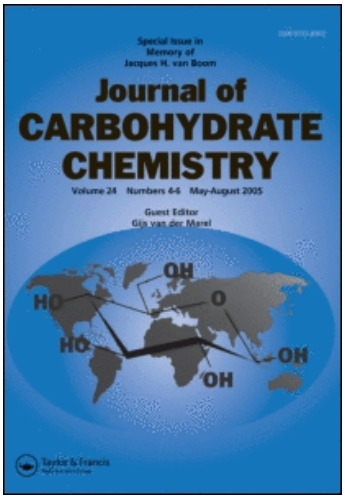

Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Synthesis of Ether-Linked Di- and Trisaccharide Derivatives Part I- Synthesis Of Disaccharides from 5,6-Anhydro-D-Glucose Derivatives

To cite this Article (1994) 'Synthesis of Ether-Linked Di- and Trisaccharide Derivatives Part I- Synthesis Of Disaccharides from 5,6-Anhydro-D-Glucose Derivatives', Journal of Carbohydrate Chemistry, 13: 5, 679 — 696
To link to this Article: DOI: 10.1080/07328309408011674
URL: http://dx.doi.org/10.1080/07328309408011674

J. CARBOHYDRATE CHEMISTRY, 13(5), 679-696 (1994)

SYNTHESIS OF ETHER-LINKED DI- AND TRISACCHARIDE DERIVATIVES

Part I- SYNTHESIS OF DISACCHARIDES FROM 5,6-ANHYDRO-D-GLUCOSE DERIVATIVES

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Received June 7, 1993 - Final Form February 8, 1994

ABSTRACT

We have synthesized a series of A-*O*-B disaccharides of the type A(6->n)B obtained by linking the D-glucose derivative (A) with each of the D-fructose, D-galactose, D-glucose, xylitol and glycerol derivatives (B). The key step in each case is the nucleophilic attack of a monosaccharide alkoxide on the C-6 site of 3-*O*-alkyl-5,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose; each reaction was performed in toluene-DMSO and using KOH as the base.

INTRODUCTION

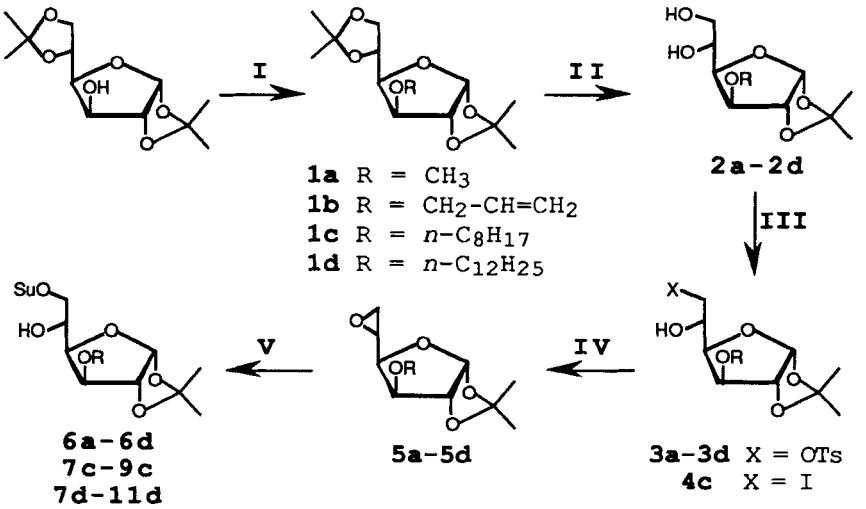
The synthesis and properties of natural disaccharides which involve coupling of the glycosyl moieties by glycosidic linkages have been extensively reported in the literature.[1] However, disaccharides which are attached by ether linkages are significantly less common. Reichrath,[2] for example, recorded the synthesis of 6-*O*-(benzyl 6-deoxy-2,3,4-tri-*O*-benzyl-α-D-glucopyranosid-6-yl)-benzyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside, using NaH as a catalyst. The same conditions were used by Paulsen[3] to synthesize various pseudodisaccharides such as 4-*O*-[1L-(1,3,5/2,4)-1,2,3,4-tetrahydroxy-5-*C*-hydroxymethylcyclohexyl]-α,β-

D-glucopyranose. In contrast, Prystas[4,5] obtained 4-*O*-(5-deoxy-β-D-ribofuranosid-5-yl)-β-D-glucopyranose derivatives using either the Lewis acid $BF_3.Et_2O$ or $SnCl_4$ as catalyst.

The work described herein was accomplished as part of a programme to synthesize di- and trisaccharide derivatives in which hexose, pentose or alditol derivatives are coupled by ether linkages. Such junctions were deliberately chosen in order to obtain compounds which are more stable to hydrolysis than those possessing glycosidic linkages. We describe in this work synthetic methods which lead to compounds with the general formula, A(6->n)B in which A is a D-glucose derivative and B is a D-glucose, D-galactose, D-fructose, xylitol or glycerol derivative.

