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HOST–GUEST COMPLEXATION OF 6-DEOXY-6-(1-PYRIDINIO) DERIVATIVES OF α-CYCLODEXTRIN (CYCLOMALTOHEXAOSE) WITH INORGANIC ANIONS IN AQUEOUS SOLUTION

YOSHIHISA MATSUI*, MASAHIKO FUJIE, AND HIROSHI SAKATE
Faculty of Agriculture, Shimane University, Nishikawatsu, Matsue 690 (Japan)
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ABSTRACT

The anions I^-, SCN^-, and Br^- formed 1:1 charge-transfer complexes with the HCO_3^- salts of bis-, tris-, and hexakis-[6-deoxy-6-(1-pyridinio)]-α-cyclodextrins in aqueous solution. Increase in the number of the pyridinio groups resulted in a remarkable increase in the binding constant, K_a. A maximum K_a value of 9×10^5 $mol^{-1}.dm^3$ was observed for the complex of the hexapyridinio derivative with I^-. Acetylation of the mono- and di-pyridinio derivatives also resulted in a significant increase in the K_a values.

INTRODUCTION

Artificial host compounds, such as crown ethers and cryptands, bind inorganic cations strongly and selectively, and they are widely used as catalysts in organic synthesis, carriers in selective extraction and transport, *etc.* In contrast, the binding of inorganic anions has been investigated much less. Macrotricyclic[1–4] and macromonocyclic[5–8] polyammonium salts and heterocyclophanes[9] bind inorganic anions selectively, but the binding constants (K_a) for most of the systems are not large.

α-Cyclodextrin (cyclomaltohexaose) and β-cyclodextrin (cyclomaltoheptaose) form inclusion complexes[10–17] with chaotropic inorganic anions such as Br^-, I^-, NO_3^-, SCN^-, and ClO_4^-, but the K_a value are small for aqueous solutions. 6-Deoxy-6-(1-pyridinio)-α-cyclodextrin (**1**) forms stable 1:1 charge-transfer (c.t.) complexes with I^-, SCN^-, and Br^-, which have characteristic u.v. absorption spectra[18]. Moreover, the K_a values for the complexes in aqueous solution were considerably larger than those for the corresponding complexes with α-cyclodextrin or methyl 6-deoxy-6-(1-pyridinio)-α-D-glucopyranoside. It was concluded that hydrophobic, van der Waals, electrostatic, and c.t. interactions are involved in the complexation.

*Author for correspondence.

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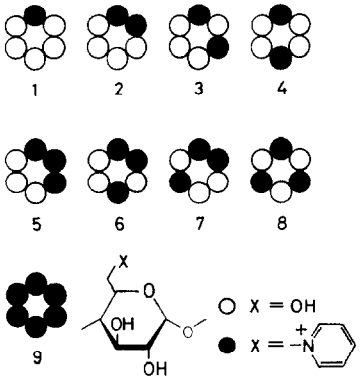

We now report on the complexation of I^-, SCN^-, and Br^- with bis- (**2–4**), tris- (**5–8**), and hexakis-[6-deoxy-6-(1-pyridinio)]-α-cyclodextrins (**9**) in aqueous solution. It was anticipated that an increase in the number of the pyridinio groups would result in large increases in the K_a values. The effect of acetylation of the mono- (**1**) and bis-pyridinio (**3**) derivatives is also reported.

EXPERIMENTAL

Materials. — α-Cyclodextrin was kindly supplied by Nihon Shokuhin Kako Co., Ltd., and dried overnight *in vacuo* at 110°. Reagent-grade pyridine was dried over CaH_2 and distilled in the presence of fresh CaH_2.

The HCO_3^- salts of **1–9** were prepared by refluxing solutions of the corresponding 6-*O*-sulfonyl- or 6-bromo-6-deoxy-α-cyclodextrins in dry pyridine, followed by elution of the products from a column of CM-cellulose with aqueous NH_4HCO_3 as described[19]. ^{1}H-N.m.r. spectroscopy (D_2O) of the products and h.p.l.c. on TSK gel CW-5PW revealed that the derivatives **1–9** were pure[19].

