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Note

The molecular and crystal structure of two trichloroethylidene acetals of epimerized monosaccharides [1]

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Recently, we reported a new method for stereospecific epimerizations of carbohydrates [1–4]. Thus, unprotected pyranosides or 1-thio-pyranosides, having a 2,3-*cis*-/3,4-*trans*- or 2,3-*trans*-/3,4-*cis*-arrangement of three contiguous OH groups (i.e., lyxose, arabinose, mannose, or galactose derivatives), react stereospecifically with carbonyl-active aldehydes or ketones in the presence of dicyclohexylcarbodiimide (DCC) as coreagent with inversion at the middle chiral carbon atom; Scheme 1. By this route, a suitable monosaccharide moiety of disaccharides can also be epimerized selectively [4c].

The key step of the reactions is the in situ formation of a cyclic imidocarbonic ester intermediate (or sometimes an isourea function) [1,2,4,5], which is attacked by a deprotonated neighbouring hemiacetal moiety in an intramolecular S_N2-type reaction forming a cyclic acetal.

The structures of the inverted sugars were supported by NMR data [1–5]. Methyl 6-deoxy-3,4-*O*-hexafluoroisopropylidene-α-L-altropyranoside, prepared from methyl α-L-rhamnoside–hexafluoroacetone–DCC [3], was investigated by X-ray crystallography [6]. We have now obtained suitable crystals of the *endo*-H configured chloral acetals 2-*O*-cyclohexylcarbamoyl-6-*O*-formyl-[(*R*)-3,4-*O*-(2,2,2-trichloroethylidene)]-α-D-altropyranosyl fluoride (**1**) [1] and methyl [(*S*)-3,4-*O*-(2,2,2-trichloroethylidene)]-α-D-

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[1] Dedicated to Professor Dr Heinz Dehne on the occasion of his 60th birthday.

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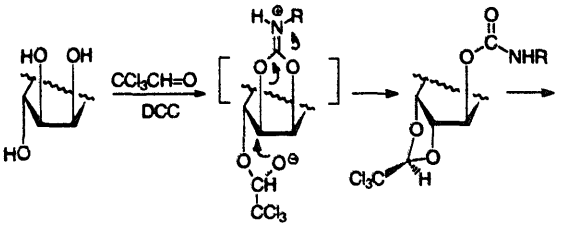
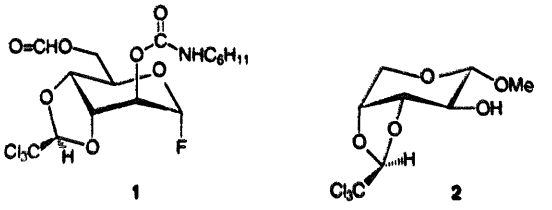


Scheme 1.

arabinopyranoside (**2**) [2], in order to give additional proof for the structure of these compounds by X-ray crystallography.



Compound **1** was prepared from methyl α-D-mannopyranoside–chloral–DCC, forming methyl 2-*O*-cyclohexylcarbamoyl-6-*O*-formyl-[(*R*)-3,4-*O*-(2,2,2-trichloroethylidene)]-α-D-altropyranoside, and its treatment with HF–nitromethane–acetic anhydride [1]. Compound **2** was synthesized from methyl α-D-lyxopyranoside–chloral–DCC, following decarbamoylation of the methyl 2-*O*-cyclohexylcarbamoyl-[(*S*)-3,4-*O*-(2,2,2-trichloroethylidene)]-α-D-arabinopyranoside formed [2]. The NMR data of compounds **1** and **2** (recorded in Me_2SO-d_6 and $CDCl_3$, respectively) allowed the conclusion that the altrosyl fluoride **1** adopts a $^1C_4$ chair conformation [1], whereas the arabinopyranoside **2** adopts a $^4C_1$ conformation [2]; formulae **1** and **2**.

The crystal structures of compounds **1** and **2** are shown in Figs. 1 and 2, respectively. The X-ray structures show, in both cases, the inversion at C-3, the *endo*-H arrangement

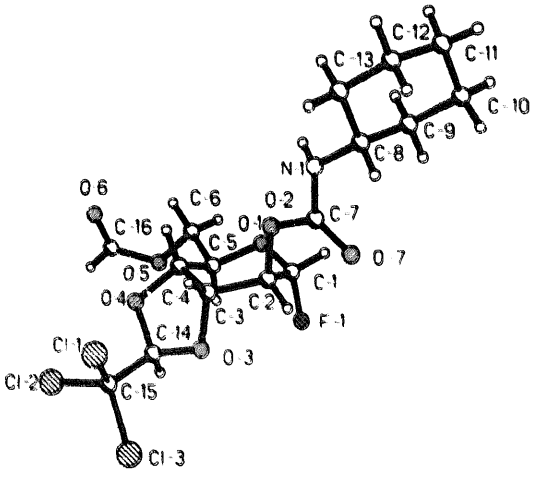


Fig. 1. Crystal structure of the altrosyl fluoride **1**.