RESULTS AND DISCUSSION

Each synthesis started from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose following the relevant sequence of reactions outlined in Scheme 1:



6: SuOH= 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (DAGlu-3-OH)

7: SuOH= 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (DAGal-6-OH)

8: SuOH= 2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (DAFru-1-OH)

9: SuOH= 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (DAFru-3-OH)

10: SuOH= 2,3:4,5-di-*O*-isopropylidene-DL-xylitol (DAXyl-1-OH)

11: SuOH= 2,3-*O*-isopropylidene-DL-glycerol (Solketal)

SCHEME 1

Step I: *Diacetone glucose alkylation leading to type **1** compounds.*

Alkyl groups (R), introduced *via* alkyl halides, were chosen in order to either regulate the lipophilicity of the final deprotected compounds obtained from the disaccharide derivatives **6-11** (R = CH_3; *n*-C_8H_{17}; *n*-$C_{12}H_{25}$) or temporarily protect the C-3-OH group (R= CH_2-CH=CH_2). These alkylations were effected with 1.2 equivalents of alkyl halide and 2.4 equivalents of KOH in toluene-DMSO. The method, described by Chellé,[6a,b] gave type **1** products in yields ranging from 83 to 92% without using either DMF as solvent or NaH as base.[7-9]

Step II: *Selective deprotection leading to type **2** compounds.*

Acid-catalyzed deprotection of type **1** compounds (**1a-1d**), in a mixture of ethanol-water (19:1) and 0.2 N sulfuric acid at 50 °C afforded the monoacetals **2a-2d** in yields ranging from 81 to 86%.

Steps III and IV: *Activation of type **2** compounds to give compounds of type **3**, **4** and **5**.*

The site C-6 of type **2** compounds was activated by the formation of either sulfonate or iodide derivatives. The sulfonate compounds **3** were synthesized using a modification of the literature method[10] in which chloroform was replaced by toluene to effect improved yields which were in the range 73 to 81%.

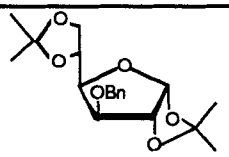
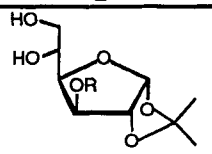
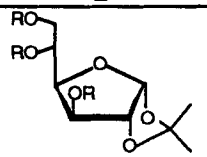
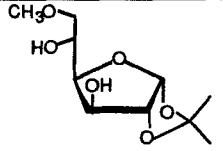
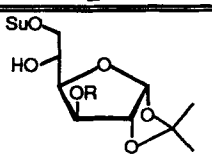
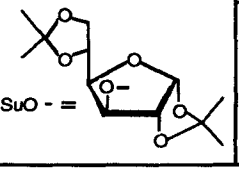
We also prepared 6-deoxy-6-iodo-1,2-*O*-isopropylidene-3-*O*-octyl-α-D-glucofuranose (**4c**) in 60% yield using the method initially described by Garegg[11] and later slightly modified by Postel.[12]

Treatment of sulfonates **3** with NaOH in either ethanol-water (9:1) or dioxane-water (9:1), furnished the anhydro derivatives **5** in good yields ranging from 88 to 93%.

Step V: *Reaction of SuOH derivatives leading to disaccharides **6-11**.*

A preliminary study of the reaction involving diacetone glucose (1.25 equiv), 5,6-anhydro-3-*O*-dodecyl-1,2-*O*-isopropylidene-α-D-glucofuranose **5d** (1 equiv) and KOH in toluene-DMSO at 40 °C showed, by HPLC analysis, the presence of three new compounds identified as **6d**, **6'd** and **6"d**. The purification of the crude product mixture by silica gel column chromatography afforded two fractions which were pure **6d** and a mixture of **6d**, **6'd** and **6"d**. The NMR data discussed below are in accordance with the structure of disaccharide **6d** identified in Scheme 1. The site of substitution on the D-glucose moieties of the disaccharide (**6d**) was determined on the basis of a comparison of ^{13}C

Table 1: Attempt at ^{13}C NMR signal assignment to disaccharide **6d** by comparison with published data*.

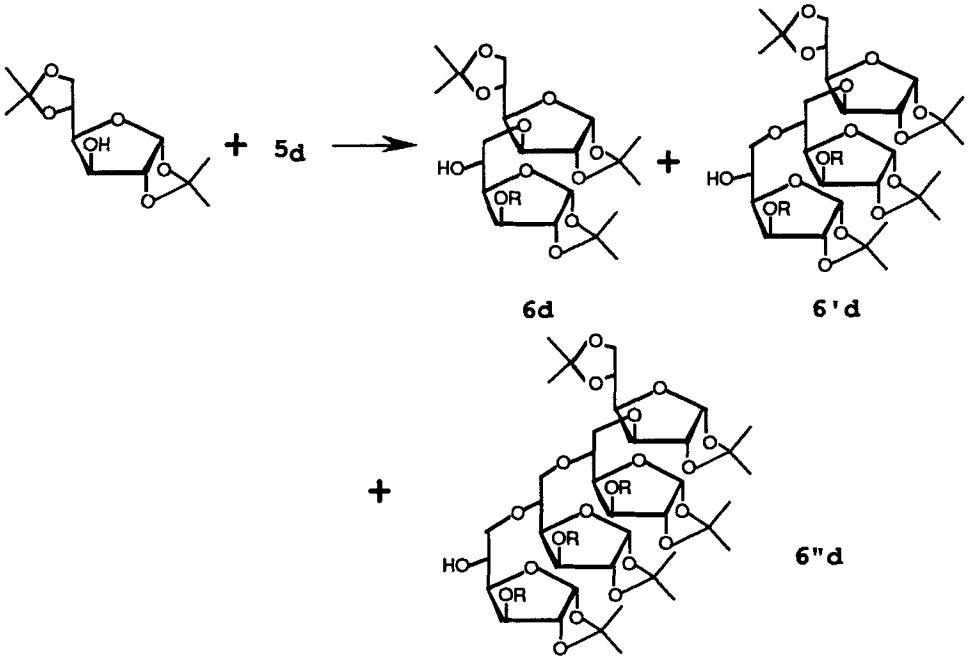
Sugar	C-1	C-2	C-3	C-4	C-5	C-6	Ref
 **1**	105.3	82.6	81.7	81.3	72.5	67.4	13
 **2**	104.92	82.67	79.69	69.32	**64.32**	**64.20**	6b
 **2'**	104.03	81.81	81.88	78.90	75.34	71.41	6b
 **2"**	104.87	**85.10**	**75.63**	79.72	69.20	73.57	6b
	104.4	83.9	82.0	81.0	68.0	73.6	
	105.4	82.5	82.1	81.2	72.6	67.6	

* ^{13}C NMR chemical shifts of unsubstituted carbons are designated in bold.