T.l.c. was performed on Kieselgel $60F_{254}$ (Merck), using acetic acid–chloroform–water (80:10:20) and detection with a saturated solution of cerium(IV) sulfate in conc. sulfuric acid. Column chromatography involved Sephadex G-15 (35 × 730 mm, Pharmacia) and/or CM-cellulose (50 × 550 mm, Serva). Each fraction (10 mL) was assayed by u.v. absorption at 270 nm and polarimetry at 589 nm.

Acetylation of **1** *and* **3**. — Typically, acetic anhydride (2 mL, 19.6 mmol) was stirred with a solution of the HCO_3^- salt of **1** (103.5 mg, 0.094 mmol) in dry pyridine (20 mL) at room temperature for 20 h. After the addition of water (2 mL), the mixture was concentrated to dryness *in vacuo*. Column chromatography (water) of the residue on Sephadex G-15 removed material with low molecular weight. Fractions (10 mL) 38–50 were combined and concentrated to dryness *in vacuo*. T.l.c. showed that the residue (134.3 mg) was not pure. An aliquot (101 mg) of the residue was eluted from a column of CM-cellulose with 0.05M NH_4HCO_3 (10-mL fractions). Fractions 110–125 were combined and concentrated to dryness *in vacuo*

to afford the acetylated derivative **10** (37.6 mg, 29%) that gave a single spot at R_F 0.53 in t.l.c. The ^{1}H-n.m.r. spectrum (270 MHz, D_2O) of **10** at 50° contained broad signals at δ 8.87, 8.66, and 8.13 due to the *o*-, *p*-, and *m*-protons, respectively, of the pyridinio group. The acetyl protons gave signals at δ 2.12 (b) and 1.88 (s) with integrated intensities in the ratio ~2:1. The sum of the peak areas indicated ~16 acetyl groups (theoretical value, 17).

The acetylated compound **11**, prepared similarly from **3** (95.7 mg, 0.079 mmol), was purified by elution from a column of CM-cellulose with 0.05M NH_4HCO_3 (2 L) followed by 0.10M NH_4HCO_3 (10-mL fractions). Fractions 310–350 were combined and concentrated to dryness *in vacuo* to afford **11** (100.4 mg, 68%), t.l.c. of which gave a single spot, R_F 0.28. The ^{1}H-n.m.r. spectrum (D_2O) of **11** contained broad signals at δ 8.85, 8.69, and 8.17, due to the *o*-, *p*- and *m*-protons of the pyridinio groups, together with signals at δ 2.13 (b) and 1.90 (s) due to ~16 acetyl groups.

RESULTS AND DISCUSSION

0.1–0.8M Solutions of the pyridinio derivatives **1–9** and the acetylated pyridinio derivatives **10** and **11** exhibited virtually no u.v. absorption at >280 nm. On the addition of KI, KSCN, or KBr to the solutions, characteristic absorption bands appeared in the region of 280–350 nm, indicating the formation of c.t. complexes[18]. The absorbance increased with increasing concentration of the inorganic salt. The K_a values for the c.t. complexes were determined by a computer curve-fitting analysis of the changes (ΔA) in absorbance at a given wavelength (290–310 nm) with the concentration (c_a) of the inorganic salt, assuming 1:1 complexation. The observed and calculated curves fitted well (Fig. 1) even for the hosts **2–9** and **11** which carry two or more pyridinio groups. In these hosts, it is possible that two or more guest anions are bound to one molecule of the host. However, only 1:1 c.t. complexation may be observable if the macrocyclic cavity of the α-cyclodextrin

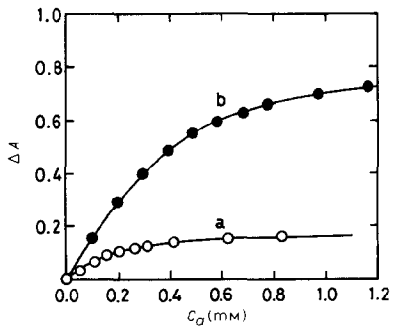

Fig. 1. Changes (ΔA) in absorbance at 300 nm of aqueous solutions containing (a) 0.10mM and (b) 0.40mM **5** with increasing concentration (c_a) of KI at 25°. The solid lines were obtained by curve-fitting analysis, assuming a 1:1 complex of **5** and I^-.

