64.30 (C-6), 60.31, 60.17, 59.98, 58.76, 58.11 and 54.62 (OCH_3), 39.32 (C-4), 25.90 ($Si-C(CH_3)_3$), 23.47 (C methylene), 18.31 ($Si-C(CH_3)_3$), −5.19 and −5.28 ($Si-(CH_3)_2$).

MS, *m/z*: 646 $(M + NH_4)^-$, 629 $(M + H)^+$, 614 $(M - OMe + NH_3)^+$, 597 $(M - OMe)^+$.

Anal calc for $C_{32}H_{56}O_{10}Si$: C, 61.12; H, 8.98. Found: C, 61.03; H, 9.07.

Benzyl [methyl 4-C-(6-O-benzyl-2,3,4-tri-O-methyl-α-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-α-D-glucopyranosid]uronate ***31***

A solution of CrO_3 (0.6 g, 6.0 mmol) in aqueous H_2SO_4 (3.5 M, 2.6 mL) was slowly added to a cooled (0 °C) solution of **30** (1.1 g, 1.75 mmol) in acetone (50 mL). After 4 h, dichloromethane was added, the mixture was poured into iced H_2O, stirred vigorously. The organic layer was washed with water until neutral, dried ($MgSO_4$), and concentrated under reduced pressure. The crude acid which was immediately dissolved in DMF (50 mL), and treated overnight at room temperature with benzyl bromide (1.1 mL, 9.25 mmol), $KHCO_3$ (1.1 g, 11 mmol) and tetrabutylammonium iodide (3.2 g, 8.66 mmol). After evaporation under reduced pressure, water and dichloromethane were added, the organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane/ethyl acetate 3:2) to give **31** (0.94 g, 87%). $[\alpha]_D$ +94 (*c* 1.1, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 7.40–7.24 (m, 10H, arom), 5.16 and 5.12 (d, 1H, J_{gem} 12.5 Hz, $COOCH_2Ph$), 4.94 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.65 and 4.44 (d, 1H, J_{gem} 12.3 Hz, OCH_2Ph), 4.43 (ddd, 1H, $J_{4ha,1'}$ 10.7 Hz, $J_{1',2'}$ 5.9 Hz, $J_{4hb,1'}$ 3.9 Hz, H-1′), 4.12 (d, 1H, $J_{4,5}$ 10.8 Hz, H-5), 3.66 (dd, 1H, $J_{6a',6b'}$ 10.5 Hz, $J_{5',6a'}$ 1.8 Hz, H-6a′), 3.60 (dd, 1H, $J_{5',6b'}$ 1.0 Hz, H-6b′), 3.57, 3.50, 3.49, 3.45 and 3.41 (s, 3H, OCH_3), 3.46 (t, 1H, $J_{2,3}$ 9.0 Hz, $J_{3,4}$ 9.0 Hz, H-3), 3.35 (dd, 1H, H-2), 3.32–3.26 (m, 3H, H-2′, H-3′, H-5′), 3.19–3.14 (m, 1H, H-4′), 2.21 (dddd, 1H, $J_{4,4hb}$ 7.8 Hz, $J_{4,4ha}$ 3.0 Hz, H-4), 1.73 (ddd, 1H, $J_{4ha,hb}$ 15.5 Hz, H-4ha), 1.66 (ddd, 1H, H-4hb).

^{13}C NMR (63 MHz) δ: 170.14 (C=O), 138.28 and 135.07 (C arom), 128.55–127.42 (C arom), 98.09 (C-1), 83.42, 82.10, 81.72, 81.43, 79.26 and 71.22 (C-2, C-3, C-2′, C-3′, C-4′, C-5′), 73.37 (OCH_2Ph), 72.15 (C-5), 71.65 (C-1′), 68.63 (C-6′); 67.24 ($COOCH_2Ph$), 60.37, 60.15, 59.84, 58.55, 58.44 and 55.69 (OCH_3), 38.78 (C-4), 24.10 (C methylene).

MS, *m/z*: 636 $(M + NH_4)^+$, 619 $(M + H)^+$, 604 $(M - OMe + NH_3)^+$, 587 $(M - OMe)^+$.

Anal calc for $C_{33}H_{46}O_{11}$: C, 64.06; H, 7.49. Found: C, 64.00; H, 7.63.

