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6-*O*-Modified *β*-Cyclodextrin Enabling Inclusion Complex Formation in Nonpolar Media

Toshiyuki Kida,[†] Yoshinori Fujino,[†] Kazuhiro Miyawaki,[‡] Eiichi Kato,[‡] and Mitsuru Akashi*,[†]

Department of Applied Chemistry, Graduate School of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565-0871, Japan

akashi@chem.eng.osaka-u.ac.jp

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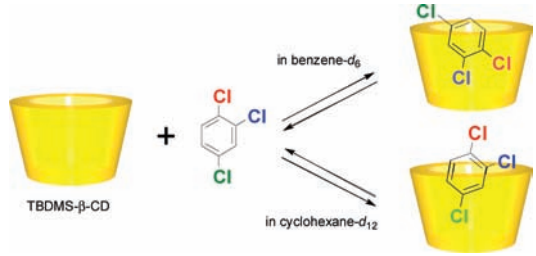
ABSTRACT



Heptakis(6-*O*-*tert*-butyldimethylsilyl)-*β*-cyclodextrin (TBDMS-*β*-CD) effectively forms inclusion complexes with chlorinated benzenes in nonpolar solvents such as benzene-d_6 and cyclohexane-d_{12}. The inclusion selectivity toward 1,2- and 1,3-dichlorobenzenes can be switched by changing the solvent from benzene-d_6 to cyclohexane-d_{12}. Moreover, 1,2,4-trichlorobenzene (90 ppm) is perfectly removed from insulating oil by using TBDMS-*β*-CD as an adsorbent.

Cyclodextrins (CDs) have been widely used as one of the most common and useful hosts in host−guest and supramolecular chemistry.[1−3] CDs can form inclusion complexes with a variety of molecules in aqueous media[4] or in several kinds of polar organic media[5,6] via the incorporation of the guests into the CD cavities. On the other hand, it has been believed that inclusion complex formation between CDs and guest molecules in nonpolar media would be extremely difficult,[7,8] because the main driving force for the inclusion of guest molecules within the CD cavity is hydrophobic interactions and/or van der Waals interactions between the guests and the CD cavity, and the enormous amount of nonpolar solvents become strong competitors for inclusion within the CD cavity. Until now, there have been a few reports on the complexation between CD derivatives and guest molecules in nonpolar solvents.[9−12] Most of them, however, have been limited to complexation through the interaction between guests and substituents on the upper and/or lower rims of the CDs, such as the cation−dipole interaction between sodium picrate and the carbonyl oxygens of peracetylated *β*-CD[9] and the hydrogen-bonding interaction between an acidic hydrogen of the guest and an ether oxygen of

[†] Osaka University
[‡] NEOS Company, Ltd.

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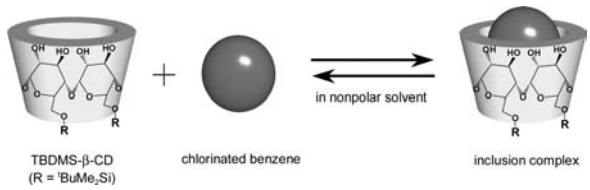

Figure 1. Schematic illustration of inclusion complex formation between TBDMS-β-CD and chlorinated benzene in nonpolar solvents.

permethylated β-CD.[10] If a CD derivative were developed that effectively forms inclusion complexes in nonpolar solvents with a variety of guest molecules, including guests with no charge and no acidic hydrogen, through direct interactions between the CD cavity and the guests, then it would open the way to new applications for CDs. For instance, such a CD derivative can be expected to allow the selective removal of persistent organic pollutants such as polychlorobiphenyls (PCBs) from oils. We report herein that heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (TBDMS-β-CD)[13] effectively formed inclusion complexes with chlorinated benzenes in nonpolar solvents such as benzene-d_6 and cyclohexane-d_{12} (Figure 1). To the best of our knowledge, this is the first example of inclusion complex formation between a CD derivative and an aromatic guest molecule possessing no charge and no acidic hydrogen in nonpolar solvents.

