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Note

Preparation of α and β anomers of 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-D-galactopyranose based upon anomerization and kinetic acetylation

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Abstract—4-Chloro-4-deoxy-α-D-galactopyranose, 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranose and 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-β-D-galactopyranose were readily prepared from 1,4:3,6-dianhydro-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside. In the study, we found an interesting anomerization phenomenon of 4-chloro-4-deoxy-D-galactose. The molar ratio of α and β anomers in solution is about 1:2 when the anomerization reaches a dynamic equilibrium, and the β anomer could completely convert to the α anomer in the process of crystallization and precipitation. The acetylation of 4-chloro-4-deoxy-D-galactopyranose is kinetically controlled, and the configuration of the starting galactose determines the configuration of the resulting acetates. The influence of the chloro group at C-4 and the *O*-acetyl group at the anomeric carbon on the galactopyranose ring conformations is discussed, based upon the crystallographic data for the α and β anomers of 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-D-galactopyranose.

Keywords: Acetylation; Anomerization; 4-Chloro-4-deoxy-D-galactopyranose; Conformation; X-Ray analysis

Carbohydrates and their derivatives are potentially useful substrates in the chemical and biological fields. To improve the function of compounds with new and attractive characteristics, structural modifications of the sugars are often required.[1,2] Structural modifications can occur by substitution with *O*-acetyl, phosphate, sulfate, or chloro, and other groups. Variation of the substitution greatly alters the characteristics of saccharides and the conformation adopted by a sugar ring. The ring conformational analysis of carbohydrates is also of interest in regard to biological activities, as well as chemical and physical properties determined by the adopted conformations of the compounds.[3]

Within sucrochemistry, the synthetic methods for various anhydrosucrose derivatives have been developed previously,[4] and the synthesis of 1,4:3,6-dianhydro-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (**1**) has been reported in our earlier paper.[5] To our knowledge, although the synthesis of anhydrosucrose derivatives have been extensively investigated, no further utilization of anhydrosucrose in organic synthesis has been reported. We attempted to hydrolyze **1** to prepare new monosaccharides and successfully obtained 4-chloro-4-deoxy-α-D-galactopyranose (**4**). In the study, we found an interesting anomerization phenomenon for the new halogenated monosaccharides. On the basis of the anomerization, the α and β anomers of the acetates of the monosaccharides were synthesized.

We report herein the preparation and the unique anomerization of 4-chloro-4-deoxy-α-D-galactopyranose, and the respective preparation of the α and β anomers of 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-D-galactopyranose based on the anomerization via different processes. The galactopyranose ring conformations of α and β anomers were analyzed also based on the crystallographic data and Cremer–Pople puckering parameters.

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Hydrolysis of 1,4:3,6-dianhydro-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (**1**)[5] with dilute sulfuric acid, followed by concentration to dryness under diminished pressure and fractionation by chromatography, afforded 4-chloro-4-deoxy-D-galactopyranose with a melting point of 147–150 °C (dec) and an optical rotation of +134.0° (*c* 0.726, MeOH). The smaller J_{12} value (4.0 Hz) observed in the ^{1}H NMR spectrum of the galactopyranose, based upon 2D NMR spectra, showed it as the α anomer **4**. Acetylation of **4** with acetic anhydride in pyridine resulted in the product (compound **2**, needles) with a melting point of 76–78 °C and an optical rotation of +146.5° (*c* 1.03, $CHCl_3$). ^{1}H and ^{13}C NMR spectral data indicated that **2** is pure 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranose. In our previous study, acetylation of D-galactose under the same conditions yielded almost pure β anomer acetate. It is obvious that the introduction of chlorine into C-4 of galactopyranose ring has altered the feature of acetylation. Furthermore, the dry concentrated residue without fraction (intermediate residue) was acetylated directly and extracted with ethyl acetate, followed fractionation by chromatography, giving a mixture of α and β anomers of 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-D-galactopyranose (α:β ≈ 1:2, mol/mol). The anomeric acetates were separated by recrystallization from absolute ethanol to afford the β anomer (compound **3**) as needles (as shown in Scheme 1) with a melting point of 176–177 °C and an optical rotation of +64.8° (*c* 0.58, $CHCl_3$). The ^{1}H and ^{13}C NMR spectral data for the three compounds are shown in Tables 1 and 2. Single-crystal X-ray analysis after recrystallization from absolute ethanol established the structure of **2** and **3** as shown in Figure 1.

