

X-Ray crystallographic study of octakis(3,6-anhydro)- γ -cyclodextrin with a highly specific cation binding ability†

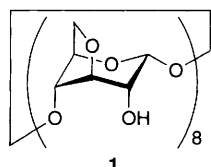
Hatsuo Yamamura,* Hideki Masuda, Yoshitaka Kawase, Masao Kawai, Yasuo Butsugan and Hisahiko Einaga

Department of Applied Chemistry, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466, Japan

Octakis(3,6-anhydro)- γ -cyclodextrin, which is composed of eight 3,6-anhydroglucoses, is analysed by X-ray crystallography to determine its unique structure which contains a hydrophilic cavity enabling specific binding to Cs⁺.

Cyclodextrins (CDs) have been an important subject of investigation in biomimetic chemistry, since they can act as hosts for hydrophobic guest compounds through predominantly hydrophobic interactions.¹ It is essential to improve the inclusion ability of CDs for further development of their host-guest chemistry. Compared with numerous studies of introducing functional groups into CDs, there have been very few studies on the modification of the CD cavity itself. We² and others³ succeeded in 3,6-anhydration of the glucose units in CD to change drastically the nature of the cavity. In particular, the poly(3,6-anhydro) derivatives acquired specific cation binding abilities.^{2d,f} For detailed discussion of their unique molecular behaviour, structural information from X-ray crystal analysis would be most instructive, as for crown ethers and cryptands. Here we report the X-ray structural analysis of octakis(3,6-anhydro)- γ -CD **1**^{2d} composed of eight 3,6-anhydroglucoses possessing specific Cs⁺ affinity. We believe this is the first example of the X-ray crystallographic study of a 3,6-anhydro-CD derivative.[§]

The result of the structural analysis of **1** using X-ray crystallography^{||} is shown in Fig. 1. The molecule of **1** which possesses C₂ symmetry consists of four crystallographically nonequivalent 3,6-anhydroglucose units. The four anhydroglucose units, restricted to a ¹C₄ conformation by intramolecular ether bridges, adopt essentially the same geometry; *i.e.* their corresponding torsion angles for the bicyclic structure are within $\pm 2^\circ$. The torsion angles which describe the interunit geometry, however, differ markedly from each other; *i.e.* the (ϕ , ψ) values^{||} are (83.3, 171.3), (148.5, 105.1), (71.6, 73.3), and (91.7, 172.8). Thus, in contrast to the cylindroconical structure of unmodified CDs,⁵ the molecular shape of **1** resembles a 'horse saddle'. This structure is stabilized by an inter-residual hydrogen bonding network between hydroxy groups at C(2) and glycosidic oxygen atoms [Fig. 1(a)]. The secondary hydroxy oxygens point inwards and the inner surface of the molecular cavity is covered by the oxygen atoms of the hydroxy groups and two types of hemiacetal oxygen atoms. Therefore, **1** is reasonably expected to include a cation in its hydrophilic cavity as do cryptands.⁶ Thirteen H₂O molecules per molecule of **1** are present, three of which participate in hydrogen bonding with the hydroxy groups of **1**.



The binding ability of **1** for 21 cations (M)^{**} was examined by the reported method^{2d} using liquid secondary ion mass spectrometry (LSIMS). Fast atom bombardment mass spectrometry (FABMS) has often been used in order to determine the cation binding ability of crown ethers.⁷ Since LSIMS is generally accepted as identical to FABMS,^{8,††} we estimated that the cation binding ability of **1** using LSIMS should be qualitatively similar. Fig. 2 shows the observed relative intensities of the [**1** + M]⁺ ion peaks, which are assumed to reflect the affinities of **1** for the given metal cations. The results indicated that **1** favoured binding of the largest ions, Cs⁺, followed by Rb⁺. Compound **1** did not show significant affinity towards other cations.

According to the crystallographic data, all of the 24 oxygen atoms of the hemiacetal and hydroxy groups which cover the inner wall of **1** are arranged approximately on the surface of a

