ChemComm

Crystallographic evaluation of the mobility of 2-naphthoic acid included in heptakis(2,6-di-*O*-methyl)-β-cyclodextrin

Kazuaki Harata

Biomolecules Department, National Institute of Bioscience and Human-Technology, 1-1 Higashi, Tsukuba, Ibaraki 305-8566, Japan. E-mail: harata@nibh.go.jp

Received (in Columbia, MO, USA) 15th September 1998, Accepted 4th December 1998

Analysis of anisotropic temperature factors of the title compound revealed the rigid-body thermal motion of 2-naphthoic acid, which has root mean squared amplitudes of 0.3 Å for translational motion and 6° for libration.

Cyclodextrins are cyclic oligosaccharides consisting of glucose units and form inclusion complexes with a variety of guest molecules. X-Ray structures of numerous crystalline complexes of cyclodextrins and their derivatives have revealed guest molecules included in the macrocyclic cavity.[1] The guest molecules have relatively high mobility in the host cavity because they are weakly bound by van der Waals forces, electrostatic forces, hydrogen bonds, *etc.* instead of chemical bonds. However, no attention has been paid to the mobility of included guest molecules. Analysis of not only the mean structure of inclusion but also the mobility of the guest molecule is essential to elucidate the characteristics of included guests. The crystallographic temperature factor is a measure of the mobility of the atoms, groups or molecules.[2] Analysis of temperature factors is expected to provide information on the dynamic state of guest molecules in crystalline complexes. Here we deal with the thermal motion of 2-naphthoic acid included in heptakis(2,6-di-*O*-methyl)-β-cyclodextrin. The crystal structure of the 1 : 1 complex has been reported.[3]† The naphthalene ring of the guest molecule is inserted into the host macrocycle from the O6 side while the carboxy group protrudes outside the host cavity.

The molecular fluctuation of 2-naphthoic acid was evaluated by the TLS method[4] which has been applied for the analysis of thermal motion of molecular crystals.[4,5] The anisotropic temperature factor is expressed by a linear combination of translation (T), libration (L) and screw motion (S), as described in eqn. (1), where G_{ijkl} and H_{ijkl} are functions of the atomic coordinates.

$$u_{ij} = \Sigma G_{ijkl}\boldsymbol{L}_{kl} + \Sigma H_{ijkl}\boldsymbol{S}_{kl} + \boldsymbol{T}_{ij} \qquad (1)$$

Tensor elements for these motions were determined by the least-squares fit to observed anisotropic temperature factors. The quantity minimized was $\Sigma w_{ij}(\Sigma G_{ijkl}\boldsymbol{L}_{kl} + \Sigma H_{ijkl}\boldsymbol{S}_{kl} + \boldsymbol{T}_{ij} - u_{ij})$.[2] The inverse value of the estimated standard deviation of u_{ij} was used as weight w_{ij}. The center of libration was so determined that the ***S*** tensor was symmetrical. The tensors of ***T***, ***L***, and ***S*** are given in Table 1. From the eigenvalues of ***T*** and ***L*** tensors, the root mean squared amplitudes of translational and rotational vibration were estimated as 0.35, 0.27 and 0.27 Å and 4.6, 5.1 and 7.7°, respectively, for the three principal axes. Therefore, 2-naphthoic acid has a rotational vibration of about 6° and a translational vibration of about 0.3 Å. The discrepancy factor for observed and calculated values of u_{eqv} (Table 2), $\Sigma|u_{eqv}^{obs}-u_{eqv}^{cal}|\Sigma u_{eqv}^{obs} = 0.048$, indicates that the magnitude of atomic thermal motion is mostly derived from the rigid-body motion. In contrast, the discrepancy factor of 0.24 for u_{ij} is large. The reason is obvious from the comparison between observed and reproduced temperature factors as shown in Fig. 1. Differences in the orientation of thermal ellipsoids are observed for C5, C6, C7, C8, O1 and O2 and significant disagreements are found in off-diagonal u_{ij} elements for these atoms. A possible explanation for the disagreement is the effect of torsional vibration of the carboxy group around the C2–C11 bond. The local motion of the carboxy group affects the libration parameters and as a result disagreement also occurs for C5, C6, C7 and C8, which are located on the other end of the guest molecule. Such internal motion is coupled with the rigid-body motion and not distinguishable. The TLS model was also applied for the host molecule, but the discrepancy factors of 0.31 and 0.50 for u_{eqv} and u_{ij}, respectively, indicate that the thermal motion of the host molecule is not a simple rigid-body motion because of the high conformational flexibility of the macrocyclic ring.