In order to investigate the reason for the different results of the two acetylations, we utilized ^{1}H NMR technology to trace the anomerization of **4** in solution. Compound **4** was dissolved in deuterated Me_2SO, and the ^{1}H NMR spectrum was recorded immediately. The recorded ^{1}H NMR spectrum indicated the presence of only α anomer at first. The α anomer converted gradually to the β anomer (**5**, as shown in Tables 1 and 2) with the passage of time, and the ^{1}H NMR spectrum showed the ratio of α to β anomers was 1:2 when the anomerization reached a dynamic equilibrium (as shown in Scheme 2). This ratio is in accord with that of the anomeric acetates from the intermediate residue. When the deuterated Me_2SO was replaced by CD_3OD, a similar anomerization was shown to exist. Therefore, **4** was dissolved in a solution of 5:1 methanol–pyridine and heated to reflux for 10 h, followed by evaporation of the methanol. Acetylation of the residual solution containing pyridine with acetic anhydride gave a mixture of α and β anomers of acetates in a ratio of 1:1.92, almost same result as the direct acetylation of the intermediate residue. On the basis of the experiments described

Table 1. ^{13}C NMR spectral data of compound **2**–**5**

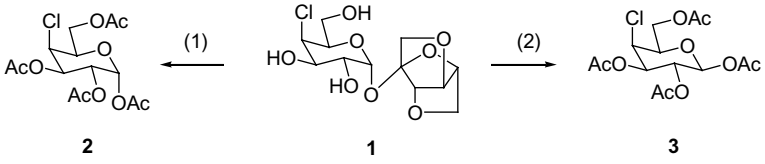
	2[a]	**3**[a]	**4**[b]	**5**[b]
1	89.6	92.2	92.7	97.9
2	66.1	67.3	68.0	72.0
3	68.3	71.7	68.7	72.1
4	58.4	57.3	65.6	64.2
5	68.9	71.9	69.0	73.4
6	63.0	62.7	61.0	60.9
	20.5	20.62		
AcO	20.7	20.69		
(CH_3)	20.8	20.72		
	20.9	20.81		
	168.7	169.0		
AcO	169.6	169.1		
(C=O)	170.35	170.1		
	170.38	170.3		

[a] In $CDCl_3$.
[b] In Me_2SO-d_6.

Table 2. ^{1}H NMR spectral data of compound **2**–**5**

	2[a]	**3**[a]	**4**[b]	**5**[b]
1	6.37(d)	5.69(d)	4.95(d)	4.31(d)
2	5.45(dd)	5.44(dd)	3.48(m)	3.23(t)
3	5.32(dd)	5.05(dd)	3.84(m)	3.60(dd)
4	4.62(d)	4.53(d)	4.36(d)	4.26(d)
5	4.43(t)	4.11(t)	4.08(t)	3.65(t)
6a	4.27(dd)	4.31(dd)	3.48(m)	3.48(t)
6b	4.20(dd)	4.24(dd)		
CH_3CO	2.03	2.06		
	2.08	2.09		
	2.14	2.128		
	2.16	2.132		
$J_{1,2}$	3.6	8.4	4.0	7.2
$J_{2,3}$	10.6	10.0		9.2
$J_{3,4}$	3.6	3.6	2.4	3.6
$J_{5,6}$	6.4	6.0	6.4	6.4
$J_{6a,6b}$	11.4	11.2		

[a] In $CDCl_3$.
[b] In Me_2SO-d_6.



