CHEMICAL & PHARMACEUTICAL BULLETIN

Vol. 28, No. 7 July 1980

Regular Articles

[Chem. Pharm. Bull. 28(7)1975—1980(1980)]

# Molecular Dynamics of Prostaglandin $F_{2\alpha}$-Cyclodextrin Complexes in Aqueous Solution[1)]

Fumitoshi Hirayama, Kaneto Uekama,[2a)] and Hideomi Koinuma[2b)]

*Faculty of Pharmaceutical Sciences, Kumamoto University[2a)] and Faculty of Engineering, University of Tokyo[2b)]*

(Received October 22, 1979)

The molecular dynamics of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and its $\alpha$- and $\beta$-cyclodextrin ($\alpha$- and $\beta$-CyD) complexes in aqueous solution were investigated by means of carbon-13 nuclear relaxation measurements. Some reorientation times calculated for $PGF_{2\alpha}$ indicated that the internal motion of the $C_{16}$–$C_{20}$ alkyl chain and the overall tumbling motion were predominantly reduced upon binding to $\alpha$- and $\beta$-CyDs, respectively. Upon inclusion of $PGF_{2\alpha}$, the internal motion of primary alcohol groups slowed down by a factor of 6 in $\alpha$-CyD and by a factor of 2 in $\beta$-CyD, in comparison with the overall motions. The stability of the inclusion complexes is discussed on the basis of dynamic coupling between the molecular motions of the host and guest molecules. Dynamic coupling coefficients of 0.12 and 0.75 were obtained for the $PGF_{2\alpha}$–$\alpha$-CyD and $PGF_{2\alpha}$–$\beta$-CyD systems, respectively, indicating a greater dynamic rigidity for the $\beta$-CyD complex as compared with the $\alpha$-CyD complex. On the basis of these observations, different inclusion modes are proposed in the $\alpha$- and $\beta$-CyD complexes.

**Keywords**——molecular dynamics of inclusion complexes; prostaglandin $F_{2\alpha}$; $\alpha$- and $\beta$-cyclodextrins; $^{13}$C-nuclear relaxation; inversion-recovery technique; correlation time; dynamic coupling coefficients; mode of inclusion in aqueous solution

We recently reported that some naturally occurring prostaglandins form inclusion complexes with $\alpha$- and $\beta$-cyclodextrins ($\alpha$-CyD, $\beta$-CyD) either in the solid phase or in solution.[3)] However, the dynamic properties of the prostaglandin molecule embedded in the hydrophobic cavity of CyDs and the actual mode of inclusion still remain unclear. Direct evidence for the inclusion in solution has been obtained by carbon-13 nuclear magnetic resonance ($^{13}$C-NMR) measurements,[4)] which afford considerable information on the environments of individual carbons. Thus, the present study was undertaken to examine the molecular motions of the

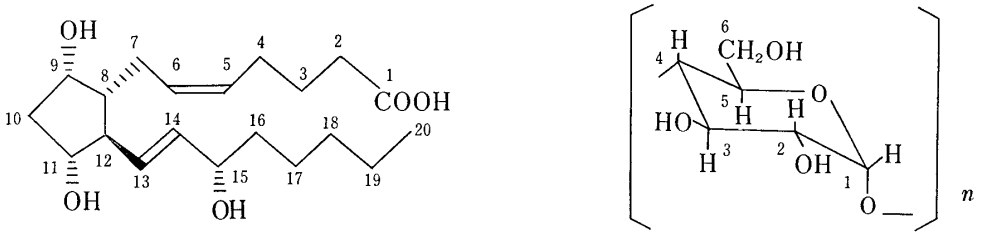
1) A part of this study was presented at the 99th Annual Meeting of the Pharmaceutical Society of Japan, Sapporo, August 1979.