As shown in Fig. 1, the largest translational motion is in the direction of the short axis of the naphthalene ring. Intermolecular contacts with host molecules impose restrictions on the movement of the guest molecule. Motion in the direction perpendicular to the molecular plane is prohibited by a methyl group and CH_2 groups,[2] which are marked with asterisks in Fig. 1. The carboxy group, which is coplanar with the naphthalene ring within an atomic deviation of 0.05 Å, forms a water-mediated hydrogen-bond bridge with an adjacent host molecule. The C1, C4, C5 and C8 atoms of the naphthalene ring have contacts with the O6 oxygen atoms of the host of 3.5–3.8 Å. Two methyl groups of an adjacent host molecule related *via* a two-fold screw axis are inserted from the secondary hydroxy side and have contacts with the C6 and C7 atoms of the naphthalene ring with a shortest distance of 3.5 Å. The center of libration (O1) is shifted by 0.83 Å towards the C2 atom from the

Table 1 TLS tensors

$\boldsymbol{T}/10^{-3}$ Å^2	$\boldsymbol{L}/10^{-3}$ rad^2	$\boldsymbol{S}/10^{-3}$ rad Å
$\begin{pmatrix} 86 & -7 & -22 \\ -7 & 76 & 8 \\ -22 & 8 & 105 \end{pmatrix}$	$\begin{pmatrix} 13 & 3 & -4 \\ 3 & 10 & -3 \\ -4 & -3 & 10 \end{pmatrix}$	$\begin{pmatrix} -2 & -3 & -2 \\ -3 & 2 & 0 \\ -2 & 0 & 0 \end{pmatrix}$

Table 2 Observed and calculated u_{eqv} (Å^2)

Atom	u_{eqv}^{obs}	u_{eqv}^{cal}	Atom	u_{eqv}^{obs}	u_{eqv}^{cal}	Atom	u_{eqv}^{obs}	u_{eqv}^{cal}
C1	0.097	0.103	C6	0.141	0.142	C11	0.109	0.113
C2	0.095	0.093	C7	0.139	0.137	O1	0.124	0.115
C3	0.107	0.099	C8	0.117	0.127	O2	0.168	0.154
C4	0.117	0.113	C9	0.088	0.100			
C5	0.133	0.136	C10	0.103	0.105			

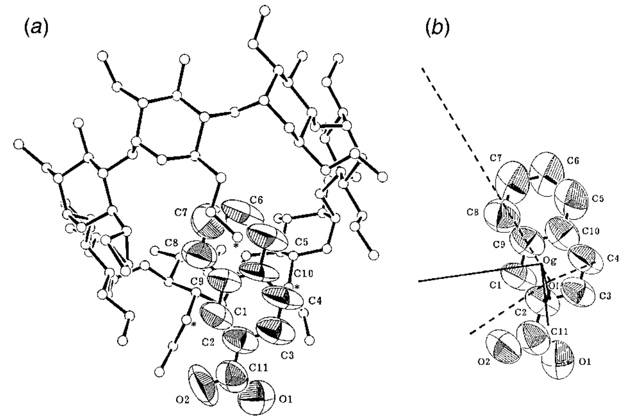

Fig. 1 ORTEP drawings of (*a*) observed and (*b*) reproduced thermal motion of 2-naphthoic acid. Principal axes of translation (solid lines) are drawn from the center of gravity (Og). The length of the axes corresponds to eigenvalues of the ***T*** tensor. Dashed lines denote principal axes of libration drawn from the center of libration (Ol).

center of gravity (Og). The largest libration is around the principal axis located on the guest plane,which makes an angle of about 30° with the long axis of the naphthalene ring. In cyclodextrin complexes, guest molecules generally have greater thermal motion than the host molecules. The present result demonstrates that rigid-body motion is predominant in the thermal motion of the guest molecule and is interpreted in terms of the TLS model.

Notes and references

† *Crystal data*: $C_{56}H_{98}O_{35}\cdot C_{11}H_8O_2\cdot 3H_2O$, M = 1557.6, space group $P2_12_12_1$, a = 15.436(2), b = 18.922(1), c = 27.852(2) Å, Z = 4, D_x = 1.270 g cm^{-3}. X-Ray diffraction data were collected on a Nonius CAD4 diffractometer at 293 K. The structure was refined for 4458 reflections with $F_o > 3\sigma(F)$ to the R value of 0.073.

1 K. Harata, *Chem. Rev.*, 1998, **98**, 1803.
2 B. T. M. Willis and A. W. Pryor, *Thermal Vibrations in Crystallography*, Cambridge University Press, London, 1975.
3 K. Harata, *J. Chem. Soc., Chem. Commun.*, 1993, 2347.
4 V. Schomaker and K. N. Trueblood, *Acta Crystallogr., Sect. B*, 1968, **24**, 63.
5 M. Kaftory and D. Dunitz, *Acta Crystallogr., Sect. B*, 1976, **32**, 617.

Communication 8/07168C