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A facile approach to anhydrogalactosucrose derivatives from chlorinated sucrose

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Abstract—Three new anhydrosucrose derivatives: 1,4:3,6-dianhydro-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (**4**), 1,4:3,6-dianhydro-β-D-fructofuranosyl 3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (**6**) and 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl-3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (**8**) were prepared from chlorinated sucrose. The structures of these anhydrides were confirmed by their ^{1}H and ^{13}C NMR spectra, ESIMS and elemental analysis. The crystal structures of **6** and the acetate of **4** (**5**) are presented. The relative reactivity of the chloromethyl groups towards S_N2 reactions in 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside was found to be in order $6 > 6' > 1'$.
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Keywords: Anhydrosucrose; Chlorinated sucrose; X-ray analysis; Relative reactivity

1. Introduction

Due to its widespread existence in all photosynthetic plants and its biological importance, sucrose and its derivatives are of interest as potentially useful substrates in the chemical and biological fields. To develop new applications for sucrose and its derivatives, structural modifications of sucrose have been extensively investigated. Some work has been previously carried out on the preparation of anhydrosucrose.[1] Treatment of 6,1′,6′-tri-*O*-tosylsucrose and its pentabenzoate with sodium ethoxide afforded a high yield of 3,6:1′4′:3′6′-trianhydrosucrose.[2] Alkaline hydrolysis of 4,6,1′-trichlorosucrose tetrabenzoate furnished 2,1′:3,6-dianhydro-4-chloro-4-deoxy-*galacto*-sucrose.[3] According to the molecular models and data from the literature,[3] the relative reactivity of the 6-, 6′- and 1′-sulfonyloxy groups towards S_N2 reactions is in the order $6 \approx 6' > 1'$. In our previous paper, we reported some work about the application and stereochemistry of glucose and xylose.[4] As the first stage of our research on sucrose, we now report a convenient method for synthesis of three new anhydrosucrose derivatives: 1,4:3,6-dianhydro-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside [1′,4′:3′,6′-dianhydro-4-chloro-4-deoxygalactosucrose, (**4**)], 1,4:3,6-dianhydro-β-D-fructofuranosyl 3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (**6**) and 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (**8**). The relative reactivity of the chloromethyl group in 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside (4,6,1′,6′-tetrachloro-4,6,1′,6′-tetradeoxygalactosucrose, **3**) was investigated in this paper.

2. Results and discussion

Treatment of 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (sucralose, **2**) with an aqueous solution of potassium hydroxide afforded a high yield of 1,4:3,6-dianhydro-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (**4**). In the ^{13}C NMR spectrum for **4**, the absence of signals

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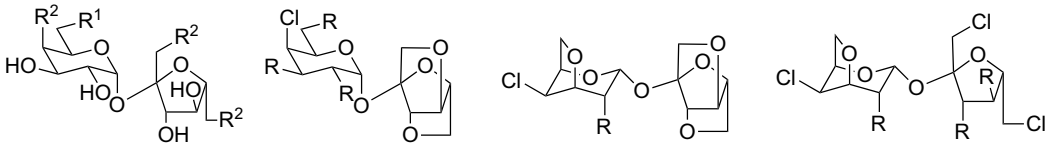