2 **1** **3**

Scheme 1. Preparation of α and β anomers of 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-D-galactopyranose. Reagents and conditions: (1) (a) 0.37 N H_2SO_4, 60 °C, 2 h; (b) separation by chromatography; (c) Ac_2O, pyridine; (2) (a) 0.37 N H_2SO_4, 60 °C, 2 h; (b) Ac_2O, pyridine; (c) separation by chromatography; (d) recrystallization from EtOH.

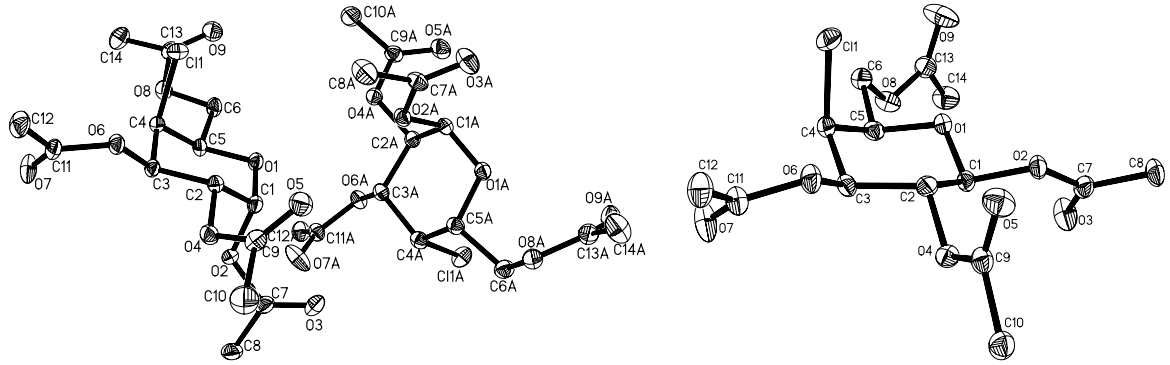
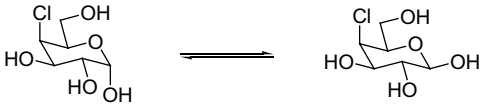


Figure 1. ORTEP of compounds **2** and **3**, hydrogens omitted.



Scheme 2. Anomerization of 4-chloro-4-deoxy-D-galactopyranose in Me_2SO.

above, we could conclude that there are α and β anomers in the intermediate residue; acetylation of 4-chloro-4-deoxy-D-galactopyranose is a kinetically controlled process, that is, the anomeric configuration of the starting galactose determines the configuration of the resulting acetates.

Since the intermediate residue is a mixture, why is the final product obtained in the hydrolysis of **1** only the α anomer of 4-chloro-4-deoxy-D-galactopyranose? The solution of **4** in methanol was heated to reflux and kept for 24 h. At the end of this time the solvent was allowed to evaporate slowly and naturally to dryness, giving a product as a white solid. The ^1H NMR spectrum of the product indicated that the product was pure 4-chloro-4-deoxy-α-D-galactopyranose, while the solution of **4** in CD_3OD after keeping at 55 °C for 20 h contained two anomers (α:β ≈ 1:1.1). It is obvious that the conversion from the β anomer to the α anomer takes place in the process of crystallization or precipitation, and the β anomer disappears at last.

Crystal data summary and refinement results for compound **2** and **3** are contained in Table 3. Single-crystal

Table 3. Crystal data summary and refinement results for compound **2** and **3**

