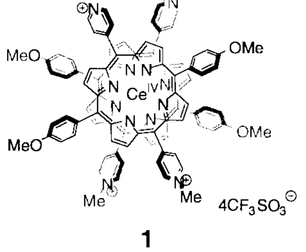
Efficient Anion Binding to Cerium(IV) Bis(porphyrinate) Double Decker Utilizing Positive Homotropic Allosterism

Masashi Yamamoto, Atsushi Sugasaki, Masato Ikeda, Masayuki Takeuchi, Karine Frimat,† Tony D. James,† and Seiji Shinkai*
Department of Chemistry & Biochemistry, Graduate School of Engineering, Kyushu University, Fukuoka 812-8581
†Department of Chemistry, University of Bath, Bath BA2 7AY, U. K.

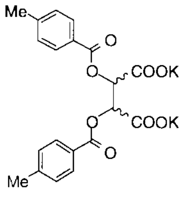
(Received February 26, 2001; CL-010160)

New cerium(IV) bis(porphyrinate) double decker bearing two pairs of anion binding sites was synthesized. This anion receptor can bind dianionic tartarate guest according to positive homotropic allosterism. Analysis using the Hill equation afforded log K (association constant) = 9.33 [(mol dm^{-3})$^{-2}$] and n (Hill coefficient) = 2.1 (± 0.1). This is the first example where "static" anion binding has been combined with the "dynamic" allosteric system.

Cation binding has a relatively long history since the discovery of macrocyclic polyethers and polyamines. In contrast, the history of anion binding is relatively short in spite of the importance in sensing nature-originated anionic species such as phosphates, carbonates, carboxylates, etc.[1] Thus, much recent research effort has been devoted towards the exploitation of new receptors for anion recognition. Typical, successful examples are the helicates of Hamilton[2] and Nabeshima,[3] the calix[4]pyrroles of Sessler,[4] the calix[4]arenes of Reinhoudt,[5] etc.[6] In these systems, the anion binding occurs "statically" between one receptor site and one guest, for which one cannot expect either switch functions or allosteric functions which frequently play important roles in nature. In order to combine "dynamic" functions with anion recognition, we designed cerium(IV) bis(porphyrinate) double decker[7,8] (**1**) bearing two anion recognition sites, each site consisting of a pair of cationic charges. It is known that this scaffold not only shows unique positive homotropic allosterism for guests which can bridge two *meso*-substituents but also is useful to realize high association constants with the aid of positive homotropic allosterism.[8,9] As expected, we found that **1** can bind D-tartarate dipotasium salt (**2**) with positive homotropic allosterism with Hill coefficient (n) = 2.



1



2 (D- or L-)

Compound **1** was synthesized by quaternization of cerium(IV) bis[5,15-(4-methoxyphenyl)-10,20-dipyridylporphyrinato][8] by CF_3SO_3Me in DMF. The product (mp > 300 °C) was identified by ^{1}H NMR and MALDI TOF MS ([**1**-$(CF_3SO_3)_2]^+$ m/z1848) spectral evidence and elemental analysis.

The first key point of this experiment was selection of measurement media. It is undoubted that less polar solvents are more favorable to the electrostatic interaction but **2** is less soluble in such solvents. To overcome this dilemma we used dicyclohexyl-18-crown-6 (DC18C6) to aid solubility of **2**. Figure 1 shows CD spectra of **1** in the presence of **2** in various mixed solvents. It has been established that only when two *meso*-substituents are bridged by chiral guests, the double deckers become CD-active.[8,9] In THF:DMSO = 1:1 v/v the solution was CD-silent. The THF solution gave CD spectra but became turbid with time and the spectra were not reproducible. On the other hand, reproducible CD spectra were obtained from the "clear" THF:MeOH = 1:1 v/v solution. In Figure 1, it is particularly noteworthy that in this mixed solvent L- and D-**2** give very strong, symmetrical CD bands, indicating that the two porphyrin planes are twisted in opposite directions by these two enantiometric guests. We thus decided to use this mixed solvent as a standard measurement medium.

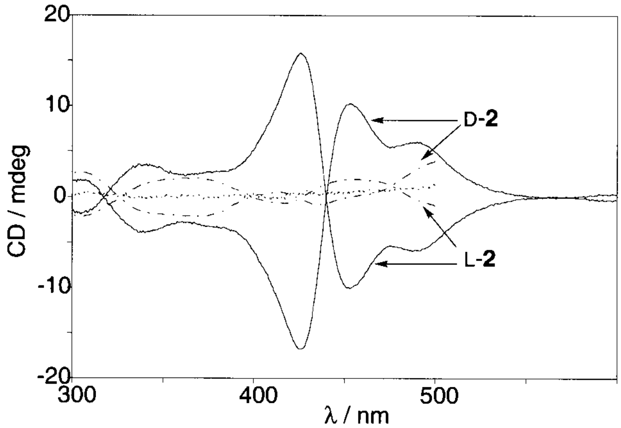


Figure 1. CD spectra of **1** (1.00×10^{-5} mol dm^{-3}) in the presence of D- or L-**2** (1.00×10^{-4} mol dm^{-3}) and DC18C6 (1.00×10^{-2} mol dm^{-3}) in THF:DMSO=1:1 v/v (----), THF (-·-·-), and THF:MeOH=1:1 v/v (——) at 25 °C with 1.0 cm cell.