1 $R^1 = R^2 = OH$
2 $R^1 = OH$, $R^2 = Cl$
3 $R^1 = R^2 = Cl$

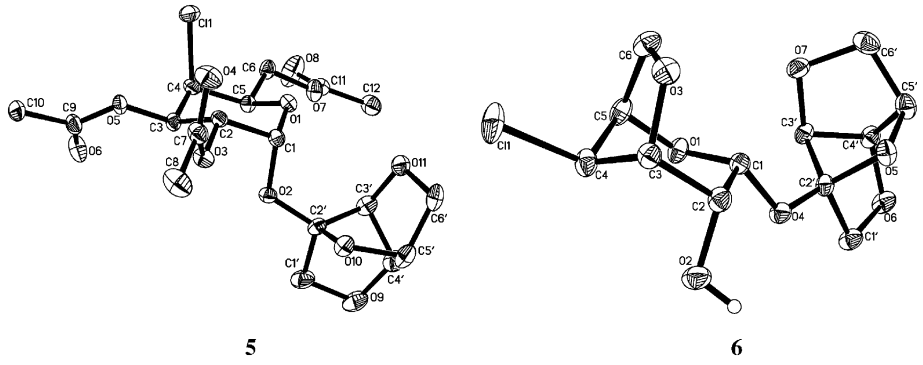
4 R = OH
5 R = OAc

6 R = OH
7 R = OAc

8 R = OH
9 R = OAc

for the chloromethyl carbon atoms that resonate in the 43–45 ppm range as shown in **2** indicated that the chlorine atoms at 1′- and 6′-position had disappeared. Furthermore, the downfield ^{13}C shifts at 71–73 ppm for C-1′ and C-6′ compared to those of **2** suggested the two carbons involved in anhydro rings, that is, the 1′,4′:3′,6′-dianhydro or the 2,1′:3′,6′-dianhydro product, must be formed. In the ^1H NMR spectrum of anhydrosucrose peracetate (compound **5**), three CH_3 signals (around 2.0 ppm) represented the presence of three CH_3CO groups in the molecule, and the downfield shift at 5.00 ppm for H-2 revealed the presence of an *O*-acetyl group at the 2-position. Therefore, we deduced that no 2,1′ linkage was formed and **4** would be 1′,4′:3′,6′-dianhydro-4-chloro-4-deoxygalactosucrose. The structure of **4** was later confirmed by the single-crystal X-ray analysis of compound **5** (Fig. 1) after **5** gave crystals suitable for X-ray analysis through recrystallization from absolute ethanol. These results reveal that the formation of the 1′,4′-anhydro ring precedes the formation of the 2,1′-anhydro ring. This is apparently due to the fact that the C-1′ is adjacent to the anomeric position,[5] and the hindrance of the neopentyl-type group of the 1′-chloromethyl group renders it less reactive than the 6′-chloromethyl group in the nucleophilic displacement reaction. From the examination of the molecular model, we note that the formation of the 3′,6′-anhydro ring makes C-1′ and O-4′ very close; therefore, 1′,4′-anhydro ring formation becomes kinetically favourable. This reaction is very similar to the nucleophilic displacement reaction of 1′,6′-di-*O*-mesylsucrose.[6] A comparison of the ^{13}C NMR spectral data of the dianhydrosucrose derivative with that of sucralose indicated that the formation of the anhydro rings on the fructose moiety caused a downfield shift of 6–7 ppm at the C-2′ atom.

Chlorination of sucrose in *N*,*N*-dimethylformamide and pyridine with thionyl chloride, followed by convenient neutralization and extraction, afforded 4,6,1′,6′-tetrachloro-4,6,1′,6′-tetradeoxygalactosucrose (**3**)[7] as a syrup. Thermal alkaline treatment of **3** in water with three molar equivalents of potassium hydroxide, followed filtration, furnished a precipitate (**6**). The filtrate was concentrated and separated by chromatography, followed by crystallization, giving a white solid (**8**). Acetylation of **6** and **8** gave acetates **7** and **9**, respectively, in high yields. By comparing the ^{13}C chemical shifts at C-6, C-1′ and C-6′ of **6** with the corresponding shifts of **3**, and the ^1H shift at H-2 of **7** with corresponding shift of **6**, we noted that three chlorine atoms had been lost, and three anhydro rings involving the three carbons had been formed in the conversion, and that only the 2-OH was presented in the molecule of **6**. Therefore, we concluded that **6** would be 3,6:1′,4′:3′,6′-trianhydro-4-chloro-4-deoxygalactosucrose. The structure of **6** was also established by X-ray analysis after recrystallization from ethyl acetate (Fig. 1). We noted that the conversion of the conformation for the galactopyranose ring from $^4C_1$ to $^1C_4$ resulted from the formation of a 3,6-anhydro ring and caused the ^{13}C upfield shifts of 7 ppm at the C-4 atom. All the ^1H and ^{13}C NMR chemical shifts are presented in Tables 1 and 2.