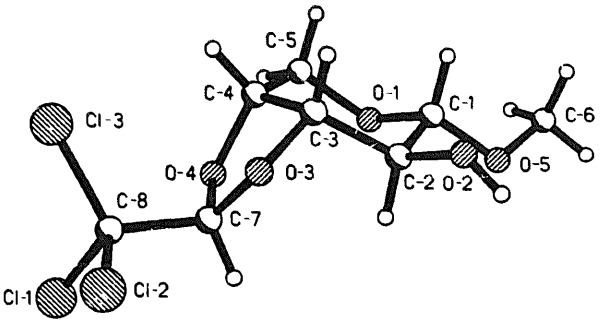


Fig. 2. Crystal structure of the arabinoside **2**.

Table 1
Atomic positional parameters and equivalent thermal parameters of 2-*O*-cyclohexylcarbamoyl-6-*O*-formyl-[(*R*)-3,4-*O*-(2,2,2-trichloroethylidene)]-α-D-altropyranosyl fluoride (**1**)

Atom	*x*	*y*	*z*	*U* (Å^2)
Cl-1	0.48515(7)	0.7671(2)	0.08725(7)	0.0485(3)
Cl-2	0.59160(10)	0.7897(2)	0.29290(7)	0.0620(3)
Cl-3	0.55116(9)	1.2203(2)	0.18140(8)	0.0571(3)
F-1	0.9188(2)	1.1030(5)	0.0619(2)	0.0748(9)
O-1	0.9508(2)	0.7072(6)	0.0836(2)	0.0566(8)
O-2	0.7560(3)	0.6535(6)	−0.0958(2)	0.0560(8)
O-3	0.7017(2)	0.9787(5)	0.0891(2)	0.0409(6)
O-4	0.7373(2)	0.6601(5)	0.1899(2)	0.0415(6)
O-5	0.9885(4)	0.5544(11)	0.3224(3)	0.0679(14)
O-6	0.9082(6)	0.2065(18)	0.3271(6)	0.124(3)
O-5′	0.9300(10)	0.3657(24)	0.2823(9)	0.086(3)
O-6′	0.9789(17)	0.6623(43)	0.3863(15)	0.162(7)
O-7	0.7393(3)	0.9171(6)	−0.2135(2)	0.0698(10)
N-1	0.7209(4)	0.5210(8)	−0.2430(3)	0.0642(12)
H-N(1)	0.7476(23)	0.4113(93)	−0.2244(16)	0.080
C-1	0.8993(4)	0.8803(8)	0.0179(3)	0.0561(12)
C-2	0.7744(4)	0.8485(8)	−0.0306(3)	0.0482(10)
C-3	0.7190(3)	0.7717(8)	0.0387(2)	0.0415(9)
C-4	0.7872(3)	0.6142(7)	0.1206(2)	0.0384(9)
C-5	0.9086(3)	0.6859(9)	0.1602(3)	0.0487(11)
C-6	0.9839(4)	0.5006(11)	0.2262(3)	0.072(2)
C-7	0.7379(3)	0.7156(9)	−0.1882(3)	0.0498(10)
C-8	0.7016(4)	0.5311(8)	−0.3456(3)	0.0544(11)
C-9	0.8037(5)	0.5599(18)	−0.3627(4)	0.116(3)
C-10	0.7871(7)	0.5629(18)	−0.4680(4)	0.139(4)
C-11	0.7259(5)	0.3511(11)	−0.5185(3)	0.077(2)
C-12	0.6241(4)	0.3184(14)	−0.5021(3)	0.088(2)
C-13	0.6396(5)	0.3163(14)	−0.3960(3)	0.092(2)
C-14	0.7022(3)	0.8998(7)	0.1779(3)	0.0374(9)
C-15	0.5865(3)	0.9149(7)	0.1834(3)	0.0400(9)
C-16	0.9442(10)	0.3815(25)	0.3608(8)	0.077(3)
C-16′	0.9383(23)	0.4811(44)	0.3663(16)	0.075(8)

Table 2
Atomic positional parameters and equivalent thermal parameters of methyl [(*S*)-3,4-*O*-(2,2,2-trichloroethylidene)]-α-D-arabinopyranoside (**2**)