Benzyl [1-O-acetyl-4-C-(6-O-benzyl-2,3,4-tri-O-methyl-α-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-6-O-tert-butyldimethylsilyl-α,β-D-glucopyranose]-uronate ***32***

A 5% solution of H_2SO_4 in acetic acid (0.150 mL) was added to a cooled (0 °C) solution of **31** (255 mg, 0.412 mmol) in acetic anhydride (25 mL). After 1 h, dichloromethane (50 mL) was added, immediately followed by saturated aqueous $NaHCO_3$ (150 mL). The organic phase was extracted three times with CH_2Cl_2, the organic layers were combined, dried ($MgSO_4$), concentrated under reduced pressure. The residue was purified by flash chromatography (5:2 cyclohexane/acetone) to give **32** (188 mg, 76%; α/β 5:1 mixture). The two anomers could be separated by chromatography on silica gel and characterized.

32 (α-anomer): $[\alpha]_D$ +73 (*c* 1.0, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 7.42–7.31 (m, 5H, arom), 6.42 (d, 1H, $J_{1,2}$ 2.9 Hz, H-1), 5.15 (s, 2H, COOCH_2Ph), 4.41 (ddd, 1H, $J_{4ha,1'}$ 11.5 Hz, $J_{1',2'}$ 5.4 Hz, $J_{4hb,1'}$ 2.7 Hz, H-1'), 4.25–4.18 (m, 3H, H-5, H-6a', H-6b'), 3.56, 3.51, 3.49, 3.44 and 3.41 (s, 3H, OCH_3), 3.48–3.39 (m, 3H, H-2, H-3, H-5'), 3.25 (dd, 1H, $J_{2',3'}$ 8.7 Hz, H-2'), 3.18 (t, 1H, $J_{3',4'}$ 8.7 Hz, H-3'), 3.01 (dd, 1H, $J_{4',5'}$ 9.5 Hz, H-4'), 2.24–2.16 (m, 1H, H-4), 2.13 and 2.08 (s, 3H, OCOCH_3), 1.80 (ddd, 1H, $J_{4,4ha}$ 2.1 Hz, H-4ha), 1.65 (ddd, 1H, $J_{4ha,4hb}$ 15.5 Hz, $J_{4,4hb}$ 8.0 Hz, H-4hb).

^{13}C NMR (63 MHz) δ: 170.90, 169.26 and 169.18 (C=O), 134.83 (C arom), 128.70–128.56 (C arom), 89.62 (C-1), 82.95 (C-3'), 81.27, 81.14, 81.07 and 69.95 (C-2, C-3, C-2', C-5'), 79.62 (C-4'), 73.90 (C-5), 71.40 (C-1'), 67.54 (COOCH_2Ph), 63.48 (C-6'), 60.35, 60.27, 59.63, 58.56 and 58.47 (OCH_3), 38.42 (C-4), 24.19 (C methylene), 20.98 and 20.61 (OCOCH_3).

MS *m/z*: 616 $(M + NH_4)^+$, 599 $(M + H)^+$.

Anal calc for $C_{29}H_{42}O_{13}$ (598.643): C, 58.18; H, 7.07. Found: C, 58.05; H, 7.12.

32 (β-anomer): $[\alpha]_D$ +22 (*c* 1.0, $CHCl_3$).

^{1}H NMR (400 MHz) δ: 7.39–7.31 (m, 5H, arom), 5.57 (m, 1H, $J_{1,2}$ 6.6 Hz, H-1), 5.17 and 5.13 (d, 1H, J_{gem} 12.0 Hz, COOCH_2Ph), 4.39 (ddd, $J_{4ha,1'}$ 11.5 Hz, $J_{1',2'}$ 5.2 Hz, $J_{4hb,1'}$ 2.7 Hz, H-1'), 4.24–4.19 (m, 2H, H-6a', H-6b'), 4.03 (d, 1H, $J_{4,5}$ 10.6 Hz, H-5), 3.55, 3.54, 3.52, 3.50 and 3.40 (s, 3H, OCH_3), 3.45 (ddd, 1H, $J_{4',5'}$ 9.3 Hz, $J_{5',6a'}$ 3.6 Hz, $J_{5',6b'}$ 3.6 Hz, H-5'), 3.30–3.24 (m, 2H, H-2, H-3), 3.22 (dd, 1H, $J_{2',3'}$ 8.5 Hz, H-2'), 3.17 (t, 1H, $J_{3',4'}$ 8.5 Hz, H-3'), 3.00 (dd, 1H, H-4'), 2.28–2.20 (m, 1H, H-4), 2.11 and 2.09 (s, 3H, OCOCH_3), 1.79 (ddd, 1H, $J_{4ha,4hb}$ 15.5 Hz, $J_{4,4ha}$ 2.3 Hz, H-4ha), 1.58 (ddd, 1H, $J_{4,4hb}$ 8.0 Hz, H-4hb).

