ORGANIC
LETTERS

2000
Vol. 2, No. 13
1803−1805

Allosteric Silver(I) Ion Binding with Peripheral π Clefts of a Ce(IV) Double Decker Porphyrin

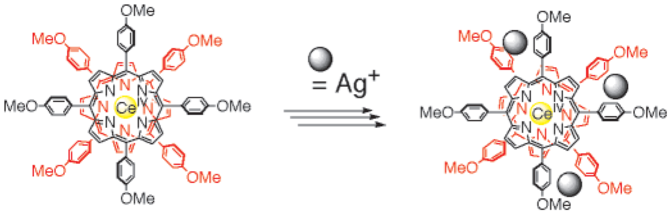
Masato Ikeda, Tomoyuki Tanida, Masayuki Takeuchi, and Seiji Shinkai*

*Department of Chemistry and Biochemistry, Graduateschool of Engineering,
Kyushu University, Fukuoka 812-8581, Japan*

seijitcm@mbox.nc.kyushu-u.ac.jp

Received March 14, 2000

ABSTRACT



1

1•Ag$^+_3$ complex

A cerium(IV) double decker porphyrin (1) bearing four 4-methoxyphenyl groups was synthesized. Compound 1 shows a positive, homotropic allosteric effect in metal recognition of Ag$^+$ ion, and the peripheral π clefts of 1 act as effective binding sites for Ag$^+$ ion.

Positive and negative allosteric effects are seen throughout nature where biological events must be efficiently regulated in response to chemical or physical signs from the outside world.[1−4] To design such artificial allosteric systems[5−14] is of great significance not only for controlling catalytic activities but also for regulating complexation properties of artificial receptors according to an allosteric manner. However, the examples reported so far are mostly heterotropic or negative allosterisms whereas homotropic, positive allosterism, which is the regulation tool with the most potential, has been very limited.[13,15] Furthermore, this approach is useful for amplifying and transforming weak chemical or

---

(1) (a) Perutz, M. F. *Annu. Rev. Biochem*. **1979**, *48*, 327. (b) Monod, J.; Changeux, J.-P.; Jacob, F. *J. Mol. Biol*. **1963**, *6*, 306. (c) Perutz, M. F.; Fermi, G.; Luisi, B.; Shaanan, B.; Liddington, R. C. *Acc. Chem. Res*. **1987**, *20*, 309.

(2) Gramdori, R.; Lavoie, T. A.; Pflumm, M.; Tian. G.; Niersbach, H.; Maas, W. K.; Fairman, R.; Carey, J. *J. Mol. Biol*. **1995**, *254*, 150.

(3) Burke, R.; Witmer, M. R.; Tredup, J.; Micanovic, R.; Gregor, K. R.; Lahiri, J.; Tramposch, K. M.; Villaframca, J. J. *Biochemistry* **1995**, *34*, 15165.

(4) (a) Filenko, A. M.; Danilova, V. M.; Sobieszek, A. *Biophys. J*. **1997**, *73*, 1593. (b) Modi, S.; Gilham, D. E.; Sutcliffe, M. J.; Lian, L.-Y.; Primrose, W. V.; Wolf, C. R.; Roberts, G. C. K. *Biochemistry* **1997**, *36*, 4461. (c) Bruzzese, F. J.; Connelly, P. R. *Biochemitry* **1997**, *36*, 10428. (d) Schetz, J. A.; Sibley, D. R. *J. Neurochem*. **1997**, *68*, 1990.

(5) Traylor, T. G.; Mitchell, M. J.; Ciconene, J. P.; Nelson, S. *J. Am. Chem. Soc*. **1982**, *104*, 4986.

(6) (a) Rebek, J., Jr. *Acc. Chem. Res*. **1984**, *17*, 258. (b) Rebek, J., Jr.; Costello, T.; Marshall, L.; Wattley, R.; Gadwood, R. C.; Onan, K. *J. Am. Chem. Soc*. **1985**, *107*, 7481. (c) Ebmeyer E.; Rebek, J., Jr. *Angew. Chem., Int. Ed. Engl*. **1990**, *29*, 1148.