	2	**3**
Empirical formula	$C_{28}H_{38}Cl_2O_{18}$	$C_{14}H_{19}ClO_9$
Formula weight	733.48	366.74
Temperature (K)	291(2)	291(2)
Crystal system	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
Unit cell dimensions		
a (Å)	9.3626(19)	5.7960(12)
b (Å)	10.239(2)	14.472(3)
c (Å)	38.098(8)	21.532(4)
V (Å^3)	3652.3(13)	1806.1(6)
Z	4	4
D_{calcd} (Mg/m^3)	1.334	1.349
Absorption coefficient (mm^{-1})	0.250	0.253
F (000)	1536	768
Crystal size (mm^3)	$0.20 \times 0.20 \times 0.18$	$0.20 \times 0.18 \times 0.18$
θ Range for data collection (°)	1.07–25.00	1.70–27.49
Index ranges	$0 \leqslant h \leqslant 11$, $-12 \leqslant k \leqslant 12$, $-45 \leqslant l \leqslant 45$	$-7 \leqslant h \leqslant 7$, $0 \leqslant k \leqslant 18$, $-27 \leqslant l \leqslant 27$
Reflections collected/unique	9195/5585 [R(int) = 0.0533]	5025/3192 [R(int) = 0.0747]
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	5585/0/435	3192/0/218
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0568$	$R_1 = 0.0531$
R indices (all data)	$wR_2 = 0.1284$	$wR_2 = 0.1641$
Goodness-of-fit on F^2	1.049	1.035
Largest diff. peak and hole	0.186 and −0.152 e Å^{-3}	0.320 and −0.312 e Å^{-3}

X-ray analysis revealed that two rotamers are present in an asymmetric unit and that the $^4C_1$ conformations of pyranose rings exist in the solid state of the acetate **2**. The primary hydroxyl groups of two rotamers in **2** are in the *tg* position (O(1)–C(5)–C(6)–O(8) = −178.2°) and the *gt* position (O(1A)–C(5A)–C(6A)–O(8A) = 66.5°), respectively, being the two favored orientations for sugars with the *galacto* configuration.[6] For acetate **3**, one asymmetric unit contains only one molecule with the primary hydroxyl group in the *gt* position (O(1)–C(5)–C(6)–O(8) = 78.3°) and the pyranose ring existing in the $^4C_1$ conformation. The regular intermolecular weak H-bonds between O(5) of carbonyl group in one molecule and H at C(1) as well as H at C(3) in the pyranose ring of another molecule (distance C(1)–H···O-5 2.559 Å, C(3)–H···O-5 2.572 Å; angle 1-C–H···O-5 140.1°, 3-C–H···O-5 140.3°) result in the closer packing of acetate **3** (as shown in Fig. 2). Then despite the presence of more kinds and higher numbers of supramolecular bonds, including C–H···O, C–H···Cl, and C═O···Cl, in acetate **2** than in acetate **3**, most of the atoms involved in the bonds are at carbon atoms outside pyranose rings (as shown in Fig. 3), which could not allow the close packing of molecules. It seems that the

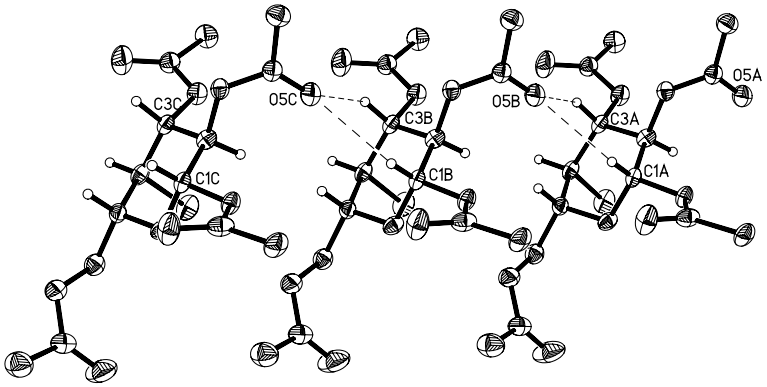


Figure 2. The weak H-bonds of **3**.

