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Structure of a Complex of Cycloheptaamylose with 1-Adamantanecarboxylic Acid*

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Abstract

The structure of cycloheptaamylose complexed with 1-adamantanecarboxylic acid (an inhibitor of phenyl ester hydrolysis by cycloheptaamylose), determined by single-crystal X-ray diffraction at 108 K, is triclinic, space group $P1$, $a = 17{\cdot}747\ (5)$, $b = 15{\cdot}255\ (5)$, $c = 15{\cdot}491\ (5)$ Å, $\alpha = 102{\cdot}54\ (1)$, $\beta = 113{\cdot}54\ (1)$ and $\gamma = 98{\cdot}87\ (1)°$, $V = 3615$ Å^3, $Z = 1$, $D_x = 1{\cdot}455$ g cm^{-3}. Two molecules of each of cycloheptaamylose and 1-adamantanecarboxylic acid per unit cell form a dimer of composition $2C_{11}H_{16}O_2.2C_{42}H_{70}O_{35}.30H_2O$. The final R was 0·11 for 6433 observed reflections (Mo $K\alpha$ radiation, $\mu = 1{\cdot}407$ cm^{-1}). Two cycloheptaamylose molecules are in a head-to-head dimer produced by tight hydrogen bonding involving the secondary hydroxyl groups on both molecules. The two 1-adamantanecarboxylic acid guests have different orientations in the cycloheptaamylose cavities and different depths of penetration.

Introduction

The cycloamyloses (cyclodextrins) are cyclic oligosaccharides containing 6 to 12 D-glucopyranose residues linked α-(1 → 4). They have attracted great attention as models for enzymes such as the serine acylase enzymes, in particular chymotrypsin (Van Etten, Sebastian, Clowes & Bender, 1967; Bender & Komiyama, 1978). Cyclohexaamylose (α-cyclodextrin), cycloheptaamylose (β-cyclodextrin) and to a lesser extent cyclooctaamylose (γ-cyclodextrin) have been studied to examine the mode of binding of organic molecules in their cavities. This complexation process is the basis for all of the wide variety of phenomena produced by the cycloamyloses including catalysis of ester hydrolysis. These phenomena and other applications of the cycloamyloses in research and industry have recently been reviewed by Saenger (1980).

Early studies showed that the cycloamyloses caused stereoselective acceleration of the cleavage of phenyl esters (Van Etten, Sebastian, Clowes & Bender, 1967; Van Etten, Clowes, Sebastian & Bender, 1967). Cycloheptaamylose is a better catalyst than cyclohexaamylose. 1-Adamantanecarboxylic acid, which binds well in the cavity of cycloheptaamylose, is a competitive inhibitor of phenyl ester hydrolysis (Van Etten, Sebastian, Clowes & Bender, 1967; Breslow & Overman, 1970). 1-Adamantanecarboxylic acid also binds to cyclohexaamylose but is probably too large to enter the cavity entirely and must sit on top (Bender & Komiyama, 1978).

The best ratio of catalyzed *vs* uncatalyzed reaction found by Bender & Komiyama (1978) for acetyl transfer to cycloheptaamylose was only 250 for the substrate *tert*-butylphenyl acetate. However, as pointed out by Breslow, Czarniecki, Emert & Hamaguchi (1980), true enzymes often achieve ratios of 10^5–10^{10} or greater. They suggested, on the basis of model building, that substrates such as *tert*-butylphenyl acetate can bind fully in the cavity in the complex but they are pulled up partly out of the cavity by formation of the tetrahedral intermediate. They proposed several types of new substrates which were selected to retain as much binding as possible while proceeding from bound substrate to bound transition state to bound tetrahedral intermediate to product. One particular class of these new substrates is based on the adamantane framework. On the basis of binding studies and model building they have proposed that in the complex of 1-adamantanecarboxylic acid with cycloheptaamylose only half of the adamantane moiety would be enclosed by the cycloheptaamylose. Breslow *et al.* (1980) discussed the kinetic results of ester hydrolysis of two adamantane derivatives on the basis of this model. In

* Adamantane is tricyclo[3.3.1.1^{3,7}]decane.

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contrast, Komiyama & Bender (1978) proposed that the cycloheptaamylose cavity would be large enough to accommodate almost completely 1-adamantanecarboxylic acid. This structural study by X-ray crystallography of the complex (Fig. 1) was undertaken to clarify the binding of the adamantane moiety in the cavity and its depth of penetration and to help understand the subsequent reactions.

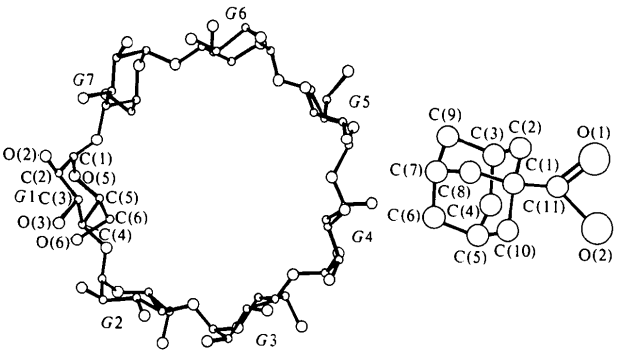

Fig. 1. The numbering scheme of the cycloheptaamylose molecule and the 1-adamantanecarboxylic acid. $G1, G2, \ldots, G7$ denote the glucose residue numbers.