(7) (a) Tabushi, I.; Kugimiya, S.; Kinnaird, M. G.; Sasaki, T. *J. Am. Chem. Soc*. **1985**, *107*, 4129. (b) Tabushi, I.; Kugimiya, S. *J. Am. Chem. Soc*. **1986**, *108*, 6926.

(8) Beer, P. D.; Rothin, A. S. *J. Chem. Soc., Chem. Commun*. **1988**, 52.

(9) Petter, R. C.; Salek, J. S.; Sikorski, C. T.; Kumaravel, G.; Lin, F.-T. *J. Am. Chem. Soc*. **1990**, *112*, 3860.

(10) Schneider, H.-J.; Ref, D. *Angew. Chem., Int. Ed. Engl*. **1990**, *29*, 1159.

(11) Sijbesma, R. P.; Nolte, R. J. *J. Am. Chem. Soc*. **1991**, *113*, 6695.

(12) Kobuke, Y.; Y. Satoh. *J. Am. Chem. Soc*. **1992**, *114*, 789.

(13) Kobayashi, K.; Asakawa, Y.; Kato, Y.; Aoyama, Y. *J. Am. Chem. Soc*. **1992**, *114*, 10307.

(14) Takeuchi, M.; Imada, T.; Shinkai, S. *J. Am. Chem. Soc*. **1996**, *118*, 10658.

(15) Takeuchi, M.; Imada, T.; Shinkai, S. *Angew. Chem., Int. Ed*. **1998**, *37*, 2096. It is known that the rate of the porphyrin ring rotation in Ce•bis(porphyrinate) double decker is comparable with or slower than the NMR time scale. However, the allosteric behavior is basically observable for the present "static" equilibrium system as long as porphyrin rings are able to rotate. See the following references: Takeuchi, M.; Imada, T.; Ikeda, M.; Shinkai, S. *Tetrahedron Lett.* **1998**, *39*, 7897. Tashiro, K.; Konishi, K.; Aida, T. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 856.

10.1021/ol005807a CCC: $19.00

physical signals into other forms, so that we can more conveniently monitor them. Previously, we demonstrated that cerium(IV) bis[tetrakis(4-pyridyl)porphyrinate] double decker binds certain dicarboxylic acids [e.g., BOC-(D- or L-)-aspartic acid (BOC-Asp)] in a positive allosteric manner (Hill coefficient 3.9) via a hydrogen-bonding interaction to form only the 1:4 complex.[15] Very recently, we reported a cerium double decker porphyrin-based novel chirality transcription system in which the guest chirality is allosterically transcribed and stored.[16] Here, it occurred to us that cerium(IV) bis-[5,10,15,20-tetraarylporphyrinate] double deckers have eight peripheral π clefts and they may act as effective binding sites where guest metals such as a silver(I) ion are recognized via cation−π interactions.[17,18] We here report a novel type of homotropic, positive allosteric recognition of Ag^+ ion by *peripheral π clefts* of cerium(IV) double decker porphyrin (**1**).

Compound **1** was synthesized from 5,10,15,20-tetrakis-(4-methoxyphenyl)porphyrin according to the method reported by Buchler and Nawra.[19] The product was identified by ^{1}H NMR (COSY at −40 °C: peaks were broadened at room temperature), MALDI-TOF-MS spectral evidence, and elemental analysis.[20]

