Carbohydrate Research, 31 (1973) 211–227

TOPOGRAPHY OF CYCLODEXTRIN INCLUSION COMPLEXES

PART II[1]. THE IODINE–CYCLOHEXA-AMYLOSE TETRAHYDRATE COMPLEX; ITS MOLECULAR GEOMETRY AND CAGE-TYPE CRYSTAL STRUCTURE

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(Received March 29th, 1973; accepted for publication, June 7th, 1973)

ABSTRACT

Iodine–cyclohexa-amylose tetrahydrate $[(C_6H_{10}O_5)_6 \cdot I_2 \cdot 4H_2O]$ crystallizes in the orthorhombic space-group $P2_12_12_1$, $a = 14.240$ Å, $b = 36.014$ Å, $c = 9.558$ Å. The structure was solved by heavy-atom techniques and refined by least-squares methods to a conventional discrepancy index R = 0.148 for the 2872 observed data. The six D-glucose residues are in the *C1* chair conformation; the conformational angles vary in magnitude from 45 to 66°, the angles O(5)-C(5)-C(6)-O(6) are close to −70°, and the six O(4) atoms are almost coplanar (r.m.s. displacement 0.13 Å). Only four of the six O(2)···O(3) intramolecular hydrogen bonds have formed, which renders the molecule less symmetrical and more conical-shaped than in the previously determined α-cyclodextrin–potassium acetate complex. The iodine molecule is coaxial with the cyclohexa-amylose molecule. The I–I distance is a conventional 2.677 Å. Close interactions between the iodine atoms and the host molecule comprise carbon atoms C(5) and C(6) and oxygen atoms O(4), with interatomic distances all equal to or greater than van der Waals contacts. Intermolecular, almost-linear, short contacts O···I–I···O with I···O distances of 3.22 and 3.07 Å indicate attractive interaction.

The molecules are arranged in herring-bone "cage-type" fashion, with the four water molecules as space-filling mediators; the structure is held together by an intricate network of hydrogen bonds.

INTRODUCTION

Cycloamyloses (cyclodextrins) are cyclic molecules consisting of six to ten, α-(1→4)-linked D-glucose residues (Fig. 1). They are able, due to their doughnut shape, to form inclusion complexes, even in aqueous solution, with guest (substrate)

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molecules ranging in character from purely hydrophobic to purely hydrophilic, provided that the guest molecule is small enough to fit into the annular aperture of the cyclodextrins[2]. For this reason, cycloamyloses have been valuable model compounds in the study of starch complexes, the "burying" of tyrosine residues, and the action of enzymes[3].

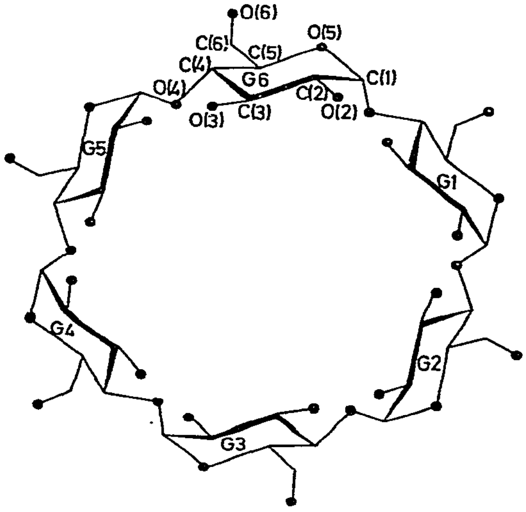

Fig. 1. Chemical formula and numbering scheme of cyclohexa-amylose used in the text; the two indices of each atom refer to the D-glucose residue and the conventional numbering of the atom, respectively.

Adduct formation has been investigated for a large number of guest molecules and, recently, the crystallographic data of 17 inclusion complexes of cyclohexa-amylose (α-cyclodextrin) were reported[1]. These results revealed that, in essence, two different forms of the cyclohexa-amylose adduct exist in crystalline state, namely, the channel and the cage-type structures. The channel structures develop when, during crystallisation, cyclohexa-amylose molecules pack on top of each other like coins to yield "endless" channels, in which the guest molecules are enclosed. The cage structures are due to the displaced (not coaxial) arrangement of cyclohexa-amylose molecules, which results in discrete, small cavities represented by the annular apertures in which the guest molecules are located.

The X-ray analysis of the channel structure of the potassium acetate–cyclohexa-amylose adduct has been reported[4], and a cage structure, the cyclohexa-amylose hexahydrate complex, has been described recently[5]. Only preliminary data are available so far for the iodine–cyclohexa-amylose adduct[6], and we now report in detail on its structure.

EXPERIMENTAL

The iodine adduct studied here and that described by James *et al.*[6] differ in method of preparation and in reported composition, the earlier formulation of the adduct being $(C_6H_{10}O_5)_6\cdot I_2\cdot 14H_2O$. We now infer that the crystals of both preparations are, in fact, of the composition $(C_6H_{10}O_5)_6\cdot I_2\cdot 4H_2O$ established by this structure analysis. Crystals for this study were prepared by placing aqueous cyclohexaamylose and ethereal iodine solutions in contact for one week. Crystal growth occurred in the aqueous phase at the liquid interface, yielding small, fragile specimens. The crystals were reddish-brown and developed as blades elongated along *c*, with (110) as the predominant face. They became opaque in air due to loss of water and darkened in the X-ray beam on long exposures (60 h) with significant diminution of diffraction intensities. As a consequence, several crystals coated with polystyrene films were used in the diffraction studies. These were of similar shapes and of approximate dimensions 0.02 × 0.04 × 0.20 mm. The space-group symmetry and approximate unit-cell dimensions were determined by Weissenberg and precession photographs. The reported unit-cell dimensions (Table I) and the diffraction intensities were measured on a Siemens automatic diffractometer, using nickel-filtered Cu radiation ($\lambda = 1.5418$ Å). No attempt was made to obtain a value for the measured density; the values for Z and the hydration number were those of pseudo-isomorphs, for which measured density values were available[1]. Intensity measurements were made by scanning reflections in the $\theta/2\theta$ mode at a rate of 3° min^{-1} with variable scan-widths. Data were collected for 2872 reflections for which θ was less than 45°. Of these reflections, 751 were observed to have intensities less than twice the estimated error in measurements and were omitted from the final refinement. The standard reflection decreased in intensity by 30% for each crystal used after three days of X-ray exposure, and the data were scaled accordingly. The intensities were corrected for Lorentz and polarization factors, but not for absorption effects.