Experimental

Crystals of the complex were prepared by heating together a 1:1 mixture of cycloheptaamylose with 1-adamantanecarboxylic acid in aqueous solution and allowing the mixture to cool slowly to room temperature. X-ray intensity data were collected at low temperature (108 K) which avoids having to seal the crystal inside a capillary tube to prevent loss of water of crystallization. The data are then free from errors due to absorption by the glass capillary tubes and high thermal vibration.

The cell parameters were determined and refined on a Picker four-circle automated diffractometer at 108 K. The intensity data, 6433 observed reflections, were also measured at 108 K on the Picker four-circle automated diffractometer. Small crystals and Mo $K\alpha$ radiation were used to minimize absorption ($\mu = 1{\cdot}407$ cm^{-1}). No absorption corrections were applied. All reflections with intensities greater than one standard deviation were used. The 6433 observed reflections constitute approximately 84% of the possible reflections in the 1 Å sphere of resolution.

Structure determination and refinement

The structure was solved using data from an isomorphous crystal structure of a complex of cycloheptaamylose with 1-propanol, solved by Stezowski and co-workers (Stezowski, Jogun, Eckle & Bartels, 1978). The atomic coordinates of cycloheptaamylose were obtained from the thesis of K. H. Jogun, supplied by Dr Stezowski. Refinement was carried out using a combination of difference Fourier synthesis and block-diagonal least-squares calculation. The quantity minimized in the least-squares refinement was $\sum w(|F_o| - |F_c|)^2$ where $w = 1/\sigma^2(F)$. The final R for the 6433 reflections with $F_o > \sigma(F)$ was 0·11. The value of R_w was 0·12. The final difference map showed no peaks with electron density greater than 0·5 e $Å^{-3}$. Scattering factors were taken from *International Tables for X-ray Crystallography* (1962) and all computer programs were from the XRAY76 system (Stewart, 1976). Isotropic thermal parameters were used for all atoms. The final fractional coordinates and thermal parameters are listed in Table 1.* Hydrogen bonding is indicated in Figs. 2 and 3.

* Lists of structure factors, bond lengths and angles, dihedral angles and hydrogen-bond lengths have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38047 (49 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Atomic parameters with e.s.d.'s in parentheses*

	Molecule 1				Molecule 2			
	x	y	z	U (Å²)	x	y	z	U (Å²)
Residue $G1$								
C(1)	2090 (10)	396 (11)	2568 (11)	2·9 (5)	7344 (9)	3083 (10)	8700 (10)	2·0 (4)
C(2)	2847 (9)	426 (10)	2261 (10)	2·0 (4)	6665 (9)	3417 (10)	8951 (10)	2·3 (4)
C(3)	2974 (9)	1270 (11)	1943 (10)	2·2 (4)	6651 (9)	4393 (10)	8810 (10)	1·7 (4)
C(4)	2146 (9)	1261 (10)	1110 (10)	1·3 (4)	7559 (9)	5041 (10)	9582 (10)	1·4 (4)
C(5)	1430 (9)	1224 (10)	1421 (10)	1·9 (4)	8238 (9)	4672 (10)	9340 (11)	2·1 (4)
C(6)	598 (12)	1120 (13)	635 (13)	5·0 (6)	9133 (9)	5196 (10)	10130 (10)	1·7 (4)
O(2)	3585 (6)	396 (7)	3036 (6)	2·1 (3)	5844 (6)	2790 (7)	8264 (7)	2·5 (3)
O(3)	3605 (6)	1275 (7)	1566 (7)	2·6 (3)	6053 (6)	4720 (7)	9081 (7)	2·2 (3)
O(4)	2289 (6)	2136 (7)	889 (6)	1·7 (3)	7568 (6)	5928 (6)	9395 (6)	1·5 (3)
O(5)	1360 (6)	418 (7)	1777 (7)	2·4 (3)	8165 (6)	3719 (7)	9585 (6)	1·7 (3)
O(6)	333 (13)	465 (14)	−28 (14)	2·5 (6)[a]	9261 (6)	5116 (7)	11080 (7)	2·0 (3)
O(6)*	−74 (13)	861 (14)	726 (14)	2·8 (6)[b]				

The population parameters for O(6) and O(6)* are $a = b = 0{\cdot}5$.

* The primary hydroxyl oxygen on this residue is disordered and appears in two positions.