Upon addition of CF_3SO_3Ag to a solution of **1** (5.0 μM) in chloroform−methanol (4:1 v/v) at 25 °C, the Soret band of **1** shifted from 400.0 to 414.0 nm with a clear isosbectic point at 404.5 nm (Figure 1). When an excess amount of tetrabutylammmonium chloride was added to the solution of **1**−Ag^+ complex, AgCl precipitated and the Soret band in the supernatant solution immediately shifted to 400.0 nm without an absorbance decrease, which is coincident with that in the absence of Ag^+ ion. Furthermore, no absorbance change in the Soret band of **1** was confirmed in the presence of alkali metal cation. These results support the view that the Ag^+ ion interacts with **1** neither by redox reaction between **1** and Ag^+ ion nor by electrostatic interaction. More importantly, the plots of absorbance change at 414 nm vs CF_3SO_3Ag concentration featured a sigmoidal curvature, indicating that the binding of Ag^+ ion to **1** is cooperative (positive, homomotoropic allosterism) (Figure 2). This cooperative guest binding was analyzed with the Hill equation:[21] $\log(y/(1-y)) = n \log[\text{guest}] + \log K$, where K and n are the association constant and Hill coefficient, respectively and $y = K/([\text{guest}]^{-n} + K)$. From the slope and the intercept of the linear plot, we obtained $\log K = 11.2$ and $n = 2.2$ (correlation coefficient 0.99). The stoichiometry of the **1**−Ag^+ complex was confirmed by the continuous variation (Job) plots.[22] A plot of absorbance change at 414.0 nm against [**1**]/([**1**] +[Ag^+]) has a maximum at 0.25 which supports the view that the complex consists of one host **1** and three Ag^+ ion. The break point of the molar ratio plot of the **1**−Ag^+ system also appeared at [Ag^+]/[**1**] = 3. These spectral data consistently support that the most likely stoichiometry of **1**−Ag^+ complex is 1:3. Probably the 1:4 **1**−Ag^+ complex is thermodynamically unfavorable because of electrostatic repulsion among Ag^+ ions bounded with peripheral π clefts. The foregoing findings indicate that the first Ag^+ ion binding facilitates a second and third Ag^+ binding by suppressing the rotational freedom of the two porphyrin planes and/or of the 4-methoxyphenyl groups.

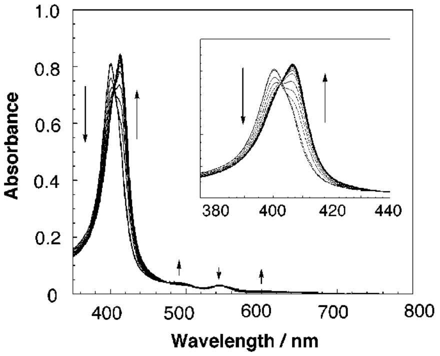


Figure 1. Concentration dependence of the UV−vis spectra: [**1**] = 5.0 μM, [CF_3SO_3Ag] = 5.0−100 μM, chloroform−methanol (4:1 v/v) at 25 °C.

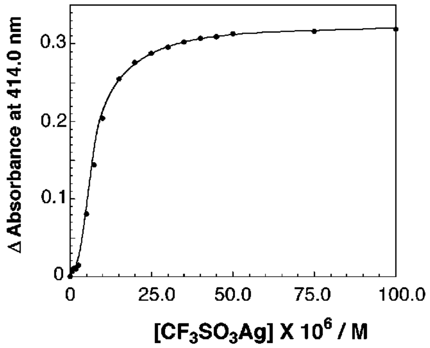


Figure 2. Plots of absorbance change at 414.0 nm for **1** vs [CF_3SO_3Ag].

To obtain further insights into the complexation mode of this allosteric **1**−Ag^+ system, we measured ^{1}H NMR spectra

---

(16) Sugasaki. A.; Ikeda, M.; Takeuchi, M.; Robertson, A.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3259.

(17) Alkali metal binding with peripheral crown ethers of phthalocyanine double decker was reported: Toupane, T.; Ahsen, V.; Simon, J. *J. Am. Chem. Soc*. **1994**, *116*, 5352.

(18) Silver(I) ion recognition with aromatic π system: (a) Pierre, J.-L.; Baret, P.; Chautemps, P.; Armand, M. *J. Am. Chem. Soc*. **1981**, *103*, 2986. (b) Kang, H. C.; Hanson, A. W.; Eaton, B.; Boekelheide, V. *J. Am. Chem. Soc*. **1985**, *107*, 1979. (c) Gano, G.; Subramaniam, G.; Brirnbaum, R. *J. Org. Chem*. **1990**, *55*, 4760. (d) Ikeda, A.; Tsuzuki, H.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2073. (e) Ikeda, A.; Shinkai, S. *J. Am. Chem. Soc*. **1994**, *116*, 3102. (f) Ikeda, A.; Tsudera, T.; Shinkai, S. *J. Org. Chem.* **1997**, *62*, 3568 and references therein.