5 **6**

Figure 1. ORTEP for compounds **5** and **6**. Hydrogen atoms are omitted.

Table 1. ^{1}H NMR chemical shifts and coupling constants for sucrose derivatives **2**–**9**

	2[a]	**3**[b]	**4**[b]	**5**[b]	**6**[b]	**7**[b]	**8**[b]	**9**[c]
H-1	5.32 d	5.23 d	5.38 d	5.78 d	5.48 d	5.67 d	5.21 d	5.45 d
H-2	3.79 dd	3.62 m	3.62 dd	5.00 dd	3.74 m	4.93 dd	4.00 t	5.14 dd
H-3	4.02 dd	3.96 m	3.82 m	5.32 dd	4.31 d	4.47 d	4.32 d	4.42 d
H-4	4.36 d	4.44 d	4.37 d	4.78 d	4.66 d	4.67 d	4.68 d	4.65 d
H-5	4.26 m	4.59 dd	3.98 t	4.49 m	4.47 m	4.59 m	4.44 s	4.49 s
H-6a	3.60 d	3.78 m	3.48 d	4.20 dd	4.09 d	4.15 d	4.12 d	3.92 dd
H-6b	3.62 m			4.08 dd	4.02 dd	4.09 dd	4.05 dd	3.78 dd
H-1′a	3.63 s	3.69 d	3.82 m	3.88 d	3.81 d	3.77 d	3.76 m	3.63 d
H-1′b		3.59 d	3.73 d	3.76 d	3.70 d	3.62 d	3.76 m	3.57 d
H-3′	4.26 m	3.87 m	4.56 m	4.46 m	4.46 d	4.44 d	3.76 m	5.63 d
H-4′	3.96 t	4.05 t	4.57 m	4.60 dd	4.59 dd	4.59 m	3.76 m	5.37
H-5′	3.92 m	3.78 m	4.51 s	4.55 s	4.56 s	4.56 s	3.76 m	4.26 m
H-6′a	3.73 dd	3.90 m	3.82 m	3.83 d	3.92 d	3.96 d	3.76 m	4.26 m
H-6′b		3.79 m		3.78 d	3.87 d	3.87 d	3.76 m	4.26 m
$J_{1,2}$	4.0	3.6	4.0	4.0	2.4	2.6	2.2	2.4
$J_{2,3}$	10.0		10.0	10.8	5.6	5.6	5.4	5.6
$J_{3,4}$	3.6	2.4	3.2	3.6		5.2	4.2	
$J_{4,5}$				1.2	1.2		1.2	
$J_{5,6a}$	6.0	7.0	6.0	7.6				8.4
$J_{5,6b}$		5.0		4.4	2.8	2.4	2.8	4.4
$J_{6a,6b}$				11.2	10.4	10.4	10.4	11.6
$J_{1'a,1'b}$		12.4	7.6	8.0	7.6	7.6		12.0
$J_{3',4'}$	8.0	8.8		3.2	3.6	3.2		7.0
$J_{4',5'}$					1.2			
$J_{5',6'a}$	5.2							
$J_{6'a,6'b}$				8.0	8.4	8.8		

[a] At 400.1 MHz in D_2O.
[b] At 400.1 MHz in Me_2SO-d_6.
[c] At 400.1 MHz in $CDCl_3$.