TABLE I

CRYSTAL DATA

Stoichiometry	$(C_6H_{10}O_5)_6\cdot I_2\cdot 4H_2O$	Cell dimensions	$a = 14.240 \pm 0.004$ Å
Molecular weight	1308.72		$b = 36.014 \pm 0.006$ Å
Crystal system	Orthorhombic		$c = 9.558 \pm 0.006$ Å
Space group	$P2_12_12_1$	Cell volume	4901.7 Å^3
Z	4	Calculated density	1.704 g.cm^{-3}

THE STRUCTURE DETERMINATION AND REFINEMENT

The structure model was derived by application of heavy-atom method, starting with phases determined by the iodine atoms in the positions reported by James *et al.*[6]. Five successive cycles of structure factors and difference Fourier calculations were required to locate the 70 independent carbon and oxygen atoms of the structure, assuming that the correct enantiomorph was known from chemical evidence. The atomic positional and isotropic thermal parameters were refined by a block-diagonal, least-squares procedure. The quantity minimized was $\Sigma w(F_0 - F_c)^2$, where the weights w were determined from a function of the form $w = 1/[1 + (bF_0 + c)^2]$. The atomic scattering factors and anomalous dispersion components for the iodine atoms were taken from standard tables[7]. The iodine scattering curve was corrected for the real component of anomalous dispersion ($\Delta f' = -1.2$ for CuKα radiation), and the imaginary component, though large ($\Delta f'' = 7.0$), was ignored, since the refinement procedure being used did not incorporate a routine for dispersion corrections. After two isotropic refinement-cycles, anisotropic thermal parameters were introduced for the iodine atoms and the oxygen atoms of the water molecules, and the refinement was continued for three additional cycles. A three-dimensional, electron-density difference map was then calculated. The dominant features of this map (± 2.5 e.Å^{-3}) were at or near the iodine positions, and were attributed to errors due to incomplete dispersion corrections and to systematic errors in the data resulting from radiation damage. In view of this, further refinement with these data appeared to be unwarranted, and the analysis was terminated at this stage. The shifts in positional parameters after the final cycle were equal to, or less than, their standard errors: ~0.03 Å for the light atoms and 0.003 Å for iodine atoms.

The crystallographic discrepancy index $R = \Sigma||F_0| - |F_c||/\Sigma|F_0|$ is 0.114 for the reflections included in the refinement and 0.148 for all recorded reflections.

Computer programs used in the analysis were local modifications of the ORFLS[8] and Zalkin Fourier summation[9] programs for the IBM 7040 computer at Göttingen; programs of X-ray 63 system[10] and ORTEP[11] for the IBM 7094 at Darmstadt, and for the UNIVAC 1108 computers at the University of Wisconsin and the Gesellschaft für wissenschaftliche Datenverarbeitung, Göttingen.

RESULTS AND DISCUSSION

The atomic positional and thermal parameters are given in Table II. Atoms of the cyclohexa-amylose molecule are identified according to D-glucose residue and conventional carbohydrate numbering within the residues, respectively, by the first and second numbers after the chemical symbols (Fig. 1). Bond distances and valence angles are presented in Tables III and IV for each D-glucose residue, and their mean values averaged for chemical equivalence are represented in Fig. 2. The maximum deviations from the mean correspond to 2.2δ in distances and 2.8δ in angles. The I–I bond distance is 2.677 Å ($\delta = 0.005$ Å). The torsional angles describing the conformation of the macro-ring are listed in Table V. In Table VI are given intramolecular O···O contact-distances and C–O···O angles falling in the range of values that indicate hydrogen-bond interactions. Intermolecular hydrogen-bond distances are listed in Table VII. Other nearest distances for van der Waals separation between molecules of the sugar–water framework structure are given in Table VIII, together with the

TABLE II

FRACTIONAL CO-ORDINATES AND THERMAL PARAMETERS[a] (Å^2)

	x	y	z	B		x	y	z	B
C(11)	.8074	.2293	.0109	3.68	C(41)	.7234	.0115	.7302	1.95
C(12)	.8632	.2132	−.0997	2.47	C(42)	.6493	−.0119	.6612	1.90
C(13)	.9228	.1802	−.0488	2.69	C(43)	.5928	.0104	.5574	4.39
C(14)	.9755	.1890	.0845	2.67	(C44)	.5553	.0451	.6430	1.90
C(15)	.9117	.2064	.1961	3.25	C(45)	.6328	.0656	.7154	3.06
C(16)	.9698	.2227	.3183	5.50	C(46)	.5968	.0988	.8026	4.52
O(12)	.8047	.2039	−.2133	4.75	O(42)	.6964	−.0399	.5888	3.04
O(13)	.9845	.1687	−.1510	3.79	O(43)	.5180	−.0082	.4946	2.46
O(14)	1.0017	.1534	.1423	2.91	O(44)	.5146	.0702	.5277	2.38
O(15)	.8659	.2398	.1286	2.99	O(45)	.6752	.0409	.8079	2.46
O(16)	1.0541	.2428	.2732	4.69	O(46)	.5283	.0885	.8980	5.02
C(21)	.4574	.1873	.1541	2.13	C(51)	1.0651	.0478	.5682	4.23
C(22)	.4844	.1876	.0051	2.78	C(52)	1.0404	.0080	.5876	3.27
C(23)	.5893	.1828	−.0160	3.36	C(53)	.9277	.0027	.5663	2.82
C(24)	.6470	.2108	.0595	3.53	C(54)	.8783	.0257	.6726	3.08
C(25)	.6130	.2155	.2104	3.05	C(55)	.9134	.0658	.6585	4.04
C(26)	.6498	.2495	.2840	3.30	C(56)	.8744	.0929	.7745	3.08
O(22)	.4362	.1557	−.0620	4.41	O(52)	1.0858	−.0162	.4928	6.60
O(23)	.6136	.1871	−.1635	4.51	O(53)	.9069	−.0355	.5949	3.46
O(24)	.7409	.2024	.0549	3.36	O(54)	.7814	.0248	.6356	2.84
O(25)	.5095	.2184	.2229	2.96	O(55)	1.0159	.0688	.6706	4.28
O(26)	.6402	.2814	.2069	4.29	O(56)	.9025	.0821	.9077	3.51
C(31)	.4241	.0829	.5329	2.24	C(61)	1.0983	.1470	.1587	4.16
C(32)	.3722	.0748	.3915	3.65	C(62)	1.1232	.1101	.1122	2.67
C(33)	.4298	.0972	.2806	1.86	C(63)	1.0719	.0812	.2012	3.74
C(34)	.4301	.1370	.3167	2.07	C(64)	1.1000	.0872	.3479	2.99
C(35)	.4609	.1445	.4598	2.33	C(65)	1.0763	.1251	.3946	2.25
C(36)	.4524	.1825	.5218	3.88	C(66)	1.1155	.1370	.5409	3.57
O(32)	.3817	.0345	.3719	3.42	O(62)	1.0942	.1052	−.0311	3.42
O(33)	.3746	.0902	.1481	4.41	O(63)	1.1047	.0433	.1622	3.79
O(34)	.4865	.1537	.2199	4.09	O(64)	1.0390	.0596	.4285	3.62
O(35)	.4202	.1203	.5657	2.80	O(65)	1.1297	.1502	.3024	3.68
O(36)	.3567	.1939	.5172	6.58	O(66)	1.2098	.1203	.5663	5.89