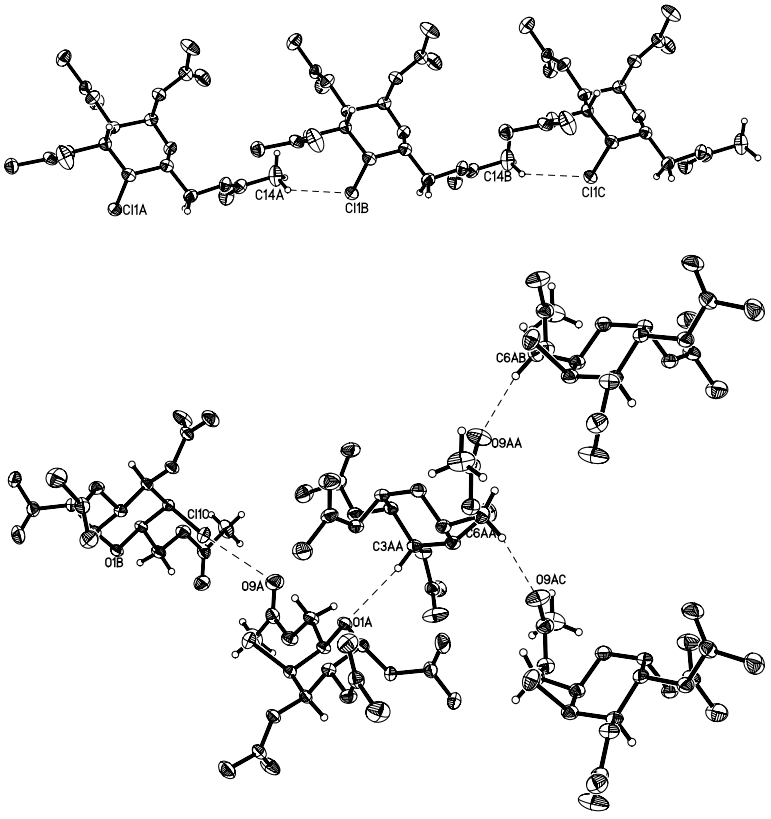


Figure 3. The supramolecular bonds of **2**.

presence of the two molecules rotated with respect to each other in one asymmetric unit lead to a relatively 'irregular' and 'looser' packing of **2**, which is also indirectly confirmed by the difference of 40 Å^3 between the cell volumes of the two anomers (V(**2**) and 2V(**3**) in Table 3). In turn, this probably explains the significant difference of 100 °C between the melting points of **2** and **3** as well as the exclusive crystallization of **3** from solution of a mixture of the two anomers.

According to the literature,[7] the α-D-galactopyranose pentaacetate has a pyranose ring close to a perfect chair with nearly equal (but with opposite sign) values for the three pairs of torsion angles, and the magnitudes of the torsion angles are 50.3–59.1°. The value of θ[8] (2.7°) and the magnitudes of the torsion angles (52.0–58.5°) for **2** clearly reveals the pyranose ring with a slight distortion. Comparing the C–O bond lengths around the anomeric carbon in **2** within the α-D-galactopyranose pentaacetate, we found that both the exocyclic C(1)–O(2) bond and the endocyclic C(1)–O(1) bond are shorter in compound **2** than in galactopyranose pentaacetate (1.424, 1.399 Å vs 1.441, 1.406 Å). In contrast to compound **2**, the pyranose ring of **3** is much greater distorted away from the perfect chair of β-D-galactopyranose pentaacetate.[1] This is shown by the larger value of θ (8.1°) and the larger magnitude of the torsion angles of the pyranose ring in **3** (48.4–65.2°). β-D-Galactopyranose pentaacetate has a relatively smaller magnitude of the torsion angles (53.3–61.5°). Both the exocyclic C(1)–O(2) bond and the endocyclic C(1)–O(1) bond around the anomeric carbon are longer in compound **3** (1.438, 1.432 Å) than in β-D-galactopyranose pentaacetate (1.408, 1.408 Å). Table 4 contains some critical bond lengths, torsion angles and Cremer–Pople puckering parameters for **2** and **3**. From the above comparison we could conclude that the equatorial *O*-acetyl group at the anomeric carbon caused greater distortion of the pyranose ring of 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-D-galactose. Meanwhile, the different orientation of the *O*-acetyl groups at the anomeric carbon resulted in the greater difference of melting points and optical rotation between the α and β anomers of 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-D-galactose as described above.

