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X-ray Structural Studies of β-Cyclodextrin Inclusion Complexes with Racemic and *S*(−)Methyl-*p*-tolylsulfoxides

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Abstract. In order to clarify the reason why the stereospecific sulfoxides undergo racemization in solution but not in the complex crystal with β-cyclodextrin (β-CD) in the solid state, a crystal structure analysis of two β-CD inclusion complexes with methyl-*p*-tolylsulfoxide (MTSO) having a chiral sulfur atom was carried out.

Key words. Methyltolylsulfoxide, cyclodextrin complex, X-ray structure.

1. Introduction

In order to clarify the reason why the stereospecific sulfoxides undergo racemization in solution but not in the complex crystal with β-cyclodextrin (β-CD) in the solid state, a crystal structure analysis of two β-CD inclusion complexes with methyl-*p*-tolylsulfoxide (MTSO) having a chiral sulfur atom was carried out.

2. Experimental

Table I shows the crystallographic data for two inclusion complexes of MTSO, in which the β-CD molecule includes a racemic *R*,*S*(±)-MTSO or a stereospecific *S*(−)MTSO (Figure 1). β-CD was dissolved in distilled hot water at 70°C and the guest sample (MTSO)

Fig. 1. The stereoisomers of methyl-*p*-tolyl-sulfoxide (MTSO): (a) *S*(−)-MTSO; (b) *R*(+)-MTSO.

Table I. Crystallographic data

Inclusion Complex	(β-CD) $R,S(\pm)$MTSO	(β-CD) $S(-)$MTSO
Chemical Formula	$(C_{42}H_{70}O_{35})_2 \cdot (C_8H_{10}OS)_3 \cdot 34\,H_2O$	$(C_{42}H_{70}O_{35})_4 \cdot (C_8H_{10}OS)_4 \cdot 68\,H_2O$
Mol. Weight	3191.0	6381.6
Crystal System	triclinic	monoclinic
Space Group	$P1$	$P2_1$
Z	1	2
Cell Dimensions		
a (Å)	19.618(3)	15.495(2)
b (Å)	15.432(1)	65.04(2)
c (Å)	15.476(3)	15.471(5)
α (°)	102.98(2)	90.0
β (°)	117.70(1)	102.60(2)
γ (°)	104.30(1)	90.0
Volume (V)	3692(2)Å^3	15216(2)Å^3
D_m (g cm^{-3})	1.433(6)	1.39(1)
D_x (g cm^{-3})	1.434	1.393
Crystal Dimensions	0.15 × 0.3 × 0.6 (mm)	0.2 × 0.2 + 0.4 (mm)
Radiation Used	CuK_α	CuK_α
No. of Reflections Used	6858	1567
R-factor	0.18	0.27

dissolved in ethanol-water mixed solvent was slowly added to the β-CD aqueous solution in a 1 : 1.2 host–guest ratio. After gradually cooling, crystals were obtained at room temperature in a few days. A crystal was sealed into a glass capillary with a small amount of mother liquor, and X-ray intensity data were collected on a Rigaku automated four-circle diffractometer with graphite-monochromatized CuK_α radiation. The crystal density was measured by the flotation method using a benzene-carbon tetrachloride mixture.

The structure determination was initiated by inspection of the Patterson function. As shown in Figure 2, the glucopyranose ring which is the building unit of the β-CD

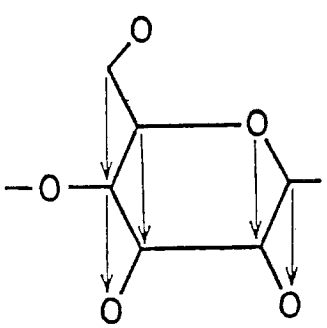

Fig. 2. The glucopyranose unit of the β-CD molecule. The arrow indicates the interatomic Patterson vector with a distance of 2.5 Å and the same direction.

molecule and takes a chairform conformation, has several C—C or C—O interatomic vectors with a distance of 2.5 Å and the same direction. Therefore the molecular orientation of β-CD was determined from the position of a Patterson peak with a distance of 2.5 Å. Then the β-CD molecule with a fixed orientation was moved by rotational and translational operations in the unit cell, and the most reasonable position of the β-CD molecule was indicated by the lowest R-factor. After successive Fourier syntheses, the structure was refined by a least-squares procedure. All the calculations were carried out by using an ACOS-850S computer at the Crystallographic Research Center, Institute for Protein Research, Osaka University.*

3. Results and Discussion

The structure of β-CD : $R,S(\pm)$-MTSO is highly isomorphous to that of β-CD : 3,4-xylidine which was recently solved by us [1]. Assuming that the molecular conformation of β-CD in β-CD : $R,S(\pm)$-MTSO should be the same as that in β-CD : 3,4-xylidine, the atomic coordinates of the β-CD molecules in β-CD : 3,4-xylidine were used and the structure refined to an R-factor of 0.18. The head-to-head dimeric structure is shown in Figure 3. The molecular orientations of the three guest molecules, $R,S(\pm)$-MTSO, are not unequivocally determined because of disorder, especially for the guest molecule