Table 2. ^{13}C NMR chemical shifts for compound **2**–**9**

	C-1	C-2	C-3	C-4	C-5	C-6	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′
2[a]	92.3	67.2	67.7	62.6	70.4	61.0	43.1	103.0	75.6	74.9	80.8	44.4
3[b]	92.0	66.7	66.9	65.2	70.0	46.2	43.8	102.7	75.7	75.1	82.5	44.3
4[b]	94.0	67.5	67.8	64.8	70.5	61.2	72.6	109.8	75.5	78.1	81.8	71.9
5[b]	90.2	67.1	67.0	60.2	67.4	63.1	72.3	109.9	75.5	78.2	82.3	72.1
6[b]	90.4	70.2	82.6	58.2	77.6	67.8	72.5	110.2	75.7	78.2	82.2	72.2
7[b]	88.2	70.1	79.1	57.7	77.8	67.8	71.9	109.7	75.4	77.5	82.0	71.9
8[b]	89.4	77.1	81.9	57.8	77.2	67.7	43.8	103.6	75.9	70.7	82.1	46.0
9[c]	88.4	78.6	80.0	57.0	76.4	68.7	43.9	104.2	75.5	70.9	81.2	44.8

[a] At 100.6 MHz in D_2O.
[b] At 100.6 MHz in Me_2SO-d_6
[c] At 100.6 MHz in $CDCl_3$.

In the ^{13}C NMR spectrum of compound **8**, the signals at 43.8 and 46.0 ppm showed the presence of two chloromethyl groups in the molecule. The ^{13}C shift at 57.8 ppm for C-4, which is very close to the corresponding resonance in **6** and **7**, indicated that the chlorine at C-4 is equatorial and confirmed the formation of the 3,6-anhydro ring on the galactose moiety. Compared to **8**, the downfield shifts of H-2, H-3′ and H-4′ observed in ^{1}H NMR spectrum of **9** indicated the existence of *O*-acetyl groups at these positions. From the above structural analysis, we presumed that **8** would be 3,6-anhydro-4,1′,6′-trichloro-4,1′,6′-trideoxygalactosucrose. The results of the alkaline treatment of **3**, which gave the 3,6-anhydride and the 3,6:1′4′:3′,6′-trianhydride, reveal that the formation of the 3,6-anhydro ring precedes the formation of the 3′,6′-anhydro ring. Combined with the analysis for the reactivity of two chloromethyl groups on the fructose moiety with the above experimental results, we could conclude that the relative reactivity of the 6-, 6′-and 1′-chloromethyl group in 4,6,1′,6′-tetrachloro-4,6,1′,6′-tetradeoxygalactosucrose towards S_N2 reactions is in order $6 > 6' > 1'$.

In order to further verify the order of relative reactivity, the thermal treatment of pure **3** (white foam, mp 62–64 °C, $[\alpha]_D^{20}$ +86.9 (*c* 0.26, MeOH), obtained by chromatographic fractionation of the syrup of **3**) with sufficient potassium hydroxide (3.5 molar equiv), gave the sole product **6** (91% yield based on **3**). Then, when

Table 3. Crystal data and structure refinement for compounds **5** and **6**

	5	**6**
Empirical formula	$C_{18}H_{23}ClO_{11}$	$C_{12}H_{15}ClO_7$
Formula weight	450.81	306.69
Crystal system	Orthorhombic	Orthorhombic
Space group	$P\,2_12_12_1$	$P\,2_12_12_1$
Unit cell dimensions		
a (Å)	9.972(2)	6.4197(13)
b (Å)	12.694(3)	10.637(2)
c (Å)	16.855(3)	18.706(4)
V (Å^3)	2133.7(7)	1277.4(4)
Z	4	4
D_{calcd} (mg/m^3)	1.403	1.595
Absorption coefficient (mm^{-1})	0.236	0.330
F (000)	944	640
Crystal size (mm^3)	$0.20\times0.20\times0.18$	$0.20\times0.18\times0.18$
θ Range for data collection (°)	2.01–25.00	2.18–27.47
Index ranges	$-11\leqslant h\leqslant 11$, $0\leqslant k\leqslant 15$, $-20\leqslant l\leqslant 19$	$-7\leqslant h\leqslant 8$, $-13\leqslant k\leqslant 0$, $-23\leqslant l\leqslant 23$
Reflections collected/unique	5265/3181 [R(int) = 0.0659]	4784/2712 [R(int) = 0.0524]
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	3181/0/272	2712/0/186
Final R indices [$I>2\sigma(I)$]	R_1 = 0.0567	R_1 = 0.0450
R indices (all data)	wR_2 = 0.1426	wR_2 = 0.1211
Goodness-of-fit on F^2	1.015	1.090