Table 4. Critical bond lengths (Å) and torsion angles (°) and Cremer–Pople puckering parameters for **2** and **3**

	2	**3**
C(1)–C(2)	1.531(6)	1.514(6)
C(2)–C(3)	1.516(6)	1.509(6)
C(3)–C(4)	1.520(6)	1.531(6)
C(4)–C(5)	1.525(6)	1.527(6)
O(1)–C(5)	1.444(5)	1.429(5)
O(1)–C(1)	1.399(5)	1.432(5)
O(2)–C(1)	1.424(5)	1.438(4)
C(5)–O(1)–C(1)–C(2)	−58.5(4)	−62.0(4)
C(1)–O(1)–C(5)–C(4)	57.9(4)	65.2(4)
C(1)–C(2)–C(3)–C(4)	−53.7(4)	−48.4(4)
C(2)–C(3)–C(4)–C(5)	52.0(4)	49.3(4)
C(3)–C(4)–C(5)–O(1)	−52.7(4)	−57.4(4)
O(1)–C(1)–C(2)–C(3)	55.9(5)	53.5(4)
Puckering parameters		
Q (Å)	0.548(4)	0.563(4)
θ (°)	2.7(4)	8.1(4)

In conclusion, the paper describes the preparation, the unique anomerization, and the acetylation of the 4-chloro-4-deoxy-D-galactopyranose as well as the separation of the α and β anomers of the tetraacetates. The influence of the chlorine atom at C-4 and the *O*-acetyl group at anomeric carbon on the conformation of the pyranose ring of both the α and β anomers of 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-D-galactopyranose are also discussed. Through the above study, we developed a facile approach to 4-chloro-4-deoxy-α-D-galactopyranose and the two anomers of 1,2,3,6-tetra-*O*-acetyl-4-chloro-4-deoxy-D-galactopyranose.

1. Experimental

1.1. General methods

^{1}H and ^{13}C NMR spectra were acquired on a Bruker AVANCE DPX-400 spectrometer with chemical shifts (δ) given in parts per million relative to Me_4Si as an internal standard. Melting points were determined on a WC-1 melting-point apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 341 Polarimeter.

1.2. Single-crystal X-ray analysis

A single crystal suitable for data collection was mounted on a Rigaku RAXIS-IV single-crystal X-ray diffractometer. The X-ray diffraction data were collected using Mo K_α radiation (λ = 0.71073 Å) 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 nonhydrogen atoms were refined with anisotropic thermal parameters. All hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinement was based on 5585 reflections and 435 variable parameters for the crystal of **2**, and 3192 reflections and 218 variable parameters for the crystal of **3**. All calculations were performed using the SHELX-97 crystallographic software package.[9] Final atomic coordinates and equivalent isotropic displacement parameters for compound **2** and **3** are given in Tables 5 and 6.

4-Chloro-4-deoxy-α-D-galactopyranose (**4**): Concentrated sulfuric acid (0.4 mL) was added to a solution of **1** (3.24 g, 10 mmol) in H_2O (40 mL). The mixture was heated to 60 °C and kept for 2 h, followed by concentration to dryness under diminished pressure and

Table 5. Selected atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for compound **2**

	x	*y*	*z*	*U* (equiv)
Cl(1)	7636(2)	798(1)	268(1)	71(1)
O(1)	8039(3)	1336(3)	1099(1)	56(1)
O(2)	7431(3)	−259(3)	1502(1)	57(1)
O(3)	6414(5)	783(4)	1952(1)	104(1)
O(4)	4933(3)	−801(3)	1162(1)	63(1)
O(5)	3480(4)	928(4)	1170(1)	88(1)
O(6)	5995(3)	−1519(3)	513(1)	57(1)
O(7)	7401(4)	−3260(3)	458(1)	87(1)
O(8)	11,115(3)	683(3)	565(1)	67(1)
O(9)	12,095(4)	2578(4)	408(1)	93(1)
C(1)	6901(5)	684(4)	1260(1)	56(1)
C(2)	6001(4)	−38(4)	986(1)	49(1)
C(3)	6926(5)	−964(4)	775(1)	49(1)
C(4)	8199(4)	−256(4)	617(1)	48(1)
C(5)	8987(5)	496(4)	903(1)	50(1)
C(6)	10,130(5)	1413(4)	774(1)	62(1)
C(7)	7128(6)	−108(5)	1848(1)	67(1)
C(8)	7782(6)	−1158(5)	2055(1)	80(2)
C(9)	3693(6)	−192(5)	1239(1)	66(1)
C(10)	2694(6)	−1089(6)	1422(2)	111(2)
C(11)	6339(6)	−2689(4)	385(1)	60(1)
C(12)	5188(7)	−3139(5)	138(1)	86(2)
C(13)	12,074(5)	1415(5)	390(1)	66(1)
C(14)	13,118(6)	586(6)	195(1)	90(2)