	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
I (1)	.7663	.1039	.2936	6.04	4.70	5.00	−.29	−.34	.34
I (2)	.7689	.1543	.4994	5.95	4.61	4.79	.28	.34	.34
O(W1)	.2409	.0778	.8156	9.65	8.58	8.31	−.34	.34	−.34
O(W2)	.2695	.0007	.8048	6.28	5.79	7.13	.33	.34	−.34
O(W3)	.2476	.2309	.3168	6.44	7.41	7.78	.34	.23	.34
O(W4)	.2778	.1684	.7627	9.14	7.95	9.29	.34	−.34	−.34

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[a] The anisotropic thermal parameters are in the form
$\exp[-1/4(h^2B_{11}a^{*2}+k^2B_{22}b^{*2}+1^2B_{33}c^{*2}+2hkB_{12}a^*b^*+2hlB_{13}a^*c^*+2klB_{23}b^*c^*)]$.
The mean e.s.d.'s of positional parameters are: $\delta(x) = .0018$, $\delta(y) = .0007$, $\delta(z) = .0030$ for light atoms; $\delta(x) = .0002$, $\delta(y) = .0001$, $\delta(z) = .0003$ for iodine atoms.

TABLE III

BOND LENGTHS[a] IN CYCLOHEXA-AMYLOSE

Atoms	*Length* (*Å*)	*Atoms*	*Length* (*Å*)	*Atoms*	*Length* (*Å*)
C(11) C(12)	1.44	C(15) O(15)	1.51	C(13) O(13)	1.38
C(21) C(22)	1.48	C(25) O(25)	1.48	C(23) O(23)	1.46
C(31) C(32)	1.57	C(35) O(35)	1.46	C(33) O(33)	1.51
C(41) C(42)	1.50	C(45) O(45)	1.39	C(43) O(43)	1.39
C(51) C(52)	1.49	C(55) O(55)	1.47	C(53) O(53)	1.43
C(61) C(62)	1.45	C(65) O(65)	1.48	C(63) O(63)	1.49
C(12) C(13)	1.54	C(11) O(15)	1.45	C(14) O(14)	1.44
C(22) C(23)	1.52	C(21) O(25)	1.50	C(24) O(24)	1.37
C(32) C(33)	1.57	C(31) O(35)	1.38	C(34) O(34)	1.36
C(42) C(43)	1.51	C(41) O(45)	1.47	C(44) O(44)	1.54
C(52) C(53)	1.63	C(51) O(55)	1.42	C(54) O(54)	1.43
C(62) O(63)	1.53	C(61) O(65)	1.45	C(64) O(64)	1.53
C(13) C(14)	1.51	C(11) O(24)	1.42	C(15) C(16)	1.55
C(23) C(24)	1.49	C(21) O(34)	1.43	C(25) C(26)	1.51
C(33) C(34)	1.48	C(31) O(44)	1.37	C(35) C(36)	1.50
C(43) C(44)	1.59	C(41) O(54)	1.31	C(45) C(46)	1.55
C(53) C(54)	1.49	C(51) O(64)	1.45	C(55) C(56)	1.58
C(63) C(64)	1.47	C(61) O(14)	1.40	C(65) C(66)	1.57
C(14) C(15)	1.54	C(12) O(12)	1.41	C(16) O(16)	1.47
C(24) C(25)	1.53	C(22) O(22)	1.48	C(26) O(26)	1.37
C(34) C(35)	1.46	C(32) O(32)	1.47	C(36) O(36)	1.42
C(44) C(45)	1.50	C(42) O(42)	1.40	C(46) O(46)	1.39
C(54) C(55)	1.53	C(52) O(52)	1.41	C(56) O(56)	1.39
C(64) C(65)	1.48	C(62) O(62)	1.44	C(66) O(66)	1.49

[a] The mean, estimated, standard deviation in bond lengths is 0.04 Å.

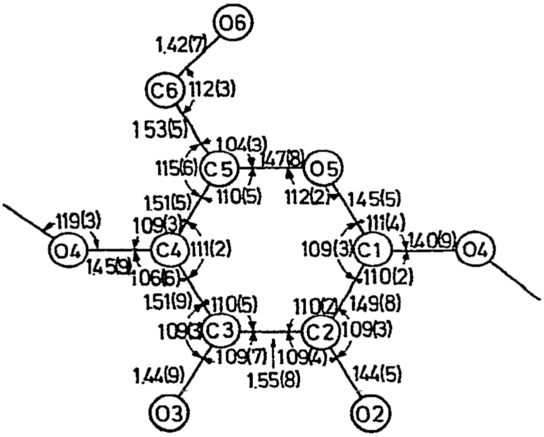

Fig. 2. Averaged bond-distances and -angles for the D-glucose residues; standard deviations are given in parentheses.

closest-approach distances between "guest" iodine molecules and the "host" cyclohexa-amylose molecules.

(*a*) *Geometry of the cyclohexa-amylose molecule*

The cyclohexa-amylose molecule in this adduct has the configuration shown in Fig. 3. The six D-glucose residues are in the conventional *C1* chair conformation

