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THE CRYSTAL AND MOLECULAR STRUCTURE OF HEXA-*O*-ACETYLCARRABIOSE DIMETHYL ACETAL

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ABSTRACT

The crystal and molecular structure of hexa-*O*-acetylcarrabiose dimethyl acetal is reported. This is the first structural study of a carrageenan fragment, and the stereochemistry of the D-galactose and 3,6-anhydro-D-galactose residues are of interest in relation to the conformations of carrageenan chains in solution and in the solid state.

INTRODUCTION

Carrageenans are a family of sulphated D-galactans which occur in the cells and intercellular regions of red algae (*Rhodophyceae*). The polysaccharides are based on an alternating sequence of α-(1→3)- and β-(1→4)-linked D-galactosyl residues, although individual carrageenan samples differ according to the location of sulphate and the degree of sulphation as well as the occurrence of 3,6-anhydro-D-galactose[1].

Molecular models, derived from X-ray fibre diffraction and model building studies, have been proposed to account for the ability of some carrageenan preparations to form gels through selective interactions with cations[2,3]. More recently, however, it has been suggested that non-specific competition by cations for water may be more important in promoting the interactions between polysaccharide chains which lead to the formation of a gel network, rather than specific conformational transitions[4].

One approach to the problem of identifying the nature of the intermolecular interactions in polysaccharides is to study oligomeric fragments by such techniques as X-ray crystallography. The data obtained may be useful for providing important stereochemical parameters for exploring conformations in solution and in the solid state.

The present investigation describes the crystal and molecular structure of

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TABLE I

DATA FOR HEXA-*O*-ACETYLCARRABIOSE DIMETHYL ACETAL

Molecular formula	$C_{26}H_{38}O_{17}$	Cell volume (Å^3)	1641.0
Molecular weight	622.5	Z	2
Crystal system	Monoclinic	$F(000)$ (e)	660.0
Space group	$P2_1$	μ (Cu K$_\alpha$) (cm^{-1})	8.77
Cell dimensions (Å)		D_c (kg.m^{-3})	1.260
a	12.567(2)		
b	8.825(1)		
c	15.671(3)		
β (deg.)	109.23(1)		

hexa-*O*-acetylcarrabiose dimethyl acetal, the first reported structural study of a fragment from carrageenans.

EXPERIMENTAL

3,6-Anhydro-4-*O*-β-D-galactopyranosyl-D-galactose dimethyl acetal hexaacetate (hexa-*O*-acetylcarrabiose dimethyl acetal) was prepared by the method described by Araki and Hirase, starting from the partial methanolysis of the mucilage of *Chondrus crispus*[5].

Crystals were grown by slow concentration of an aqueous ethanolic solution. A crystal (0.68 × 0.14 × 0.13 mm) was sealed in a Lindemann glass capillary and set on an Enraf-Nonius CAD-4F diffractometer. Accurate unit-cell parameters were determined by a least-squares fit of measurements of 32 reflections with $25° < \theta < 34°$. The crystal data are given in Table I.

The intensity data were collected in the $\omega - 2\theta$ scan mode, using Nickel-filtered Cu-K$_\alpha$ radiation up to $\theta = 70°$ for a total of 6790 reflections (h − 15 to 15, k − 10 to 0, l −19 to 19) of which 5467 were non-zero. The control reflection 4 − 3 − 7 was measured every hour of exposure time (164 measurements overall), with an average value of 2006.0 counts and a standard deviation (of the distribution) of 80.9 (4.0%). Lorentz and polarisation corrections were applied, but no absorption correction was made. The data were merged using the SHELX program[6] to give 3022 unique reflections, merging $R = 0.02$, of which 2819 with $F_o > 4\sigma(F_o)$ were used in the following calculations.

STRUCTURE DETERMINATION AND REFINEMENT

The structure was solved by integrated Patterson-search and direct methods, using the SHELX-84 and PATSEE suites of programs[7,8]. The orthogonal coordinates of the average ring for the galactopyranose moiety were chosen, from the literature, as the search-fragment[9]. The default parameters were used throughout and the best solution on the basis of the combined figure of merit showed, by tangent expansion and Fourier recycling, the complete structure.