TABLE I

BINDING CONSTANTS (K_a, $mol^{-1}.dm^3$) FOR HOST–ANION COMPLEXES IN AN AQUEOUS SOLUTION AT 25°

Host	I^-	SCN^-	Br^-
α-CD	1.32×10^a	2.28×10^a	0.87 ± 0.02^b
1	$(1.36 \pm 0.02) \times 10^2$	$(2.86 \pm 0.07) \times 10^2$	8.4 ± 0.2
2	$(1.13 \pm 0.02) \times 10^3$	$(1.15 \pm 0.01) \times 10^3$	$(3.9 \pm 0.2) \times 10$
3	$(1.44 \pm 0.02) \times 10^3$	$(2.01 \pm 0.02) \times 10^3$	$(3.8 \pm 0.1) \times 10$
4	$(1.32 \pm 0.02) \times 10^3$	$(1.85 \pm 0.02) \times 10^3$	$(3.6 \pm 0.1) \times 10$
5	$(0.97 \pm 0.06) \times 10^4$	$(0.68 \pm 0.02) \times 10^4$	$(2.8 \pm 0.1) \times 10^2$
6	$(1.64 \pm 0.07) \times 10^4$	$(1.23 \pm 0.01) \times 10^4$	$(3.0 \pm 0.4) \times 10^2$
7	$(1.51 \pm 0.06) \times 10^4$	$(1.15 \pm 0.01) \times 10^4$	$(3.6 \pm 0.3) \times 10^2$
8	1.11×10^4		
9	$(9.0 \pm 1.1) \times 10^5$	$(1.3 \pm 0.2) \times 10^5$	$(1.3 \pm 0.2) \times 10^4$
10	$(5.4 \pm 0.1) \times 10^2$	$(4.6 \pm 0.2) \times 10^2$	9.2 ± 2.7
11	$(5.7 \pm 0.5) \times 10^3$	$(2.2 \pm 0.2) \times 10^3$	$(8.7 \pm 1.3) \times 10$

[a]Ref. 14. [b]Ref. 15.

moiety plays an important role. The K_a value for the c.t. complex of the non-macrocyclic analogue of **1**, namely, methyl 6-deoxy-6-(1-pyridinio)-α-D-gluco-pyranoside, with I^- is much smaller than that for a macrocyclic **1**–I^- system[18]. Thus, the macrocyclic cavities are essential for the formation of stable c.t. complexes.

The K_a values for 1:1 c.t. complexes of **1**–**11** with I^-, SCN^-, and Br^- are summarized in Table I. An increase in the number of pyridinio group(s) resulted in a remarkable increase in the K_a value. Thus, I^- was bound to the mono-, di-, tri-, and hexa-pyridinio derivatives more strongly than to α-cyclodextrin by factors of ~10, ~100, ~1000, and ~70,000, respectively. The K_a value (9×10^5 $mol^{-1}.dm^3$) for the **9**–I^- system is the largest reported thus far for the complexation of inorganic anions. SCN^- was also strongly bound to **9**, but the K_a value was ~7 times less than that for the corresponding I^- system. In contrast, SCN^- bound to α-cyclodextrin more strongly than I^- by a factor of ~2. The reversal of the guest selectivity may be attributed to a difference in c.t. interactions of the pyridinio group and the guest anions. U.v. spectrophotometry revealed[18] that the c.t. interactions of the pyridinio group with I^- are much stronger than those with SCN^-. Br^- interacts very weakly with α-cyclodextrin. The modification of the host with the pyridinio group(s) resulted in a remarkable increase in the K_a value for Br^-, but the K_a values were always much smaller than those for the corresponding I^- systems. This fact implies that the guest selectivity is largely dependent on the macrocyclic cavity of the host. The di- and tri-pyridinio derivatives involve three and four regioisomers, respectively. However, no significant differences in the K_a values were observed between the regioisomers; thus, the position of the pyridinio groups is not important in the complexation with anions.

