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Unique Catalytic Effect of a Cyclodextrin Host on Photodimerization of Coumarin in Nonpolar Solvents

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ABSTRACT

Heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (TBDMS-β-CD) formed inclusion complexes with coumarin in benzene and cyclohexane. The inclusion mode of coumarin within the TBDMS-β-CD cavity was different between these solvents. Photodimerization of coumarin in the solvents was remarkably accelerated by the inclusion within the TBDMS-β-CD cavity. In particular, the largest rate increase was observed when 1.0 equivalent of TBDMS-β-CD was added to coumarin.

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Over the past few decades, the development of artificial supramolecular hosts exhibiting high affinity for specific organic guests[1] and their application to synthetic and analytical fields[2] have been actively carried out. In particular, much attention has been paid to catalytic reactions utilizing supramolecular hosts.[3] Cyclodextrins (CDs) and their derivatives which possess sub-nano scaled cavities have been widely utilized as supramolecular hosts and catalysts.[1a,b,4] However, in most cases, catalytic reactions using CDs have been limited to aqueous media[4a,c,d] and several kinds of polar organic media.[5] On the other hand, catalytic reactions with CDs in nonpolar media were rarely carried out. Recently, our research group reported that 6-*O*-modified CDs, such as heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (TBDMS-β-CD) and heptakis(6-*O*-triisopropylsilyl)-β-cyclodextrin (TIPS-β-CD), effectively formed inclusion complexes with aromatic compounds, including chlorinated benzenes[6] and pyrene[7] in nonpolar solvents. These findings opened the way to the application of CDs in nonpolar media. In particular, CD derivatives exhibiting high inclusion ability towards organic substrates in nonpolar media could have great potential as effective catalysts for a variety of reactions, including reactions that have not been successfully carried out in water or polar media. Herein, we report for the first time the catalytic ability of 6-*O*-modified CD towards the photodimerization of coumarin in nonpolar solvents.

TBDMS-β-CD was chosen as a 6-*O*-modified CD host, based on our recent findings.[6,7] Figure 1 shows the ^{1}H NMR

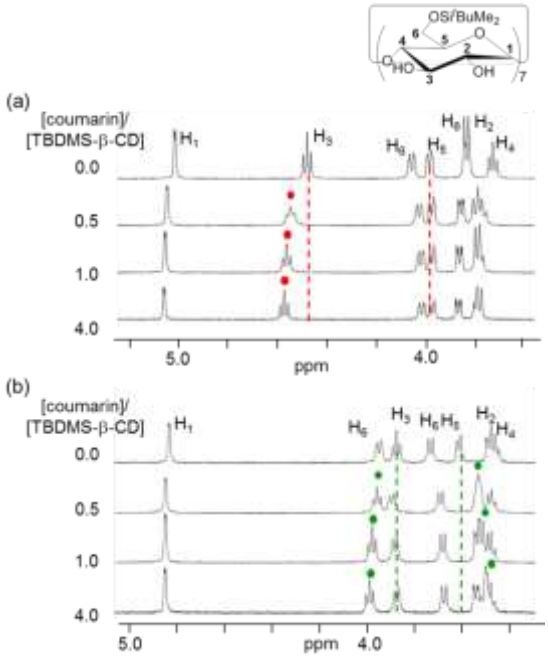

Figure 1. ^{1}H NMR spectral changes observed for TBDMS-β-CD (1.0×10^{-3} M) (a) in benzene-d_6 and (b) in cyclohexane-d_{12} upon addition of coumarin at 10 °C.

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spectral changes of TBDMS-β-CD after the addition of coumarin in benzene-d_6 and cyclohexane-d_{12} at 10 °C. Upon addition of coumarin, a remarkable shift in the H_3 and/or H_5 proton signals of TBDMS-β-CD was observed in both solvents, suggesting the formation of a TBDMS-β-CD–coumarin complex. In benzene-d_6, the H_3 proton signal of TBDMS-β-CD was shifted downfield, whereas little shift of the H_5 signal was observed. On the other hand, an upfield shift of the H_5 signal as well as a downfield shift for the H_3 signal was observed in cyclohexane-d_{12}. These results imply that there is some difference in the inclusion mode of coumarin within the TBDMS-β-CD cavity between these two solvents.