In order to estimate the stoichiometry between **1** and **2** we measured the CD spectra at high **1** concentration (1.00 × 10^{-4} mol dm^{-3}) as a function of D-**2** concentration (Figure 2A). The presence of isosbestic points suggests that the CD-active species is yielded in one step from **1**. As shown in a plot of CD intensity vs. [D-**2**], the CD intensity increases almost linearly up to [D-**2**]/[**1**] < 2.0 and then is saturated, resulting in a clear breakpoint at [D-**2**]/[**1**] =2.0. The result supports the view that (i) the association constant (K) between **1** and D-**2** is large and (ii) the CD-active species consists of a 1:2 stoichiometry.[10]

The cooperative guest binding profile, if it occurs, can be analyzed according to the Hill equation: $\log(y/(1-y)) = n \log[\text{guest}] + \log K$, where K and n are the association constant and Hill coefficient, respectively and $y = K/([\text{guest}]^{-n} + K)$.[11]

In order to determine the K we decreased the **1** concentra-

Copyright © 2001 The Chemical Society of Japan

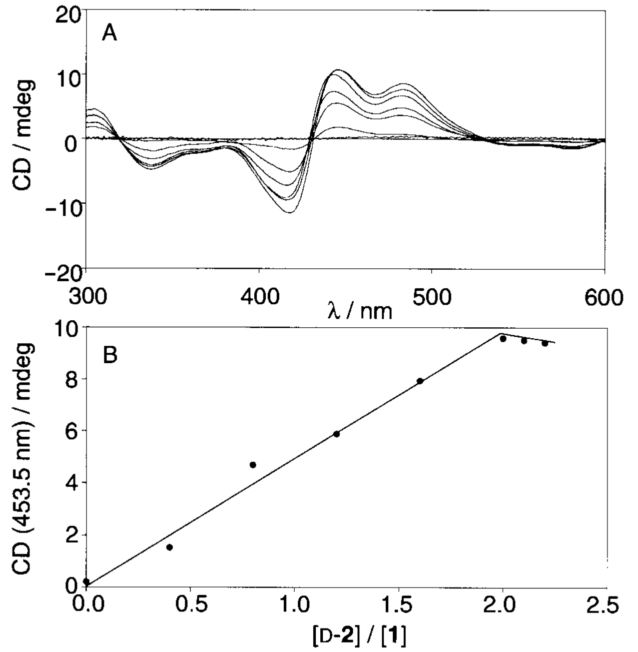


Figure 2. (A) CD spectral change of **1** (1.00×10^{-4} mol dm^{-3}) and (B) plots of CD intensity (at 453.5 nm) vs [D-**2**] at 25 °C with 1.0 mm cell. At [D-**2**] / [**1**] > 2.4, the solution became turbid because of precipitated D-**2**.

tion to 1.00×10^{-5} mol dm^{-3} (Figure 3).[12] Very interestingly, the plot shows a sigmoidal curvature characteristic of positive homotropic allosterism: that is, the binding of first D-**2** facilitates the binding of second D-**2**.

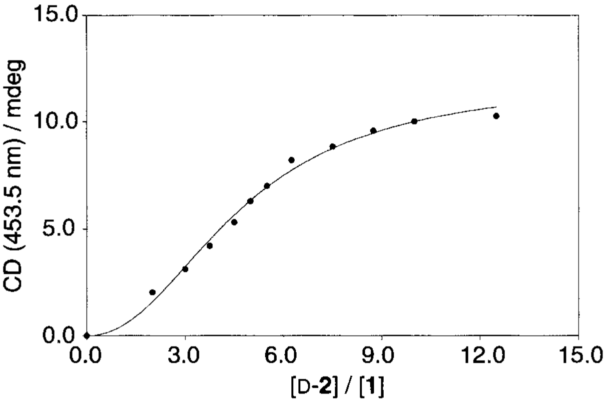


Figure 3. Plot of CD intensity (at 453.5 nm) vs [D-**2**]: [**1**]=1.00×10^{-5} mol dm^{-3}: for other measurement conditions see a caption to Figure 1.

