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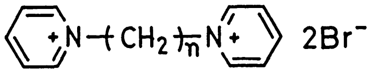
# Stability and Exchange Properties of Through-ring Cyclodextrin Complexes. Effects of Chain Length in Polymethylene Bis[1-pyridinium] as Guest Molecules1)

Hide SAITO, Hiroaki YONEMURA, Hiroshi NAKAMURA, and Taku MATSUO*
Department of Organic Synthesis, Faculty of Engineering,
Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812

On the basis of $^1H$ NMR spectra, polymethylene bis(1-pyridinium) and α-CD were concluded to afford a rotaxane-type complex. Signals due to the originally equivalent pair of protons in the polymethylene- and pyridinium groups were split into a pair of distinct signals on the complexation. Free energy of activation for the site-exchange in the complex increased with the number of methylene groups (n=8—12) and reached an asymptotic value (ca. 72 kJ/mol).

Cyclodextrin (CD) is known as the most capable receptor for molecular recognition in aqueous phase.2) In addition to hydrophobic binding to the cavity of CD, charges on the substrate has been known to play important roles in the molecular recognition.3) The incorporation mode has mainly been deduced from NMR spectroscopic studies, which afford time-averaged structural informations during rapid exchange between the CD complex and unbound, free species in the NMR-time scale. ESR time scale has been found fast enough for detecting the signals due to bound and free species separately.4)

Distinct NMR signals due to bound and free species were detected, for the first time, by the present authors, when the guest molecules were donor-acceptor linked compounds with a relatively long alkyl group as the spacer.5,6) A viologen unit was used as the acceptor site, and the viologen moiety was suggested to lead the spacer group entering into CD cavity on complex formation. Complexation of CD with viologen derivatives has been studied by several authors,7,8) but no one has implied the viologen unit as the site of entrance on complex formation. Then, the study was here extended to investigate the role of the leading head by the use of a series of the following symmetric compounds with two pyridinium groups linked via a polymethylene chain:



CnBPy 2Br (n=6,8,9,10,and 12)

The investigated compounds ($C_nBPy$ 2Br) were prepared and purified by usual methods. Extra pure grade α-CD was used as supplied from Tokyo Kasei Inc. The NMR spectra of $D_2O$ solution were recorded by the use of a JEOL JNM-GSX 400 NMR spectrometer.

The $^1H$ NMR spectra for $C_{10}BPy$ with α-CD in three different concentrations are summarized in Fig. 1. In the absence of α-CD, the spectra (Fig. 1 (a)) clearly