TABLE II

FRACTIONAL COORDINATES AND U_{eq} (Å^2) OF THE NON-HYDROGEN ATOMS

Atom	*Reducing residue*				*Non-reducing residue*			
	x	*y*	*z*	U_{eq}*	*x*	*y*	*z*	U_{eq}*
C-1	1.2410(4)	−0.0185(0)	0.9005(4)	0.086	0.8061(3)	−0.2834(10)	0.6942(2)	0.051
C-2	1.1206(3)	−0.0167(10)	0.8396(3)	0.061	0.8124(3)	−0.3449(10)	0.6055(2)	0.051
C-3	1.0578(3)	−0.1405(10)	0.8702(3)	0.056	0.6938(3)	−0.3764(10)	0.5409(2)	0.051
C-4	0.9324(3)	−0.1512(10)	0.8200(2)	0.052	0.6277(3)	−0.4732(10)	0.5859(3)	0.053
C-5	0.8805(4)	−0.1819(11)	0.8953(3)	0.068	0.6337(3)	−0.4036(10)	0.6768(3)	0.055
C-6	0.9853(5)	−0.2166(12)	0.9750(3)	0.083	0.5860(4)	−0.4994(12)	0.7352(3)	0.077
O-2	1.0661(3)	0.1265(9)	0.8389(2)	0.067	0.8621(2)	−0.2323(9)	0.5642(2)	0.059
O-3	1.0697(3)	−0.1231(10)	0.9625(2)	0.070	0.7057(2)	−0.4498(9)	0.4634(2)	0.060
O-4	0.9154(2)	−0.2693(9)	0.7544(2)	0.054	0.6794(2)	−0.6223(9)	0.6041(2)	0.059
O-5	0.8333(3)	−0.0443(10)	0.9157(3)	0.090	0.7491(2)	−0.3888(9)	0.7317(2)	0.056
O-6	—	—	—	—	0.4611(2)	−0.4956(10)	0.6871(2)	0.084
CAC-1	1.3122(11)	0.2501(19)	0.9388(6)	0.210	—	—	—	—
OAC-1	1.2919(4)	0.1214(11)	0.8747(3)	0.120	—	—	—	—
CAC-2	1.4133(6)	−0.1336(21)	0.9366(7)	0.181	—	—	—	—
OAC-2	1.2936(4)	−0.1296(12)	0.8857(4)	0.137	—	—	—	—
CA-2	1.0306(6)	0.2005(12)	0.7608(4)	0.095	0.9736(4)	−0.2474(11)	0.5744(3)	0.069
OA-2	1.0325(7)	0.1526(12)	0.6927(3)	0.164	1.0301(3)	−0.3480(10)	0.6156(3)	0.089
CM-2	0.9944(10)	0.3565(13)	0.7717(6)	0.136	1.0095(6)	−0.1230(12)	0.5263(4)	0.097
CA-3	—	—	—	—	0.6196(4)	−0.4319(11)	0.3842(3)	0.072
OA-3	—	—	—	—	0.5413(4)	−0.3517(11)	0.3774(2)	0.101
CM-3	—	—	—	—	0.6384(6)	−0.5256(14)	0.3111(4)	0.108
CA-4	—	—	—	—	0.6345(4)	−0.7312(10)	0.5425(3)	0.070
OA-4	—	—	—	—	0.5564(3)	−0.7112(10)	0.4747(2)	0.081
CM-4	—	—	—	—	0.6953(5)	−0.8777(11)	0.5700(5)	0.100
CA-5	0.7269(6)	−0.0143(12)	0.8704(4)	0.098	—	—	—	—
OA-5	0.6722(5)	−0.0931(12)	0.8112(4)	0.143	—	—	—	—
CM-5	0.6864(7)	0.1315(15)	0.8980(7)	0.146	—	—	—	—
CA-6	—	—	—	—	0.3999(5)	−0.5457(14)	0.7345(6)	0.110
OA-6	—	—	—	—	0.4391(5)	−0.5816(15)	0.8105(4)	0.176
CM-6	—	—	—	—	0.2782(6)	−0.5535(19)	0.6803(7)	0.157

*$U_{eq} = 1/3\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i \mathbf{a}_j$.

The structure was then refined isotropically ($R = 0.140$, unit weights) and anisotropically, minimising the function $\Sigma w|F_o| - |F_c|)^2$ where $w = 3.0764/[\sigma^2(F_o) + 0.000853(F_o)^2]$, together with anisotropic refinement of the overall scale factor. Subsequent difference Fourier syntheses revealed all the hydrogen atoms. These were included in the later refinement: the methyl groups were refined as rigid groups and the remaining hydrogen atoms were refined positionally with fixed U_{iso} values equal to the U_{eq} of the carrier atoms. The final R and R_w values are 0.0537 and 0.0759, respectively. In the final cycle of SFLS refinement, the average shift/e.s.d. is 0.080. The final difference Fourier synthesis shows maximum and minimum electron densities of 0.26 and −0.26 $eÅ^{-3}$, respectively. The atomic scattering factors used were taken from the International Tables for X-Ray Crystallography[10].