NMR data obtained for a variety of known *O*-alkyl derivatives of 1,2-*O*-isopropylidene-α-D-glucofuranose (Table 1).[6b,13]

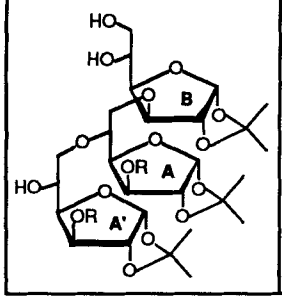
The signals for C-1 of all D-glucose moieties in the 1,2-*O*-isopropylidene form were found to be similar for the range of compounds selected for the study. However, differences were observed for signals assigned C-2 and C-3. An alkyl substituent attached by an ether linkage at C-3 resulted in a shielding effect on C-2 (Δ 1.2-3.3 ppm) and a deshielding effect on C-3 (Δ 4.0-6.5 ppm); such evidence is supportive of the structure **6d** in which the SuO group is attached by the C-3 carbon. Likewise, either an alkyl or sugar attached at C-6, resulted in a deshielding effect on C-5 (Δ 3.7-4.9 ppm). The major effect of substitution was a large deshielding effect (Δ ≈ 9.4 ppm) observed for the signal assigned to C-6. These results further support the structure assigned to **6d** in which there is a liaison between C-6 and C-3' and a free OH group on C-5.

Compounds **6'd** and **6"d** (identified in Scheme 2) can result, from the consecutive nucleophilic attack of **6d** and **6'd** respectively, in their respective alkoxide ion forms, at the least hindered carbon C-6 of the anhydro derivative **5d**.



SCHEME 2

Table 2: Attempt at ^{13}C NMR signal assignments for the 5,6-deacetalized trisaccharide obtained from **6'd**.



	C-1	C-2	C-3	C-4	C-5	C-6
B	105.4	82.3	80.1	78.4	67.7	64.9
A	105.0	81.8	82.3	78.9	74.6	71.4
A'	104.9	83.7	81.7	81.4	69.0	70.8

A convenient preparative separation of the mixture **6d, 6'd** and **6"d** was not achieved. However, their 5,6-deacetalized derivatives were relatively easy to separate using silica gel column chromatography. Structural characterisation of these derivatives by NMR spectroscopy (Table 2) supported the structural assignments for **6'd** and **6"d** shown in Scheme 2.

The assignment of signals in the ^{13}C NMR spectrum corresponding to C-5 and C-6 of the monosaccharide units A, B and A' were made by comparison with the spectral assignments of compounds **2, 2'** and **2"** (Table 1). The ^{13}C NMR spectrum of the 5,6-deacetalized tetrasaccharide was not well resolved, however we clearly distinguished four signals corresponding to four C-1 carbons in the 105 ppm area. The earlier structural assignments were supported by elemental analysis (experimental section).

Before preparing the series of A-*O*-B disaccharides, we studied the influence of temperature and the relative amount of diacetone glucose with respect to **5c** (R = *n*-C_8H_{17}), on the proportions of products obtained in step **V** (Table 3).

The results presented in Table 3 show that a reduction in temperature and the doubling of proportions of DAGlu-3-OH with respect to substrate **5c** favoured the formation of **6c**. At 40 °C, an excess of 150% of diacetone glucose in comparison with substrate led to 92% of the desired disaccharide **6c** and 8% of trisaccharide **6'c**. We also observed the formation of a small amount of monoacetal **2c** resulting

Table 3: Influence of temperature and the relative amount of DAGlu-3-OH on the proportions of products (**6c, 6'c, 6"c**) obtained, using toluene-DMSO (1:1) (KOH/DAGlu-3-OH = 2).

Reaction (n°)	SuOH/**5c**	T°C	Time (h)	Remaining **5c** (%)	Distribution of products (%)		
					6c	**6'c**	**6"c**
1	1.25	80	4	5	60	33	7
2	1.25	40	24	5	76	21	3
3	2.50	40	24	4	92	8	0
4	2.50	20	48	20	93	7	0

from competitive attack of HO^- on the anhydro substrate. Other attempts showed that the variation of proportions of DMSO modify the rate of reaction but do not affect proportions of the products formed.

The synthesis of **6c** was also attempted from **3c** and **4c**, using the conditions applied to reaction n°3 in Table 3. The tosyl (**3c**) and iodo (**4c**) derivatives were completely consumed after an hour to give the anhydro derivative **5c**; after 24 hours the relative proportions of **6c** and **6'c** were close to those of the above reaction n°3. However, after purification, yields of **6c** obtained were 50 and 43% respectively. In contrast, **6c** was obtained in 73% yield starting from **5c**.

These results prompted us to prepare all of the type **6** disaccharides (SuOH = DAGlu-3-OH and R = CH_3; CH_2-CH=CH_2; *n*-C_8H_{17}; *n*-$C_{12}H_{25}$) using the conditions of reaction n°3 of Table 3; the yields ranged from 68 to 79%, after purification.

We also applied the latter reaction conditions to the synthesis of other disaccharides with the general formula A(6->n)B. The B units were introduced by reaction of the acetal derivatives (SuOH ≠ DAGlu-3-OH), defined in Scheme 1, with the D-glucose (A) unit as its anhydro derivative **5** (Table 4).