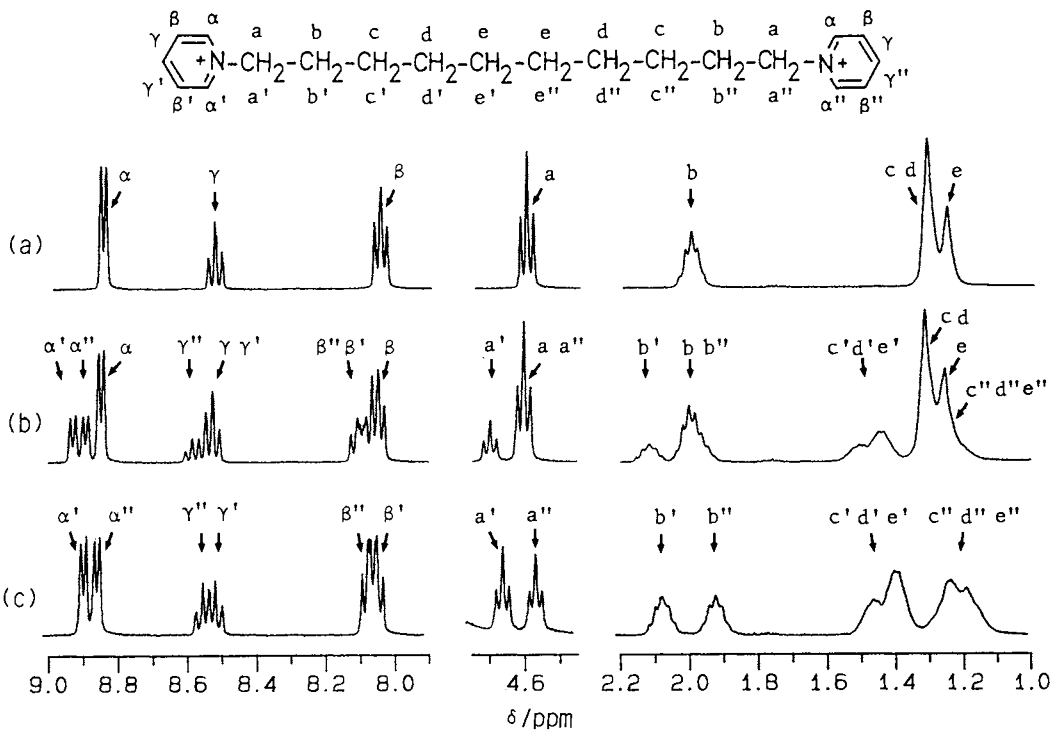


Fig. 1. Effects of α-CD on $^1$H NMR spectra for $C_{10}$BPy 2Br (10 mM) in $D_2O$ solutions at 5 °C: (a), without α-CD; (b), with α-CD (5 mM); and (c), with α-CD (100 mM). Signal assignments, as confirmed by COSY's and NOE measurements, for the protons of left and right halves are shown by letters with a prime and a double prime, respectively.

indicate that the chemically equivalent protons of the linked compound are located at the same electromagnetic environment as shown by the assignments for the free molecule at the top of Fig. 1. On the addition of α-CD, a new set of signals, which are denoted by the letters with a prime or a double prime, became evident, and the intensities increased at the expense of the corresponding signals for the free species at higher α-CD concentrations (Fig. 1 (b) and (c)). Then, the new signals are reasonably explained by complexation between $C_{10}$BPy and α-CD. The signal shapes for the complexed species could easily be recognized in Fig. 1 (c) without disturbance from those of the free species. It should be noted that each group of originally equivalent protons in $C_{10}$BPy affords a pair of new signals with equal intensity on complexation with α-CD.

On the basis of the above observation, it is concluded that the lifetime of the complexed species is long enough to be separately detected in NMR time scale at 5 °C. In addition, the complexation is suggested to create electromagnetically asymmetric microenvironment along the spacer chain.

Similar behaviors were observed with $^1$H NMR spectra of other three homologues ($C_n$BPy : n = 8, 9, and 12) in the presence of α-CD. No distinct signals for α-CD complexes were detected, however, in the case of the linked compound with the shortest spacer (n=6). The assignments of $^1$H NMR signals for $C_{10}$BPy in Fig. 1(c) were confirmed by the use of H-H, H-C COSY's and intramolecular NOE measurements. Detailed analysis of the chemical shifts proved that the induced shifts could be explained by electromagnetic difference between two sections as indicated by a prime and a double prime in the structural formula at the top of Fig. 1: the signals for the methylene protons with a prime were always observed at higher (or lower) fields with respect to those of the corresponding counterpart with a double prime. In other words, the complex-induced chemical shifts suggest evolution of electromagnetic gradient along to the spacer chain.[9] The size of the complex-induced chemical shift for a given pair of protons rapidly decreased with the spacer chain length (Fig. 2). In addition, larger induced shifts were observed with the protons at the central part of the spacer as compared with those at either end of the linked compound in all of the four $C_nBPy$ (n = 8, 9, 10, and 12): $\Delta\nu(\gamma'-\gamma'') \cong \Delta\nu(\beta'-\beta'') < \Delta\nu(\alpha'-\alpha'') < \Delta\nu(a'-a'') < \Delta\nu(b'-b'')$. Both diamagnetic anisotropy and electrostatic gradient in α-CD must be responsible for the observed trend in the Δν-values. All of these observations strongly support the previously suggested model of the novel complex with CD ring around the spacer chain. The CD complexes, as described here, may be considered as a homologue of roatxanes.[10]

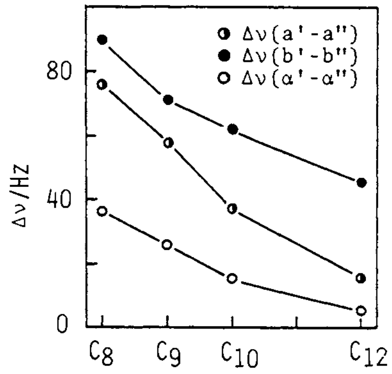


Fig. 2. Complex-induced chemical shift difference for four linked compounds $C_nBPy$ in $D_2O$ solutions.