Acetylation of **1** and **3** resulted in a significant increase in K_a values for I^-. Thus, I^- was bound to **10** and **11** more strongly than to **1** and **3**, respectively, by a factor of ~4. The microenvironment of the pyridinio group(s) may become more

hydrophobic after acetylation, which is advantageous not only for hydrophobic interactions of the hosts and the chaotropic I^- but also for c.t. and electrostatic interactions. Similar, though less favorable, effects of the acetylation were observed for SCN^- and Br^- systems.

Inorganic anions such as ClO_4^-, Cl^-, and SO_4^{2-} do not form c.t. complexes with the pyridinio group. However, they retarded[18] the complexation of the hosts **1–11** with I^- strongly (ClO_4^-) or weakly (Cl^- and SO_4^{2-}). The complexation of the hosts with these inorganic anions is currently under investigation.

REFERENCES

1 E. Graf and J.-M. Lehn, *J. Am. Chem. Soc.*, 98 (1976) 6403–6405.
2 J.-M. Lehn, E. Sonveaux, and A. K. Willard, *J. Am. Chem. Soc.*, 100 (1978) 4914–4916.
3 J.-M. Lehn, *Acc. Chem. Res.*, 104 (1978) 49–57.
4 F. P. Schmidtchen, *Top. Curr. Chem.*, 132 (1986) 101–133.
5 B. Dietrich, M. W. Hosseini, J.-M. Lehn, and R. B. Sessions, *J. Am. Chem. Soc.*, 103 (1981) 1282–1283.
6 J. Cullinane, R. I. Gelb, T. N. Margulis, and L. J. Zompa, *J. Am. Chem. Soc.*, 104 (1982) 3048–3053.
7 E. Kimura, M. Kodama, and T. Yatsunami, *J. Am. Chem. Soc.*, 104 (1982) 3182–3187.
8 R. I. Gelb, B. T. Lee, and L. J. Zompa, *J. Am. Chem. Soc.*, 107 (1985) 909–916.
9 I. Tabushi, Y. Kimura, and K. Kamamura, *J. Am. Chem. Soc.*, 100 (1978) 1304–1306.
10 F. Cramer, W. Saenger, and H.-Ch. Spatz, *J. Am. Chem. Soc.*, 89 (1967) 14–20.
11 K. Mochida, A. Kagita, Y. Matsui, and Y. Date, *Bull. Chem. Soc. Jpn.*, 46 (1973) 3703–3707.
12 R. P. Rohrbach, L. J. Rodriguez, E. M. Eyring, and J. F. Wojcik, *J. Phys. Chem.*, 81 (1977) 944–948.
13 A. Buvari and L. Barcza, *Inorg. Chim. Acta*, 33 (1979) L179–L180.
14 H. Hoeiland, L. H. Hald, and O. J. Kvammen, *J. Solution Chem.*, 10 (1981) 775–784.
15 R. I. Gelb, L. M. Schwartz, M. Radeos, and D. A. Laufer, *J. Phys. Chem.*, 87 (1983) 3349–3354.
16 J. P. Diard, E. Saint-Aman, and D. Serve, *J. Electroanal. Chem. Interfacial Electrochem.*, 189 (1985) 113–120.
17 I. Sanemasa, M. Fujiki, and T. Deguchi, *Bull. Chem. Soc. Jpn.*, 61 (1988) 2663–2665.
18 Y. Matsui, M. Fujie, and K. Hanaoka, *Bull. Chem. Soc. Jpn.*, 62 (1989) 1451–1457.
19 Y. Matsui, M. Fujie, and H. Sakate, *Bull. Chem. Soc. Jpn.*, 61 (1988) 3409–3415.