U (equiv) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Table 6. Selected atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for compound **3**

	x	*y*	*z*	*U* (equiv)
Cl(1)	6207(2)	6662(1)	251(1)	77(1)
O(1)	4134(5)	4864(2)	862(1)	56(1)
O(2)	6365(5)	4124(2)	1588(1)	54(1)
O(3)	3411(6)	3129(2)	1775(2)	92(1)
O(4)	6340(4)	5757(2)	2332(1)	52(1)
O(5)	10,190(5)	5759(3)	2268(2)	78(1)
O(6)	6394(6)	7352(2)	1562(2)	63(1)
O(7)	3480(7)	8377(3)	1576(2)	101(1)
O(8)	−13(6)	4755(3)	97(2)	74(1)
O(9)	1790(9)	3904(4)	−613(3)	131(2)
C(1)	4755(6)	4870(3)	1505(2)	47(1)
C(2)	6063(7)	5745(3)	1664(2)	51(1)
C(3)	4762(7)	6601(3)	1471(2)	49(1)
C(4)	3876(7)	6541(3)	802(2)	55(1)
C(5)	2634(7)	5618(3)	718(2)	51(1)
C(6)	1803(8)	5457(3)	68(2)	64(1)
C(7)	5504(10)	3269(3)	1723(2)	63(1)
C(8)	7312(9)	2593(3)	1817(3)	70(1)
C(9)	8405(7)	5758(3)	2575(2)	55(1)
C(10)	8296(9)	5759(3)	3275(2)	71(1)
C(11)	5517(9)	8214(3)	1619(2)	65(1)
C(12)	7422(10)	8904(4)	1703(3)	79(2)
C(13)	178(10)	4022(4)	−254(3)	74(1)
C(14)	−1782(11)	3360(5)	−139(3)	98(2)

U (equiv) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

fractionation by chromatography with 8:1 $CHCl_3$–MeOH, afforded **4** (1.81 g, 91% yield): mp 147–150 °C (dec), $[\alpha]_D^{20}$ +134.0 (*c* 0.726, MeOH). ESIMS: $[M+Na]^+$ 221. Anal. Calcd for $C_6H_{11}ClO_5$: C, 36.29; H, 5.58. Found: C, 36.06; H, 5.69.

1,2,3,6-Tetra-*O*-acetyl-4-chloro-4-deoxy-α-D-galactose (**2**): Compound **4** obtained above (1.81 g, 9.1 mmol) was mixed with pyridine (15 mL), Ac_2O (10 mL), and catalytic amount of DMAP. The mixture was stirred at ambient temperature and monitored by TLC. After the disappearance of starting sugar, absolute EtOH (10 mL) was added. The mixture was continued to stir for 20 min, then partitioned by EtOAc and H_2O. The EtOAc layer was washed with water (20 mL × 2), dried over anhyd Na_2SO_4 and evaporated, affording compound **2** as a white solid (3.00 g, 82% yield from **1**). Recrystallization from absolute EtOH gave a needle product: mp 76–78 °C, $[\alpha]_D^{20}$ +146.5 (*c* 1.03, $CHCl_3$). ESIMS: $[M+Na]^+$ 389. Anal. Calcd for $C_{14}H_{19}ClO_9$: C, 45.85; H, 5.22. Found: C, 45.66; H, 5.37.