In these reactions, the proportion of trisaccharide is higher than when SuOH = DAGlu-3-OH, but yields of isolated disaccharides remained satisfactory (> 61%). For the disaccharides **7c-11d**, the assigned C-6

Table 4: Synthesis of disaccharide derivatives and distribution of the products formed (under reaction n° 3 conditions, 24 h).

5	SuOH	Distribution (HPLC)			Yield %	δ(ppm) of liaison	
		Dis.	**Tris.**	**Tetras.**		C-6	C-n(*)
5c	DAGal-6-OH	85	14.5	0.5	64(**7c**)	73.4	70.2
	DAFru-1-OH	80	15	5	61(**8c**)	73.9	73.0
	DAFru-3-OH	87	12.5	0.5	63(**9c**)	75.2	78.9
5d	DAGal-6-OH	84	15	1	64(**7d**)	73.4	70.2
	DAFru-1-OH	87	13	0	79(**8d**)	73.9	73.0
	DAFru-3-OH	86	14	0	72(**9d**)	75.2	78.9
	DAXyl-1-OH	82	18	0	73(**10d**)	72.9;72.7	71.1;70.7
	Solketal	80	20	0	65(**11d**)	72.9;72.7	66.3;66.1

* Chemical shifts are noted C_n' in the experimental section.

^{13}C NMR signals showed the same characteristic deshielding effect as that induced by the SuO substituent in compound **6d**. This comparison supports the structures of the disaccharides identified in Scheme 1.

CONCLUSIONS

We have obtained in good yield, using a facile and original method, disaccharides with the general structure A-O-B in which D-glucose (A) is linked to a variety of either hexoses or alditols with an ether junction. The product range obtained can be conveniently extended to give access to numerous compounds of differing character according to the nature of R and of the second substituent R_1 introduced at site C-5. Further possibilities include alternative derivatisation at site C-6 when B = D-glucose and the number of deprotected acetal groups are varied.

The partial deprotection of unit B gives access to trisaccharide derivatives which could be further modified. The methodology discovered

in this work can also be used to obtain various series of disaccharides from anhydro derivatives of other sugars such as either D-xylose, D-mannose or D-fructose.

EXPERIMENTAL

General Procedures. Reactions were monitored by either HPLC (Waters 721), using either of the reverse phase columns RP-18 (Merck) or PN 27-196 (Waters) or by GLC (Girdel) using an OV 17 or SE 30 column. Preparative chromatography was performed on silica gel (Matrex 60 mesh) with a hexane-acetone gradient. Specific rotations were determined with a JASCO-DIP 970 polarimeter (Prolabo) and melting points with an electrothermal automatic apparatus. ^{13}C NMR spectra were recorded using a Brücker WP 300 spectrometer. The ^{13}C signal assignment of the C_2, C_3, C_4 carbons of the D-glucose moiety for compounds **6a-11d**, as well as that of the C_1 carbons when both monosaccharide units are D-glucose, can result in problems of interpretation because the chemical shifts are very close.

Type **1** *O*-alkyl diacetal derivatives, namely, **1,2:5,6-di-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (1a)**, **3-*O*-allyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1b)**, **1,2:5,6-di-*O*-isopropylidene-3-*O*-octyl-α-D-glucofuranose (1c)**, **3-*O*-dodecyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1d)**, were synthesized in accordance with the method described by Chellé.[6a,b]

Type **2** *O*-alkyl monoacetal derivatives, namely, **1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (2a)**, **3-*O*-allyl-1,2-*O*-isopropylidene-α-D-glucofuranose (2b)**, **1,2-*O*-isopropylidene-3-*O*-octyl-α-D-glucofuranose (2c)** and **3-*O*-dodecyl-1,2-*O*-isopropylidene-α-D-glucofuranose (2d)**, were synthesized in accordance with the method described in our previous work.[6a,b;14]

1,2-*O*-isopropylidene-3-*O*-methyl-6-*O*-tosyl-α-D-glucofuranose (3a). *p*-Toluenesulphonyl chloride (9.6 g, 50 mmol) dissolved in toluene (50 mL) was slowly added to a stirred pyridine (50 mL) solution of **2a** (11 g, 47 mmol) at 0 °C. After 48 h at 5 °C, crushed ice and aqueous-HCl (9:1) (50 mL) were added to the mixture and two phases separated. The aqueous phase was

extracted with toluene (2 x 25 mL); the organic phases were pooled, dried (Na_2SO_4) and concentrated to give 15.2 g of crude product which was purified on a silica gel column eluted with hexane-acetone (17:3) to give 14.2 g (78%) of **3a** as a syrup. $[\alpha]_D^{25}$ -30.4° (*c* 1.2, $CHCl_3$); lit.[15] $[\alpha]_D^{25}$ -22.1° (*c* 1.0, $CHCl_3$). ^{13}C NMR ($CDCl_3$) δ: C_1 (105.0), C_2 (82.7), C_3 (82.0), C_4 (79.0), C_5 (74.2), C_6 (67.5), 2xCH_3 (26.1-26.7), CMe_2 (111.8), C'_1 (144.9), C_{ortho} (129.8), C_{meta} (128.0), C_{para} (132.6), CH_3 (21.5), OCH_3 (58.2).