Table 1 (*cont.*)

	Molecule 1				Molecule 2			
	x	*y*	*z*	*U* (Å²)	*x*	*y*	*z*	*U* (Å²)
Residue *G*2								
C(1)	2091 (10)	2128 (11)	−92 (11)	2·5 (5)	7872 (9)	6722 (10)	10229 (10)	1·8 (4)
C(2)	2888 (9)	2716 (10)	−59 (10)	2·2 (4)	7142 (9)	7234 (11)	10026 (11)	2·3 (4)
C(3)	3142 (9)	3677 (10)	662 (11)	2·2 (4)	7001 (9)	7522 (10)	9104 (10)	1·6 (4)
C(4)	2370 (9)	4095 (10)	221 (10)	1·7 (4)	7852 (9)	8196 (11)	9325 (11)	2·2 (4)
C(5)	1574 (9)	3483 (10)	128 (10)	1·6 (4)	8547 (9)	7704 (10)	9577 (11)	2·1 (4)
C(6)	761 (10)	3791 (11)	−442 (11)	2·6 (5)	9457 (11)	8335 (13)	9917 (13)	4·4 (6)
O(2)	3579 (6)	2262 (7)	261 (7)	2·9 (3)	6384 (6)	6649 (7)	9922 (7)	2·2 (3)
O(3)	3870 (6)	4232 (7)	653 (7)	2·5 (3)	6356 (7)	8053 (8)	8967 (7)	3·4 (3)
O(4)	2574 (6)	4970 (7)	945 (7)	2·3 (3)	7747 (6)	8399 (7)	8434 (7)	2·2 (3)
O(5)	1403 (6)	2523 (7)	−492 (6)	1·8 (3)	8621 (6)	7324 (7)	10398 (7)	2·0 (3)
O(6)	708 (7)	3860 (7)	−1387 (7)	3·0 (3)	9595 (9)	9099 (10)	10819 (9)	6·3 (4)
Residue *G*3								
C(1)	2467 (10)	5739 (11)	555 (11)	2·7 (5)	7914 (9)	9372 (10)	8472 (10)	1·5 (4)
C(2)	3305 (9)	6500 (10)	1097 (10)	1·6 (4)	7134 (9)	9500 (10)	7691 (11)	2·2 (4)
C(3)	3576 (9)	6877 (10)	2192 (10)	2·0 (4)	6931 (9)	8891 (10)	6705 (10)	1·8 (4)
C(4)	2850 (9)	7262 (10)	2288 (10)	1·7 (4)	7710 (9)	9208 (10)	6501 (10)	1·9 (4)
C(5)	2042 (9)	6426 (11)	1804 (11)	2·6 (5)	8507 (9)	9083 (10)	7320 (10)	1·9 (4)
C(6)	1284 (11)	6754 (12)	1878 (12)	4·1 (5)	9287 (10)	9476 (11)	7218 (11)	3·0 (5)
O(2)	3940 (6)	6130 (7)	888 (7)	2·0 (3)	6430 (6)	9290 (7)	7939 (7)	2·4 (3)
O(3)	4333 (6)	7663 (7)	2655 (7)	3·0 (3)	6186 (6)	9066 (7)	5986 (7)	2·6 (3)
O(4)	3079 (6)	7587 (7)	3321 (6)	1·7 (3)	7547 (6)	8543 (7)	5558 (6)	1·9 (3)
O(5)	1823 (7)	6096 (8)	777 (8)	3·5 (3)	8643 (6)	9604 (7)	8276 (7)	2·7 (3)
O(6)	1188 (8)	7532 (9)	1472 (9)	5·6 (4)	9359 (6)	10445 (7)	7240 (7)	2·9 (3)
Residue *G*4								
C(1)	3054 (10)	8527 (11)	3664 (11)	2·7 (5)	7615 (9)	8934 (10)	4844 (10)	1·7 (4)
C(2)	3891 (9)	9018 (11)	4583 (11)	2·4 (4)	6786 (8)	8595 (10)	3894 (10)	1·2 (4)
C(3)	4030 (9)	8548 (11)	5390 (11)	2·2 (4)	6576 (9)	7559 (10)	3479 (10)	1·8 (4)
C(4)	3256 (9)	8555 (10)	5628 (10)	2·0 (4)	7294 (9)	7310 (10)	3268 (10)	1·6 (4)
C(5)	2411 (10)	8122 (11)	4707 (11)	2·9 (5)	8120 (9)	7657 (11)	4232 (11)	2·3 (4)
C(6)	1653 (10)	8288 (11)	4901 (11)	2·8 (5)	8863 (10)	7498 (12)	4036 (12)	3·7 (5)
O(2)	4606 (6)	9051 (7)	4332 (6)	2·0 (3)	6150 (6)	8884 (7)	4141 (7)	2·4 (3)
O(3)	4768 (6)	9051 (7)	6268 (7)	2·2 (3)	5783 (6)	7266 (7)	2577 (7)	2·5 (3)
O(4)	3334 (6)	7994 (7)	6259 (6)	1·9 (3)	7098 (6)	6306 (7)	2924 (6)	1·8 (3)
O(5)	2379 (6)	8559 (7)	3935 (7)	2·2 (3)	8296 (6)	8657 (6)	4636 (6)	1·6 (3)