2) Location: *a*) *5-1, Oe-honmachi, Kumamoto 862, Japan*; *b*) *Hongo, Bunkyo-ku, Tokyo 113, Japan.*

3) *a*) K. Uekama, F. Hirayama, S. Yamasaki, M. Otagiri, and K. Ikeda, *Chem. Lett.*, **1977**, 1389; *b*) K. Uekama, F. Hirayama, K. Ikeda, and K. Inaba, *J. Pharm. Sci.*, **66**, 706 (1977); K. Uekama, F. Hirayama, Y. Yamada, K. Inaba, and K. Ikeda, *ibid.*, **68**, 1059 (1979); *c*) K. Uekama and F. Hirayama, *Chem. Pharm. Bull.*, **26**, 1195 (1978); *d*) K. Uekama, F. Hirayama, and M. Daiguji, *Chem. Lett.*, **1978**, 327; F. Hirayama and K. Uekama, *Chem. Pharm. Bull.*, **27**, 435 (1979).

4) J.P. Behr and J.M. Lehn, *J. Am. Chem. Soc.*, **98**, 1743 (1976); Y. Inoue, Y. Katono, and R. Chujo, *Bull. Chem. Soc. Jpn.*, **52**, 1692 (1979).

inclusion complexes of prostaglandin $F_{2\alpha}$[5] ($PGF_{2\alpha}$) with $\alpha$- and $\beta$-CyDs by means of $^{13}C$-nuclear relaxation measurements. $PGF_{2\alpha}$ was chosen as a guest molecule for the measurements of $^{13}C$ spin-lattice relaxation times ($T_1$), because it is relatively stable and is water-soluble.



$PGF_{2\alpha}$

$n=6$ : $\alpha$-CyD
$n=7$ : $\beta$-CyD

Chart 1. Structures of $PGF_{2\alpha}$ and CyDs with Conventional Carbon Numbering

## Experimental

**Materials**——$PGF_{2\alpha}$ was a gift from Ono Pharmaceutical Industries Co., Ltd. $\alpha$- and $\beta$-CyDs were gifts from Teijin Ltd. and were used after recrystallization from water. Deuterium oxide ($D_2O$) used had an isotopic purity of 99.75% (Merck Co.) and other materials were of analytical reagent grade.

**$^{13}C$-NMR Studies**——The NMR spectra were taken on a JEOL PFT-100 spectrometer operating at 25.03 MHz, interfaced with a JEOL EC-100 Fourier transform computer with a 16 K memory. The NMR spectra were recorded for degassed solutions of $PGF_{2\alpha}$ (0.1 M) in the absence and presence of CyD in 0.1 M sodium borate buffer (pH meter reading of 9.3) in 10 mm spinning tubes at ambient temperature (about 37°) using $D_2O$ solvent as a deuterium lock, under conditions of proton noise decoupling (2.5 kHz noise bandwidth). The concentrations employed for $\alpha$- and $\beta$-CyDs were 0.1 M and 0.05M, respectively, because the stability constant of $\beta$-CyD complex is larger than that of $\alpha$-CyD complex by a factor of about 2.[6] The $^{13}C$ chemical shifts were referenced to external tetramethylsilane with accuracy of $\pm 0.025$ ppm. All peaks were assigned according to the previous paper.[3c] The spin-lattice relaxation time ($T_1$) measurements were carried out by the inversion-recovery technique, ($-180°$-$t$-$90°$-$T$-) with $T>5T_1$ for most carbons being measured.[7] In general, an average of 1500 accumulations with 8192 data points was made at a sweep width of 5000 Hz. The $T_1$ values were obtained by least-squares analyses of $\ln(A_\infty - A_t)$ *vs.* $t$, where $A_\infty$, $A_t$, and $t$ are the peak intensity at $\infty$ (after a single 90° pulse), the peak intensity at time $t$, and the pulse interval time in seconds, respectively. The slope of the line was taken as $-1/T_1$, with an accuracy of $\pm 10\%$.