3-*O*-allyl-1,2-*O*-isopropylidene-6-*O*-tosyl-α-D-glucofuranose (3b). The above procedure was applied to **2b** (17 g, 65.4 mmol) and *p*-toluenesulphonyl chloride (12.9 g, 67.7 mmol) to give 21.8 g (81%) of **3b** as a syrup, after elution on a silica gel column with hexane-acetone (22:3); $[\alpha]_D^{25}$ -76.7° (*c* 1.4, $CHCl_3$). The ^{13}C NMR spectrum of the glucosyl moiety was identical to that of **3a**; R= CH_2-CH=CH_2: C_α (73.5), C_β (134.1), C_γ (117.0). This compound was recently synthesized in a mixture of methylene chloride-pyridine[16] without giving the specific rotation.

1,2-*O*-isopropylidene-3-*O*-octyl-6-*O*-tosyl-α-D-glucofuranose (3c). Likewise, **2c** (33.2 g, 100 mmol) and *p*-toluenesulphonyl chloride (22 g, 115 mmol) gave 36.5 g (75%) of **3c** as a syrup, after elution on a silica gel column with hexane-acetone mixture(89:11); $[\alpha]_D^{25}$ -52.4° (*c* 1.0, $CHCl_3$). ^{13}C NMR spectrum of the glucosyl moiety was identical to that of **3a**; R= *n*-C_8H_{17}; C_α (70.6), C_β (31.8), 5xCH_2 (29.5-22.6), CH_3 (14.1).

Anal. Calcd for $C_{24}H_{38}O_8S$ (486.6): C, 59.24; H, 7.87. Found: C, 59.01; H, 7.92.

3-*O*-dodecyl-1,2-*O*-isopropylidene-6-*O*-tosyl-α-D-glucofuranose (3d). Likewise, **2d** (31.2 g, 80.4 mmol) and *p*-toluenesulphonyl chloride (18.3 g, 96 mmol) gave 31.8 g (73%) of **3d** as a syrup, after elution on a silica gel column with hexane-acetone (23:2); $[\alpha]_D^{25}$ -19.0° (*c* 1.2, $CHCl_3$). The ^{13}C NMR spectrum of the glucosyl moiety was identical to that of **3c**.

Anal. Calcd for $C_{28}H_{46}O_8S$ (542.8): C, 61.97; H, 8.54. Found: C, 61.80; H, 8.72.

6-deoxy-6-iodo-1,2-*O*-isopropylidene-3-*O*-octyl-α-D-glucofuranose (4c). Iodine (9.2 g, 36.2 mmol) dissolved in DMF (30 mL) was slowly added to a stirred solution of **2c** (9.9 g, 29.8 mmol) and Ph_3P (15.8 g, 60.3 mmol) in DMF (75 mL). After 4 h at room temperature, a saturated solution of $NaHCO_3$ (10 mL) and ether (50 mL) were added to the mixture and the phases separated. The aqueous phase was extracted with ether (2x20 mL). Concentration of the pooled organic phases gave a syrupy residue which was chromatographed on a silica gel column eluted with hexane-acetone (9:1) to yield 7.8 g (60%) of **4c** as a syrup; $[\alpha]_D^{25}$ -35.6° (*c* 1.1, $CHCl_3$). ^{13}C NMR ($CDCl_3$) δ: C_1 (104.1), C_2 (81.4), C_3 (81.1), C_4 (80.7), C_5 (67.7), C_6 (12.2), 2xCH_3 (25.9;25.4), CMe_2 (110.4), C_α (69.7), C_β (30.8), 5xCH_2 (28.7-21.6), CH_3 (13.1).

Anal. Calcd for $C_{17}H_{31}O_5I$ (442.3): C, 46.16; H, 7.06. Found: C, 46.50; H, 7.25.

5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (5a). To a stirred solution of **3a** (13.7 g, 35.3 mmol) in dioxane-water (9:1) (150 mL) was added NaOH (35 g, 87.5 mmol). After 1 h at room temperature, the mixture was neutralized with a saturated solution of NH_4Cl (75 mL) and the aqueous phase extracted with toluene (2x25 mL). The combined organic phases were concentrated and the resulting residue chromatographed on a silica gel column eluted with hexane-acetone (22:3) to yield 6.6 g (87%) of **5a** as a syrup; $[\alpha]_D^{25}$ -62.4° (*c* 1.1, $CHCl_3$); lit.[17] $[\alpha]_D^{12}$ -67° (*c* 4.0, $CHCl_3$). ^{13}C NMR ($CDCl_3$) δ: C_1 (105.1), C_2 (82.6), C_3 (82.6), C_4 (81.6), C_5 (47.8), C_6 (46.3), 2xCH_3 (25.9; 26.6), CMe_2 (111.3), OCH_3 (58.2).

3-*O*-allyl-5,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose (5b). The above procedure was applied to **3b** (20.7 g, 49.9 mmol) and NaOH (5 g, 125 mmol) to give 11.3 g (93%) of **5b** as a syrup, after elution on a silica gel column with hexane-acetone(93:7); $[\alpha]_D^{25}$ -51.7° (*c* 0.9, $CHCl_3$). The ^{13}C NMR spectrum of the glucosyl moiety was identical to that of **5a** with: C_α (73.5), C_β (134.1), C_γ (117.1).

Anal. Calcd for $C_{12}H_{18}O_5$ (242.3): C, 59.49 H, 7.49. Found: C, 59.79; H, 7.35.

5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-octyl-α-D-glucofuranose (5c). Likewise, **3c** (35.5 g, 72.9 mmol) and NaOH (7.3 g, 182.5 mmol) gave 21 g (92%) of **5c** as a syrup, after elution on silica gel column with hexane-acetone (19:1); $[\alpha]_D^{25}$ -34.4° (*c* 1.3, $CHCl_3$). The ^{13}C NMR spectrum of the glucosyl moiety was identical to that of **5a** with R= *n*-C_8H_{17}; C_α (70.6), C_β (31.8), 5xCH_2 (29.5-22.6), CH_3 (14.0).