TABLE IV

VALENCE BOND ANGLES[a] IN CYCLOHEXA-AMYLOSE

Atoms	*Angle* (°)	*Atoms*	*Angle* (°)	*Atoms*	*Angle* (°)
O(15)C(11)C(12)	111	C(11)C(12)O(12)	110	C(14)C(15)C(16)	111
O(25)C(21)C(22)	107	C(21)C(22)O(22)	107	C(24)C(25)C(26)	115
O(35)C(31)C(32)	111	C(31)C(32)O(32)	105	C(34)C(35)C(36)	121
O(45)C(41)C(42)	107	C(41)C(42)O(42)	107	C(44)C(45)C(46)	113
O(55)C(51)C(52)	108	C(51)C(52)O(52)	114	C(54)C(55)C(56)	114
O(65)C(61)C(62)	107	C(61)C(62)O(62)	110	C(64)C(65)C(66)	116
C(11)C(12)C(13)	113	O(12)C(12)C(13)	113	C(16)C(15)O(15)	105
C(21)C(22)C(23)	113	O(22)C(22)C(23)	108	C(26)C(25)O(25)	105
C(31)C(32)C(33)	104	O(32)C(32)C(33)	112	C(36)C(35)O(35)	104
C(41)C(42)C(43)	111	O(42)C(42)C(43)	108	C(46)C(45)O(45)	107
C(51)C(52)C(53)	109	O(52)C(52)C(53)	107	C(56)C(55)O(55)	104
C(61)C(62)C(63)	110	O(62)C(62)C(63)	108	C(66)C(65)O(65)	101
C(12)C(13)C(14)	112	C(12)C(13)O(13)	111	O(15)C(11)O(24)	109
C(22)C(23)C(24)	114	C(22)C(23)O(23)	111	O(25)C(21)O(34)	107
C(32)C(33)C(34)	110	C(32)C(33)O(33)	102	O(35)C(31)O(44)	112
C(42)C(43)C(44)	105	C(42)C(43)O(43)	116	O(45)C(41)O(54)	112
C(52)C(53)C(54)	108	C(52)C(53)O(53)	107	O(55)C(51)O(64)	111
C(62)C(63)C(64)	107	C(62)C(63)O(63)	110	O(65)C(61)O(14)	113
C(13)C(14)C(15)	112	O(13)C(13)C(14)	110	O(24)C(11)C(12)	108
C(23)C(24)C(25)	111	O(23)C(23)C(24)	105	O(34)C(21)C(22)	111
C(33)C(34)C(35)	113	O(33)C(33)C(34)	111	O(44)C(31)C(32)	111
C(43)C(44)C(45)	112	O(43)C(43)C(44)	110	O(54)C(41)C(42)	110
C(53)C(54)C(55)	108	O(53)C(53)C(54)	108	O(64)C(51)C(52)	110
C(63)C(64)C(65)	111	O(63)C(63)C(64)	107	O(14)C(61)C(62)	111
C(14)C(15)O(15)	107	C(13)C(14)O(14)	105	C(15)C(16)O(16)	114
C(24)C(25)O(25)	114	C(23)C(24)O(24)	112	C(25)C(26)O(26)	113
C(34)C(35)O(35)	115	C(33)C(34)O(34)	106	C(35)C(36)O(36)	109
C(44)C(45)O(45)	107	C(43)C(44)O(44)	103	C(45)C(46)O(46)	112
C(54)C(55)O(55)	113	C(53)C(54)O(54)	106	C(55)C(56)O(56)	112
C(64)C(65)O(65)	106	C(63)C(64)O(64)	103	C(65)C(66)O(66)	111
C(15)O(15)C(11)	112	O(14)C(14)C(15)	105	C(11)O(24)C(24)	121
C(25)O(25)C(21)	114	O(24)C(24)C(25)	111	C(21)O(34)C(34)	120
C(35)O(35)C(31)	114	O(34)C(34)C(35)	112	C(31)O(44)C(44)	122
C(45)O(45)C(41)	110	O(44)C(44)C(45)	109	C(41)O(54)C(54)	117
C(55)O(55)C(51)	113	O(54)C(54)C(55)	108	C(51)O(64)C(64)	121
C(54)O(65)C(61)	111	O(64)C(64)C(65)	109	C(61)O(14)C(14)	116

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[a] The mean, estimated, standard deviation in valence angles is 2.4°.

(1a2e3e4e5e) established previously for the molecule in the potassium acetate adduct[4]. The conformational angles ($\delta = 3°$) around the D-glucose rings vary in magnitude from 45–66°, as compared with 52–66° in the potassium acetate adduct, 49–68° in mono- and di-saccharides, and 55.8–61.7° for an ideal pyranoid ring[12,13]. Corresponding angles in the six D-glucose residues differ in extremes by 5δ [about bonds C(4)-C(5) and C(5)-O(5)], indicating deformations which are probably due ultimately to the molecular packing in the crystal and due to the fitting of the cyclohexa-amylose molecule to the dimensions of the iodine. The conformational angles O(5)-C(5)-C(6)-O(6) are −70 ±8° (Table V), and thus lie in the range most commonly found in the pyranose sugars.

TABLE V

SELECTED CONFORMATIONAL ANGLES[a]

Atoms	*D-Glucose residue*					
	1	*2*	*3*	*4*	*5*	*6*
	Angle (degrees)					
h i j k						
O(5)C(5)C(6)O(6)	−73	−76	−73	−63	−62	−78
O(5)C(1)O(4')C(4')	112	102	107	100	97	104
C(2)C(1)O(4')C(4')	−127	−142	−129	−141	−144	−136
C(1)O(4')C(4')C(3')	120	129	135	126	121	160
C(1)O(4')C(4')C(5')	−122	−107	−101	−115	−123	−82

[a] Angle, measured clockwise, between projections of bonds h-i and j-k viewed along bond i-j. (') denotes atom of adjacent D-glucose residue. Estimated, standard deviation in angles is 3°.

TABLE VI

INTRAMOLECULAR HYDROGEN-BOND O···O DISTANCES AND C–O···O ANGLES

Atoms		*Distance (Å)*	*Atoms*			*Angle (°)*
O(12)	O(23)	2.83	C(12)	O(12)	O(23)	119
O(22)	O(33)	3.22[a]	C(23)	O(23)	O(12)	114
O(32)	O(43)	2.74	C(22)	O(22)	O(33)	115
O(42)	O(53)	3.00	C(33)	O(33)	O(22)	105
O(52)	O(63)	3.83[a]	C(32)	O(32)	O(43)	124
O(62)	O(13)	3.00	C(43)	O(43)	O(32)	117
			C(42)	O(42)	O(53)	116
			C(53)	O(53)	O(42)	105
			C(52)	O(52)	O(63)	102
			C(63)	O(63)	O(52)	107
			C(62)	O(62)	O(13)	115
			C(13)	O(13)	O(62)	107

[a] Non-bonding distances included for comparison.