Job plots using a NMR method showed maxima at ratios of [TBDMS-β-CD] to ([TBDMS-β-CD]+[coumarin]) around 0.6 in both benzene-d_6 and cyclohexane-d_{12} (Figure S1), indicating that the TBDMS-β-CD–coumarin complex exists as a mixture of 1 : 1 (or 2 : 2) and 2 : 1 stoichiometries. In cyclohexane-d_{12}, the relative abundance of the 2 : 1 TBDMS-β-CD–coumarin complex to the 1 : 1 (or 2 : 2) complex appeared to be higher than that in benzene-d_6.

The UV spectral changes of coumarin against the TBDMS-β-CD concentration in benzene and cyclohexane were also observed (Figure S2), supporting the formation of inclusion complexes in these solvents.

In the NOESY spectra of the inclusion complexes between TBDMS-β-CD and coumarin in benzene-d_6 and cyclohexane-d_{12} (Figure 2), cross peaks were clearly observed between H_3 and/or H_5 protons of TBDMS-β-CD and all protons of coumarin. This observation confirmed that coumarin 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 all coumarin protons were observed, whereas cross peaks between the H_5 protons of the host and the coumarin protons were barely observed. This result indicates that a coumarin molecule is included with its long axis almost perpendicular to the axis of TBDMS-β-CD, similar to the case of previously reported complexes between TIPS-β-CD and pyrene in benzene-d_6.[7] In contrast, cross peaks were observed between the H_5 protons as well as the H_3 protons of the host and all protons of coumarin in cyclohexane-d_{12}. This observation suggests that the long axis of the incorporated coumarin molecule tilts to the axis of TIPS-β-CD, and thus the coumarin molecule penetrates more deeply into the CD cavity as compared with the case of benzene-d_6. These results showed that there was a difference in the penetration mode of coumarin between benzene-d_6 and cyclohexane-d_{12} solvents. This solvent effect on coumarin inclusion is consistent with the case of pyrene inclusion into the TIPS-β-CD cavity.[7]

Next, we examined the photodimerization of coumarin in benzene and cyclohexane in the presence and absence of TBDMS-β-CD. Photoirradiations were carried out using a high-pressure mercury arc lamp (400 W, Pyrex cut off), according to the previous reports.[8] Course of the reaction was followed by ^{1}H-NMR. It is known that the photodimerization of coumarin gives four isomeric products (Scheme 1), and the

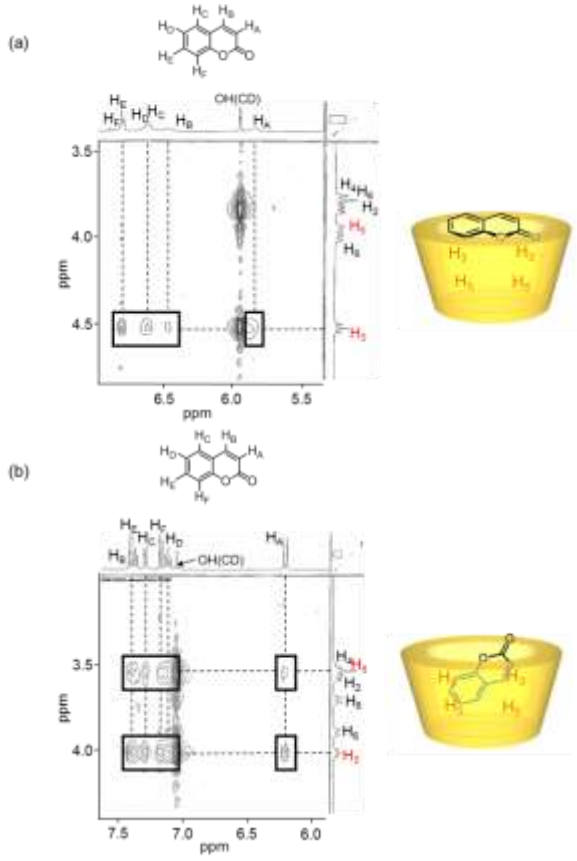
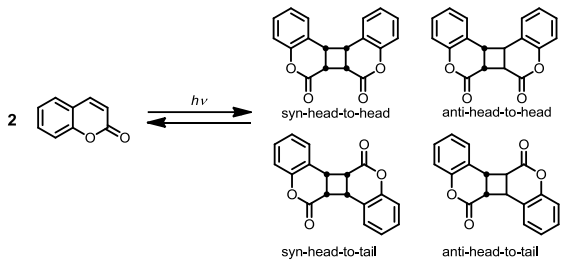