(19) Buchler, J. W.; Nawra, M. *Inorg. Chem*. **1994**, *33*, 2830.

(20) **1**: δ (CH_2Cl_2, −40 °C) 4.15 (s, 24H), 6.48 (d, J = 8.0 Hz, 8H), 6.91 (d, J = 8.0 Hz, 8H), 7.77 (d, J = 8.0 Hz, 8H), 8.37 (s, 16H), 9.54 (d, J = 8.0 Hz, 8H), m/z (MALDI-TOF MS) 1606.88 (calcd for $[\mathbf{1} + H]^+$ 1606.76). Anal. Calcd for $C_{96}H_{72}CeN_8O_8 \cdot 0.75C_6H_3Cl_3$: C, 69.21; H, 4.42; N, 6.42. Found C, 69.51; H, 4.79; N, 6.22.

(21) Baldwin, J.; Chothia, C. *J. Mol. Biol*. **1979**, *129*, 175. (b) Connors, K. A. *Binding Constants*; John Wiley: New York, 1987.

(22) Job, A. *Ann. Chim. (10th series)* **1928**, *9*, 113.

for [**1**]/CF_3SO_3Ag = 1:0 and 1:20 at seven different temperatures (between −40 and 25 °C in CD_2Cl_2:CD_3OD = 4:1 v/v, between 25 and 50 °C in $Cl_2CDCDCl_2$:CD_3OD = 4:1 v/v). The selected spectra are shown in Figure 3. In the presence of Ag^+, 4-methoxyphenyl protons and β-pyrrole protons shifted to lower magnetic field at all temperatures except for the ‘e’ proton of the 4-methoxyphenyl moiety.[23] Furthrmore, 4-methoxyphenyl protons coalesce at 50 °C in the absence of Ag^+ ion (A), whereas they do not coalesce at even 50 °C with excess Ag^+ ion (B). These results strongly indicate that Ag^+ ion is bound to “*peripheral π clefts*” of **1** so that bounded Ag^+ ion can suppress the rotational freedom of 4-methoxyphenyl groups. On the other hand, the spectral change in the β-pyrrole protons, which is associated with the rotation of the porphyrin rings, is scarcely induced. Judging from the preceding examples for our developed positive, homotoropic allosteric systems,[15,16] however, it is reasonable that Ag^+ ion binding suppresses the rotational freedom of both the 4-methoxyphenyl groups and the two porphyrin planes. In addition, we measured ^1H NMR spectra for various mixtures of **1** and CF_3SO_3Ag in $CD_2Cl_2-CD_3OD$ (4:1 v/v). The selected spectra for [**1**]/CF_3SO_3Ag = 1, 5, and 20 at −40 and −80 °C are shown in Figure 4. In the case of [**1**]/CF_3SO_3Ag = 1, the peaks for the **1**−Ag^+ complex appear separately from those for free **1**. Four different kinds of pyrrole protons are observed at −80 °C, which are assignable to the 1:0, 1:1, 1:2, and 1:3 **1**−Ag^+ complexes, respectively. On the other hand, in the case of [**1**]/CF_3SO_3Ag = 5 or 20, there is only one species assignnable, the 1:3 (**1**−$3Ag^+$) complex. In such a 1:3 (**1**−$3Ag^+$) complexation mode, the structure of the **1**−Ag^+ complex becomes nonsymmetrical. Presumably, the intramolecular Ag^+ ions exchange between peripheral π clefts of **1** faster than the NMR time scale even at −80 °C. This is why we cannot observe peak separation assignable to the nonsymmetrical structures. We tried to estimate the ratio of equilibrium constants K_2/K_1 and K_3/K_2 for the association of **1** and CF_3SO_3Ag. From the ratio of the integral intensities of free **1** and **1**−Ag^+ complexes, we obtained the values 1.61 for K_2/K_1 and 0.53 for K_3/K_2, respectively. These results also support that the binding of Ag^+ to **1** is cooperative. In conclusion, we demonstrated that **1** shows a positive, homotoropic allosteric effect in the molecular recognition of Ag^+ ion and the peripheral π clefts of **1** act as effective binding sites for the Ag^+ ion. The present system is readily applicable to the regulation of association ability or catalytic activity. We believe that further elaboration of the present system will lead to a more generalized concept for allosterism in porphyrin chemistry not only in artificial systems but also in biological systems.