**Viscosity Measurements**——The viscosity ($\eta$) of the sample solution was measured with an Epprecht Rheomat-15 viscometer (Contraves AG, Switzerland) at 37°. The $\eta$ values for $PGF_{2\alpha}$ (0.1M), $PGF_{2\alpha}$–$\alpha$-CyD (0.1 M/0.1 M), and $PGF_{2\alpha}$–$\beta$-CyD (0.1M/0.05M) were found to be 0.0127, 0.0132, and 0.0130 poise, respectively.

## Results and Discussion

### Effects of CyDs on the Molecular Dynamics of $PGF_{2\alpha}$

$^{13}C$ Spin-lattice relaxation times ($T_1$) for free $PGF_{2\alpha}$ and its mixtures with $\alpha$- and $\beta$-CyDs were measured by the inversion-recovery method. The $^{13}C$-NMR spectrum of each system consisted of only one set of peaks, indicating that the chemical exchange process expressed by Eq. (1) is sufficiently rapid on the $^{13}C$-NMR time scale,

$$PGF_{2\alpha} + \text{CyDs} \underset{}{\overset{K}{\rightleftarrows}} PGF_{2\alpha}\text{—CyDs} \qquad \text{Eq. (1)}$$

5) (5*Z*, 9$\alpha$, 11$\alpha$, 13*E*, 15*S*)-9,11,15-Trihydroxyprosta-5,13-dien-1-oic acid.
6) K. Uekama, F. Hirayama, and T. Irie, *Chem. Lett.*, **1978**, 661.
7) K. Uekama, F. Hirayama, and H. Koinuma, *Chem. Lett.*, **1977**, 1393; K. Uekama, F. Hirayama, N. Matsuo, and H. Koinuma, *ibid.*, **1978**, 703.

where $K$ is the stability constant of the inclusion complex. Since $PGF_{2\alpha}$ forms 1: 1 inculsion complexes with both $\alpha$- and $\beta$-CyDs in aqueous solution,[3c] the apparent $T_1$ value ($T_1^{obs}$) of $PGF_{2\alpha}$ in the presence of CyDs is expressed by Eq. (2), in the limit of a rapid exchange process:

$$\frac{1}{T_1^{obs}} = (1-\alpha)\cdot\frac{1}{T_1^{o}} + \alpha\cdot\frac{1}{T_1^{c}} \qquad \text{Eq. (2)}$$

where $T_1^{o}$ and $T_1^{c}$ are relaxation times for the free and the complexed $PGF_{2\alpha}$, respectively, and $\alpha$ is the complexed fraction of $PGF_{2\alpha}$. Taking into account the amounts of free and complexed species present in the mixtures, the $T_1^{c}$ values were calculated by Eq. (2), using the previously reported stability constants (390 $M^{-1}$ for $\alpha$-CyD complex and 740 $M^{-1}$ for $\beta$-CyD complex at 25°).[6] The values of $NT_1^{o}$ and $NT_1^{c}$ are listed in Table I,[8] where $N$ is the number of hydrogen atoms attached to the carbon. The conventional prostaglandin numbering is used throughout. Considering the relaxation data, the $PGF_{2\alpha}$ molecule appears to be made up of three characteristic portions from a dynamic point of view, *i. e.*, the alkyl side chain, the carboxylic acid side chain, and the cyclopentane ring and its immediate neighborhood, where the flexibility decreases in that order. The alkyl side chain exhibits a great deal of segmental motion, particularly at the $C_{16}$–$C_{20}$ carbons. Although the carboxylic acid side chain has relatively little segmental motion due to the presence of the $C_5$–$C_6$ double bond, the $C_3$ and $C_4$ carbons behave like the alkyl carbons in a fatty acid.[9] The reduced segmental motion observed for the $C_2$ carbon may be a result of effective anchoring of the terminal carboxylic group. In spite of the rigidity due to the half-chair conformation, a little internal