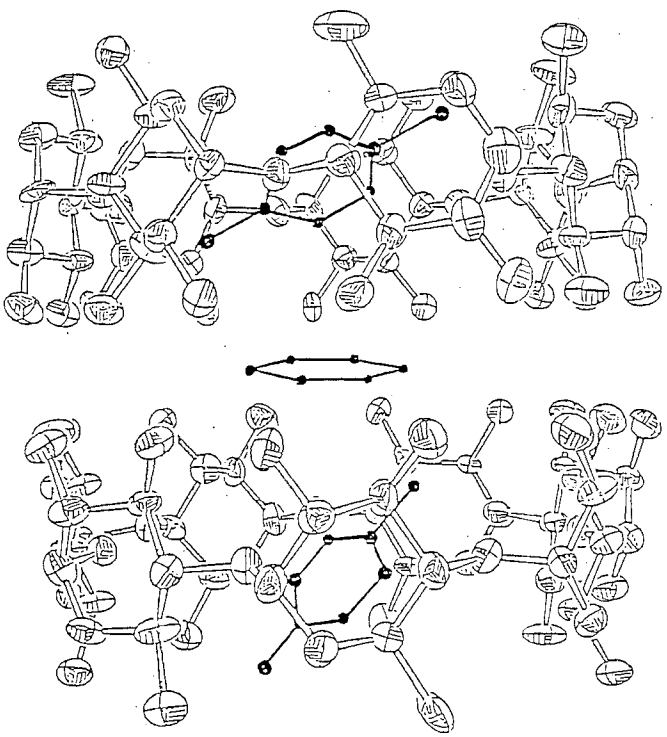

Fig. 3. The head-to-head type molecular structure of β-CD : $R,S(\pm)$MTSO. The side chain of the guest MTSO molecule sandwiched between two β-CD molecules is not shown because of the disordered structure.

* Tables of atomic coordinates and temperature factors have been deposited at the Cambridge Crystallographic Data Center.

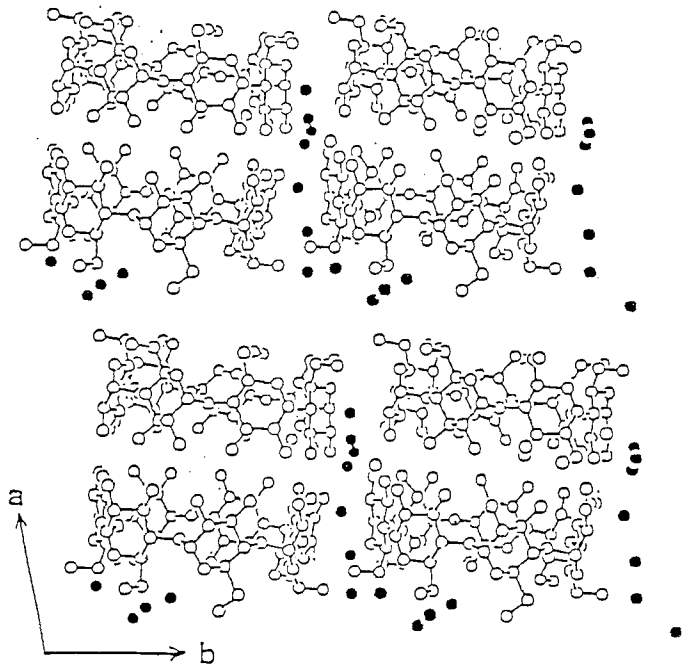

Fig. 4. The crystal structure of β-CD : *R,S*(±)MTSO. The black circles indicate the solvent water molecules. For clarity, the guest MTSO molecules are not shown in the figure.

