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1 : 2 HOST-GUEST BINDING BY DOUBLE γ-CYCLODEXTRIN

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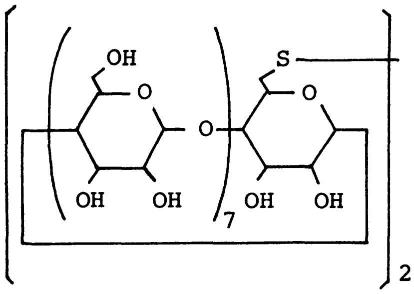
A double γ-cyclodextrin host bridged with a disulfide bond included two molecules of methyl orange with an association constant (1.06×10^{11} M^{-2}) which is the largest value ever reported for 1 : 2 (host : guest) bindings of γ-cyclodextrin, demonstrating the collaboration of the two cyclodextrin parts on guest binding.

γ-Cyclodextrin can bind two guest molecules in the cavity (1 : 2 host-guest association), being in marked contrast to the binding behavior of α or β-cyclodextrins, 1 : 1 host-guest association.[1] This unique character of γ-cyclodextrin has been applied for energy transfer, excimer formation, charge-transfer complex formation,[2,3] and photochemical reaction[4] between two guests which are included in the same cavity. This unique character must be applicable for many bimolecular reactions. In this paper, we wish to describe the first successful enhancement of this unique character by chemical modification of γ-cyclodextrin with γ-cyclodextrin.[5]

A double γ-cyclodextrin (**1**) was prepared by air oxidation of 6-deoxy-6-mercapto-γ-cyclodextrin which was synthesyzed from 6-deoxy-6-tosyloxyl-γ-cyclodextrin.[6] The double cyclodextrin (**1**) bound ethyl and methyl oranges, which were detected by the difference electronic spectra. The association ratios were determined to be 1 : 2 (host : guest) by Job's treatment[7] of the difference spectra (Eq. 1). Eq. 1 gives Eq. 2[4] by neglecting the terms of $[C]^2$ and $[C]^3$, where $[\mathbf{1}]_0$ and $[Dye]_0$ are the initial concentrations of **1** and the dye, [C] is the concentration of the inclusion complex, $(Dye)_2(\mathbf{1})$, $\Delta\varepsilon$ is the difference of the molecular extinction coefficient, $(\varepsilon_C - 2\varepsilon_{Dye})$, and ΔA is the difference absorption induced by complex formation. A plot of $[\mathbf{1}]_0[Dye]_0^2/\Delta A$ vs. $[Dye]_0([Dye]_0 + 4[\mathbf{1}]_0)$ for the experimental values gave a good straight line from which K was obtained (Table 1).[8] Binding of γ-cyclodextrin was elucidated to include two guest molecules (methyl or ethyl oranges). Reported values[2-4] of K between γ-cyclodextrin and two aromatic compounds fall between 10^6 M^{-2} and 10^8



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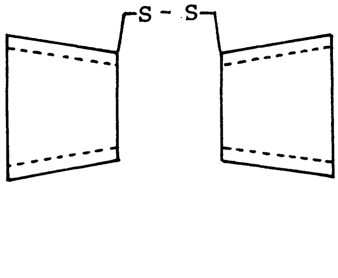

$$\mathbf{1} + 2\cdot\text{Dye} \underset{}{\overset{K}{\rightleftharpoons}} (\text{Dye})_2(\mathbf{1}) \qquad (1)$$

$$[1]_0[\text{Dye}]_0^{\,2}/\Delta A = [\text{Dye}]_0([\text{Dye}]_0 + 4[1]_0)/\Delta\varepsilon + 1/(K\cdot\Delta\varepsilon) \qquad (2)$$

Table 1. Association constants, K/M^{-2}, between cyclodextrin and methyl or ethyl oranges[a)]

Cyclodextrin	Methyl Orange	Ethyl Orange
γ-Cyclodextrin	8.67×10^{6}	4.36×10^{7}
Double γ-cyclodextrin (1)	1.06×10^{11}	3.60×10^{10}

a) 0.05 M carbonate buffer, pH 10.60, 25 °C.

M^{-2}, which was observed also in the present association between γ-cyclodextrin and two methyl oranges[9)] or two ethyl oranges. Introduction of γ-cyclodextrin as a second binding site brought about large increase in association constants, 12200-times for methyl orange and 825-times for ethyl orange. It is interesting to note that the binding of methyl orange by **1** was stronger than that of ethyl orange although the latter dye was included by γ-cyclodextrin more tightly than the former one. This implies that the combination of two tight binding sites does not necessarily produce the effective collaboration of them.

Thus, the two γ-cyclodextrins in **1** could bind guests collaboratively with the largest 1 : 2 association constant ever reported for γ-cyclodextrin.

References

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2) A. Ueno, Y. Tomita, and T. Osa, J. Chem. Soc., Chem. Commun., 1983, 976, and references cited therein.
3) K. Takamura, S. Inoue, and F. Kusu, Polym. Bull., 9, 233 (1983).
4) T. Tamaki, Chem. Lett., 1984, 53.
5) Chemical modification of β-cyclodextrin with β-cyclodextrin has been reported. I. Tabushi, Y. Kuroda, and K. Shimokawa, J. Am. Chem. Soc., 101, 1614 (1979); A. Harada, M. Furue, and S. Nozakura, Polym. J., 12, 29 (1980).
6) The structural assignment of **1** was carried out by the elemental analysis, H NMR, and IR spectra. The disulfide structure of **1** was supported by the reduction of **1** to 6-deoxy-6-mercapto-γ-cyclodextrin with dithiothreitol.
7) P. Job, Ann. Chim. Phys., 9, 113 (1928).
8) The concentration of methyl orange and the concentration range of **1** were as follows. 2.12×10^{-6} M and $1.95 \times 10^{-7} - 1.91 \times 10^{-6}$ M. The concentration of ethyl orange and the concentration range of **1** were as follows. 8.70×10^{-6} M and $5.35 \times 10^{-7} - 5.13 \times 10^{-6}$ M.
9) The reported value at 20 °C is 16×10^{6} M^{-2}. H. Hirai, N. Toshima, and S. Uenoyama, Polym. J., 13, 607 (1981).

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