Table I. Relaxation Times[a] for $PGF_{2\alpha}$($NT_1^{o}$) and Its $\alpha$- and $\beta$-CyD Complexes($NT_1^{c}$) in 0.1 M Sodium Borate-$D_2O$ Buffer[b]

| Carbon | $PGF_{2\alpha}$ alone $NT_1^{o}$ | $\alpha$-CyD system | | $\beta$-CyD system | |
|---|---|---|---|---|---|
| | | $NT_1^{c}$ | $NT_1^{c}/NT_1^{o}$ | $NT_1^{c}$ | $NT_1^{c}/NT_1^{o}$ |
| 1 | —[c] | —[c] | | —[c] | |
| 2 | 0.54 | 0.45 | 0.83 | 0.29 | 0.54 |
| 3 | 1.22 | 0.80 | 0.66 | 0.78 | 0.64 |
| 4 | 0.73 | 0.79 | 1.08 | 0.45 | 0.62 |
| 5 | 0.44 | 0.39 | 0.89 | 0.29 | 0.66 |
| 6 | 0.47 | 0.42 | 0.89 | 0.38 | 0.81 |
| 7 | 0.55 | 0.60 | 1.10 | 0.20 | 0.36 |
| 8 | 0.31 | 0.28 | 0.90 | 0.16 | 0.52 |
| 9 | 0.32 | 0.30 | 0.94 | 0.11 | 0.34 |
| 10 | 0.52 | 0.53 | 1.02 | 0.25 | 0.48 |
| 11 | 0.39 | 0.39 | 1.00 | 0.20 | 0.51 |
| 12 | 0.32 | 0.30 | 0.94 | 0.18 | 0.56 |
| 13 | 0.39 | 0.37 | 0.95 | 0.28 | 0.72 |
| 14 | 0.39 | 0.36 | 0.92 | 0.32 | 0.82 |
| 15 | 0.40 | 0.34 | 0.85 | 0.42 | 1.05 |
| 16 | 1.53 | 1.31 | 0.86 | 1.14 | 0.75 |
| 17 | 0.74 | 0.54 | 0.73 | 0.70 | 0.95 |
| 18 | 1.58 | 0.72 | 0.46 | 1.11 | 0.70 |
| 19 | 2.76 | 1.03 | 0.37 | 1.87 | 0.68 |
| 20 | 7.56 | 2.49 | 0.33 | 5.18 | 0.69 |

*a*) All values in sec.
*b*) pH meter reading of 9.3.
*c*) $T_1$ was too long for the recycle time employed.

8) Under these experimental conditions, the viscosity change of $PGF_{2\alpha}$ solution was negligibly small on addition of $\alpha$- or $\beta$-CyD (see "Experimental").
9) C. Chachaty, Z. Wolkowsky, F. Pirion, and G. Lukas, *J. Chem. Soc. Chem. Commun.*, **1973**, 951.

freedom, probably due to anisotropic motion, still remains at the $C_{10}$ carbon of the cyclopentane ring. These observations are in accord with those of Conover *et al.*[10]

Although the main dynamic features of $PGF_{2\alpha}$ described above did not change markedly even in the presence of CyDs, comparison of $NT_1^c/NT_1^o$ values in details can give some insight into the inclusion mode of $PGF_{2\alpha}$–CyD complexes. Upon binding to $\alpha$-CyD, significant changes at the $C_2$, $C_3$, and $C_{15}$–$C_{20}$ carbons were noted, indicating that the internal motion of $PGF_{2\alpha}$ is reduced as a consequence of the coupling of its motion to that of $\alpha$-CyD. In contrast, most of the $NT_1^c$ value decreased in the $\beta$-CyD system because of the larger cavity. This size dependency implies complementarity between host and guest molecules and suggests that the $PGF_{2\alpha}$ molecule is included within the CyD cavities.[11]