O(6)	1756 (7)	9268 (7)	5345 (7)	3·0 (3)	8923 (7)	7904 (8)	3305 (8)	4·1 (3)
Residue *G*5								
C(1)	3268 (10)	8345 (11)	7133 (11)	2·5 (5)	7041 (8)	5880 (10)	1961 (10)	1·2 (4)
C(2)	4045 (10)	8273 (11)	8008 (11)	2·7 (5)	6194 (9)	5168 (10)	1327 (10)	1·9 (4)
C(3)	4045 (10)	7243 (11)	7863 (11)	2·6 (5)	6088 (9)	4414 (10)	1835 (10)	2·0 (4)
C(4)	3210 (8)	6767 (10)	7849 (10)	1·3 (4)	6804 (9)	3980 (10)	1936 (10)	1·7 (4)
C(5)	2458 (9)	6837 (10)	6977 (10)	2·1 (4)	7690 (9)	4690 (10)	2491 (10)	2·0 (4)
C(6)	1589 (10)	6431 (11)	6918 (12)	3·3 (5)	8405 (9)	4259 (11)	2462 (11)	2·3 (4)
O(2)	4810 (6)	8774 (7)	8028 (7)	2·4 (3)	5505 (6)	5630 (7)	1200 (7)	2·3 (3)
O(3)	4740 (6)	7166 (7)	8707 (6)	1·8 (3)	5314 (6)	3697 (7)	1182 (7)	2·7 (3)
O(4)	3190 (6)	5778 (7)	7655 (6)	1·7 (3)	6792 (6)	3371 (7)	2526 (7)	2·0 (3)
O(5)	2534 (6)	7855 (7)	7128 (7)	2·5 (3)	7678 (6)	5441 (6)	2029 (6)	1·5 (3)
O(6)	1572 (9)	6809 (10)	7843 (9)	6·3 (5)	8221 (7)	3808 (7)	1459 (7)	3·1 (3)
Residue *G*6								
C(1)	3096 (8)	5366 (9)	8349 (9)	1·0 (4)	6804 (9)	2427 (10)	2165 (10)	1·7 (4)
C(2)	3773 (9)	4865 (10)	8666 (10)	1·6 (4)	5982 (9)	1765 (10)	2028 (10)	1·9 (4)
C(3)	3696 (9)	4158 (10)	7746 (10)	1·6 (4)	5980 (9)	1901 (10)	3034 (11)	2·3 (4)
C(4)	2837 (9)	3463 (10)	7274 (10)	2·1 (4)	6792 (9)	1714 (10)	3731 (10)	1·5 (4)
C(5)	2155 (9)	3956 (11)	7028 (11)	2·3 (4)	7600 (9)	2311 (10)	3772 (10)	1·7 (4)
C(6)	1238 (10)	3302 (11)	6688 (11)	2·5 (5)	8388 (9)	2029 (11)	4345 (11)	2·4 (3)
O(2)	4605 (6)	5515 (7)	9195 (7)	2·6 (3)	5236 (6)	1935 (7)	1339 (7)	3·1 (3)
O(3)	4361 (6)	3676 (7)	8054 (7)	2·7 (3)	5236 (6)	1275 (7)	2898 (7)	2·6 (3)
O(4)	2746 (6)	2871 (6)	6373 (6)	1·4 (3)	6826 (6)	1919 (7)	4693 (6)	1·8 (3)
O(5)	2275 (6)	4698 (7)	7903 (6)	2·0 (3)	7512 (6)	2227 (7)	2801 (7)	2·5 (3)
O(6)	1251 (6)	2857 (7)	7414 (7)	2·3 (3)	8286 (7)	1083 (8)	3849 (8)	3·8 (3)
Residue *G*7								
C(1)	2525 (9)	1873 (10)	6213 (10)	1·8 (4)	6840 (8)	1189 (9)	5140 (9)	1·0 (4)
C(2)	3207 (9)	1468 (11)	6051 (11)	2·4 (4)	6103 (9)	1055 (10)	5397 (10)	1·8 (4)
C(3)	3217 (9)	1603 (10)	5138 (10)	2·2 (4)	6202 (9)	1950 (10)	6165 (10)	1·9 (4)
C(4)	2360 (9)	1044 (10)	4277 (11)	2·1 (4)	7059 (9)	2170 (10)	7063 (10)	1·7 (4)
C(5)	1661 (10)	1430 (11)	4467 (11)	2·8 (5)	7777 (9)	2238 (10)	6747 (11)	2·0 (4)
C(6)	763 (11)	851 (12)	3721 (12)	3·7 (5)	8642 (10)	2402 (11)	7609 (11)	2·8 (5)
O(2)	4023 (6)	1941 (7)	6903 (7)	2·2 (3)	5325 (6)	843 (7)	4528 (7)	1·9 (3)
O(3)	3860 (6)	1204 (7)	4951 (7)	2·0 (3)	5507 (6)	1968 (7)	6412 (7)	2·5 (3)
O(4)	2351 (6)	1211 (6)	3392 (6)	1·7 (3)	7173 (6)	3046 (7)	7727 (7)	1·9 (3)
O(5)	1730 (6)	1423 (7)	5420 (7)	2·7 (3)	7625 (6)	1419 (7)	5994 (6)	1·8 (3)
O(6)	603 (7)	−90 (8)	3882 (7)	3·3 (3)	8662 (6)	1683 (7)	8073 (7)	2·2 (3)