insufficient potassium hydroxide (1.3 molar equiv) was used in the reaction at room temperature, the main product **8** was obtained in a yield of 86% along with only a little of **6** (4%).

Details of the crystal structure determinations for compounds **5** and **6** are given in Table 3, and the ORTEP depictions with atom numbering are shown in Figure 1. Some selected torsion angles, bond lengths and Cremer–Pople[8] puckering parameters of compounds **5** and **6** are listed in Table 4. With a θ value of 3.2(3)°, the galactopyranose ring of **5** retains the $^4C_1$ conformation, close to a perfect chair (θ 0.00°). This is also shown by the magnitude of the torsion angles of the ring (53.4–59.1°). Then the large θ value of 160.5(3)° and greater magnitude of the torsion angles in **6** (46.1–75.7°) indicate that the pyranose ring of **6** is altered to exist in the $^1C_4$ conformation, opposite to that in **5**, and distorted towards an E_4-form ring to a certain extent. The large puckering amplitude of **6** (Q 0.680 Å) also shows much more puckering than the nearly normal pyranose ring of **5** (0.568 Å). The interaction between the molecules in the stacking is shown in Figure 2. The molecules are regularly bounded by the intermolecular hydrogen bonds between O-7 in the dianhydrofructose moiety of one molecule and 2-OH in the anhydrogalactose moiety of the next one (distance 2-OH···O-7 1.90(5) Å, angle 2-OH···O-7 173(5)°). Because of this interaction, the O(7)–C(3′) bond length in **6** is longer than that of the corresponding bond in **5** (Table 4). Except for the bond length, there are almost

Table 4. Selected torsion angles (°) and bond length (Å) and Cremer–Pople puckering parameters for **5** and **6**

	5	**6**
C(1)–C(2)–C(3)–C(4)	−57.3(5)	60.2(3)
O(1)–C(1)–C(2)–C(3)	58.4(5)	−46.1(3)
C(5)–O(1)–C(1)–C(2)	−59.1(5)	50.1(3)
C(4)–C(5)–O(1)–C(1)	56.7(5)	−67.6(3)
C(3)–C(4)–C(5)–O(1)	−53.4(6)	75.7(3)
C(2)–C(3)–C(4)–C(5)	54.4(6)	−72.1(3)
C(6′)–O(11)–C(3′)–C(4′)	−26.3(6)	−25.1(3)
C(3′)–O(11)–C(6′)–C(5′)	−10.6(5)	−11.0(3)
C(6′)–O(11)–C(3′)–C(2′)	72.9(6)	72.5(3)
O(1)–C(1)	1.420(6)	1.433(3)
O(1)–C(5)	1.425(6)	1.444(3)
C(1)–C(2)	1.519(7)	1.518(4)
C(2)–C(3)	1.524(7)	1.530(4)
C(3)–C(4)	1.514(7)	1.522(4)
C(4)–C(5)	1.531(7)	1.521(4)
O(11)–C(6′)	1.461(7)	1.461(4)
O(11)–C(3′)	1.415(7)	1.423(3)
Galactopyranose ring		
Q (Å)	0.568(5)	0.680(3)
θ (°)	3.2(5)	160.5(3)

O(11) in **5** corresponds to O(7) in **6**.