Mono-, di-, and trichlorobenzenes were chosen as guest molecules. Figure 2 illustrates the shift of the ^{1}H NMR signals of TBDMS-β-CD induced by complexation with 1,2,4-trichlorobenzene (1,2,4-TCBz) in benzene-d_6 and

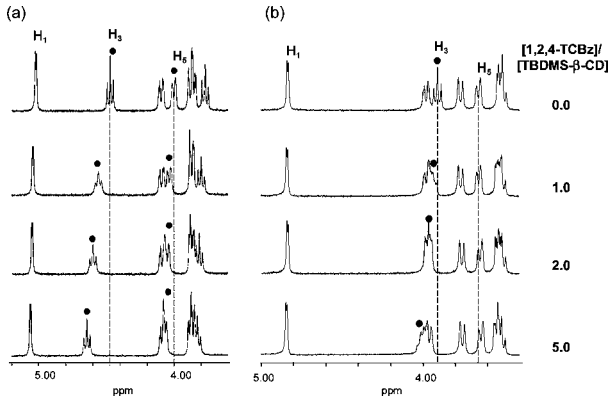

Figure 2. ^{1}H NMR spectral changes observed for TBDMS-β-CD (1.0×10^{-3} M) upon addition of 1,2,4-TCBz (a) in benzene-d_6 and (b) in cyclohexane-d_{12} at 25 °C.

cyclohexane-d_{12}. A shift of the H_3 and H_5 proton signals of TBDMS-β-CD was observed in both solvents, suggesting

Table 1. Association Constants between TBDMS-β-CD and Chlorinated Benzenes in Benzene-d_6 and Cyclohexane-d_{12} at 25 °C

	association constant (M^{-1})	
guest	in benzene-d_6	in cyclohexane-d_{12}
chlorobenzene (MCBz)	*a*	9 ± 5
1,2-dichloronbenzene (1,2-DCBz)	190 ± 10	410 ± 20
1,3-dichloronbenzene (1,3-DCBz)	680 ± 90	130 ± 20
1,4-dichloronbenzene (1,4-DCBz)	2 ± 1	2 ± 1
1,2,4-trichlorobenzene (1,2,4-TCBz)	1400 ± 120	140 ± 20
1,3,5-trichlorobenzene (1,3,5-TCBz)	48 ± 14	5 ± 2

[a] The shift of proton signals of TBDMS-β-CD upon addition of chlorobenzene was not observed.

that the guest molecule was incorporated within the cavity of the host. In benzene-d_6, the H_3 and H_5 proton signals were clearly shifted downfield, whereas a downfield shift of the H_3 signal and a slight upfield shift of the H_5 signal were observed in cyclohexane-d_{12}. This result implies that there should be some difference in the mode of guest inclusion within the TBDMS-β-CD cavity between these solvents. Job plots obviously indicated that TBDMS-β-CD formed a 1:1 complex with 1,2,4-TCBz in these solvents (see Figures S12 and S15, Supporting Information). Table 1 summarizes the association constants between TBDMS-β-CD and various chlorinated benzenes including 1,2,4-TCBz in benzene-d_6 and cyclohexane-d_{12}. Their inclusion complex formation was strongly affected by the number and position of chlorine substituents on the benzene ring of the guest molecule. Although little association with chlorobenzene (MCBz), 1,4-dichlorobenzene (1,4-DCBz), and 1,3,5-trichlorobenzene (1,3,5-TCBz) was observed, TBDMS-β-CD exhibited moderate to high inclusion ability toward 1,2- and 1,3-dichlorobenzenes (1,2- and 1,3-DCBzs) and 1,2,4-TCBz. These results suggest that the inclusion complex formation between TBDMS-β-CD and the chlorinated benzenes in the nonpolar solvents is mainly caused by dipole−dipole interactions between the host cavity and the guest molecule, as well as by the steric fit of the guest into the host cavity. In particular, the increasing order of the association constants between TBDMS-β-CD and di- and trichlorobenzenes in cyclohexane-d_{12} is very consistent with the increasing order of dipole moments of the guests (1,2-DCBz ($\mu = 2.26$ D) > 1,3-DCBz ($\mu = 1.38$ D) ≈ 1,2,4-TCBz ($\mu = 1.26$ D) > 1,3,5-TCBz ($\mu = 0.28$ D) > 1,4-DCBz ($\mu = 0$ D)).[14] Interestingly, TBDMS-β-CD showed inclusion selectivity for 1,3-DCBz over 1,2-DCBz in benzene-d_6 but showed the reverse selectivity for the same guests in cyclohexane-d_{12}, demonstrating that the inclusion selectivity can be controlled by the type of solvent employed. The inclusion ability of TBDMS-β-CD toward the trichlorobenzenes in benzene-d_6 was much higher than that in cyclohexane-d_{12}. In particular, TBDMS-β-CD showed about a 10-fold higher inclusion ability toward 1,2,4-TCBz in benzene-d_6 as compared to that in cyclohexane-d_{12}. These results support