Table 1 (*cont.*)

	Molecule 1				Molecule 2			
	x	*y*	*z*	*U* (Å²)	*x*	*y*	*z*	*U* (Å²)
1-Adamantanecarboxylic acid								
C(1)	2997 (11)	4731 (11)	4112 (12)	2·5 (4)	8766 (11)	5306 (11)	5804 (13)	2·8 (5)
C(2)	3396 (25)	5166 (28)	5261 (30)	15·6 (15)	9121 (11)	6282 (12)	6541 (13)	3·2 (5)
C(3)	4410 (15)	5294 (16)	5948 (17)	6·4 (7)	8583 (12)	6495 (12)	7064 (13)	3·4 (5)
C(4)	4716 (18)	5846 (19)	5387 (20)	9·2 (9)	7667 (12)	6395 (13)	6269 (14)	3·8 (5)
C(5)	4613 (16)	5473 (17)	4458 (19)	7·7 (8)	7245 (12)	5364 (13)	5493 (13)	3·6 (5)
C(6)	4542 (21)	4386 (24)	4072 (25)	12·3 (12)	7241 (12)	4664 (14)	6094 (14)	5·6 (6)
C(7)	4273 (17)	3807 (18)	4575 (19)	8·0 (8)	8152 (11)	4776 (11)	6867 (12)	2·6 (5)
C(8)	3154 (21)	3763 (22)	4055 (24)	11·4 (11)	8713 (11)	4590 (12)	6352 (13)	3·1 (5)
C(9)	4276 (17)	4252 (18)	5553 (19)	7·8 (8)	8484 (12)	5762 (13)	7615 (14)	4·3 (5)
C(10)	3527 (22)	5282 (24)	3675 (25)	13·3 (11)	7845 (12)	5186 (13)	4995 (14)	3·6 (5)
C(11)	2079 (12)	4609 (13)	3505 (14)	4·2 (5)	9300 (12)	5124 (13)	5271 (14)	3·8 (5)
O(1)	1656 (9)	4986 (10)	3851 (11)	6·2 (4)	9498 (7)	5688 (8)	4863 (8)	4·4 (3)
O(2)	1756 (10)	4078 (10)	2591 (11)	6·8 (5)	9606 (9)	4390 (10)	5303 (11)	6·1 (4)
Water of crystallization								
	x	*y*	*z*	*U* (Å²)	*x*	*y*	*z*	*U* (Å²)
W(1)	6356 (22)	9593 (24)	441 (8)	1·2 (7)[c]	*W*(16) 1821 (18)	8062 (20)	196 (21)	16·6 (11)
W(2)	6311 (7)	8091 (20)	1284 (19)	1·9 (8)[d]	*W*(17) 3568 (11)	8647 (12)	676 (12)	9·8 (6)
W(3)	−349 (7)	6774 (8)	2434 (7)	3·4 (3)	*W*(18) 620 (10)	3989 (11)	4563 (11)	8·5 (5)
W(4)	9110 (8)	2071 (8)	17 (8)	4·5 (4)	*W*(19) −460 (6)	187 (7)	4742 (7)	2·9 (3)
W(5)	365 (7)	8469 (8)	2324 (8)	3·6 (3)	*W*(20) −68 (13)	2570 (14)	2817 (15)	11·0 (7)
W(6)	1852 (7)	−18 (8)	7173 (8)	4·3 (4)	*W*(21) 782 (8)	5702 (9)	8637 (9)	5·4 (4)
W(7)	603 (7)	947 (8)	6717 (7)	3·3 (3)	*W*(22) 8330 (17)	9100 (18)	2193 (19)	14·1 (9)
W(8)	116 (8)	3729 (9)	1484 (9)	5·2 (4)	*W*(23) 894 (20)	8899 (23)	9157 (23)	22·3 (14)
W(9)	7835 (7)	1907 (8)	656 (8)	4·3 (4)	*W*(24) 3397 (16)	1181 (18)	8433 (18)	15·3 (9)
W(10)	5068 (11)	2450 (12)	9388 (12)	9·3 (6)	*W*(25) 1835 (21)	8870 (22)	8416 (23)	16·3 (12)
W(11)	4754 (7)	663 (8)	7588 (8)	3·9 (3)	*W*(26) 5073 (16)	490 (17)	9558 (18)	6·8 (7)[f]
W(12)	541 (7)	6114 (8)	3941 (8)	4·5 (4)	*W*(27) 5289 (9)	−621 (9)	2512 (10)	5·4 (4)
W(13)	4631 (10)	7577 (11)	482 (10)	7·8 (5)	*W*(28) 3860 (15)	103 (17)	15 (18)	14·1 (8)
W(14)	6458 (13)	941 (15)	8934 (14)	3·0 (6)[e]	*W*(29) 6411 (20)	9000 (22)	1581 (23)	7·5 (9)[g]
W(15)	8522 (12)	1012 (13)	2137 (13)	10·7 (6)	*W*(30) 5765 (16)	−285 (16)	70 (18)	3·9 (7)[h]