Figure 2. Partial NOESY spectra and proposed structure of the 1 : 1 complexes between TBDMS-β-CD (1.0×10^{-3} M) and coumarin (1.6×10^{-2} M) (a) in benzene-d_6 and (b) in cyclohexane-d_{12}.



Scheme 1. Photodimerization of coumarin.

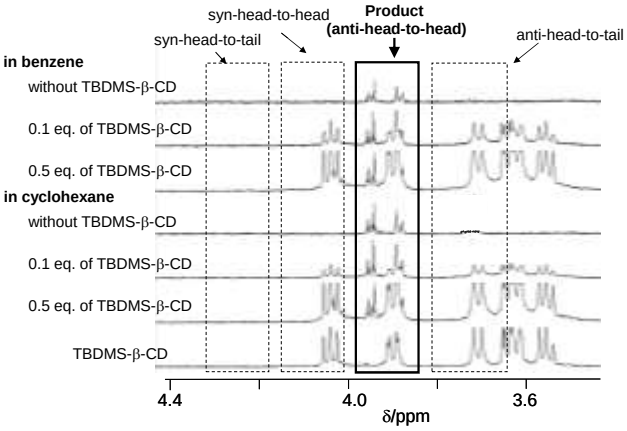


Figure 3. Partial ^{1}H NMR spectra of the dimers (the cyclobutane proton region) obtained upon irradiation of coumarin at 10 °C for 24 h in benzene and cyclohexane in the absence and presence of TBDMS-β-CD (solvent : $CDCl_3$).

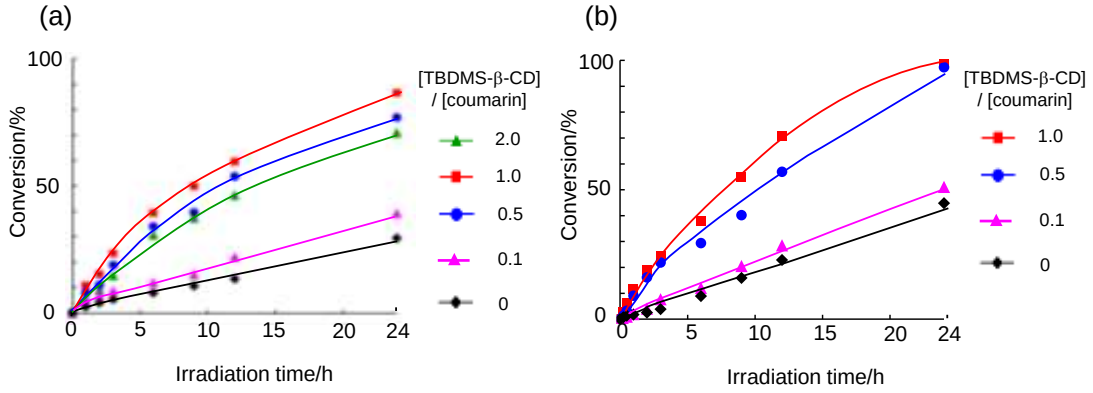


Figure 4. Time course of the photodimerization of coumarin (0.027 mmol) in the presence of different amounts of TBDMS-β-CD in (a) benzene and (b) cyclohexane (10 mL) at 10 °C.

product distribution is dependent on the reaction environment.[4b,8] Contrary to our prediction based on the above-mentioned results on the inclusion mode of coumarin within the TBDMS-β-CD cavity in benzene and cyclohexane solvents (Figure 2), photoirradiation of coumarin in these solvents gave the same sole product, anti-head-to-head cyclobutane dimer, regardless of the presence of TBDMS-β-CD and the type of solvent (Figure 3).