The potential parameters and U_{eq} values of the heavy atoms are listed in Table II. Hydrogen atom coordinates, anisotropic thermal vibration parameters, and the observed and calculated structure factors have been deposited*.

RESULTS AND DISCUSSION

A view of the molecule with the numbering of the atoms is shown in Fig. 1[11].

Molecular geometry. — Tables of bond lengths and angles involving the non-hydrogen atoms have been deposited*. The values conform to those observed in other D-galactose analogues[12,13].

As generally happens in pyranosyl compounds, the anomeric C-1′–O-4 bond at the glycosidic junction is shorter than the C-1′–O-5′ bond. This difference is due to the anomeric effect, which also seems to influence the exocyclic C-5′–C-6′ and C-6′–O-6′ bonds since these are shorter and longer, respectively, than the accepted values for a C–C and C–O single bond.

In the present structure, the β-(1→4) glycosidic linkage has bond lengths C-4–O-4 [1.430(5) Å], C-1′–O-4 [1.392(4) Å], and valence angle C-4–O-4–C-1′ [115.6(3)°] in agreement with the literature values[13]. The relative ring-to-ring orientation is described, according to Sundaralingam[14], by the dihedral angles φ = O-5′–C-1′–O-4–C-4 and ψ = C-1′–O-4–C-4–C-3, which are −91.7(7)° and −172.6(5)°, respectively. As shown in Table III, the expected $^4C_1$ chair conformation is found for the pyranose residue with C-3′ and O-5′ displaced out of the least-squares plane defined by C-1′,2′,4′,5′ by 0.63(1) and −0.69(1) Å. The 3,6-anhydro-D-galactose residue shows a half-chair conformation with C-6 and O-3 displaced out of the least-squares plane defined by C-3,4,5 by −0.29(1) and 0.35(1) Å, whereas the five-membered ring in the crystal and molecular structure of methyl 3,6-anhydro-α-D-galactopyranoside[15] shows an envelope conformation.

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*The vibrational parameters U_{ij} of the heavy atoms, their bond lengths and bond angles, the coordinates and U_{iso} values of the H atoms, and a list of F_o and F_c structure factors are deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/344/*Carbohydr. Res.*, 155 (1986) 11–17.

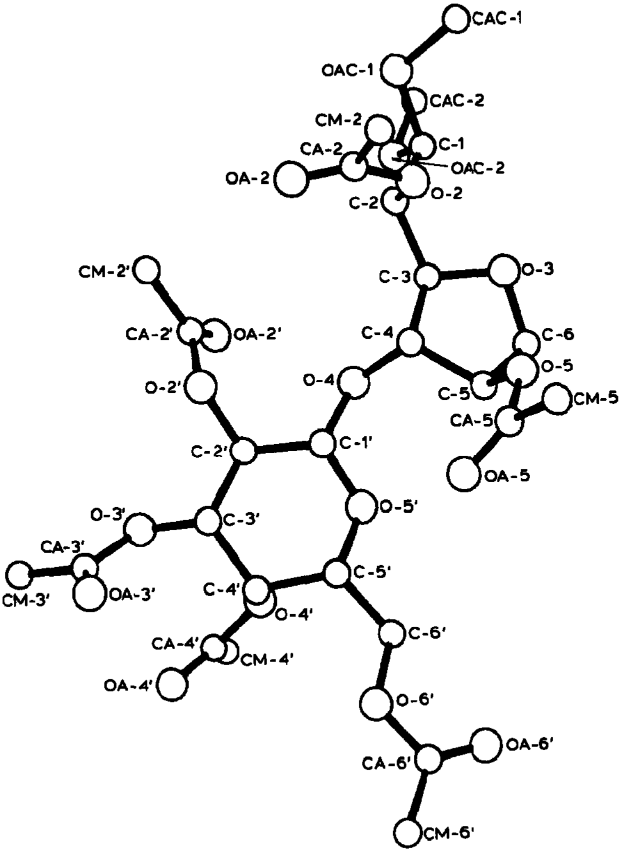

Fig. 1. Conformation and atom numbering of hexa-*O*-acetylcarrabiose dimethyl acetal. CA, CM, and OA refer to the carbonyl C, methyl C, and carbonyl O of the acetyl groups; CAC and OAC refer to the C and O of the acetal groups.

Deviations from the ideal symmetry[16] are given in terms of the asymmetry parameters $\Delta C_s = 0.6°$ and $\Delta C_2 = 3.6°$, respectively, for the pyranose and furanose rings. These are roughly parallel, the angle between their least-squares planes being 20.9°.

