CHEMISTRY LETTERS, pp. 2097-2100, 1994.

Stereoselective Formation of a 2:1 Molecular Complex between α-Cyclodextrin and Carbazole-Viologen Linked Compound with a Long Alkyl Chain as the Spacer[1)]

Hiroaki YONEMURA, Tsuyoshi NOJIRI, and Taku MATSUO*
Department of Chemical Science and Technology, Faculty of Engineering,
Kyushu University, Fukuoka 812

Analysis of ^{1}H NMR spectra revealed a novel mode of complexation between α-cyclodextrin (CD) and a carbazole-viologen linked compound with 16 methylene units in the spacer. The complexation afforded a stable rotaxane-type CD complex, where two α-CDs encased the spacer chain. NOE experiments confirmed selective formation of unique isomer among four possible orientations of the encasing α-CD.

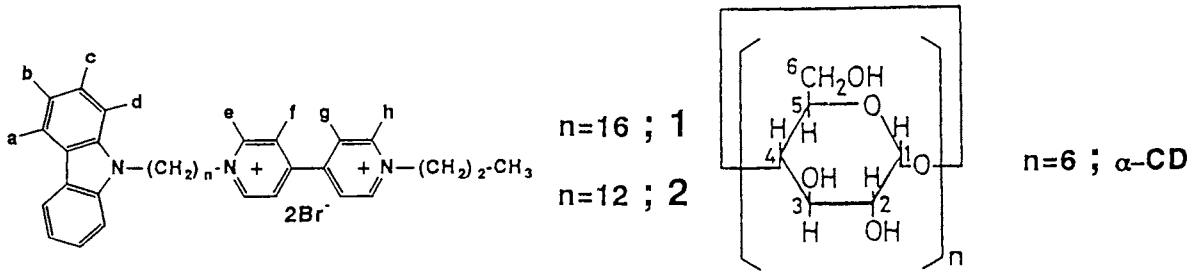
Rotaxanes afford one of the most interesting supramolecular systems, as represented by "Through-Ring Cyclodextrin (CD) Complexes".[2)] Extremely long-living, through-ring CD complexes were obtained by the use of either α- or β-CD, when the guest molecules were donor-acceptor linked compounds. The viologen unit proved to be a unique acceptor for this purpose, while phenothiazine-,[3)] carbazole-,[4)] or anthracene moiety[5)] served as the donor site. In all of these cases, one-to-one stoichiometry in the host-to-guest ratios was confirmed by the use of ^{1}H NMR spectroscopy. Similar 1:1 molecular complexes were also observed with α-CD complexes of polymethylene bis(1-pyridinium).[6)] In this case, the chemical shifts of originally equivalent protons were split into an asymmetric pair, and the reason was ascribed to electric field gradient in the inner cavity of encasing α-CD.

Kamachi and his associates reported a novel group of rotaxanes, in which many α-CD molecules were threaded on polyethylene glycol. The threaded α-CDs were suggested to align pairwise in head-to-head orientation.[7)] The complexation process has not been studied in details since the threaded complexes were hardly soluble.

On the basis of the above consideration, a carbazole-viologen linked compound with sixteen methylene groups as the spacer was prepared and the α-CD complexes were carefully investigated by ^{1}H NMR spectroscopy. The study revealed that two α-CD molecules were threaded stepwise by the linked compound. Stereospecific complexation proceeded and a single conformation among four possible isomers of the 2:1 complex was obtained.

The linked compounds (**1** and **2**) were prepared according to the standard procedures. ^{1}H NMR spectra (400 MHz) were measured with a D_2O solution. The chemical shifts were measured by the use of DSS solution in a capillary tube as an external standard. Stoichiometry of α-CD complex was investigated by the use of 0.1 mM (1M=1 mol dm^{-3}) solution of **1** to avoid micellar formation. 2D-NMR and NOE difference spectra were measured by use of 1 mM solution of **1** in the presence of α-CD to obtain spectra with good S/N ratios (Fig. 1). Assignments of the proton signals, as denoted in the following molecular formulae, were carried out by the aid

of COSY and NOE techniques:



On the addition of α–CD to the solutions of either **1** or **2**, distinct signals due to complexed species were clearly observed apart from uncomplexed species in the chemical shift-region for α–CD and aromatic protons. The spectra for the protons in CD- and viologen moieties became much more complicated, when the linked compound with a shorter spacer (**2**) was replaced by that with a longer spacer (**1**) under the same α–CD concentration. The detailed analysis of the spectra, by the use of 2D-NMR, revealed that the CD-proton signals of the complexes consisted of two sets as shown in Fig. 1A. On the addition of excess amount of α–CD, the aromatic proton signals for the complexed **1** were observed as a single set (Fig.1B).