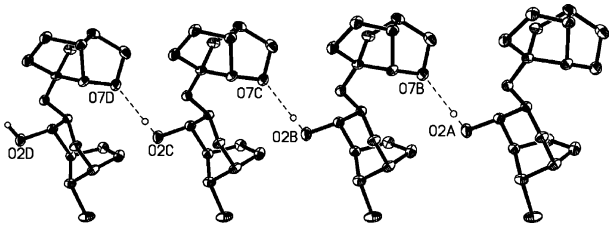


Figure 2. Perspective ORTEP view of molecules of compound **6**, showing the intermolecular hydrogen bonds. Hydrogen atoms are omitted.

no differences in the dianhydrofructose moiety between **5** and **6** due to the rigidity of the ring, in spite of the great differences in the galactopyranose moiety. In addition, the replacement of the α-OH with a β-Cl group at C-4 caused more regular molecular stacking and higher density in **6** (1.595 Mg/m^3) than in 1,4:3,6-dianhydro-β-D-fructofuranosyl 3,6-anhydro-α-D-glucopyranoside (D_{calcd} 1.57 Mg/m^3).[9]

3. Experimental

3.1. General methods

^1H and ^{13}C NMR spectra were acquired on a Bruker AVANCE DPX-400 spectrometer at 25 °C. The ^1H and ^{13}C NMR chemical shifts (δ), given in parts per million, were referenced to internal tetramethylsilane (Me_4Si). Melting points were determined on a WC-1 melting-point apparatus and are uncorrected. Optical rotations were determined on a Perkin–Elmer 341 polarimeter. Elemental analysis were carried out on a MOD 1106 analyzer. Mass spectra were taken with a Bruker Esquire 3000 mass spectrometer. Thin-layer chromatography (TLC) was performed on glass plates precoated with silica gel (5–40 μm) to monitor the reactions and certify the purity of the reaction products. Visualization was accomplished by spraying chromatograms with 10% ethanolic sulfuric acid and charring them on a hot plate. Column chromatography was carried out on silica gel (200–300 mesh).

3.2. X-ray diffraction

X-ray diffraction measurements were made on a Rigaku RAXIS-IV imaging plate with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The orthorhombic crystal was selected and mounted on a glass fibre. All data were collected at a temperature of 291(2) K and corrected for Lorentz polarization effects. The structure was solved via direct methods and expanded using the Fourier technique. The non-hydrogen atoms were refined with anisotropic thermal parameters. Hydroxyl hydrogen atoms were refined with isotropic thermal parameters. Other hydrogen atoms were included but not refined. All calculations were performed using the SHELX-97 crystallographic software package.[10]

3.3. Acetylation procedure

To a solution of 300 mg of anhydrosucrose in pyridine (1.0 mL), Ac_2O (0.5 mL) and a catalytic amount of DMAP were added. The mixture was stirred for 1 h at ambient temperature, and then absolute EtOH (2 mL) was added. After 30 min, the mixture was partitioned between EtOAc and water. The EtOAc layer was washed with satd aq $NaHCO_3$ (5 mL × 2), water (5 mL × 3), dried over anhydrous Na_2SO_4 and evaporated, affording anhydrosucrose acetate.

3.4. 1,4:3,6-dianhydro-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (4) and 1,4:3,6-dianhydro-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranoside (5)

To a solution of sucralose[11] (**2**, 19.9 g, 0.05 mol, Tate & Lyle product) in water (100 mL) was added a solution of KOH (9.8 g, 0.175 mol) in water (50 mL). The mixture was heated to 55 °C under stirring and kept for 4 h. After the sucralose disappeared by TLC detection, the solution was evaporated under diminished pressure. The residue was dissolved with 2-PrOH (50 mL) and dried over anhydrous Na_2SO_4. Evaporation of the dry solution gave **4** as a white foamy solid (14.5 g, 89%): mp 90–92 °C, $[\alpha]_D^{20}$ +229.5 (*c* 0.44, MeOH). ESIMS: $[M+Na]^+$ 347. Anal. Calcd for $C_{12}H_{17}ClO_8$: C, 44.39; H, 5.28. Found: C, 44.23; H, 5.34.