Atom	*x*	*y*	*z*	*U* (Å²)
Cl-1	0.8652(2)	0.48484(13)	0.45478(5)	0.0773(4)
Cl-2	1.1394(2)	0.66205(11)	0.53126(6)	0.0718(4)
Cl-3	1.2609(2)	0.39271(13)	0.52778(7)	0.0857(5)
O-1	0.5353(4)	0.2533(2)	0.71229(11)	0.0460(6)
O-2	0.7893(4)	0.5454(3)	0.78283(14)	0.0521(7)
H-O(2)	0.6787(21)	0.5893(34)	0.7942(19)	0.080
O-3	0.9946(4)	0.5111(2)	0.64718(12)	0.0472(6)
O-4	0.7923(5)	0.3548(2)	0.59234(12)	0.0490(6)
O-5	0.4015(5)	0.3866(2)	0.79470(12)	0.0488(6)
C-1	0.5979(6)	0.3406(3)	0.7645(2)	0.0416(8)
C-2	0.7192(6)	0.4557(3)	0.7334(2)	0.0397(8)
C-3	0.9312(6)	0.4144(3)	0.6951(2)	0.0429(8)
C-4	0.8928(7)	0.2974(3)	0.6513(2)	0.0474(9)
C-5	0.7339(7)	0.1977(4)	0.6812(2)	0.0566(10)
C-6	0.2955(8)	0.2999(4)	0.8414(2)	0.0634(11)
C-7	0.8714(6)	0.4822(3)	0.5885(2)	0.0436(8)
C-8	1.0313(7)	0.5020(4)	0.5285(2)	0.0548(10)

of the cyclic acetal moiety, as well as the different chair conformations of **1** ($^4C_1$) and **2** ($^1C_4$). The corresponding positional and isotropic thermal parameters of the non-hydrogen atoms as well as the bond lengths and angles of these compounds are summarized in Tables 1–4.

Compound **2** forms an interesting network of hydrogen bonds and short contacts. While layers are formed by hydrogen bonds between the hydrogen at O-2 and the ring O-1 (211.1 pm) in the next molecule, the layers are packed via short contacts between O-5 and a hydrogen at C-3 as well as between O-2 and one of the hydrogens at C-5.

The speciality of the crystal lattice of compound **1** is the one-dimensional linkage via short contacts. These contacts occur between chlorine atoms (335.9 pm) and between F-1 and the hydrogens at C-6 (246.3 and 243.6 pm). Additional short contacts can be found between O-7 and a hydrogen of C-13 in the cyclohexyl moiety (258.0 pm) as well as between the carbonyl oxygen O-6 and the hydrogen at C-14 (232.4 pm). However, one must take into consideration that there is a disorder problem of the formyl group at C-6. The refinement, including distance restraints, provided optimal results with a ratio of 2:1 in the site occupation factors for O-5, C-16, O-6, and the other positions O-5′, C-16′ and O-6′. The prevalence of one occupation might be explained by the fact that the short contact mentioned above is only between O-6 and the hydrogen at C-14. There are no short contacts of O-6′.

The puckering parameters [7] for the altropyranose ring in **1** are $Q = 0.479(4)$ Å (puckering amplitude), $\Theta = 18.3(5)°$, and $\Phi = 333.2(17)°$; for the 6-membered ring in **2**, $Q = 0.532(4)$ Å (puckering amplitude), $\Theta = 161.9(4)°$, and $\Phi = 219.3(13)°$. These parameters were obtained by Platon calculations [8].

1. Experimental

Single crystals of dimensions 0.82 × 0.37 × 0.21 mm and 0.98 × 0.50 × 0.38 mm for **1** and **2** were used for the investigations. The unit cells were determined from 48 and 52 reflections, respectively. The unit cell parameters and other data of interest for **1** and **2** are listed in Table 5. The data collections were performed on a Siemens P4 four-circle-diffractometer using an Mo K_α normal focus sealed tube and a graphite monochromator. In both cases, the data were collected in a routine ω-scan, for **1** within the range of $3.5° < 2\Theta < 45°$, and within $3.5° < 2\Theta < 48°$ for **2**. The structures were resolved using Directs Methods (Siemens SHELXTL). The data sets were refined on F^2 [9]. All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were put into their theoretical positions and refined according to the riding model [10]. For the