Rather simple signals due to 1-position of α–CD at around 5 ppm were examined in details under various α–CD concentrations (Fig. 2). The H-1" / H-1' ratio of the signal intensities increased with α–CD concentration up to 0.4 mM (Figs. 2A, 2B and 2C). In large excess of α–CD (2 mM) with respect to **1** (0.1 mM), the integrated signal intensity for H-1" became identical to that for H-1' (Fig. 2D). Aromatic proton spectra for the α–CD complex of **1**, under this condition, was exactly the same as that in Fig. 1B. In addition, the corresponding intensity of the carbazole protons (a") was found to be one third of that for H-1' or H-1". The two signals (H-1' and H-1") are thus assigned to the proton at the 1-position of the two α–CDs in different electromagnetic environments of the 2:1 complex.

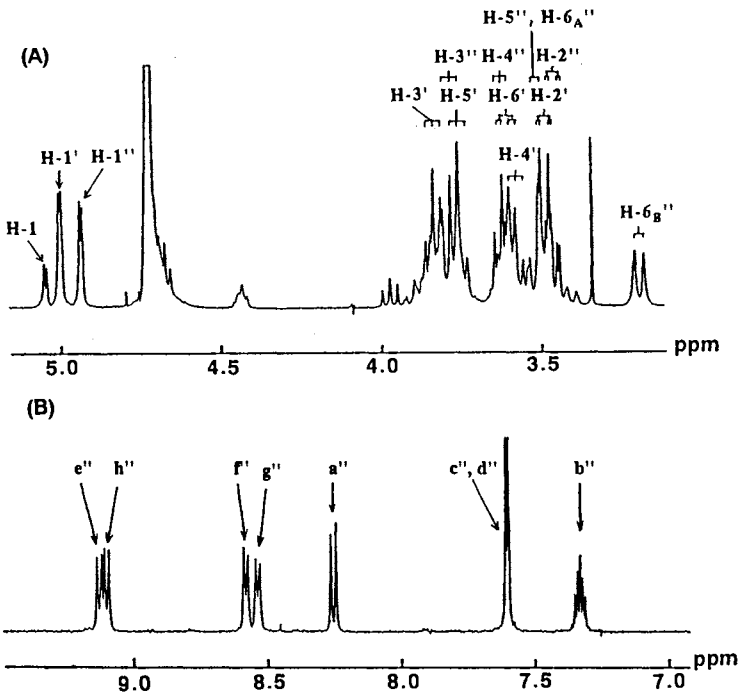


Fig. 1. Assignment of ^1H signals, as obtained by 2D-NMR spectroscopy, on complexation between **1** (1 mM) and α–CD (2 mM for (A),and 10 mM for (B)) in D_2O solution at 30°C. The complexed species are indicated by letters either with a single prime (a' ~ h' and H-1' ~ H-6') or with a double prime (H-1" ~ H-6").

The H-1' signal was clearly more intense than H-1" signal (Figs. 2A and 2B). The proton signal due to 1:1 complex was suggested to be hidden in H-1'. Equilibrium constants for the formation of the 1:1 and 2:1 complexes were accordingly evaluated from the

integrated intensities of the three signals (H-1, H-1' and H-1") in various α–CD concentrations: K_1, 1.4 x 10^4 M^{-1} and K_2, 1.8 x 10^4 M^{-1}. As to aromatic protons also, distinct signals due to the 1:1 and the 2:1 complexes could be observed apart from the signal due to free species (Fig. 3). The signals due to viologen moiety (e/e'/e" and h/h'/h") afforded the same K_1- and K_2 values as obtained above.

