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TIGHT INCLUSION OF AN ACID GUEST INTO THE CAVITY OF CYCLODEXTRIN BEARING AN AMINO MOIETY IN DIMETHYL SULFOXIDE

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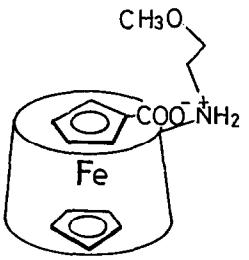
Abstract: Circular dichroism measurements show that β-cyclodextrin with an amino moiety has a strong binding ability for ferrocenecarboxylic acid in dimethyl sulfoxide via an acid-base interaction.

Cyclodextrins provide hydrophobic environment in aqueous solutions and can include a variety of lipophilic guests in their cavities.[1] The presence of water, therefore, has been considered to be important for the inclusion phenomenon. Although Siegel and Breslow observed that cyclodextrins still have binding ability in dimethyl sulfoxide and dimethylformamide, the association constants are usually very small.[2] On the other hand, Willner and Goren modified β-cyclodextrin with a diazacrown ether to bind alkali-metal p-nitrophenolates in dimethylformamide.[3] We wish to report here that β-cyclodextrin has a strong binding ability in dimethyl sulfoxide when it has an amino moiety and the guest compound is an acid.

We have prepared 6-deoxy-6-(2-methoxyethylamino)-β-cyclodextrin (1) by reaction of 6-O-tosyl-β-cyclodextrin with a large excess of 2-methoxyethylamine in dimethylformamide at 50 °C. Recrystallization of the crude product from a mixed solvent of n-butanol, ethanol and water afforded the pure dihydrate of 1 in ca. 30% yield.[4]



Complex of 1 and FcCOOH

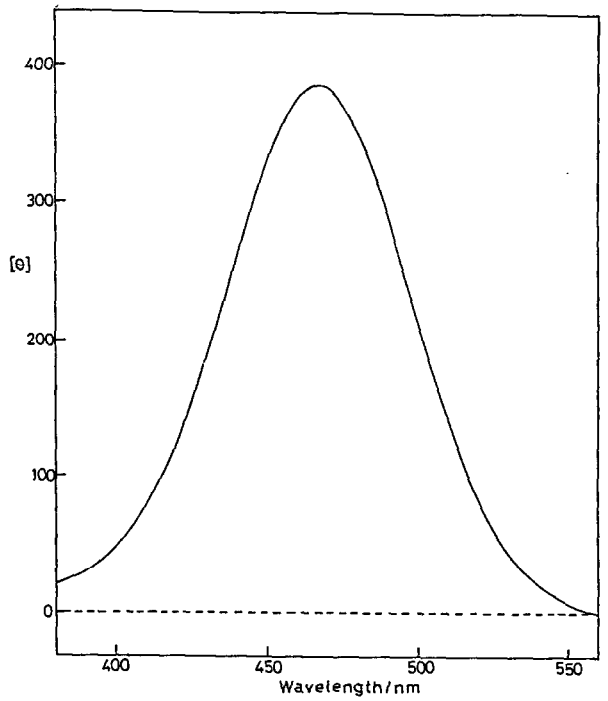


Fig. 1. Circular dichroism spectra of FcCOOH (4.55×10^{-3} M) in the presence of 1 (——) or β-cyclodextrin (----) in dimethyl sulfoxide. The concentrations of 1 and β-cyclodextrin were 4.55×10^{-3} M.