^{13}C NMR (63 MHz) δ: 170.95, 169.17 and 168.89 (C=O), 134.89 (C arom), 128.58–128.49 (C arom), 93.66 (C-1), 84.33, 82.98, 82.76 and 81.20 (C-2, C-3, C-2', C-3'), 79.54 (C-4'), 76.01 (C-5), 71.04 (C-1'), 69.97 (C-5'), 67.43 (COOCH_2Ph), 63.42 (C-6'), 60.30, 60.22, 59.76, 59.40 and 58.56 (OCH_3), 38.01 (C-4), 23.96 (C methylene), 21.02 and 20.83 (OCOCH_3).

MS, *m/z*: 616 $(M + NH_4)^+$, 599 $(M + H)^+$.

Anal calc for $C_{29}H_{42}O_{13}$: C, 58.18; H, 7.07. Found: C, 58.09; H, 6.90.

Benzyl [4-C-(6-O-acetyl-2,3,4-tri-O-methyl-α-D-glucopyranosylmethyl)-4-deoxy-2,3-di-O-methyl-6-O-tert-butyldimethylsilyl-(α,β)-D-glucopyranose]-uronate ***33***

Freshly prepared hydrazinium acetate (110 mg, 1.19 mmol) was added to a solution of **32** (230 mg, 0.38 mmol) in DMF (8 mL). After 1 h, saturated aqueous sodium chloride (40 mL) was introduced and the product was extracted by ethyl acetate. The solution was dried ($MgSO_4$) and concentrated under reduced pressure and the residue was purified by flash chromatography (cyclohexane/ethyl acetate/acetone 5:2:2) to give **33** (170 mg, 80%).

33 (α anomer):

^{1}H NMR (400 MHz) δ: 7.43–7.30 (m, 5H, arom), 5.46 (d, 1H, $J_{1,2}$ 2.6 Hz, H-1), 5.20 and 5.13 (d, 1H, J_{gem} 12.2 Hz COOCH_2Ph), 4.42 (d, 1H, $J_{4,5}$ 7.0 Hz, H-5), 4.31 (ddd, 1H, $J_{4ha,1'}$ 11.2 Hz, $J_{1',2'}$ 4.8 Hz, $J_{4hb,1'}$ 3.3 Hz, H-1'), 4.26–4.18 (m, 2H, H-6a', H-6b'), 3.58, 3.51, 3.50, 3.43 and 3.37 (s, 3H, OCH_3), 3.58–3.49 (m, 2H, H-3, H-5'), 3.29 (dd, 1H, $J_{2,3}$ 6.5 Hz, H-2), 3.27–3.21 (m, 2H, H-2', H-3'), 3.02 (dd, 1H, *J* 9.5 Hz, *J* 8.0 Hz, H-4'), 2.35–2.27 (m, 1H, H-4), 2.06 (s, 3H, OCOCH_3), 1.87 (ddd, 1H, $J_{4ha,4hb}$ 15.2 Hz, $J_{4,4ha}$ 4.7 Hz, H-4ha), 1.77 (ddd, 1H, $J_{4,4hb}$ 8.5 Hz, H-4hb).

^{13}C NMR (63 MHz) δ: 170.97 and 170.59 (C=O), 135.25 (arom), 128.52–128.37 (C arom), 89.89 (C-1), 83.15, 81.42, 80.37, 79.79, 78.79, 73.07, 71.92 and 69.93 (C-2, C-3, C-5, C-1', C-2', C-3', C-4', C-5'), 67.02 (COOCH_2Ph), 63.56 (C-6'), 60.43, 60.34, 58.83, 58.61 and 58.54 (OCH_3), 36.74 (C-4), 24.34 (C methylene), 20.78 (OCOCH_3).

33 (β anomer):

^{1}H NMR (400 MHz) δ: 4.76 (d, 1H, $J_{1,2}$ 5.5 Hz, H-1), 4.40–4.34 (m, 1H, H-1'), 4.04 (d, 1H, $J_{4,5}$ 9.0 Hz, H-5), 3.14 (dd, 1H, $J_{2,3}$ 7.0 Hz, H-2), 2.07 (s, 3H, OCOCH_3).

^{13}C NMR (63 MHz) δ: 96.60 (C-1).

MS, *m/z*: 574 $(M + NH_4)^+$, 556 $(M - OH + NH_3)^+$, 539 $(M - OH)^+$.

Anal calc for $C_{27}H_{40}O_{12}$ (556.606): C, 58.26; H, 7.24. Found: C, 58.38; H, 7.35.