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the hypothesis that the mode of guest inclusion into the CD cavity is different between these solvents.

NMR studies are effective for obtaining useful information on the inclusion complex structure. In the ROESY spectra of the inclusion complexes between TBDMS-β-CD and 1,2,4-TCBz in benzene-d_6 and cyclohexane-d_{12} (see Figures S18 and S21, Supporting Information), clear correlations were observed between the aromatic protons of 1,2,4-TCBz and the H_3 protons of TBDMS-β-CD, confirming that 1,2,4-TCBz was incorporated within the cavity of TBDMS-β-CD in these solvents. In benzene-d_6, clear cross peaks between the H_3 protons of the host and the H_a and H_c protons of 1,2,4-TCBz were observed. On the other hand, in cyclohexane-d_{12}, distinct cross peaks were observed between the H_3 protons of the host and the H_a and H_b protons of the guest, but there was only a slight cross peak between the host H_3 protons and the guest H_c proton. These results show that there is a clear difference in inclusion complex structure in benzene-d_6 and in cyclohexane-d_{12}.

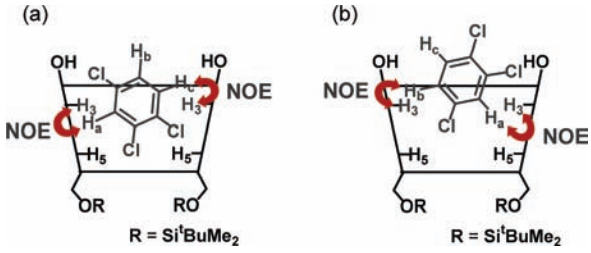

Figure 3. Proposed structures of the inclusion complexes between TBDMS-β-CD and 1,2,4-TCBz (a) in benzene-d_6 and (b) in cyclohexane-d_{12}.

Figure 3 shows the proposed structures of the inclusion complexes between TBDMS-β-CD and 1,2,4-TCBz in benzene-d_6 and cyclohexane-d_{12}, based on the ROESY spectra and CPK-modeling studies.

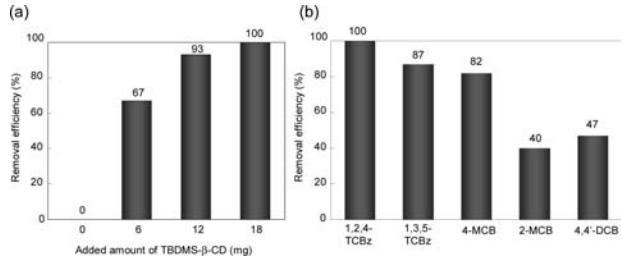

Figure 4. (a) Removal efficiency of 1,2,4-TCBz from insulating oil as a function of the amount of TBDMS-β-CD added. (b) Removal efficiency of various chlorinated aromatic compounds from insulating oil with TBDMS-β-CD (20 mg). The initial concentration of chlorinated aromatic compounds in the insulating oil (240 mg) was 90 ppm.