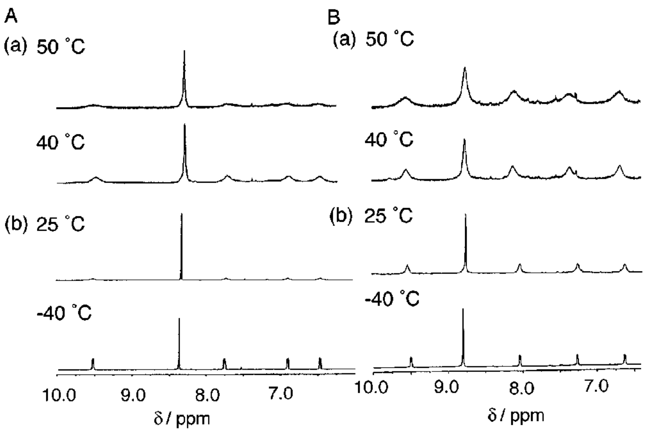


Figure 3. Aromatic proton regions of the ^1H NMR spectra of **1** (A) and mixture of **1** with 20 equiv of CF_3SO_3Ag (B) at various tempratures ((a) $Cl_2CDCDCl_2$:CD_3OD = 4:1 v/v, (b) CD_2Cl_2:CD_3OD = 4:1 v/v).

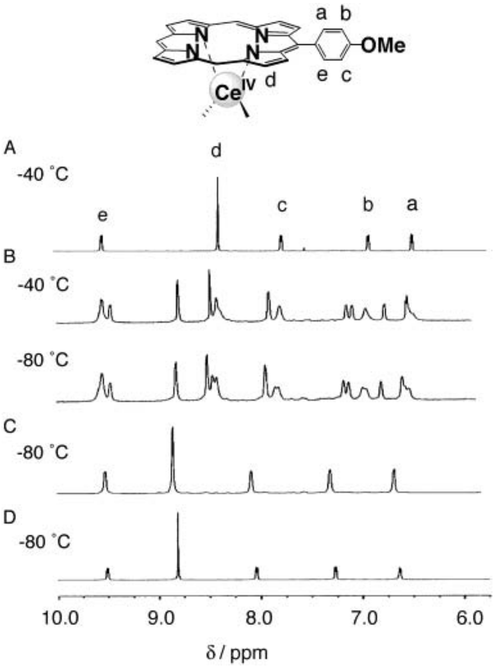


Figure 4. Aromatic proton regions of the ^1H NMR spectra of **1** (A) and mixture of **1** with 1, 5, and 20 equiv of CF_3SO_3Ag, (B), (C), and (D), respectively (in $CD_2Cl_2-CD_3OD$ (4:1 v/v)).

Acknowledgment. This work was supported by a Grant-in-Aid for COE Research (Design and Control of Advanced Molecular Assembly Systems) from the Ministry of Education, Science and Culture, Japan (#08CE2005).

Supporting Information Available: A Job plot and molar ratio plot of the **1**−Ag^+ system. A Hill plot and Scatchard plot of Figure 2. This material is available free of charge via the Internet at http://pubs.acs.org.

OL005807A

---

[23] Δδ: +0.15 (a, *exo o*-H), +0.35 (b, *exo* m−H), +0.26 (c, *endo m* − H), +0.43 (d, β-pyrrole H), −0.04 (e, *endo o*-H), +0.13(−O*Me*).