To gain further insight into the molecular motions, the effective correlation times ($\tau_{eff}$) were calculated. The major relaxation of at least one protonated carbon is known to be overwhelmingly dominated by $^{13}C$–$^1H$ dipole-dipole interactions.[12] In this case, $T_1$ is given by

$$\frac{1}{NT_1} = \frac{\hbar^2 \cdot \gamma_C^2 \cdot \gamma_H^2}{r_{CH}^6} \cdot \tau_{eff} \qquad \text{Eq. (3)}$$

where $\gamma_C$ and $\gamma_H$ are the gyromagnetic ratios of $^{13}C$ and $^1H$ nuclei, respectively, $r_{CH}$ is the C–H distance,[13] and $\tau_{eff}$ is the effective correlation time for molecular reorientation. The reorientation time for the internal motion ($\tau_i$) is faster than the overall one ($\tau_{over}$), as approximated by Eq. (4),[12] because of the multiple internal motions of $PGF_{2\alpha}$.

$$\frac{1}{\tau_i} \approx \frac{1}{\tau_{eff}} - \frac{1}{\tau_{over}} \qquad \text{Eq. (4)}$$

As a measure of the overall molecular reorientation (assumed to be pseudo-isotropic), the averaged $NT_1$ value for the most rigid portion of the $PGF_{2\alpha}$ molecule ($C_8$, $C_9$, $C_{11}$, and $C_{12}$ ring carbons) was used. This assumption is appropriate, since the observed mean $NT_1$ value (0.34 sec) for these carbons was in good agreement with the theoretical value (0.38 sec) calculated from Eq. (5).[14]

$$\frac{1}{NT_1} = \frac{\hbar^2 \cdot \gamma_C^2 \cdot \gamma_H^2 \cdot \eta \cdot f_r \cdot V_m}{r_{CH}^6 \cdot \kappa \cdot T} \qquad \text{Eq. (5)}$$

where $\kappa$ is Boltzmann's constant, $\eta$ is the viscosity of the solution,[15] $f_r$ is a microviscosity factor,[16] $T$ is the absolute temperature,[17] and $V_m$ is the molecular volume of $PGF_{2\alpha}$.[18]

Table II summarizes the correlation times for overall rotation ($\tau_{over}$) and for several internal motions ($\tau_i$) calculated by means of Eq. (3) and (4), respectively, where carbons $C_2$, $C_3$, $C_{10}$, $C_{19}$, and $C_{20}$ were chosen to evaluate the extent of the terminal group fixation induced by inclusion complexation. Considering the correlation times in Table II, a clear difference between the molecular motions of the $\alpha$- and $\beta$-CyD complexes is apparent. Upon binding to $\alpha$-CyD, the $\tau_{over}$ and $\tau_i$ values hardly changed. However, the internal motions of the $C_{19}$ and $C_{20}$ carbons[19] slowed down by a factor of 3.3 and those of the $C_2$ and $C_3$ carbons were

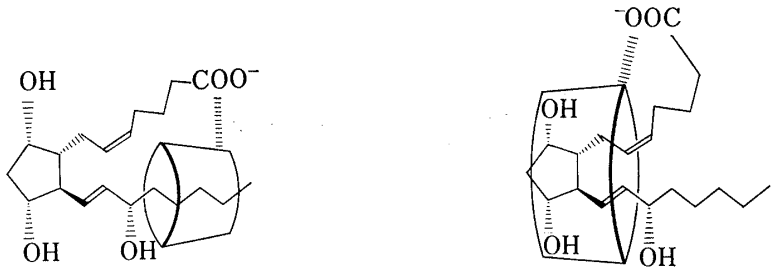
10) W.W. Conover and J. Fried, *Proc. Nat. Acad. Sci. U.S.A.*, **71**, 2157 (1974).
11) To confirm inclusion complexation, the $T_1$ values of the $PGF_{2\alpha}$–CyD system were compared with those of the $PGF_{2\alpha}$–glucose system. In the latter system, no appreciable $T_1$ change of $PGF_{2\alpha}$ carbons was observable even in the presence of 0.5—1.0 M glucose.
12) J.R. Lyerla and G.C. Levy, *Top. Carbon-13 NMR Spectrosc.*, **1**, 79 (1974).
13) Assumed to be 1.09 Å (D. Doddrell, V. Glushko, and A. Allerhand, *J. Chem. Phys.*, **56**, 3683 (1972)).
14) U. Edlung, C. Holloway, and G.C. Levy, *J. Am. Chem. Soc.*, **98**, 5069 (1976).
15) 0.0127 poise for 0.1 M $PGF_{2\alpha}$ solution (see "Experimental").
16) $f_r$ is assumed to be unity.
17) 310 °K.
18) 399 Å$^3$, estimated by the atomic increment method (J.T. Edward, *J. Chem. Edu.*, **47**, 261 (1970)).
19) In the case of the $C_{20}$ moiety, appreciable competition from other mechanisms such as spin rotation may also arise, because of the extremely free rotation.