Thermodynamic parameters for complexation between TBDMS-β-CD and 1,2,4-TCBz in benzene-d_6, which were determined by ^{1}H NMR titration at different temperatures, revealed that the complexation was enthalpy-driven ($\Delta H = -62$ kJ/mol, $\Delta S = -0.15$ J/mol K), supporting that dipole−dipole interactions between the host cavity and the guest molecule work as a main driving force for inclusion complex formation.

In sharp contrast to TBDMS-β-CD, permethylated α- and β-CDs and heptakis(2,3-di-*O*-benzyl)-β-CD did not form any inclusion complexes with the chlorinated benzenes in benzene-d_6 and cyclohexane-d_{12}. TBDMS-α-CD and TBDMS-γ-CD, which possess smaller and larger rings than TBDMS-β-CD, respectively, showed little inclusion ability toward these chlorinated benzenes in the nonpolar solvents. These findings reveal that the 6-*O*-*tert*-butyldimethylsilylated β-CD skeleton is essential for inclusion complex formation with chlorinated benzenes in nonpolar solvents.

The inclusion ability of TBDMS-β-CD toward chlorinated aromatics in nonpolar solvents has great potential for the removal of toxic chlorinated aromatics, such as PCBs, contaminated in oils. Figure 4a shows the removal efficiency of 1,2,4-TCBz (the percentage of 1,2,4-TCBz removed) from insulating oil as a function of the amount of TBDMS-β-CD (a solid adsorbent) added. The removal efficiency of 1,2,4-TCBz increased with an increase in the amount of TBDMS-β-CD added. It is noteworthy that 1,2,4-TCBz was completely removed when more than 18 mg of TBDMS-β-CD (8 wt % of insulating oil, 78-fold the molar quantity of 1,2,4-TCBz) was added. This adsorption efficiency is much higher than that of a channel-type γ-CD assembly previously reported.[15] The adsorption ability of TBDMS-β-CD toward various chlorinated aromatics in insulating oil was also evaluated (Figure 4b). TBDMS-β-CD showed high adsorption ability toward 1,3,5-TCBz as well as 1,2,4-TCBz. It is interesting that TBDMS-β-CD showed moderate to high adsorption ability toward 2-chlorobiphenyl (2-MCB), 4-chlorobiphenyl (4-MCB), and 4,4′-dichlorobiphenyl (4,4′-DCB), although little complex formation between TBDMS-β-CD and these chlorinated biphenyls was observed in benzene-d_6 and cyclohexane-d_{12} solutions. This phenomenon suggests that TBDMS-β-CD can work as a powerful adsorbent that allows the selective removal and extraction of persistent organic pollutants such as PCBs from oils.

In conclusion, we demonstrated that 6-*O*-*tert*-butyldimethylsilylated β-CD effectively formed inclusion complexes with chlorinated benzenes in nonpolar solvents. Their inclusion complex formation was strongly affected by the size, shape, and dipole moment of the guest molecule as well as by the type of solvent. Interestingly, the inclusion selectivity toward 1,2- and 1,3-dichlorobenzenes was switched by changing the solvent from benzene-d_6 to cyclohexane-d_{12}. It is expected that this CD host can function not only as a powerful adsorbent for PCBs in oils but also as an effective chiral selector in nonpolar solvents by utilizing the cooperative effect of the inclusion of the guest within the CD cavity mainly through the dipole−dipole interactions and hydrogen-bonding interactions between the hydroxyl groups on the CD rim and an appropriate functional group in the guest molecule. Further studies on inclusion

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complex formation between TBDMS-β-CD and various aromatic guests including chiral molecules in nonpolar solvents are now in progress in our laboratory.

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Supporting Information Available: Experimental details, ^{1}H NMR titration curves for complex formation, Job plots for complexes, and ROESY spectra of complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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