TABLE VII

INTERMOLECULAR[a] HYDROGEN-BOND DISTANCES AND ANGLES

Atoms		*Distance (Å)*	*Atoms*		*Distance (Å)*
O(12)	OW(3)g	2.68	O(42)	O(56)k	2.70
O(13)	O(26)g	2.90	O(43)	O(63)j	2.69
O(16)	O(23)g	2.87	O(46)	O(53)j	2.83
O(16)	OW(3)a	2.82	O(52)	OW(2)k	2.79
O(22)	O(46)d	2.78	O(56)	O(62)c	2.91
O(22)	OW(4)d	2.85	O(62)	OW(1)e	2.74
O(26)	OW(4)m	2.68	O(63)	OW(2)k	2.75
O(32)	OW(2)i	2.58	O(66)	OW(1)a	2.87
O(36)	OW(3)	2.80	O(66)	OW(4)a	2.73
O(36)	OW(4)	2.76	OW(1)	OW(2)	2.81

Atoms			*Angle (°)*	*Atoms*			*Angle (°)*
C(12)	O(12)	OW(3)g	105	C(62)	O(62)	O(56)d	120
C(13)	O(13)	O(26)g	116	C(62)	O(62)	OW(1)e	110
C(16)	O(16)	O(23)g	142	O(56)d	O(62)	OW(1)e	120
C(16)	O(16)	OW(3)a	133	C(63)	O(63)	O(43)k	112
O(23)g	O(16)	OW(3)a	84	C(63)	O(63)	OW(2)k	127
C(22)	O(22)	O(46)d	121	O(43)k	O(63)	OW(2)k	117
C(22)	O(22)	OW(4)d	120	C(66)	O(66)	OW(1)a	119
O(46)d	O(22)	OW(4)d	116	C(66)	O(66)	OW(4)a	100
C(23)	O(23)	O(16)h	112	OW(1)a	O(66)	OW(4)a	73
C(26)	O(26)	O(13)h	134	O(62)f	OW(1)	O(66)b	98
C(26)	O(26)	OW(4)m	116	O(62)f	OW(1)	OW(2)	119
O(13)h	O(26)	OW(4)m	99	O(66)b	OW(1)	OW(2)	121
C(32)	O(32)	OW(2)i	116	O(32)l	OW(2)	O(52)j	124
C(36)	O(36)	OW(3)	134	O(32)l	OW(2)	O(63)j	113
C(36)	O(36)	OW(4)	106	O(32)l	OW(2)	OW(1)	111
OW(3)	O(36)	OW(4)	120	O(52)j	OW(2)	O(63)j	87
C(42)	O(42)	O(56)k	118	O(52)j	OW(2)	OW(1)	84
C(43)	O(43)	O(63)j	118	O(63)j	OW(2)	OW(1)	133
C(46)	O(46)	O(22)c	101	O(12)h	OW(3)	O(16)b	96
C(46)	O(46)	O(53)j	113	O(12)h	OW(3)	O(36)	120
O(22)c	O(46)	O(53)j	130	O(16)b	OW(3)	O(36)	136
C(52)	O(52)	OW(2)k	130	O(22)c	OW(4)	O(26)n	129
C(53)	O(53)	O(46)k	117	O(22)c	OW(4)	O(36)	103
C(56)	O(56)	O(42)j	127	O(22)c	OW(4)	O(66)b	126
C(56)	O(56)	O(62)c	112	O(26)n	OW(4)	O(36)	100
O(42)j	O(56)	O(62)c	121	O(26)n	OW(4)	O(66)b	104
				O(36)	OW(4)	O(66)b	77

[a] The letters after the atom numbers (Table II) denote the symmetry transformations:

none	x	y	z	g	0.5+x	0.5−y	−z
a	1.0+x	y	z	h	−0.5+x	0.5−y	−z
b	−1.0+x	y	z	i	0.5−x	−y	−0.5+z
c	x	y	1.0+z	j	1.5−x	−y	0.5+z
d	x	y	−1.0+z	k	1.5−x	−y	−0.5+z
e	1.0+x	y	−1.0+z	l	0.5−x	−y	0.5+z
f	−1.0+x	y	1.0+z	m	0.5+x	0.5−y	1.0−z
				n	−0.5+x	0.5−y	1.0−z

The twists about the bonds involving bridging O(4)-atoms (Table V) are such as to confer on the molecule the general shape of a truncated cone, the larger base of which is formed by the twelve oxygen atoms, O(2) and O(3), as shown in Fig. 3. The least-squares plane through the ring of six O(4) atoms is given by the equation

$$-0.1026X-0.6610Y-0.7433Z+6.1248=0,$$

where the r.m.s. displacement of the atoms from the plane is 0.13 Å. The distances from the plane atoms O(6) at one base and atoms O(2) and O(3) at the other are, respectively, 1.94 ±0.36 and 3.01 ±0.50 Å. That the molecule manifests appreciable flexibility at the C-O(4) linkages is indicated by the significant differences in the

TABLE VIII

INTERMOLECULAR NON-BONDING DISTANCES[a]

A. Distances between the host cyclohexa-amylose and iodine molecules less than 4.25 Å

Atoms		*Distance (Å)*	*Atoms*		*Distance (Å)*
I(1)	O(14)	4.06	I(2)	C(15)	4.01
I(1)	O(24)	4.23	I(2)	C(16)	4.15
I(1)	C(41)k	4.20	I(2)	O(12)c	3.32
I(1)	C(42)k	3.74	I(2)	C(25)	4.17
I(1)	O(42)k	3.07	I(2)	O(23)c	4.08
I(1)	O(53)k	3.97	I(2)	C(55)	4.09
I(1)	O(56)d	4.24	I(2)	C(56)	3.75

B. Other non-bonding distances less than 3.6 Å

Atoms		*Distance (Å)*	*Atoms*		*Distance (Å)*
C(11)	OW(3)g	3.55	O(35)	OW(4)	3.26
C(12)	O(25)g	3.43	O(35)	O(66)b	3.00
C(12)	OW(3)g	3.33	O(36)	O(66)b	3.41
C(13)	O(56)d	3.57	C(42)	O(56)k	3.58
O(13)	O(56)d	3.23	C(43)	O(63)j	3.56
O(13)	O(56)d	3.38	O(42)	O(45)k	3.25
O(15)	C(22)g	3.37	O(43)	C(54)k	3.47
C(23)	C(46)d	3.49	O(43)	O(56)k	3.01
C(26)	OW(4)m	3.50	O(43)	C(63)j	3.53
O(22)	C(46)d	3.33	O(45)	C(53)j	3.27
O(23)	C(46)d	3.20	O(45)	O(53)j	2.99
C(31)	O(66)b	3.35	O(46)	O(52)j	3.20
C(32)	O(66)b	3.29	O(55)	OW(1)a	3.51
C(32)	OW(2)i	3.49	O(55)	O(62)c	3.33
C(36)	OW(4)	3.43	C(62)	OW(1)e	3.49
O(32)	C(52)k	3.31	C(66)	OW(4)a	3.33
O(33)	O(52)k	3.10	O(65)	OW(3)a	3.36
O(33)	O(46)d	3.24	OW(1)	OW(4)	3.34

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[a] The symmetry transformations denoted by letters are those given in Table VII.