As in other acetylated carbohydrate derivatives, the secondary acetate groups are so arranged that the carbonyl O nearly eclipses the H at the corresponding ring C. These torsion angles are in the range 7.5–31.8° (average, 19.6°).

The orientation of the primary acetate at C-6' falls into the theoretically predicted range of conformations for acetyl groups in galactosaccharides[17]. The *trans*–*gauche*$^{-}$–*trans* conformation along the C-5'–C-6'–O-6' sequence is observed.

Molecular packing. — The molecules are held in the crystal by Van der Waals forces only; no short atom contacts are observed. The packing ratio, volume/number of non-hydrogen atoms in the unit cell, is 19.1, in agreement with

TABLE III

TORSION ANGLES (DEGREES)

	Reducing residue	*Non-reducing residue*
Endocyclic torsion angles		
C-5–O-5–C-1–C-2	—	−66.1(7)
O-5–C-1–C-2–C-3	—	57.7(7)
C-1–C-2–C-3–C-4	—	−51.4(9)
C-2–C-3–C-4–C-5	—	51.1(7)
C-3–C-4–C-5–O-5	—	−56.9(8)
C-4–C-5–O-5–C-1	—	65.5(8)
O-3–C-3–C-4–C-5	−15.0(9)	—
C-3–C-4–C-5–C-6	−11.2(9)	—
C-4–C-5–C-6–O-3	34.2(8)	—
C-4–C-3–O-3–C-6	37.6(9)	—
C-5–C-6–O-3–C-3	−45.6(8)	—
Exocyclic torsion angles		
C-1–C-2–O-2–CA-2	117.3(6)	99.4(6)
C-2–C-3–O-3–CA-3	—	−153.0(7)
C-3–C-4–O-4–CA-4	—	−96.0(5)
C-4–C-5–O-5–CA-5	90.3(7)	—
C-5–C-6–O-6–CA-6	—	−166.8(8) t
C-4–C-5–C-6–O-6	—	−70.9(7) g^-
O-2–C-2–C-3–O-3	−68.7(5)	68.0(8)
O-3–C-3–C-4–O-4	−137.2(6)	53.2(5)
O-4–C-4–C-5–O-5	−140.9(5)	—
O-5–C-5–C-6–O-3	−80.4(6)	61.3(7)
O-5–C-5–C-6–O-6	—	170.7(6) t
OAC-1–C-1–C-2–O-2	−49.5(5)	—
OAC-2–C-1–C-2–O-2	−165.3(5)	—
CAC-1–OAC-1–C-1–C-2	105.1(7)	—
CAC-2–OAC-2–C-1–C-2	175.1(7)	—

that for the packing of sugars without H-bonds[12,13]. The molecules are oriented in the cell with the rings approximately perpendicular to the *b* axis and with the long axis parallel to the *a–c* plane diagonal (Fig. 2).

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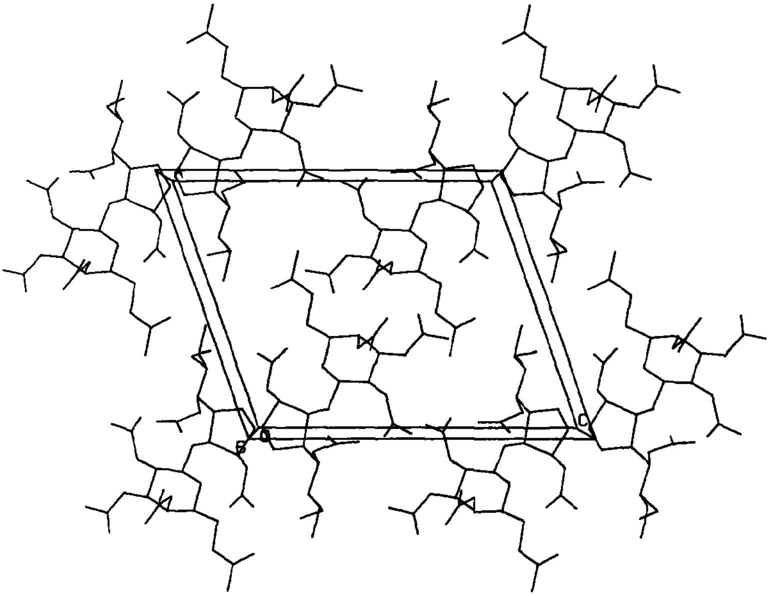

Fig. 2. Molecular packing.

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