The population parameters for the waters of crystallization are $c = 0{\cdot}3$, $d = 0{\cdot}3$, $e = 0{\cdot}5$, $f = 0{\cdot}6$, $g = 0{\cdot}5$, $h = 0{\cdot}5$.

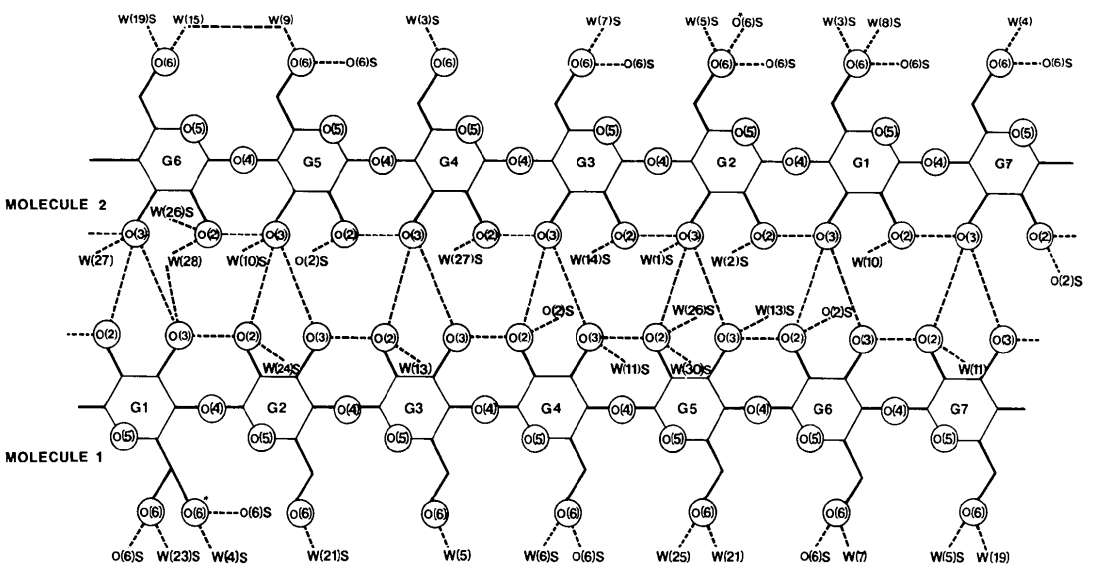

Fig. 2. The cycloheptaamylose dimer displayed diagrammatically in a linear arrangement. The intramolecular hydrogen bonds and those possible for the primary and secondary hydroxyl groups are shown.

Discussion

In addition to two complex units, the asymmetric unit contains thirty water molecules. The two cycloheptaamylose molecules form a head-to-head dimer by means of several strong hydrogen bonds between the secondary hydroxyl groups on adjacent molecules (Fig. 2). This dimer is almost identical in dimensions and

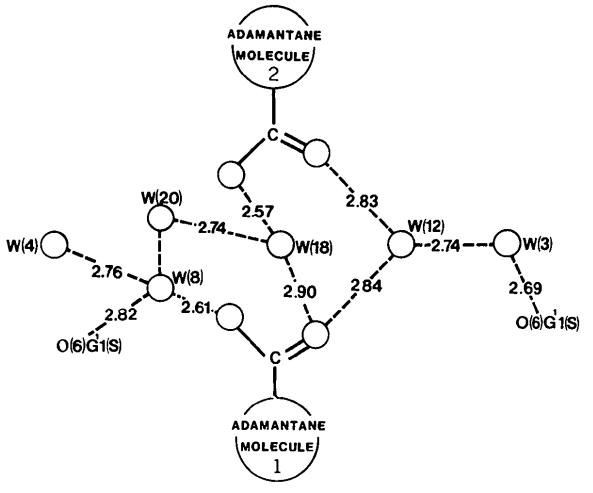

Fig. 3. Linking of the 1-adamantanecarboxylic acid by hydrogen bonding *via* water molecules; $\sigma = 0{\cdot}03$ Å for bond lengths.

conformation to that previously observed by us for complexes of cycloheptaamylose with substituted benzoic acids and phenols (space group $C2$; Hamilton, Sabesan & Steinrauf, 1981). The main difference is that in the $C2$ form the two halves of the dimer are related by the crystallographic twofold axis. This results in the overcrowding of the guest molecules around the twofold axis and the guests are consequently disordered. In this present $P1$ form there are no crystal-symmetry requirements and the guests are not subjected to symmetry restrictions. The hydrogen bonding which forms the dimer appears to be very similar in the $P1$ and $C2$ crystal forms (*i.e.* those hydrogen bonds involving only the secondary hydroxyl groups of the cycloheptaamylose molecules). A detailed comparison of the structures will be deferred to another publication.