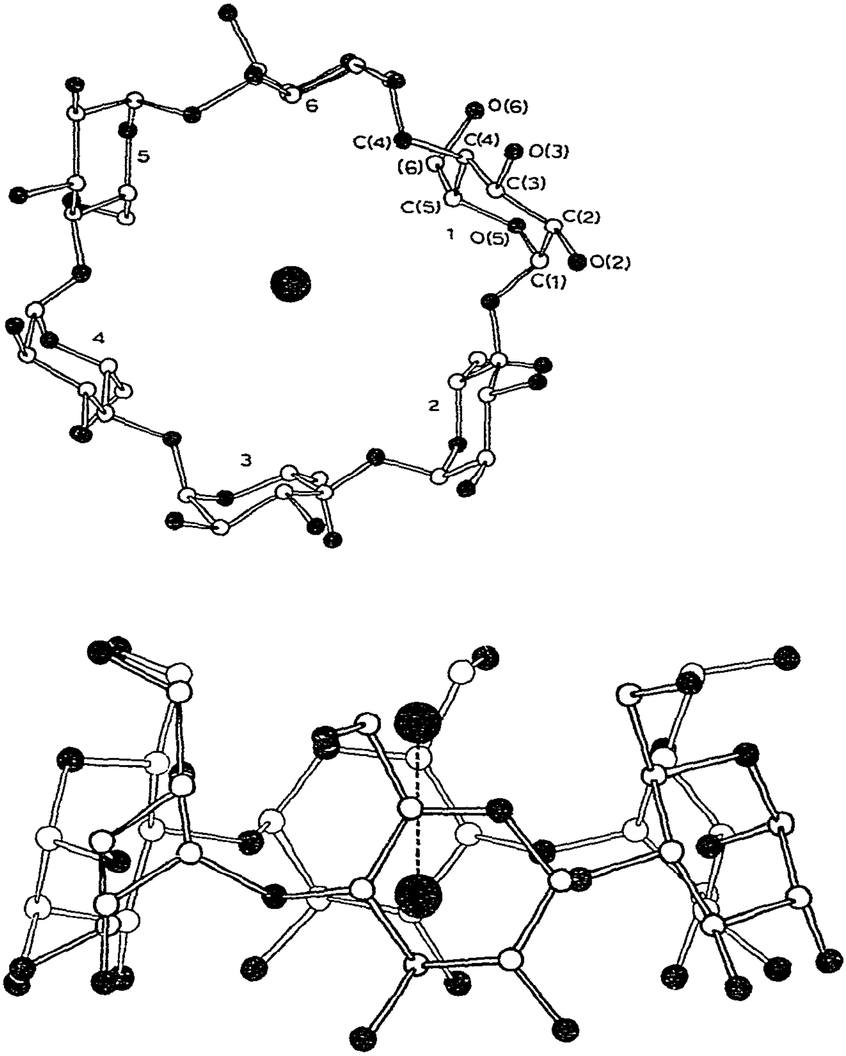

Fig. 3. Different views of the cyclohexa-amylose–iodine adduct.

conformation angles (12δ) about the C(4)-O(4) bonds (Table V). The observed distortions are again attributed to molecular packing. The molecule in the potassium acetate adduct is more cylindrical (and symmetric); this is apparently a consequence of the co-operative effects of intermolecular hydrogen-bonding between O(3) and O(6) atoms along the channel wall and intramolecular hydrogen-bonding between O(2) and O(3) atoms of contiguous D-glucose residues, since both would oppose large and non-uniform twists about of the α-(1 → 4) linkages. Also, a twofold, crystallographic symmetry-axis is co-linear with the molecular axis and gives extra molecular symmetry; in the iodine adduct, no such symmetry axis is present, and, here, only four of the six possible intramolecular O(2)···O(3) distances (Table VI) are within the range of acceptable hydrogen-bonding values (<3.0 Å).

The limited accuracy of this analysis precludes useful comparisons of bond lengths and angles with those reported for D-glucose residues in other sugar structures. However, it should be noted that the large valence angles (119 ±3°) at the linking O(4) atoms are in good agreement with values (119.1°) found in the potassium acetate adduct.

(*b*) *Geometry of Inclusion*

The atomic arrangement within the $(C_6H_{10}O_5)_6 \cdot I_2$ complex is presented in various projections in Fig. 3, and stereoscopically in Figs. 4 and 5, where the D-glucose residues of adjacent molecules that complete the cage enclosure are also shown.

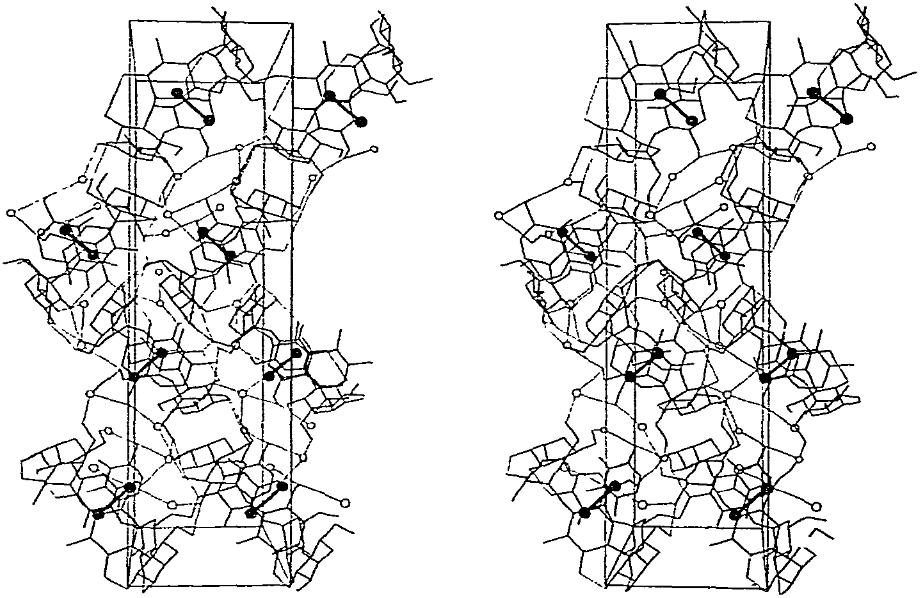

Fig. 4. Stereo view of the structure as seen down the crystallographic *a*-axis. Hydrogen bonds are indicated by thin lines, interatomatic bonds by heavier lines, iodine atoms by black dots, and water oxygen-atoms by open circles.