Treatment of **4** (300 mg) according to the acetylation procedure in Section 3.3 and crystallization from absolute EtOH afforded **5** as needles (387 mg, 93%): mp 130–131 °C, $[\alpha]_D^{20}$ +223.4 (*c* 0.54, $CHCl_3$). ESIMS: $[M+Na]^+$ 473. Anal. Calcd for $C_{18}H_{23}ClO_{11}$: C, 47.96; H, 5.14. Found: C, 47.80; H, 5.19.

3.5. 1,4:3,6-Dianhydro-β-D-fructofuranosyl 3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (6) and 1,4:3,6-dianhydro-β-D-fructofuranosyl 2-*O*-acetyl-3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (7)

To an ice-cold solution of dried sucrose (**1**, 2.0 g, 5.8 mmol) in *N*,*N*-dimethylformamide (5 mL) and pyridine (30 mL) was added dropwise $SOCl_2$ (4.2 mL, 58 mmol) over 20 min. The mixture was gradually heated to 105 °C and kept for 6 h, then cooled to room temperature. MeOH (25 mL) and 28% ammonia water (25 mL) was added in sequence to the reaction mixture. The temperature was raised to 60 °C and maintained for 2 h. The solution was evaporated under reduced pressure to dryness. The residue was dissolved in EtOAc, and the solution was washed with water three times. The solution was dried over anhyd Na_2SO_4 and concentrated to give crude 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside (**3**, 1.4 g) as a syrup. The syrup was dissolved in MeOH (3 mL) and added to a solution of KOH (0.65 g, 11.6 mmol) in water (10 mL). After the mixture was heated to 80 °C and kept for 2 h, a precipitate was formed. The mixture was cooled to room temperature, followed by filtration and washing with MeOH, to afford **6** (650 mg, 36.5% yield from sucrose). Crystallization from EtOAc gave the product as needles with mp 220–221 °C, $[\alpha]_D^{20}$ +137.5 (*c* 0.08, $CHCl_3$). ESIMS: $[M+Na]^+$ 329. Anal.

Calcd for $C_{12}H_{15}ClO_7$: C, 46.99; H, 4.93. Found: C, 46.87; H, 4.98.

Treatment of **6** (300 mg) according to the acetylation procedure in Section 3.3 afforded **7** (310 mg, 91%): mp 142–143 °C, $[\alpha]_D^{20}$ +122.5 (*c* 0.58, $CHCl_3$). ESIMS: $[M+Na]^+$ 371. Anal. Calcd for $C_{14}H_{17}ClO_8$: C, 48.22; H, 4.91. Found: C, 48.09; H, 4.95.

3.6. 1,6-Dichloro-1,6-dideoxy-β-D-fructofuranosyl 3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (8) and 3,4-di-*O*-acetyl-1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 2-*O*-acetyl-3,6-anhydro-4-chloro-4-deoxy-α-D-galactopyranoside (9)

Treatment of dried sucrose (**1**, 2.0 g, 5.8 mmol), following the description above, afforded crude **3**. Compound **3** was dissolved in MeOH (2 mL), and a solution of KOH (0.20 g, 3.6 mmol) in water (5 mL) was added. The mixture was stirred at room temperature for 16 h. After TLC indicated the disappearance of **3**, the solution was adjusted with dilute hydrochloric acid to pH 7–8 and concentrated under reduced pressure. The residual syrup was separated by column chromatography with 8:1 $CHCl_3$–EtOAc to give **8** (778 mg, overall yield 35.3%): mp 53–55 °C, $[\alpha]_D^{20}$ +12.6 (*c* 0.72, MeOH), ESIMS: $[M+Na]^+$ 401. Anal. Calcd for $C_{12}H_{17}Cl_3O_7$: C, 37.97; H, 4.51. Found: C, 37.88; H, 4.56.