Table II. Some Correlation Times of $PGF_{2\alpha}$ in Free and Complexed States

| System | Correlation time ($\times 10^{10}$ sec) | | | | | |
|---|---|---|---|---|---|---|
| | Overall | Internal | | | | |
| | $\tau_{over}$ | $\tau_i^2$ | $\tau_i^3$ | $\tau_i^{10}$ | $\tau_i^{19}$ | $\tau_i^{20}$ |
| $PGF_{2\alpha}$ alone | 1.4 | 2.2 | 0.52 | 2.5 | 0.19 | 0.065 |
| $PGF_{2\alpha}$-α-CyD | 1.5 | 3.5 | 0.96 | 2.1 | 0.65 | 0.21 |
| $PGF_{2\alpha}$-β-CyD | 3.0 | 3.5 | 0.74 | 4.8 | 0.27 | 0.093 |

Superscripts of $\tau$ represent the carbon number in $PGF_{2\alpha}$.

reduced slightly but significantly. In fact, the internal motion of the terminal methyl group ($C_{20}$) in the complexed state is decoupled from the overall motion only by a factor of 7, while that in the free state is fully decoupled by a factor of 22. These results apparently indicate that the alkyl portion ($C_{16}$–$C_{20}$) of $PGF_{2\alpha}$ is predominantly included within the α-CyD cavity. The slightly reduced motion of the $C_2$ and $C_3$ carbons may arise from the anchoring of the terminal carboxyl group by α-CyD outside the cavity, as shown in Chart 2A. This mode of inclusion was supported by the construction of a Corey–Pauling–Koltun (CPK) molecular model, *i. e.*, the smaller entrance of the α-CyD cavity (4.5 Å)[20] fitted well with the alkyl chain.




A : α-CyD complex B : β-CyD complex

Chart 2. Proposed Inclusion Modes for $PGF_{2\alpha}$-CyD Complexes in Aqueous Solution

In contrast to the α-CyD system, all the correlation times including $\tau_{over}$ were significantly changed by the binding to β-CyD. The reduction of the overall rotation of $PGF_{2\alpha}$ may be mainly due to the change in $\tau_i^{10}$ value, which represents internal motion around the cyclopentane ring. It is also noteworthy that the internal motion of the $C_{19}$ and $C_{20}$ carbons were fully decoupled from the overall rotation by factors of 11 and 33, respectively. This indicates that the terminal methyl group is located outside the β-CyD cavity, displaying free rotation. Refering to the above observation, a possible structure of the $PGF_{2\alpha}$-β-CyD complex may be illustrated as shown in Chart 2B. This depiction is also admissible on the basis of examination of a CPK model, together with the following considerations: (1) the five-membered ring is well fitted to the β-CyD cavity, (2) the greater fixation of the carboxylic acid side chain compared with the alkyl side chain may be due to the anchoring of the carboxyl group by β-CyD, (3) free rotation of the $C_{20}$ methyl group, and (4) steric hindrance of the $C_{15}$ hydroxy group.

**Effect of $PGF_{2\alpha}$ on the Molecular Dynamics of CyDs**

The $NT_1$ values and correlation times for CyDs in the presence of $PGF_{2\alpha}$ are listed in Table III. These values can be considered to be those for the complexes, since CyDs are exclusively

20) D.W. Griffiths and M.L. Bender, *Advan. Catal.*, **23**, 209 (1973).