Anal. Calcd for $C_{17}H_{30}O_5$ (314.4): C, 64.54; H, 9.62. Found: C, 64.40; H, 9.69.

5,6-anhydro-3-*O*-dodecyl-1,2-*O*-isopropylidene-α-D-glucofuranose (5d). Likewise, **3d** (30.4 g, 56 mmol) and NaOH (5.6 g, 140 mmol) gave 18 g (87%) of **5d** as a syrup, after elution on a silica gel column with hexane-acetone (19:1); $[\alpha]_D^{25}$ -33.6° (*c* 1.2, $CHCl_3$). The ^{13}C NMR spectrum of the glucosyl moiety was identical to that of **5c**.

Anal. Calcd for $C_{21}H_{38}O_5$ (370.5): C, 68.07; H, 10.33. Found: C, 68.32; H, 10.20.

Synthesis of Disaccharides

Powdered KOH (5 equiv), anhydrous Na_2SO_4 and type **5** compound (1 equiv) were added to a stirred solution of the appropriate acetal SuOH (2.5 equiv) in toluene-DMSO (1:1) (100 g/L). After 24 h at 40 °C, the mixture was filtered and neutralized with a saturated solution of NH_4Cl. The aqueous phase was extracted with toluene and the solvent concentrated under vacuum. The desired disaccharide was isolated after purification on a silica gel column eluted with a hexane-acetone gradient; the composition of mixtures were determined by HPLC analysis.

6-*O*-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (6a). The above procedure applied to **5a** (13.2 g, 61 mmol) and DAGlu-3-OH (39 g, 150 mmol) yielded 7.7 g of a mixture of **6a** and **6'a** in the ratio 7:3 after silica gel column chromatography, using hexane-acetone (92.5:7.5) as the eluent. Further elution with hexane-acetone (91:9) gave 19.4 g (68%) of pure **6a** as a syrup; $[\alpha]_D^{25}$ +63.1° (*c* 1.5, C_2H_5OH). ^{13}C NMR ($CDCl_3$)

δ: C_1 (104.4), C_2 (83.9), C_3 (82.0), C_4 (81.0), C_5 (68.0), C_6 (73.6), $C_{1'}$ (105.4), $C_{2'}$ (82.5), $C_{3'}$ (82.1), $C_{4'}$ (81.2), $C_{5'}$ (72.6), $C_{6'}$ (67.6), 6xCH_3 (25.9; 26.6), 3xCMe_2 (111.7; 111.7; 109.0), OCH_3 (58.2).

Anal. Calcd for $C_{22}H_{36}O_{11}$ (476.5): C, 55.45; H, 7.61. Found: C, 55.70; H, 7.40.

6-*O*-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)-3-*O*-allyl-1,2-*O*-isopropylidene-α-D-glucofuranose (6b). Likewise, **5b** (9.7 g, 40 mmol) and DAGlu-3-OH (26 g, 100 mmol) gave 3.3 g of a mixture of **6b** and **6'b** in the ratio 1:3 after elution on a silica gel column with hexane-acetone mixture (93:7). Further elution with hexane-acetone mixture (23:2) gave 15.8 g (79%) of pure **6b** as a syrup; $[\alpha]_D^{25}$ +32.1° (*c* 1.4, $CHCl_3$). The ^{13}C NMR spectrum of glucosyl moieties was identical to that of **6a**: C_α (73.6), C_β (134.3), C_γ (117.0).

Anal. Calcd for $C_{24}H_{38}O_{11}$ (502.5): C, 57.38 H, 7.62. Found: C, 57.64; H, 7.58.

6-*O*-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)-1,2-*O*-isopropylidene-3-*O*-octyl-α-D-glucofuranose (6c). Likewise, **5c** (5.0 g, 15.9 mmol) and DAGlu-3-OH (10.4 g, 40 mmol) gave 1.9 g of a mixture of **6c** and **6'c** in the ratio 7:3 after purification on a silica gel column eluted with hexane-acetone (93:7). Further elution with hexane-acetone (23:2) gave 6.8 g (73%) of pure **6c** as a syrup; $[\alpha]_D^{25}$ -43.2° (*c* 1.4, $CHCl_3$). The ^{13}C NMR spectrum of glucosyl moieties was identical to that of **6a**; R = *n*-C_8H_{17}; C_α (70.6), C_β (31.7), 5xCH_2 (29.5-22.6), CH_3 (13.9).

Anal. Calcd for $C_{29}H_{50}O_{11}$ (574.7): C, 60.61; H, 8.77. Found: C, 60.59; H, 8.85.

6-*O*-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)-3-*O*-dodecyl-1,2-*O*-isopropylidene-α-D-glucofuranose (6d). Likewise, **5d** (6.8 g, 18.4 mmol) and DAGlu-3-OH (24 g, 92.3 mmol) gave 3.3 g of a mixture of **6d** and **6'd** in the ratio 8:1 after purification on a silica gel column eluted with hexane-acetone (42:3). Further elution with hexane-acetone (93:7) gave 7.75 g (67%) of pure **6d** as a syrup; $[\alpha]_D^{25}$ -48.1° (*c* 1.2, $CHCl_3$). The ^{13}C NMR spectrum of glucosyl moieties was identical to that of **6c**.

Anal. Calcd for $C_{33}H_{58}O_{11}$ (630.7): C, 62.83; H, 9.27. Found: C, 62.92; H, 9.31.