Table 1. The second-order rate constants for the photodimerization of coumarin in benzene and cyclohexane in the absence and presence of TBDMS-β-CD at 10 °C.

Entry	Solvent	TBDMS-β-CD (eq.)	k_2[a] (10^6 $s^{-1}M^{-1}$)
1	benzene	0	3.5 (1.0)
2	benzene	0.1	5.8 (1.7)
3	benzene	0.5	25 (7.1)
4	benzene	1.0	33 (9.4)
5	benzene	2.0	20 (5.7)
6	cyclohexane	0	9.0 (1.0)
7	cyclohexane	0.1	12 (1.3)
8	cyclohexane	0.5	27 (3.0)
9	cyclohexane	1.0	35 (3.9)

[a]The values in parentheses denote relative rate constants.

Plots of the product yields versus irradiation time at 10 °C at different [TBDMS-β-CD]/[coumarin] feed ratios are shown in Figure 4.[9] Second-order rate constants k_2 of the photodimerization of coumarin in benzene and cyclohexane are summarized in Table 1. The dimerization of coumarin in these solvents was accelerated upon the addition of TBDMS-β-CD. In the benzene solvent, the addition of more than 0.1 equivalent of TBDMS-β-CD to coumarin clearly accelerated the reaction (Table 1, entries 2-5), indicating that TBDMS-β-CD functions as a catalyst for this reaction. In particular, the rate of photodimerization in the presence of 1.0 equiv. of TBDMS-β-CD was 9.4 times faster than in the absence of TBDMS-β-CD (Table 1, entry 4). The acceleration of reaction rates by TBDMS-β-CD can be explained by considering that the coumarin in the excited state is effectively stabilized by inclusion within the TBDMS-β-CD cavity. An increase in the addition amount of TBDMS-β-CD from 0.5 to 1.0 equiv. to coumarin enhanced the reaction rate, whereas 2.0 equiv. of TBDMS-β-CD somewhat decreased the reaction rate (Table 1, entries 3-5). This result may imply that the 1 : 1 (or 2 : 2) TBDMS-β-CD–coumarin inclusion complex participates in the acceletaion of the photodimerization, while the 2 : 1 TBDMS-β-CD–coumarin inclusion complex inhibits the photodimerization. In the case of cyclohexane solvent, a similar but smaller accelerating effect of TBDMS-β-CD was observed. This difference in the accelerating effect between benzene and cyclohexane solvents may be due to the difference in the inclusion mode of coumarin within the TBDMS-β-CD cavity or the difference in the abundance ratio of the 2 : 1 TBDMS-β-CD–coumarin complex between these solvents. When the photodimerization of coumarin was carried out in toluene-d_8 where the formation of TBDMS-β-CD–coumarin complex was not observed spectroscopically (Figure S3), no acceleration of the reaction rate was observed even in the presence of 1.0 equiv. of TBDMS-β-CD. These results support that the TBDMS-β-CD–coumarin inclusion complex plays a crucial role in the acceleration of photodimerization of coumarin.

In summary, we have demonstrated that TBDMS-β-CD forms inclusion complexes with coumarin in benzene and cyclohexane, and functions as a catalyst for the photodimerization of coumarin in such nonpolar solvents. To the best of our knowledge, this is the first example of the utilization of CD derivatives as a catalyst in nonpolar solvents. Further studies on the application of CD derivatives as a supramolecular catalyst for other reactions in nonpolar solvents are now in progress in our laboratory.

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9. In the case of cyclohexane solvent, the addition of more than 1.0 equiv. of TBDMS-β-CD was not examined due to its low solubility in cyclohexane at 10 ºC.

Supplementary Material