Table III. Relaxation Times($NT_1$) and Rotational Correlation Times($\tau$) of CyDs in Complexed States

| System | $NT_1$ (sec) | | | | | | | $\tau$ ($\times 10^{10}$ sec) | |
|---|---|---|---|---|---|---|---|---|---|
| | $C_1$ | $C_2$ | $C_3$ | $C_4$ | $C_5$ | $C_6$ | $\langle NT_1 \rangle$[a] | $\tau_{over}$ | $\tau_i^{CH_2OH}$ |
| α-CyD | 0.135 | 0.124 | 0.132 | 0.123 | 0.136 | 0.140 | 0.130 | 3.6 | 20.3 |
| β-CyD | 0.123 | 0.119 | 0.114 | 0.112 | 0.113 | 0.138 | 0.116 | 4.0 | 8.8 |

a) The mean values of $NT_1$ for $C_1$—$C_5$.

in the complexed states under the experimental conditions used (85.2% for α-CyD and 97.4% for β-CyD, as estimated from the $K$ values). The mean $NT_1$ value ($\langle NT_1 \rangle$) of the $C_1$—$C_5$ carbons was taken to calculate the effective correlation times ($\tau_{over}$) for the overall molecular motions of CyDs.[4] The $NT_1$ value of the $C_6$ carbon was found to be larger than those of other ring carbons, showing the existence of internal rotation of the primary alcohol group about the $C_5$–$C_6$ bond. The correlation time ($\tau_i^{CH_2OH}$) for this rotation was calculated from Eq. (6),[12]

$$\frac{1}{NT_1} = \frac{\hbar^2 \cdot \gamma_C^2 \cdot \gamma_H^2}{r_{CH}^6} \cdot \tau_{over}\left[A + B \cdot \frac{6\tau_i^{CH_2OH}}{6\tau_i^{CH_2OH} + \tau_{over}} + C \cdot \frac{3\tau_i^{CH_2OH}}{3\tau_i^{CH_2OH} + 2\tau_{over}}\right] \quad \text{Eq. (6)}$$

where $A$, $B$, and $C$ are defined as follows:

$$A = \frac{1}{4} \cdot (3\cos^2\theta - 1)^2 \quad \text{Eq. (7)}$$

$$B = \frac{3}{4} \cdot \sin^2 2\theta \quad \text{Eq. (8)}$$

$$C = \frac{3}{4} \cdot \sin^4\theta \quad \text{Eq. (9)}$$

In these equations, $\theta$ is the angle between the relaxation vector and the principal axis of rotation ($\theta = 109°$ for rotation of the tetrahedral $C_6$–H bond about the $C_5$–$C_6$ bond). The overall reorientation times obtained for CyDs were in the range expected from the molecular sizes and were in fair agreement with those reported by Lehn *et al.*[4] Upon inclusion of $PGF_{2\alpha}$, the internal rotation of the primary alcohol group slowed down by a factor of 6 in α-CyD and by a factor of 2 in β-CyD, in comparison with the overall motions. Thus, it is reasonable to assume that the primary alcohol group of α-CyD participates in the anchoring of the $PGF_{2\alpha}$ carboxyl group at the smaller entrance side of the cavity through hydrogen bonding[4] (see Chart 2A).

It is suggested that the stability of the molecular complex should be described in terms of dynamic coupling between the molecular motions of the host and guest molecules, as well as thermodynamic stability.[4] In the present cases, dynamic coupling coefficients of 0.12 and 0.75 were obtained from the date in Table III for the $PGF_{2\alpha}$-α-CyD and $PGF_{2\alpha}$-β-CyD systems, respectively, indicating an appreciable decoupling, particularly for the former system. In sharp contrast, the dynamic rigidity expected for the β-CyD complex may result in a larger stability constant for inclusion complexation in aqueous solution.