Table 3
Bond lengths (Å) and angles (°) of compound **1**

Atoms		Distance	Atoms		Distance	Atoms		Distance
1	2		1	2		1	2	
Cl-1	C-15	1.765(4)	O-5	C-16	1.359(12)	C-3	C-4	1.511(5)
Cl-2	C-15	1.769(4)	O-5	C-6	1.458(6)	C-4	C-5	1.519(5)
Cl-3	C-15	1.773(4)	O-6	C-16	1.127(14)	C-5	C-6	1.521(7)
F-1	C-1	1.395(5)	O-5′	C-16′	1.39(2)	C-8	C-9	1.448(7)
O-1	C-1	1.373(6)	O-5′	C-6	1.484(9)	C-8	C-13	1.494(8)
O-1	C-5	1.448(5)	O-6′	C-16′	1.14(2)	C-9	C-10	1.517(7)
O-2	C-7	1.368(5)	O-7	C-7	1.196(6)	C-10	C-11	1.477(9)
O-2	C-2	1.431(5)	N-1	C-7	1.337(6)	C-11	C-12	1.440(7)
O-3	C-14	1.405(4)	N-1	C-8	1.471(5)	C-12	C-13	1.533(6)
O-3	C-3	1.449(5)	N-1	H-N(1)	0.71(6)	C-14	C-15	1.534(5)
O-4	C-14	1.411(5)	C-1	C-2	1.524(6)			
O-4	C-4	1.436(4)	C-2	C-3	1.527(5)			

Atoms			Angle	Atoms			Angle	Atoms			Angle
1	2	3		1	2	3		1	2	3	
C-1	O-1	C-5	113.9(3)	O-3	C-3	C-2	109.3(3)	C-8	C-9	C-10	113.3(5)
C-7	O-2	C-2	115.1(3)	C-4	C-3	C-2	116.1(3)	C-11	C-10	C-9	111.9(6)
C-14	O-3	C-3	107.2(3)	O-4	C-4	C-3	101.6(3)	C-12	C-11	C-10	111.6(5)
C-14	O-4	C-4	106.7(3)	O-4	C-4	C-5	110.1(3)	C-11	C-12	C-13	113.5(4)
C 16	O-5	C-6	113.8(7)	C-3	C-4	C-5	112.2(3)	C-8	C-13	C-12	111.4(5)
C-16′	O-5′	C-6	112.5(16)	O-1	C-5	C-4	110.4(3)	O-3	C-14	O-4	108.2(3)
C-7	N-1	C-8	122.7(4)	O-1	C-5	C-6	103.7(3)	O-3	C-14	C-15	111.6(3)
C-7	N-1	H-N(1)	121.3(3)	C-4	C-5	C-6	113.6(4)	O-4	C-14	C-15	108.8(3)
C-8	N-1	H-N(1)	108.5(3)	O-5	C-6	C-5	106.9(4)	C-14	C-15	Cl-1	112.3(3)
O-1	C-1	F-1	109.7(4)	C-5	C-6	O-5′	113.4(6)	C-14	C-15	Cl-2	108.8(3)
O-1	C-1	C-2	114.4(4)	O-7	C-7	N-1	126.6(4)	Cl-1	C-15	Cl-2	109.8(2)
F-1	C-1	C-2	108.0(4)	O-7	C-7	O-2	123.2(4)	C-14	C-15	Cl-3	107.7(3)
O-2	C-2	C-1	107.4(3)	N-1	C-7	O-2	110.2(4)	Cl-1	C-15	Cl-3	109.3(2)
O-2	C-2	C-3	104.4(3)	C-9	C-8	N-1	112.0(4)	Cl-2	C-15	Cl-3	108.8(2)
C-1	C-2	C-3	112.9(3)	C-9	C-8	C-13	110.9(5)	O-6	C-16	O-5	127.1(10)
O-3	C-3	C-4	101.6(3)	N-1	C-8	C-13	110.8(4)	O-6′	C-16′	O-5′	122.3(27)

Table 4
Bond lengths (Å) and angles (°) of compound **2**

Atoms		Distance	Atoms		Distance	Atoms		Distance
1	2		1	2		1	2	
Cl-1	C-8	1.776(4)	O-2	H-O(2)	0.82	O-5	C-6	1.438(5)
Cl-2	C-8	1.775(4)	O-3	C-7	1.410(4)	C-1	C-2	1.520(5)
Cl-3	C-8	1.752(4)	O-3	C-3	1.438(4)	C-2	C-3	1.514(5)
O-1	C-1	1.432(4)	O-4	C-7	1.401(4)	C-3	C-4	1.514(5)
O-1	C-5	1.434(5)	O-4	C-4	1.448(4)	C-4	C-5	1.511(5)
O-2	C-2	1.420(4)	O-5	C-1	1.378(4)	C-7	C-8	1.536(5)