O-[Benzyl 4-C-(6-O-acetyl-2,3,4-tri-O-methyl-α-D-glucopyranosylmethyl)-4-desoxy-2,3-di-O-methyl-(α,β)-D-glucopyranosyluronate]-trichloroacetimidate ***34***

Trichloroacetonitrile (1.5 mL, 15 mmol) and DBU (30 μL, 0.2 mmol) were added to a solution of **33** (280 mg, 0.503 mmol) in dichloromethane (15 mL). After 40 min at room temperature, the solution was concentrated under reduced pressure and the residue was purified by flash chromatography (cyclohexane/ethyl acetate 17:10, containing 1% Et_3N) to give **34** (306 mg, 87%; α/β 10:1).

34 (α anomer):

^{1}H NMR (400 MHz, C_6D_6) δ: 8.49 (s, 1H, NH), 7.25–7.00 (m, 5H, arom), 6.72 (d, 1H, $J_{1,2}$ 3.4 Hz, H-1), 5.15 and 4.94 (d, 1H, J_{gem} 12.2 Hz, COOCH_2Ph), 4.67 (dd, 1H, $J_{6a',6b'}$ 11.8 Hz, $J_{5',6a'}$ 2.0 Hz, H-6a'), 4.65 (d, 1H, $J_{4,5}$ 11.2 Hz, H-5), 4.62 (ddd, 1H, $J_{4ha,1'}$ 11.5 Hz, $J_{1',2'}$ 5.5 Hz, $J_{4hb,1'}$ 2.7 Hz, H-1'), 4.40 (dd, 1H, $J_{5',6b'}$ 5.0 Hz, H-6b'), 3.70 (ddd, 1H, $J_{4',5'}$ 10.0 Hz, H-5'), 3.69 (t, 1H, $J_{2,3}$ 9.5 Hz, $J_{3,4}$ 9.5 Hz, H-3), 3.50, 3.41, 3.40, 3.13 and 3.04 (s, 3H, OCH_3), 3.31 (dd, 1H, $J_{2',3'}$ 9.5 Hz, $J_{3',4'}$ 8.0 Hz, H-3'), 3.25 (dd, 1H, H-2'), 3.23 (dd, 1H, H-2), 3.11 (dd, 1H, H-4'), 2.63 (dddd, 1H, $J_{4,4hb}$ 8.0 Hz, $J_{4,4ha}$ 2.2 Hz, H-4), 1.98 (ddd, 1H, $J_{4ha,4hb}$ 15.5 Hz, H-4ha), 1.86 (s, 3H, OCOCH_3), 1.82 (ddd, 1H, H-4hb).

^{1}H NMR (400 MHz) δ: 8.64 (s, 1H, NH), 6.61 (d, 1H, $J_{1,2}$ 2.8 Hz, H-1), 4.46 (ddd, 1H, $J_{4ha,1'}$ 11.5 Hz, $J_{1',2'}$ 6.0 Hz, $J_{4hb,1'}$ 3.0 Hz, H-1'), 4.34 (d, 1H, $J_{4,5}$ 11.0 Hz, H-5), 2.37–2.27 (m, 1H, H-4).

^{13}C NMR (63 MHz, C_6D_6) δ: 170.22 and 169.27 (C=O), 161.24 (C=NH), 135.64 (C arom), 128.89–128.47 (C arom), 94.67 (C-1), 84.02, 82.19, 82.05, 81.93, 80.59, 75.02, 72.31 and 70.53 (C-2, C-3, C-5, C-1', C-2', C-3', C-4', C-5'), 67.54 ($COOCH_2Ph$), 63.83 (C-6'), 60.40, 60.24, 59.94, 58.30 and 57.85 (OCH_3), 39.22 (C-4), 24.55 (C, methylene), 20.57 ($OCOCH_3$).

34 (β anomer):

^{1}H NMR (400 MHz, C_6D_6) δ: 8.65 (s, 1H, NH), 5.76 (s, 1H, $J_{1,2}$ 7.0 Hz, H-1), 4.41 (ddd, 1H, $J_{4ha,1'}$ 11.5 Hz, $J_{1',2'}$ 5.0 Hz, $J_{4hb,1'}$ 2.6 Hz, H-1'), 4.08 (d, 1H, $J_{4,5}$ 10.8 Hz, H-5), 2.31–2.23 (m, 1H, H-4).

Anal calc for $C_{29}H_{40}NO_{12}Cl_3$ (700.994): C, 49.69; H, 5.75; N, 2.00. Found: C, 49.80; H, 5.94; N, 2.14.

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