The iodine (guest) and enveloping cyclohexa-amylose (host) molecules are nearly coaxial (Fig. 3). The nearest guest–host separations (Table VIII) in radial directions are those between iodine atom I(2) and carbon atoms C(5) and C(6), some of which are in van der Waals contact at distances 3.75–4.17 Å, and those between I(1) and O(4), all of which are at distances exceeding contact separations, taking Pauling's van der Waals radii: 2.15 Å for iodine, 1.40 Å for oxygen, and 2.00 Å for methylene carbon[15]. Thus, for the iodine molecule, the environment in directions normal to its bond axis is mainly polar at I(1) and hydrophobic at I(2).

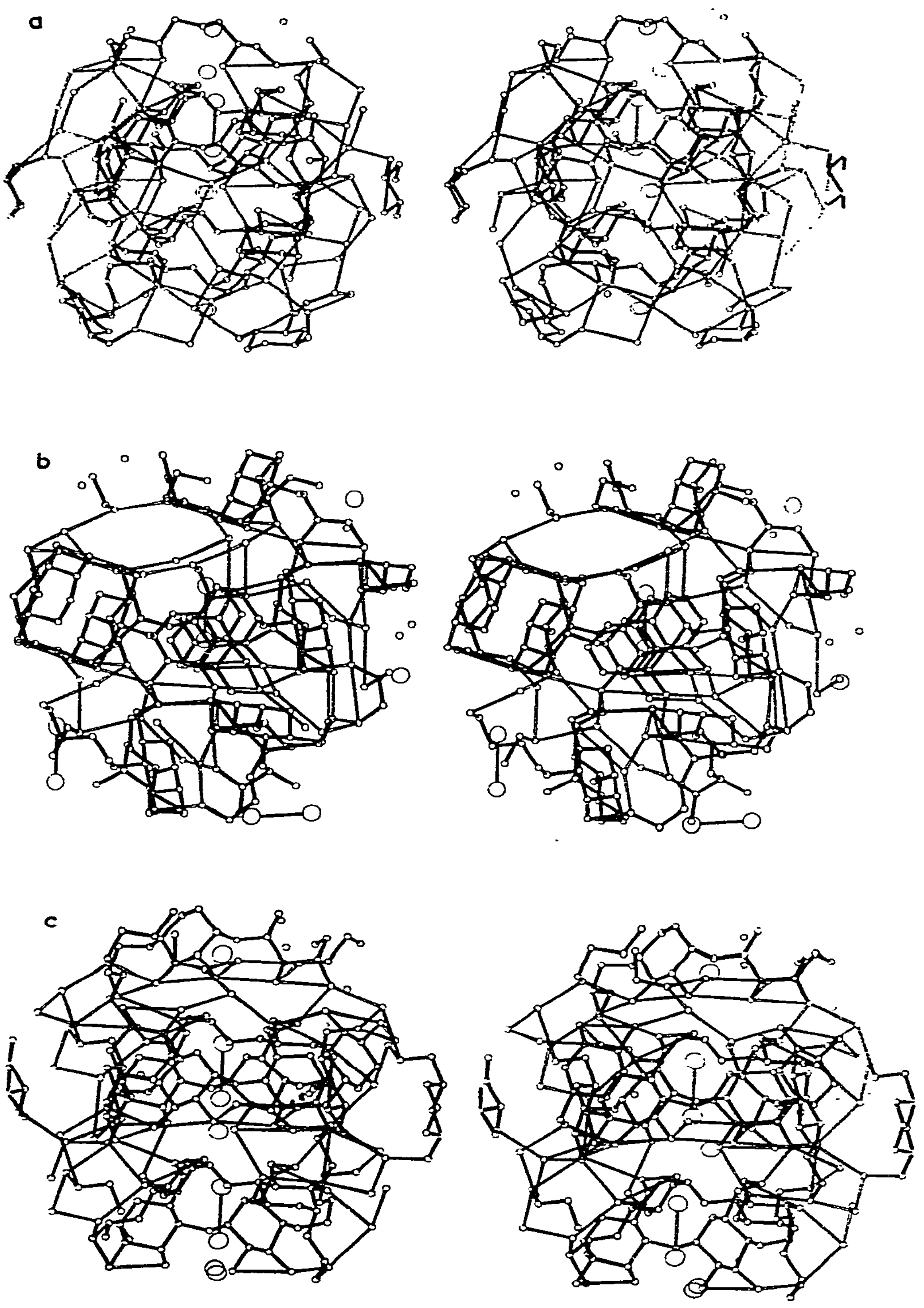

Fig. 5. Stereo view of one complete cyclohexa-amylose–iodine complex, with surrounding atoms within a sphere of enclosure of 10-Å radius. Intramolecular, interatomic distances are drawn with heavy lines, hydrogen bonds are indicated by double lines, iodine atoms are represented by the 50% probability, thermal ellipsoids. (a) A view along the I-I vector. (b) A view along the crystallographic *a*, axis. The *b*- and *c*-axes are oriented at ~45° with respect to the I-I vector, *i.e.*, going from the left, lower corner to the right, upper corner within the plane of the paper, and from the left, upper corner to the right, lower corner, respectively. (c) A view as in (b), but the molecule was rotated about the I-I vector by 90°. Now, the *a*-axis is within the plane of the paper, from left to right.

In the axial directions, the shortest intermolecular contacts to both iodine atoms are from oxygen atoms of symmetry-related cyclohexa-amylose molecules at distances of 3.07 Å, I(1)···O(42), and 3.32 Å, I(2)···O(12), as shown in Fig. 5 and Table VIII. The atoms O(42)···I(1)-I(2)···O(12) are roughly co-linear, the angular deviations of O(42) and O(12) from the I(1)-I(2) bond-axis being within 13°. The difference between the I···O distances is significant, and the smaller is appreciably less than the sum (3.55 Å) of conventional van der Waals radii[15], indicating attractive interactions.

(c) *Molecular packing and hydrogen-bonding scheme*

The packing of the cyclohexa-amylose–iodine complex molecules within the unit cell is depicted in detail in a stereo view along the crystallographic *a*-axis (Fig. 4) and schematically in Fig. 6. The herring-bone arrangement of the conical molecules causes the formation of "cages" due to the blocking of the annular apertures of the cyclohexa-amylose molecules. The O(6) side of the cage is closed by the O(2),O(3) rim of a contiguous molecule and the O(2), O(3) side is closed mainly by the cone wall of a molecule related by the screw operation parallel to *c*.