Atoms			Angle	Atoms			Angle	Atoms			Angle
1	2	3		1	2	3		1	2	3	
C-1	O-1	C-5	111.6(3)	O-2	C-2	C-1	111.1(3)	O-4	C-7	O-3	108.8(3)
C-2	O-2	H-O(2)	109.5(2)	C-3	C-2	C-1	111.4(3)	O-4	C-7	C-8	111.6(3)
C-7	O-3	C-3	106.3(3)	O-3	C-3	C-4	102.0(3)	O-3	C-7	C-8	108.6(3)
C-7	O-4	C-4	107.4(3)	O-3	C-3	C-2	110.5(3)	C-7	C-8	Cl-3	112.4(3)
C-1	O-5	C-6	115.2(3)	C-4	C-3	C-2	113.6(3)	C-7	C-8	Cl-2	108.4(3)
O-5	C-1	O-1	109.3(3)	O-4	C-4	C-5	111.1(3)	Cl-3	C-8	Cl-2	109.6(2)
O-5	C-1	C-2	107.1(3)	O-4	C-4	C-3	101.9(2)	C-7	C-8	Cl-1	108.1(3)
O-1	C-1	C-2	108.2(3)	C-5	C-4	C-3	114.1(3)	Cl-3	C-8	Cl-1	110.0(2)
O-2	C-2	C-3	107.8(3)	O-1	C-5	C-4	112.9(3)	Cl-2	C-8	Cl-1	108.2(2)

Table 5
Crystal data and structure determination and refinement data for **1** and **2**

	1	**2**
Molecular formula	$C_{16}H_{21}Cl_3FNO_7$	$C_8H_{11}Cl_3O_5$
Molecular weight	464.69	293.52
Melting point	104–106 °C [1]	115–116 °C [2]
Crystal system	Monoclinic	Orthorhombic
Space group	$P2_1$	$P2_12_12_1$
Cell dimensions:		
a	12.9590(10)	5.8140(10)
b	5.6170(10)	10.3680(10)
c	15.0350(10)	20.073(2)
α	90	90
β	111.410(10)	90
γ	90	90
Cell volume (Å^3)	1018.9(2)	1210.0(3)
Z	2	4
$F(000)$	480	600
μ (Mo K_α) cm^{-1}	5	7.6
Density (calcd)	1.515	1.611
% Decay of standards	7.8	8.12
Number of reflections	3086	1898
Number of independent reflections used for refinement	2639	1570
Reflections observed	2515	1533
Number of parameters	268	146
$R1$ for observed reflections	0.0396	0.0427
$R1$ for all	0.0419	0.0434
w$R2$ for all	0.1066	0.1153
S	1.046	1.064

refinement of the positions of the disordered formyl group atoms in **1** the advantages of SHELXL-93 calculations, including distance restraints, were used [10]. The density in the final difference Fourier map was between 0.246 and −0.26 for **1** and 0.194 and −0.28 for **2**. [2]

References

[1] R. Miethchen and D. Rentsch, *Synthesis*, (1994) 827–831.
[2] R. Miethchen and D. Rentsch, *Liebigs Ann. Chem.*, (1994) 1191–1197.
[3] R. Miethchen, D. Rentsch, and M. Michalik, *Liebigs Ann. Chem.*, (1994) 219–222.
[4] (a) R. Miethchen and D. Rentsch, *J. Prakt. Chem. / Chem.-Ztg.*, 337 (1995) 422–423; (b) R. Miethchen, D. Rentsch, and M. Frank, *J. Carbohydr. Chem.*, 15(1) (1996) in press; (c) R. Miethchen, D. Rentsch, M. Frank, and A. Lipták, *Carbohydr. Res.*, 281 (1996) 61–68.
[5] E. Vowinkel and P. Gleichenhagen, *Tetrahedron Lett.*, (1974) 139–142.
[6] J. Kopf, G. Sheldrick, D. Rentsch, H. Reinke, and R. Miethchen, *Acta Crystallogr., Sect. C*, 51 (1995) 1198–1201.
[7] D. Cremer and J.A. Pople, *J. Am. Chem. Soc.*, 97 (1975) 1354–1358.
[8] A.L. Spek, Platon-93, University of Utrecht, 1993.
[9] G.M. Sheldrick, *Acta Crystallogr., Sect. A*, 46 (1990) 467.
[10] G.M. Sheldrick, SHELXL-93, Universität Göttingen, 1993.

[2] Further details of the crystal structure investigations are available on request from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftliche Information mbH, D-76344 Eggenstein-Leopoldshafen, Germany, on quoting the depository number CSD-401978 (**1**) and CDS-401979 (**2**), the names of the authors, and the journal citation.