1,2,3,6-Tetra-*O*-acetyl-4-chloro-4-deoxy-β-D-galactose (**3**): Concentrated H_2SO_4 (0.4 mL) was added to a solution of **1** (3.24 g, 10 mmol) in H_2O (40 mL). The mixture was heated to 60 °C and kept for 2 h, followed by concentration to dryness under diminished pressure. The residue obtained was acetylated directly in the presence of a catalytic amount of DMAP with Ac_2O in pyridine. After completion of the acetylation, absolute EtOH (10 mL) was added. The mixture was allowed to stir for 20 min, then partitioned by EtOAc and H_2O. The EtOAc layer was washed with H_2O (20 mL × 2), concentrated, and fractioned by chromatography with 10:1 $CHCl_3$–EtOAc to give a mixture of α and β anomers of acetates in a ratio of 1:2. The anomeric acetates were separated by crystallization from hot absolute EtOH to afford compound **3** as needles (1.86 g, 51% yield from **1**): mp 176–177 °C, $[\alpha]_D^{20}$ +64.8 (*c* 0.58, $CHCl_3$). ESIMS: $[M+Na]^+$ 389. Anal. Calcd for $C_{14}H_{19}ClO_9$: C, 45.85; H, 5.22. Found: C, 45.69; H, 5.45.

2. Supplementary materials

Complete crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC 250116 (compound **2**) and CCDC 250117 (compound **3**). 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, deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

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References

1. Thibodeaux, D. P.; Johnson, G. P.; Stevens, E. D.; French, A. D. *Carbohydr. Res.* **2002**, *337*, 2301–2310.
2. Teranishi, K. *Carbohydr. Res.* **2002**, *337*, 613–619.
3. James, L. C.; Roversi, P.; Tawfik, D. S. *Science* **2003**, *299*, 1362–1367.
4. (a) Chowdhary, M. S.; Hough, L.; Anthony, C. *Carbohydr. Res.* **1986**, *147*, 49–56; (b) Guthrie, R. D.; Jenkins, I. D.; Thang, S.; Yamasaki, R. *Carbohydr. Res.* **1988**, *176*, 306–313; (c) Isaacs, N. W.; Kennard, C. H. L. G.; O'Donnell, W.; Richards, G. N. *J. Chem. Soc., Chem. Commun.* **1970**, 360–361; (d) Bolton, C. H.; Hough, L.; Khan, R. *Carbohydr. Res.* **1972**, *21*, 133–143; (e) Khan, R. *Carbohydr. Res.* **1972**, *22*, 441–445; (f) Buchanan, J. G.; Cummerson, D. A.; Turner, D. M. *Carbohydr. Res.* **1972**, *21*, 283–293; (g) Khan, R.; Jenner, M. R.; Mufti, K. S. *Carbohydr. Res.* **1975**, *39*, 253–262; (h) Ball, D.; Bissett, H. F. H.; Chalk, R. C. *Carbohydr. Res.* **1977**, *55*, 149–163; (i) Gurjar, M. K.; Hough, L.; Richardson, A. C. *Carbohydr. Res.* **1980**, *78*, C21–C23; (j) Chiu, A. K. B.; Gurjar, M. K.; Hough, L.; Sincharoenkul, L. V.; Richardson, A. C. *Carbohydr. Res.* **1982**, *100*, 247–261.
5. Liu, F. W.; Liu, H. M.; Ke, Y.; Zhang, J. *Carbohydr. Res.* **2004**, *339*, 2651–2656.
6. Tvaroška, I.; Taravel, F. R.; Utille, J. P.; Carver, J. P. *Carbohydr. Res.* **2002**, *337*, 353–367.
7. Roslund, M. U.; Klika, K. D.; Lehtilä, R. L.; Tähtinen, P.; Sillanpää, R.; Leino, R. *J. Org. Chem.* **2004**, *69*, 18–25.
8. Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358.
9. Sheldrick, G. M. *SHELXS-97*; Göttingen, Germany, 1997.