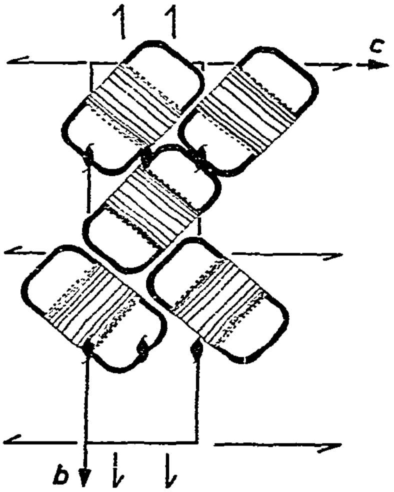

Fig. 6. Schematic packing-scheme of the cyclohexa-amylose–iodine adducts, as viewed down the crystallographic *a*-axis, showing the blocking of the torii by contiguous molecules.

The cyclohexa-amylose molecules are held together by an intricate network of hydrogen bonds between the hydroxyl groups (Figs. 4 and 5), with the water molecules as space-filling mediators in some cases. The hydrogen-bonding contacts listed in Tables VI and VII are depicted graphically in Figs. 7 and 8. Bonds to ether oxygen-atoms O(4) and O(5) were omitted in Fig. 7; O···O distances and C–O···O and O···O···O angles (Tables VII and VIII) are in the conventional range, 107 ±35°. Since no hydrogen atoms could be located in this analysis, hydrogen-bonding interactions were taken as O···O distances less than 2.9 Å.

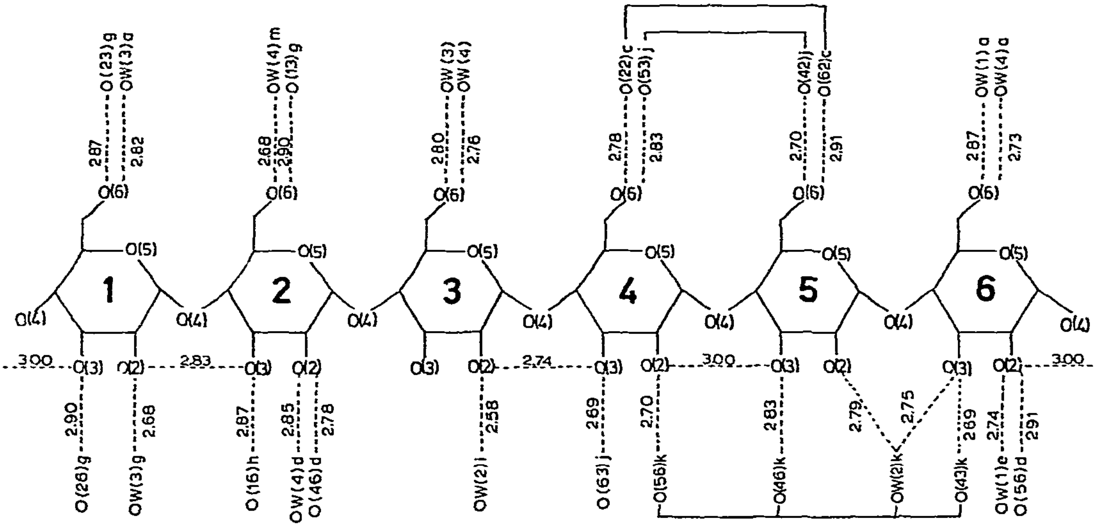

Fig. 7. Hydrogen-bonding scheme indicating all hydroxyl O···O distances <3.0 Å.

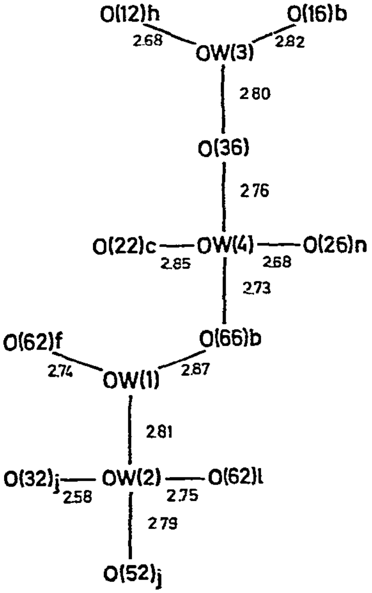

Fig. 8. Hydrogen-bonding scheme involving the four molecules of water of hydration.

One out of the total of 26 hydroxyl groups (18 from the cyclohexa-amylose and 8 from the water molecules), O(33), does not form hydrogen bonds; all the other hydroxyl groups are involved in two hydrogen bonds, except O(52) with only one, and O(62) with three hydrogen bonds of which two are >2.9 Å. Water molecules W(1) and W(3) form three hydrogen bonds which are in an arrangement close to tetrahedral (Fig. 8).

The four water molecules and their symmetry-related mates are in hydrogen-bonding contact with five of the O(2) and O(3), and six of the O(6) hydroxyl groups of D-glucose residues 1, 2, 3, 6, but with only one and zero, respectively, of the hydroxyl groups of D-glucose residues 4 and 5; instead, the O(2) and O(3) hydroxyl-groups of the latter D-glucose residues are in direct hydrogen-bonding contact with the hydroxyl groups of another cyclohexa-amylose molecule related by symmetry element *k*, $(1.5-x, -y, -0.5+z)$, a *c*-screw operation (indicated by a jaw in Fig. 7). This contact between two cyclohexa-amylose molecules, which is not mediated by water molecules, is the already-mentioned closing of the cyclohexa-amylose void, the "cage", at the O(2),O(3) side by the cone wall of another molecule related by a *c*-screw axis. Furthermore, the O(6) hydroxyl-groups of D-glucose residues 4 and 5 are bonded to two other cyclohexa-amylose molecules related by symmetry operations c and j, respectively (see the jaws in Fig. 7).

The stereoscopic Figs. 5 demonstrate this peculiar packing arrangement in detail. In Fig. 5a, the water molecules are located above and below and on the left-hand side of the central cyclohexa-amylose molecule, indicating that the hydrogen bonds for the translational packing of cyclohexa-amylose molecules along *a* (in the vertical direction in the plane of the paper in Fig. 5a) are mediated by water molecules; this accounts for the length of the *a*-axis, 14.240 Å, while the measured outer-diameter of a cyclohexa-amylose space-filling model is only ~13.5 Å[1]. It is also apparent from Fig. 5c that, in the indicated direction *a*, water molecules are located between the cyclohexa-amylose molecule in the centre and the next, translational equivalent D-glucose residues on the far right and far left.

ACKNOWLEDGMENTS

One of the authors (R. K. M.) acknowledges a generous grant from the Alexander von Humboldt Stiftung. The Deutsche Forschungsgemeinschaft supported these studies by providing the automatic diffractometer.

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