When the reaction was performed with **5d** (10.2 g, 27.6 mmol) and DAGlu-3-OH (8.9 g, 34.5 mmol), a mixture of **6d**, **6'd** and **6"d** was obtained. These compounds were separated after partial hydrolysis (0.2 N (H_2SO_4); 50 °C in ethanol-water 19:1) and column chromatography to give:

- 9.4 g of the 5,6-deprotected disaccharide after elution with hexane-acetone (7:3); $[\alpha]_D^{25}$ -36.9° (*c* 1.6, $CHCl_3$).

Anal. Calcd for $C_{30}H_{54}O_{11}$ (590.7): C, 61.00; H, 9.21. Found: C, 60.78; H, 9.52,

- 3.9 g of the 5,6-deprotected trisaccharide after elution with hexane-acetone (4:1): mp 68-70°C; $[\alpha]_D^{25}$ -37.8° (*c* 1.2, $CHCl_3$).

Anal. Calcd for $C_{51}H_{92}O_{16}$ (961.1): C, 63.72; H, 9.65. Found: C, 63.87; H, 9.52,

- 1.1 g of the 5,6-deprotected tetrasaccharide after elution with hexane-acetone (17:3); $[\alpha]_D^{25}$ -40.9° (*c* 1.1, $CHCl_3$).

Anal. Calcd for $C_{72}H_{130}O_{21}$ (1331.3): C, 64.93; H, 9.84. Found: C, 64.81; H, 9.56.

6-*O*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl)-1,2-*O*-isopropylidene-3-*O*-octyl-α-D-glucofuranose (7c). Likewise, **5c** (5.0 g, 15.9 mmol) and DAGal-6-OH (10.4 g, 40 mmol) gave 2.8 g of a mixture of **7c** and **7'c** in the ratio 7:3 after elution on a silica gel column with hexane-acetone (93.5:6.5). Further elution with hexane-acetone (92.5:7.5) gave 5.9 g (64%) of pure **7c** as a syrup; $[\alpha]_D^{25}$ -50.1° (*c* 0.8, $CHCl_3$). ^{13}C NMR ($CDCl_3$) δ: C_1 (105.0), C_2 (82.6), C_3 (82.3), C_4 (79.7), C_5 (67.7), C_6 (73.4), $C_{1'}$ (96.2), $C_{2'}$ (70.7), $C_{3'}$ (70.5), $C_{4'}$ (71.1), $C_{5'}$ (66.8), $C_{6'}$ (70.2), 6x*C*H_3 (26.7; 24.3), *C*Me_2 (111.5), 2x*C*Me_2 (108.5; 109.2), C_α (70.6), C_β (31.7), 5x*C*H_2 (29.5-22.6), *C*H_3 (13.9).

Anal. Calcd for $C_{29}H_{50}O_{11}$ (574.7): C, 60.61; H, 8.77. Found: C, 61.05; H, 8.90.

6-*O*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl)-3-*O*-dodecyl-1,2-*O*-isopropylidene-α-D-glucofuranose (7d). Likewise, **5d** (3.7 g, 10 mmol) and DAGal-6-OH (6.5 g, 25

mmol) gave 1.9 g of a mixture of **7d** and **7'd** in the ratio 8:1 after purification on a silica gel column eluted with hexane-acetone (42:3). Further elution with hexane-acetone (93:7) gave 4.03 g (64%) of pure **7d** as a syrup; $[\alpha]_D^{25}$ -47.4° (*c* 1.2, $CHCl_3$). The ^{13}C NMR spectrum of glycosyl moieties was identical to that of **7c**.

Anal. Calcd for $C_{33}H_{58}O_{11}$ (630.7): C, 62.83; H, 9.27. Found: C, 63.02; H, 9.37.

6-*O*-(1-deoxy-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranos-1-yl)-1,2-*O*-isopropylidene-3-*O*-octyl-α-D-glucofuranose (8c) Likewise, **5c** (4.1 g, 13 mmol) and DAFru-1-OH (8.4 g, 32.3 mmol) gave 2.5 g of a mixture of **8c**, **8'c** and **8"c** in the ratio 2:2:1 after elution on a gel silica column with hexane-acetone (93:7); 4.53 g (61%) of pure **8c** as a syrup was obtained by further elution with hexane-acetone (23:2); $[\alpha]_D^{25}$ -38.0° (*c* 1.2, $CHCl_3$). ^{13}C NMR ($CDCl_3$) δ: C_1 (105.0), C_2 (82.4), C_3 (82.1), C_4 (79.7), C_5 (67.5), C_6 (73.9), $C_{1'}$ (73.0), $C_{2'}$ (102.4), $C_{3'}$ (70.3), $C_{4'}$ (70.1), $C_{5'}$ (70.8), $C_{6'}$ (60.9), 6xCH_3 (26.6-23.9), CMe_2 (111.4), 2xCMe_2 (108.3), C_α (70.6), C_β (31.8), 5xCH_2 (29.6-22.5), CH_3 (13.9).

Anal. Calcd for $C_{29}H_{50}O_{11}$ (574.7): C, 60.61; H, 8.77. Found: C, 60.80 H, 8.69.

6-*O*-(1-deoxy-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranos-1-yl)-3-*O*-dodecyl-1,2-*O*-isopropylidene-α-D-glucofuranose (8d).Likewise, **5d** (2.7 g, 7.3 mmol) and DAFru-1-OH (4.7 g, 28 mmol) gave 0.7 g of a mixture of **8d** and **8'd** in the ratio 1:2 after chromatography on a silica gel column eluted with hexane-acetone (47:3). Further elution with hexane-acetone (93:7) gave 3.63 g (79%) of pure **8d** as a syrup; $[\alpha]_D^{25}$ -30.9° (*c* 1.1, $CHCl_3$). The ^{13}C NMR spectrum of glycosyl moieties was identical to that of **8c**.