The main interest in the present crystal structure is the position of the 1-adamantanecarboxylic acid in the cycloheptaamylose cavity. As can be seen from Fig. 4, the guest is oriented in each crystallographically independent complex with the carboxylic acid group pointing to the primary hydroxyl end of the cycloheptaamylose (Fig. 5). Fig. 6 shows how completely the guests are enclosed. In our discussion of the benzoic acids and their orientation in the cycloheptaamylose dimer (Hamilton, Sabesan & Steinrauf, 1981) we concluded that dimer formation is equivalent to the 'capping' of the cycloheptaamylose by chemical modification as described by Breslow *et al.* (1980). In the crystal structure the access of the water is restricted at the secondary hydroxyl end of the cycloheptaamylose by the dimer 'cap' and the 1-adamantanecarboxylic acid orients itself so that the carboxylic acid group can be solvated at the open primary hydroxyl end. This agrees with the work of Bergeron, Channing, McGovern & Roberts (1979), who concluded from NMR studies in solution with a number of carboxylic acid guests and cycloheptaamylose that solvation of the polar groups was the most important factor in the positioning and stability of the guest in the cycloheptaamylose cavity.

The carboxylic acid groups of two neighboring adamantane molecules (along the direction of the molecular sevenfold axis) are twisted approximately 90° with respect to each other and are linked by two water molecules $W(12)$ and $W(18)$ (Figs. 3 and 4). There is no direct hydrogen bonding of the carboxylic acid groups to the primary hydroxyl groups. The primary hydroxyl groups are all in the *gauche–gauche* conformation except for that of the disordered primary hydroxyl of residue 1 of molecule 1, which is 50% in the *gauche–gauche* conformation and 50% in the *gauche–trans* conformation. Thus the primary hydroxyl groups point away from the cycloheptaamylose cavity (and the guest) and are hydrogen bonded to the remaining water molecules (28 positions) which form a water channel parallel to the cycloheptaamylose channel, *i.e.* parallel to the molecular sevenfold axis. Some of the primary and secondary hydroxyl groups are linked to those on a parallel cycloamylose column *via* hydrogen bonding to the water channel. The water channel thus contributes greatly to the stability of the crystal. A similar packing arrangement was found in the $C2$ form (Hamilton, Sabesan & Steinrauf, 1981).

The orientation and the depth of penetration of the two guests in the two crystallographically independent complexes are different. As seen in Fig. 4 the guest in the bottom half of the cycloheptaamylose dimer (molecule 2) is sitting so that its adamantane moiety is some distance from the secondary hydroxyl end and its carboxylic acid group is slightly beyond the primary hydroxyl oxygens. In fact the centroid of the adamantane moiety (excluding the carboxylic acid group) lies just outside the circle formed by the C(5) and O(5) atoms of the cycloheptaamylose and approximately

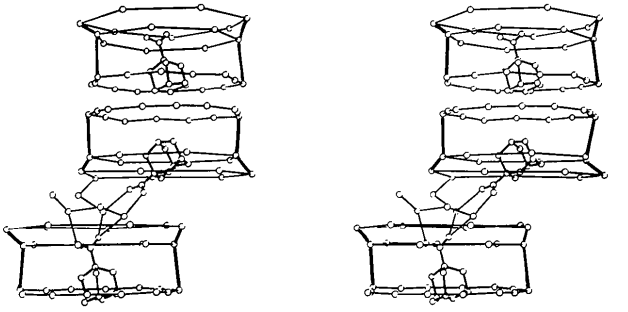

Fig. 4. Stereoview of the dimer of the complex plus an additional complex unit related by a cell translation. The cycloheptaamylose is represented by its primary hydroxyl, secondary hydroxyl and glycosidic oxygen atoms. These are joined to form rings. Omission of the carbon atoms allows the position of the 1-adamantanecarboxylic acid molecules to be appreciated.

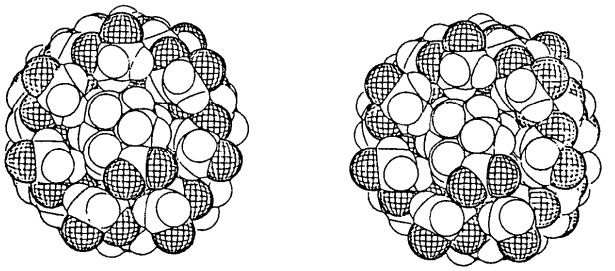

Fig. 5. Stereoview of a space-filling model of one of the cycloheptaamylose complex units. It is viewed down the sevenfold molecular axis from the primary hydroxyl end.