In addition, intermolecular NOEs were clearly observed between the inner protons (H-3', H-5', H-3", H-5", and H-6"$_A$) of α–CDs and the spacer methylene protons of **1**. These NMR spectroscopic evidence confirmed formation of a stable 2:1 complex between α–CD and **1**.

Detailed studies of NMR spectra indicated that formation of the 2:1 complex proceeded via stereospecific pathway as described below. As to the first complexation step, the narrower rim of α–CD was concluded to be in contact with carbazole moiety, since an intermolecular NOE was clearly observed between H-6"$_B$ proton and carbazole protons (c" and/or d") (Fig. 1).

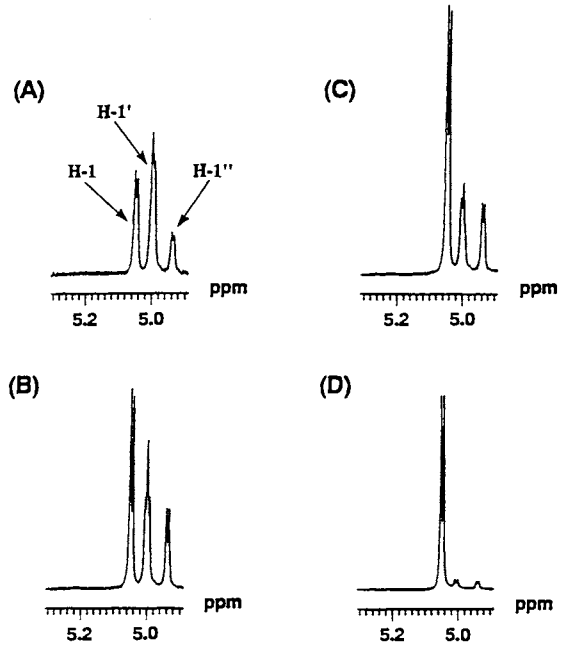


Fig. 2. Variation of NMR signals for ^1H at 1-position of α–CD on complexation with **1** (0.1 mM) in D_2O solution at 30°C. The spectra at four different α–CD concentration : (A) 0.1 mM, (B) 0.2 mM, (C) 0.4 mM, and (D) 2 mM.

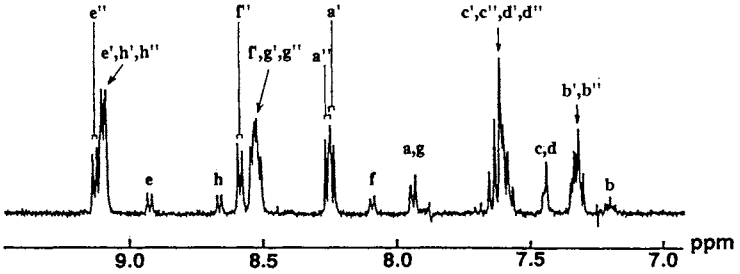


Fig.3. ^1H NMR spectra of aromatic moieties **1** (0.1 mM) in the presence of α–CD (0.2 mM) in D_2O solution at 30°C. The 1:1 and the 2:1 complexed species are indicated by letters with a single prime (a' ~ h') and a double prime (a" ~ h"), respectively.

Stereospecificity in the second complexation step was also indicated, when proton signals around viologen moieties (e, h and l) of the 2:1 complex were compared with those of an reference compound (decyl bisviologen, BC10V in Fig. 4). In the case of the reference compound (BC10V), originally equivalent protons (e,e"; h,h"; l-CH_2 and l"-CH_2) afforded two sets of NMR signals on complexation with α–CD. A pair of rather broad multiplets (2.15 and 1.99 ppm) were observed with l-CH_2 and l"-CH_2. Ring protons adjacent to nitrogen atom likewise afforded a pair of signals : (a) a closely located double doublet (9.13 and 9.08 ppm), and (b) a rather broad singlet with shoulders (9.00 ppm). The double doublet signals were assigned to viologen (e" and h") in contact with wider rim of α–CD, since exactly the same ring proton signals have been observed with previously reported 1:1 through-ring α–CD complexes of carbazole-viologen linked compounds.[8] The other broad singlet was consequently assigned to viologen unit (e and h) at narrower rim of α–CD.