Treatment of **8** (300 mg) according to the acetylation procedure in Section 3.3 afforded **9** (376 mg, 94%): mp 112–113 °C, $[\alpha]_D^{20}$ −9.2 (*c* 0.54, $CHCl_3$), ESIMS: $[M+Na]^+$ 527. Anal. Calcd for $C_{18}H_{23}Cl_3O_{10}$: C, 42.75; H, 4.58. Found: C, 42.58; H, 4.66.

4. Supplementary data

Complete crystallographic data for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 249375 (**5**) and CCDC No. 249376 (**6**). Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK. (Fax: +44 1223 336033, e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

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References

1. Teranishi, K. *Carbohydr. Res.* **2002**, *337*, 613–619; Luis Jimenez, J. L.; Garcia Fernandez, J. M.; Gadelle, A.; Defaye, J. *Carbohydr. Res.* **1997**, *303*, 367–372; Chowdhary, M. S.; Hough, L.; Anthony, C. *Carbohydr. Res.* **1986**, *147*, 49–56; Guthrie, R. D.; Jenkins, I. D.; Thang, S.; Yamasaki, R. *Carbohydr. Res.* **1988**, *176*, 306–313.
2. Isaacs, N. W.; Kennard, C. H. L.; O'Donnell, G. W.; Richards, G. N. *J. Chem. Soc., Chem. Commun.* **1970**, 360–361; Bolton, C. H.; Hough, L.; Khan, R. *Carbohydr. Res.* **1972**, *21*, 133–143; Khan, R. *Carbohydr. Res.* **1972**, *22*, 441–445; Buchanan, J. G.; Cummerson, D. A.; Turner, D. M. *Carbohydr. Res.* **1972**, *21*, 283–293; Khan, R.; Jenner, M. R.; Mufti, K. S. *Carbohydr. Res.* **1975**, *39*, 253–262; Ball, D.; Bissett, H. F. H.; Chalk, R. C. *Carbohydr. Res.* **1977**, *55*, 149–163; Gurjar, M. K.; Hough, L.; Richardson, A. C. *Carbohydr. Res.* **1980**, *78*, C21–C23.
3. Chiu, A. K. B.; Gurjar, M. K.; Hough, L.; Sincharoenkul, L. V.; Richardson, A. C. *Carbohydr. Res.* **1982**, *100*, 247–261.
4. Liu, H.-M.; Zhang, F.; Zhang, J.; Li, S. *Carbohydr. Res.* **2003**, *338*, 1737–1743; Liu, H.-M.; Zhang, F.; Zou, D.-P. *Chem. Commun. (Cambridge)* **2003**, *16*, 2044–2045; Liu, H.-M.; Zou, D.-P.; Zhang, F.; Zhu, W.-G.; Peng, T. *Eur. J. Org. Chem.* **2004**, 2103–2106; Liu, H.-M.; Xu, W.; Liu, Z.-Z. *Carbohydr. Res.* **2001**, *331*, 229–232.
5. Richardson, A. C. *Carbohydr. Res.* **1969**, *10*, 395–402.
6. Buchanan, J. G.; Cummerson, D. A. *Carbohydr. Res.* **1972**, *21*, 293–296.
7. Liu, H.-M.; Ke, Y.; Liu, Z.-Z. *Chin. J. Magn. Reson.* **2003**, *20*, 357–361.
8. Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358.
9. Isaacs, N. W.; Kennard, C. H. L. *J. Chem. Soc., Perkin. Trans. 2* **1972**, 582–585.
10. Sheldrick, G. M. SHELXS-97; Göttingen: Germany, 1997.
11. Hough, L. et al. *Carbohydr. Res.* **1972**, *21*, 144–147.