Thermodynamic parameters for the complex formation were also obtained by the use of $^1H$ NMR, and the data are summarized in Table 1. The stability of the complex rapidly increased with the spacer chain length as one would expect on the basis of hydrophobic interaction. Temperature effects on the line shapes revealed the dynamic features of the complex. The coalescence temperature of the signals due to the b' and b" are listed in Table 1. The free energy of activation for the site exchange process at $T_c$, as evaluated from the Eyring's equation for absolute reaction rates, rapidly approached an asymptotic value (ca. 72 kJ/mol) with the increase of the spacer chain length. Free energy difference between the complex and dissociated species was less than 11 kJ/mol. Then, the energy profile for the rate process involving the asymmetric, through-ring CD complex may be depicted as in Fig. 3. The exchange of the two electromagnetically different site must proceed via dissociation of the complex. Since population of the dissociated species is extremely small at 5 °C, new complex formation is suggested to follow immediately. Starting from complex A, the orientation of α-CD must be inverted to ob-

Table 1. Relevant Parameters for the Complex Formation and the Exchange Process

| $C_n$ | $K/M^{-1}$ a) | $T_c/°C$ b) | Δν/Hz b) | $\Delta G_c^{\ddagger}/kJ\cdot mol^{-1}$ b) |
|---|---|---|---|---|
| $C_8$ | 110 | 43.9 | 90 | 62.0±0.1 |
| $C_9$ | 640 | 63.4 | 71 | 66.6±0.1 |
| $C_{10}$ | 2200 | 76.4 | 62 | 69.7±0.1 |
| $C_{12}$ | 4800 | 69.0 | 45 | 69.1±0.1 |

a) Evaluated with a solution containing $C_nBPy$ (10 mM) and α-CD (10 mM or 30 mM) at 5 °C.
b) Obtained with a solution containing $C_nBPy$ (10 mM) and α-CD (100 mM).

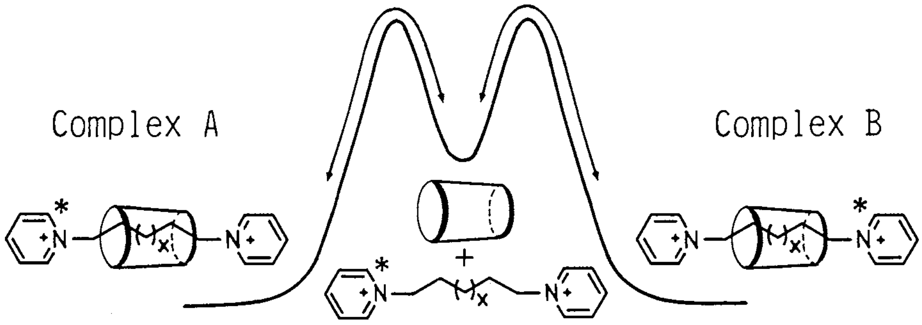


Fig. 3. Schematic presentation of energy surface for complex dissociation and site exchange process.

tain a new complex with opposite order of the chemical shifts for the proton signals (complex B). Consequently, the reaction rate for the pyridinium group to go through the α-CD ring is concluded to be twice as large as that for the exchange process. The reaction rate is extremely small in comparison with the case of ordinary complexes between CD and hydrophobic guests, whose lifetimes are too short to be separately detected by NMR. One of the reasons may be ascribed to the fact that pyridinium group must be dehydrated before getting into the cavity of α-CD.

References

1) Contribution No. 921 from Department of Organic Synthesis, Faculty of Engineering, Kyushu University.
2) M. L. Bender and M. Komiyama, "Cyclodextrin Chemistry," Springer-Verlag, New York, (1978); I. Tabushi, Acc. Chem. Res., 15, 66 (1982).
3) R. J. Bergeron, P. S. Burton, J. Am. Chem. Soc., 104, 3664 (1982).
4) Y. Kotake and E. G. Janzen, J. Am. Chem. Soc., 111, 2066 (1989).
5) H. Yonemura, H. Nakamura, and T. Matsuo, Chem. Phys. Lett., 155, 157 (1989).
6) H. Yonemura, H. Saito, S. Matsushima, H. Nakamura, and T. Matsuo, Tetrahedron Lett., 30, 3143 (1989); H. Yonemura, H. Saito, H. Nakamura, and T. Matsuo, submitted for publication.
7) I. Willner, E. Adar, Z. Goren, and B. Steinberger, New J. Chem., 11, 769 (1987).
8) A. Diaz, P. A. Quintela, J. M. Schuette, and A. E. Kaifer, J. Phys. Chem., 92, 3537 (1988).
9) M. Sakurai, M. Kitagawa, H. Hoshi, Y. Inoue, and R. Chujo, Chem. Lett., 1988, 895; H. Kitagawa, H. Hoshi, M. Sakurai, Y. Inoue and R. Chujo, Bull. Chem. Soc. Jpn., 61, 4225 (1988).
10) Chemical shift differences induced in CD-rotaxane were suggested in the following example: H. Ogino, J. Am. Chem. Soc., 103, 1303 (1981).

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