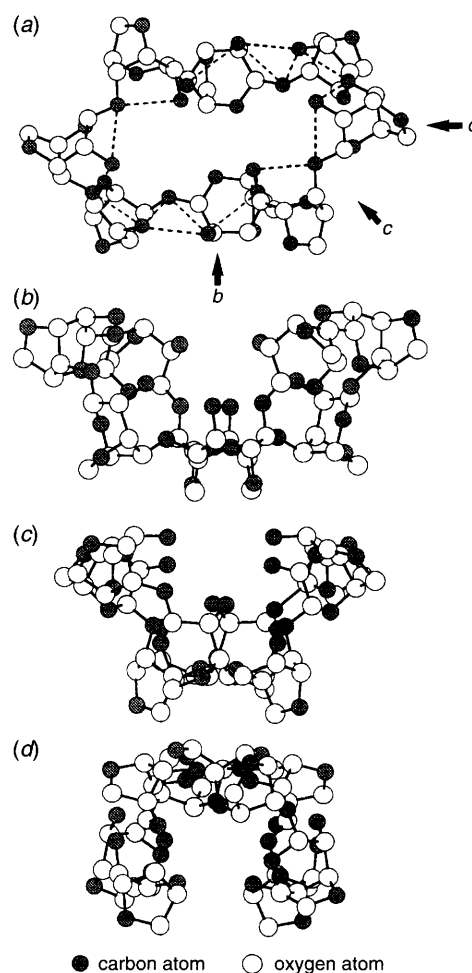


Fig. 1 Molecular structure of **1**; (a) top view looking down the y axis; (b)–(d) side views of Fig. 1(a); dotted lines indicate possible hydrogen bonds

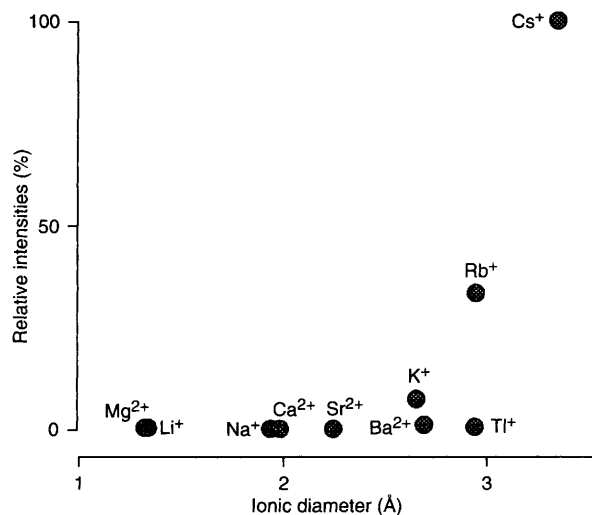


Fig. 2 Relative intensities of $[1 + M]^+$ ions in the LSIMS spectra

sphere. The radius of the optimized sphere is calculated as 4.66 Å and the standard deviation of each oxygen atom from the spherical surface is 1.05 Å. Considering the ionic radius of Cs⁺ (1.67 Å) and the van der Waals radius of oxygen (1.52 Å), the cavity radius of 4.66 Å suggests that the oxygen atoms of the cavity of **1** may be accessible to Cs⁺ upon slight conformational change, which accounts for the strong affinity of **1** towards Cs⁺.

In summary, we have demonstrated a unique structure of free **1** which possesses a characteristic Cs⁺ binding ability. We are now studying the molecular structures of metal complexes of per(3,6-anhydro)-CDs.

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Footnotes

† We have already reported some of these findings at the 67th National Meeting of the Chemical Society of Japan, Tokyo, March 31st, 1994, Abstract of Papers II, 3 D2 34, p. 831.

‡ These workers also synthesized hexakis(3,6-anhydro)- α -CD and heptakis(3,6-anhydro)- β -CD. See reference 3.

§ Professor J. F. Stoddart reported that a full set of X-ray data for heptakis(3,6-anhydro)- β -CD had been collected but that a structural solution had not yet been achieved.^{3b,c}

¶ Crystal data for **1**: C₄₈H₆₄O₃₂·14H₂O; dimensions, 0.1 × 0.25 × 0.25 mm; monoclinic, space group C2; *a* = 22.200(2), *b* = 10.305(1), *c* =

15.406(1) Å; β = 123.08(1)°; *U* = 2953.3 Å³; *Z* = 2; scan mode, ω -2 θ ; ω -2 θ_{\max} = 60°; *D_c* = 1.59 Mg m⁻³; μ = 1.034 mm⁻¹; λ = 0.71073 Å; *T* = 293 K; 3252 observed reflections with 2766 [*I_o* ≤ 3 σ (*I_o*)] used. Data were collected on an Enraf-Nonius CAD4-EXPRESS diffractometer. The structure was solved by direct methods using the SIR88 program and refined to *R* = 0.053, *R'* = 0.071. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/31.

|| Torsion angles ϕ , ψ refer to O–C(1)–O–C(4') and C(1)–(O)–C(4')–C(3'), respectively; see ref. 4.

** We examined the binding ability of **1** towards Li⁺, Na⁺, K⁺, Rb⁺, Cs⁺, Mg²⁺, Ca²⁺, Sr²⁺, Ba²⁺, Tl⁺, Ag⁺, Fe³⁺, Ni²⁺, Co²⁺, Cu²⁺, Zn²⁺, Pb²⁺, NH₄⁺, MeNH₃⁺, Me₂NH₂⁺ and Me₃NH⁺.

†† This was also supported by the fact that the cation binding study of hexakis(3,6-anhydro)- α -CD using LSIMS gave the same result as that using FABMS (unpublished work).

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