Figure 1 shows circular dichroism spectra of ferrocenecarboxylic acid (FcCOOH, 4.55×10^{-3} M (M = mol l^{-1})) when measured at 25 °C in the presence of 1 or β-cyclodextrin. The spectrum in the presence of 1 reveals a strong induced circular dichroism band in the absorption region of FcCOOH around 467 nm, indicating the inclusion of the guest acid in the chiral cavity of 1. This result contrasts to the absence of any induced dichroism band in the presence of β-cyclodextrin. The different behavior between the two hosts should be ascribable to the effect of the amino moiety in 1, the moiety leading the guest acid into the cavity by an acid-base interaction. This argument was confirmed by the decrease in the intensity of the dichroism band caused by acid and base additives, the peak intensity shown in Figure 1 becoming 76% and 36% of the original value in the presence of acetic acid (0.39 M) and 2-methoxyethylamine (1.05×10^{-2} M), respectively. These observations should arise from the competitive acid-base interactions; acetic acid tends to interact with the amino moiety of 1 in place of FcCOOH,

while 2-methoxyethylamine forms an acid-base complex with FcCOOH, both resulting in the exclusion of FcCOOH from the cavity of 1.

Figure 2 shows the intensity of the dichroism band as a function of the ratio of FcCOOH and 1. The obtained curve is a saturation one, affording the maximum value 690 for the molecular ellipticity [θ]. The analysis of these data[5] gave an association constant 600 ± 44 M^{-1}. Since β-cyclodextrin shows no binding behavior for FcCOOH under the present conditions, the acid-base interaction is solely responsible for the strong binding of 1. The acid-base interaction is usually much stronger in organic solvents than in water as shown by the slightly promoted binding in aqueous solution reported for other cyclodextrin system.[6] The strong acid-base interaction, therefore, can serve as a powerful means to construct inclusion chemistry of cyclodextrins in organic solvents.

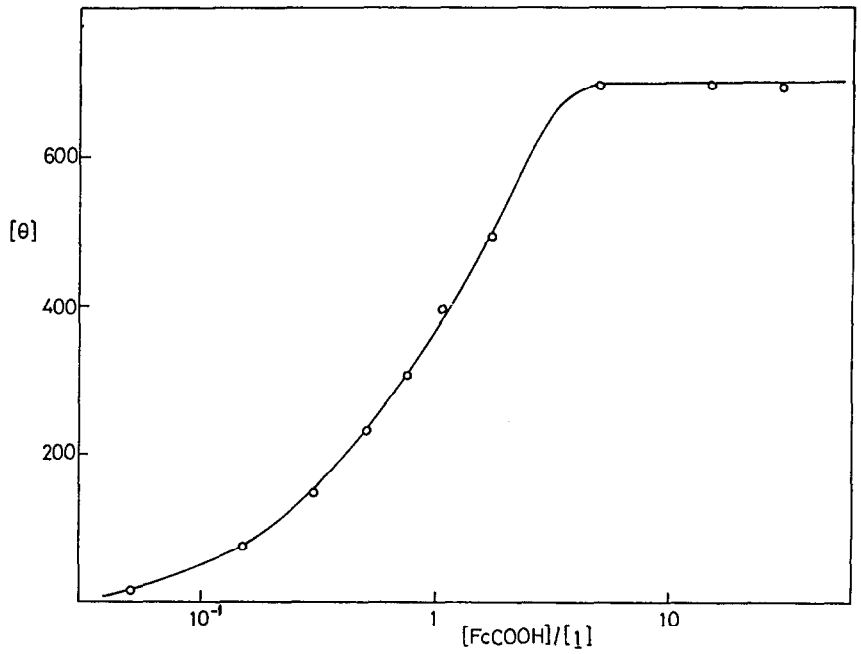


Fig. 2. Molecular ellipticity of 1 in dimethyl sulfoxide as a function of the ratio of FcCOOH and 1

Although this communication presents only one example, the idea may generally be applicable and similar strong binding should be attained when cyclodextrins bearing an acid moiety are used for amine guests. Studies on

chiral recognition through inclusion complexes with enantiomeric guests are now under way on this basis.

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4. 1: R_f 0.29 (NH_4OH, H_2O, AcOEt, i-PrOH 1:4:3:5 by volume); Satisfactory ^1H NMR was obtained; Elemental analysis, Found (Calc'd for $C_{45}H_{77}O_{35}N,2H_2O$) C, 43.95 (44.00); H, 6.99 (6.66); N, 1.07 (1.14).

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