Anal. Calcd for $C_{33}H_{58}O_{11}$ (630.7): C, 62.83; H, 9.27. Found: C, 63.02; H, 9.37.

6-*O*-(3-deoxy-1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranos-3-yl)-1,2-*O*-isopropylidene-3-*O*-octyl-α-D-glucofuranose (9c). Likewise, **5c** (6 g, 19 mmol) and DAFru-3-OH (12.4 g, 47.7 mmol) gave 3.5 g of a mixture of **9c** and **9'c** in the ratio 3:1 after purification on a silica gel column eluted

with hexane-acetone mixture (93:7). Further elution with hexane-acetone (23:2) gave 6.85 g (62%) of pure **9c** as a syrup; $[\alpha]_D^{25}$ -83.6° (*c* 1.2, $CHCl_3$). ^{13}C NMR (CDCl3) δ: C_1 (105.0), C_2 (82.2), C_3 (82.1), C_4 (79.7), C_5 (68.2), C_6 (75.2), $C_{1'}$ (71.9), $C_{2'}$ (104.3), $C_{3'}$ (78.9), $C_{4'}$ (76.7), $C_{5'}$ (73.5), $C_{6'}$ (60.4), 6xCH_3 (27.8-25.9), CMe_2 (111.4), 2xCMe_2 (111.8; 109.0), C_α (70.6), C_β (31.7), 5xCH_2 (29.6-22.5), CH_3 (13.9).

Anal. Calcd for $C_{29}H_{50}O_{11}$ (574.7): C, 60.61; H, 8.77. Found: C, 60.90 H, 8.63.

6-*O*-(3-deoxy-1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranos-3-yl)-3-*O*-dodecyl-1,2-*O*-isopropylidene-α-D-glucofuranose (9d). Likewise, **5d** (3.0 g, 8.1 mmol) and DAFru-3-OH (5.2 g, 20 mmol) gave 1.1 g of a mixture of **9d** and **9'd** in the ratio 1:1 following purification on a silica gel column eluted with hexane-acetone (47:3). Further elution with hexane-acetone (93:7) gave 3.7 g (72%) of pure **9d** as a syrup; $[\alpha]_D^{25}$ -76.7° (*c* 1.2, $CHCl_3$). The ^{13}C NMR spectrum of glycosyl moieties was identical to that of **9c**.

Anal. Calcd for $C_{33}H_{58}O_{11}$ (630.7): C, 62.83; H, 9.27. Found: C, 62.95; H, 9.21.

6-*O*-(1-deoxy-2,3:4,5-di-*O*-isopropylidene-DL-xylit-1-yl)-3-*O*-dodecyl-1,2-*O*-isopropylidene-α-D-glucofuranose (10d). Likewise, **5d** (2.5 g, 6.75 mmol) and DAXyl-1-OH (3.9 g, 16.8 mmol) gave 0.9 g of a mixture of **10d** and **10'd** in the ratio 1:2 after purification on a silica gel column eluted with hexane-acetone (24:1). Further elution with hexane-acetone (19:1) gave 2.97 g (73%) of pure **10d** as a syrup; $[\alpha]_D^{25}$ -19.2° (*c* 1.3, $CHCl_3$). ^{13}C NMR ($CHCl_3$) δ: C_1 (105.0), C_2 (82.6), C_3 (82.3), C_4 (79.7), C_5 (67.7), C_6 (72.9; 72.7), $C_{1'}$ (71.1; 70.7), $C_{2'}$ (75.4;75.3), $C_{3'}$ (77.0;76.8), $C_{4'}$ (74.2; 74.1), $C_{5'}$ (64.8), 6xCH_3 (26.7-24.3), CMe_2 (110.5), 2xCMe_2 (110.5; 108.6), C_α (69.7), C_β (30.9), 9xCH_2 (29.7-22.6), CH_3 (13.9).

Anal. Calcd for $C_{32}H_{38}O_{10}$ (602.8): C, 63.76; H, 9.69. Found: C, 63.85; H, 9.60.

6-*O*-(1-deoxy-2,3-*O*-isopropylidene-DL-glycer-1-yl)-3-*O*-dodecyl-1,2-*O*-isopropylidene-α-D-glucofuranose (11d). Likewise,

5d (3.2 g, 8.65 mmol) and solketal (2.85 g, 22 mmol) gave 1.3 g of a mixture of **11d** and **11'd** in the ratio 1:1 after purification on a gel silica column eluted with hexane-acetone (87:13). Further elution with hexane-acetone (17:3) gave 2.82 g (65%) of pure **11d** as a syrup; $[\alpha]_D^{25}$ -21.3° (*c* 1.3, $CHCl_3$). ^{13}C NMR ($CDCl_3$) δ: C_1 (105.0), C_2 (82.6), C_3 (82.3), C_4 (79.7), C_5 (67.7), C_6 (72.9; 72.7), $C_{1'}$ (66.1; 66.3), $C_{2'}$ (72.8;72.6), $C_{3'}$ (69.5), 4xCH_3 (26.5-24.3), CMe_2 (111.5), CMe_2 (109.9), C_α (70.6), C_β (31.7), 9xCH_2 (29.5-22.6), CH_3 (13.9).

Anal. Calcd for $C_{27}H_{30}O_8$ (502.7): C, 64.51; H, 10.02. Found: C, 64.80: H, 9.90.

ACKNOWLEDGMENTS

We thank Pr. G. Mackenzie for assistance with the English language, the Biopôle de Picardie and the Centre de Valorisation des Glucides for financial support.

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