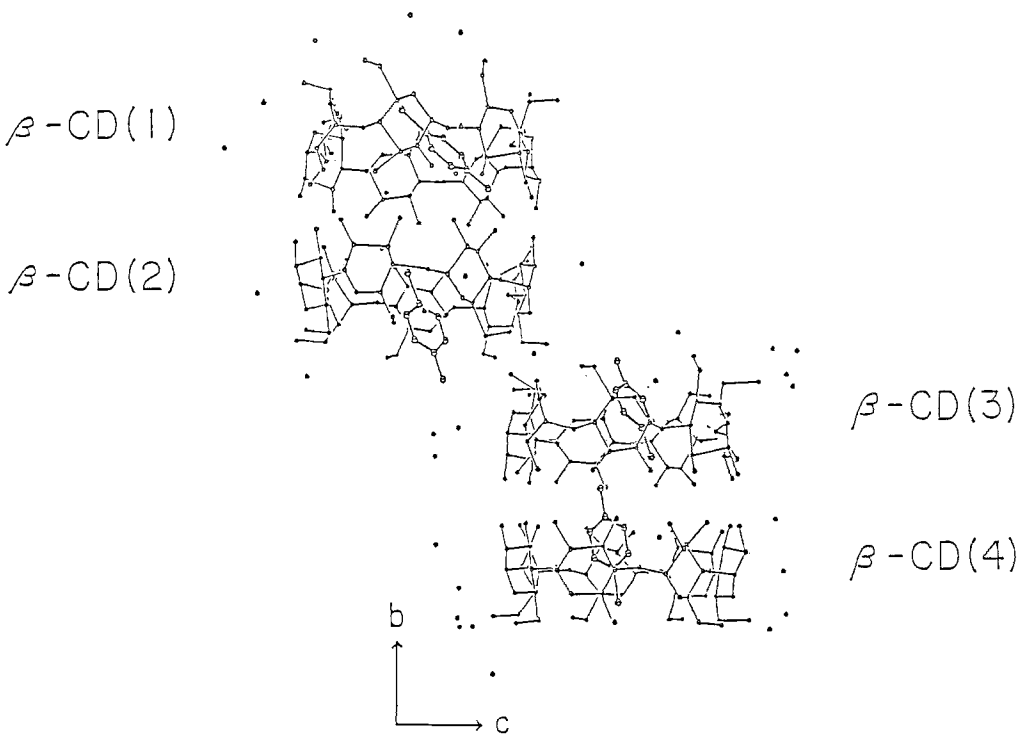

Fig. 5. The molecular packing of β-CD : *S*(−)MTSO. The black circles indicate the solvent water molecules. Four β-CD molecules are crystallographically independent of each other.

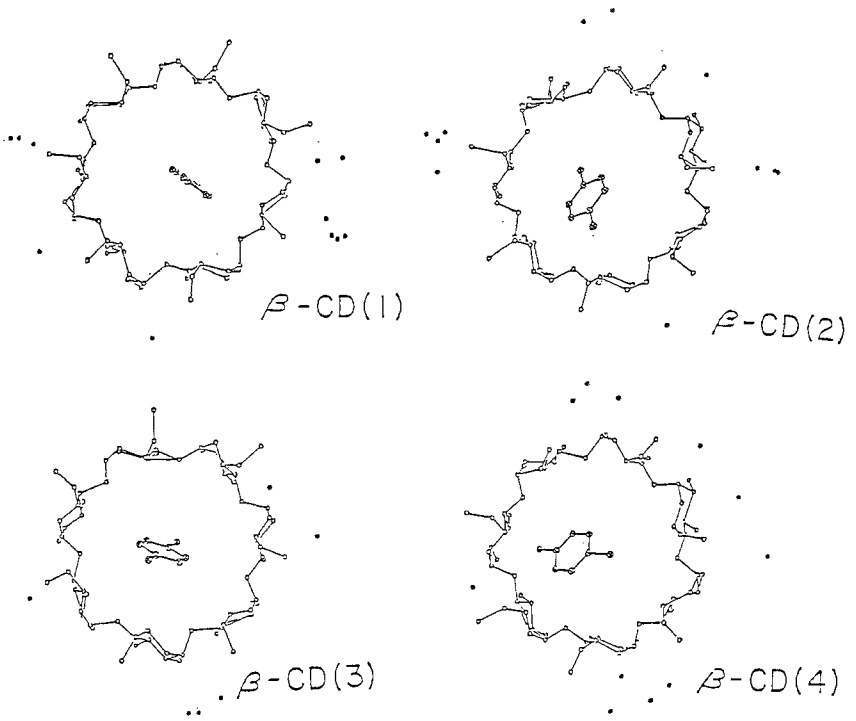

Fig. 6. The host–guest interaction modes in β-CD : *S*(−)MTSO. The black circles indicate the solvent water molecules.

sandwiched between two β-CD molecules. As shown in Figure 4, the molecular packing in the crystals is of the brick type structure similar to that found in β-CD : salicylic acid [2].

The host-guest interactions in the crystal of β-CD : *S*(−)MTSO complex are shown in Figures 5 and 6. The host-guest ratio is 2 : 2 similar to that in the β-CD : *p*-ethylaniline complex [3], but as already indicated in Table I, two crystallographically independent dimeric molecules are piled up as shown in Figure 5. The positions of the guest molecules in the β-CD cavity are presented in Figure 6. These are tentative and it was not possible to determine the definitive positions unequivocally because of the disordered structure.

Unfortunately, we have not yet succeeded in the crystallization of β-CD : *R*(+)MTSO and, therefore, it cannot be concluded why the chiral sulfoxides undergo racemization in solution, but not in the solid state as they are all included in the β-CD cavities.

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