On the formation of 2:1 complex between α-CD and **1**, only a single set of signals due to the relevant protons (e", h"(Fig. 1), and l"-CH_2 (2.03 ppm)) was observed. Two sets of signals should be observed, as discussed with α-CD complex of the reference compound, if either orientation of α-CD is allowed in the second complexation step. The second α-CD is thus concluded to take a single orientation on encasing the terminal viologen unit in the complexation process. Both chemical shifts and multiplet structure of the relevant protons (e", h", l"-CH_2) of the 2:1 complex agree reasonably well with those of the reference compound, if α-CD molecules are threaded in a head-to-tail orientation. Thermodynamic properties of the present CD complex and the origin of stereospecificity in the complexation process are under investigation.

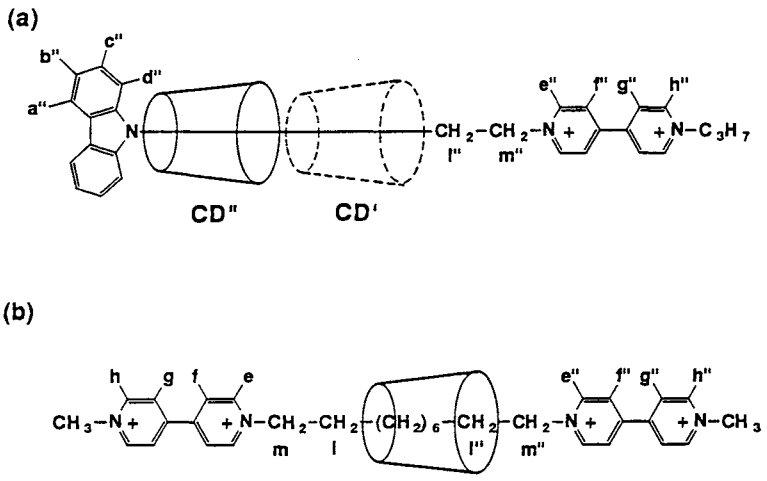


Fig. 4. Schematic presentation of stereospecificity in the formation of through-ring complexes : (a) complexation between α-CD and **1**, and (b) complexation between α-CD and a reference compound (BC10V).

The authors are grateful to Center of Advanced Instrumental Analysis, Kyushu University for the measurement of ^1H NMR by a 400 MHz spectrometer. Financial support from the Ministry of Education, Science and Culture (Grants in Aid for Scientific Research No.06218224, No.06239250, No.6750849, No.06226263, No.05750738, and No.05453192) is deeply appreciated.

References

1) Contribution No. 1003 from the Department of Chemical Science and Technology, Faculty of Engineering, Kyushu University.
2) J. F. Stoddart, Angew. Chem., Int. Ed. Engl., **31**, 846 (1992).
3) H. Yonemura, H. Saito, S. Matsushima, H, Nakamura, and T. Matsuo, Tetrahedron Lett., **30**, 3143(1989).
4) H. Yonemura, M. Kasahara, H. Saito, H, Nakamura, and T. Matsuo, J. Phys. Chem., **96**, 5765 (1992).
5) A. Toki, H. Yonemura, and T. Matsuo, Bull. Chem. Soc. Jpn., **66**, 3382 (1993).
6) H. Saito, H. Yonemura, H. Nakamura, and T. Matsuo, Chem. Lett.,535 (1990).
7) A. Harada, J. Li, and M. Kamachi, Nature, **356** ,325 (1992).
8) The same stereospecificity was also encountered in 1:1 through-ring complex formation between α-CD and the following linked compounds with a poly-methylene group as the spacer: phenothiazine-viologen, anthracene-viologen, and carbazole-trimethylammonium. The stereospecificity in rotaxane-formation with α-CD was lost, when a viologen unit was linked to a trimethylammonium group via a poly-methylene group. Intramolecular interaction between the polar group and the hydrophobic moiety at the end of the linked compound might be responsible for the stereospecificity of the 1:1 complex.

(Received August 1, 1994)