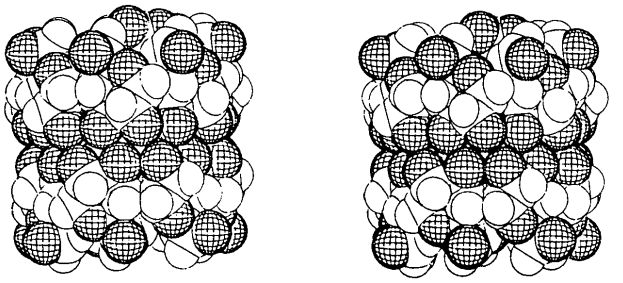

Fig. 6. Stereoview of a space-filling model of the cycloheptaamylose complex dimer seen perpendicular to the sevenfold molecular axis. The interlocking of the secondary hydroxyl oxygen atoms which hydrogen bond to form the dimer is spectacular. The guest molecules are almost completely enclosed in the cycloheptaamylose cavities. The carboxylic acid of guest 2 sticks out further than that of guest 1.

1·4 Å from the circle formed by the C(1) and C(4) atoms. The interior of the cavity is not a smooth cone or cylinder but has a constriction in the neighborhood of the O(4) atoms and another in the neighborhood of C(5) atoms (Fig. 3). Atoms C(5) and O(4) of each residue protrude farthest into the cycloheptaamylose cavity and form constrictions to the entrance of the guest molecules. The average distances of C(5) and O(4) of the cycloheptaamylose from the molecular sevenfold axis are 5·10 (2) and 5·03 (2) Å for molecule 1 and 5·06 (2) and 5·08 (2) Å for molecule 2. Thus the centroid of the guest (which corresponds approximately to the widest cross section of the guest) is located on the solvent side of C(5) of the cycloheptaamylose and in a region where the fit of the guest in the cavity is tight and the van der Waals contacts strong. In the case of guest 1 the centroid of the adamantane moiety lies just above the circle formed by the C(2) and C(3) atoms of cycloheptaamylose on the secondary hydroxyl side of this circle. The distance of the centroid from the circle formed by the C(1) and C(4) atoms of the cycloheptaamylose is approximately 2 Å. Thus the adamantane moiety of guest 1 lies partly in the hydrophobic space produced at the secondary hydroxyl end by dimer formation. Thus its position does not place the widest cross section of the adamantane moiety at the constriction produced by O(4). It is located in a wider part of the cavity where the van der Waals contacts are weaker. In addition to the different depths of penetration for the two guest molecules, the adamantane rings are slightly rotated with respect to each other about an axis through C(1) and C(7) of the adamantane ring. In the dimer unit the closest approach of the adamantane rings is 4·25 (7) Å between atom C(6) on guest 1 and atom C(5) on guest 2.

Another significant difference between the two guest molecules is that the temperature parameters of guest 1 are, on average, twice those of guest 2 (Table 1). This could be caused by two conditions: the binding constants of the two guests are different or guest 1 may not have full occupancy. The latter situation can be dismissed because loss of partner in this scheme (Fig. 3) would require substitution of water to solvate the carboxylic acid group of the remaining guest and no evidence was found for disordered water molecules in this area. The final difference Fourier map was very flat, showing no peaks with electron density greater than 0·3 e $Å^{-3}$. It seems reasonable to conclude that the high temperature parameters for all atoms of guest 1 reflect its less-favorable environment (looser fit) and probably weaker binding to the cycloheptaamylose.

In conclusion, in the two crystallographically independent complexes of cycloheptaamylose with 1-adamantanecarboxylic acid, the guest occupies a different position in each complex. The orientation of the guest in the cavity and its depth of penetration are controlled by the constrictions in the cavity produced around atoms C(5) and O(4) of the cycloheptaamylose and by the ability of the carboxylic acid group to be solvated at the open primary hydroxyl end. Access to water at the secondary hydroxyl end is limited by the dimerization of the cycloheptaamylose.

The binding of the 1-adamantanecarboxylic acid is different in the two orientations. The preferred position of the guest has the carboxylic acid group protruding further from the cavity at the primary hydroxyl end. The guests are further stabilized by hydrogen bonding *via* water between adjacent molecules along the direction of the molecular sevenfold axis.

The guest positions suggest entry of one guest from the secondary hydroxyl end of the cycloheptaamylose and entry of the other from the primary hydroxyl end. Since guest 1 would be in a very unfavorable position in a monomer unit, it is possible that before crystallization the guest can move along the cavity to its final observed position after dimerization takes place.

In solution additional arrangements of the complex are possible, including inversion of each of the guest positions found in the crystal. This is a consequence of the secondary hydroxyl end being open in solution and allowing solvation of the carboxylic acid group.

Our structural results are in agreement with Komiyama & Bender (1978) and in disagreement with

Breslow *et al.* (1980). The cycloheptaamylose cavity is large enough to accommodate completely the 1-adamantanecarboxylic acid.

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