From analysis of the data according to the Hill equation[11] we obtained log K = 9.33 [(mol dm^{-3})$^{-2}$] and n = 2.1 (± 0.1) (correlation coefficient 0.98). The results clearly establish that the binding of dianionic D-**2** to **1** occurs "cooperatively". This process can be illustrated as in Figure 4: that is, the first anionic guest binding is achieved by the electrostatic interaction with two cationic charges, but this process is not energetically favorable because the ΔH gain from the electrostatic interaction is effected by the ΔS penalty arising from the suppression of the porphyrin plane rotation. On the other hand, the second anionic guest binding is readily achieved because the remaining two cationic charges are already preorganized for guest binding.

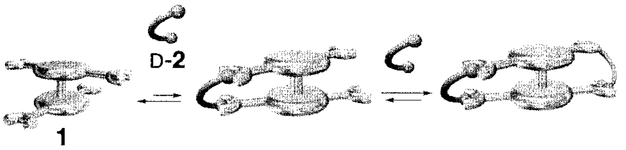


Figure 4. Schematic representation of allosteric binding of dianionic D-**2** guests to tetracationic **1** host.

The foregoing findings indicate that the binding of the first dianionic guest suppressed the rotational freedom of the two porphyrin planes and the remote second binding site is aligned for the highly cooperative binding of the second guest. As a result, two pairs of cationic charges in **1** can cooperatively bind these dianionic guest molecules with high association constants and give CD-active species. We believe that the concept demonstrated in the present system will help in further development of new receptor system for anion recognition.

References and Notes

1 For review on anion receptor see: a) P. A. Gale, *Coord. Chem. Rev.*, **199**, 181 (2000). b) T. M. Snowden and E. V. Anslyn, *Curr. Opin. Cell Biol.*, **3**, 740 (1999). c) F. P. Schmidtchen and M. Berger, *Chem. Rev.*, **97**, 1609 (1997).

2 a) M. S. Goodman, V. Jubian, B. Linton, and A. D. Hamilton, *J. Am. Chem. Soc.*, **117**, 11610 (1995). b) M. S. Goodman, V. Jubian, and A. D. Hamilton, *Tetrahedron Lett.*, **36**, 2551 (1995).

3 a) T. Nabeshima, A. Hashiguchi, S. Yazawa, T. Haruyama, and Y. Yano, *J. Org. Chem.*, **63**, 2788 (1998). b) T. Nabeshima, T. Inaba, N. Furukawa, T. Hosoya, and Y. Yano, *Inorg. Chem.*, **32**, 1407 (1993). c) T. Nabeshima, T. Inaba, and N. Furukawa, *Tetrahedron Lett.*, **28**, 6211 (1987).

4 a) P. Anzenbacher, Jr., A. C. Try, H. Miyaji, K. Jursíková, V. M. Lynch, M. Marquez, and J. L. Sessler, *J. Am. Chem. Soc.*, **122**, 10268 (2000). b) P. A. Gale, J. L. Sessler, W. E. Allen, N. A. Tvermoes, and V. Lynch, *Chem. Commun.*, **1997**, 665.

5 a) B. H. M. Snellink-Ruël, M. M. G. Antonisse, J. F. J. Engbersen, P. Timmerman, and D. N. Reinhoudt, *Eur. J. Org. Chem.*, **2000**, 165. b) H. Boerrigter, L. Grave, J. W. M. Nissink, L. A. J. Chrisstoffels, J. H. van der Mass, W. Verboom, F. de Jong, and D. N. Reinhoudt, *J. Org. Chem.*, **63**, 4174 (1998).

6 For recent reports on anion receptors see: a) D. H. Lee, K. H. Lee, and J. I. Hong, *Org. Lett.*, **3**, 5 (2001). b) P. D. Beer, N. Berry, M. G. B. Drew, O. D. Fox, M. E. Padilla-Tosta, and S. Patell, *Chem. Commun.*, **2001**, 199. c) M. J. Deetz, M. Shang, and B. D. Smith, *J. Am. Chem. Soc.*, **122**, 6201 (2000). d) Y. Kubo, M. Tsukahara, S. Ishihara, and S. Tokita, *Chem. Commun.*, **2000**, 653. e) S. Sasaki, M. Mizuno, K. Naemura, and Y. Tobe, *J. Org. Chem.*, **65**, 275 (2000). f) M. H. Al-Sayah, and N. R. Branda, *Angew. Chem. Int. Ed.*, **39**, 945 (2000).

7 Aida et al. showed that this class of double deckers is applicable to novel chiral recognition and molecular switches: a) K. Tashiro, K. Konishi, and T. Aida, *J. Am. Chem. Soc.*, **122**, 7921 (2000). b) Y. Mizuno, T. Aida, and K. Yamaguchi, *J. Am. Chem. Soc.*, **122**, 5278 (2000). c) K. Tashiro, K. Konishi, and T. Aida, *Angew. Chem., Int. Ed. Engl.*, **36**, 856 (1997).

8 a) M. Ikeda, M. Takeuchi, A. Sugasaki, A. Robertson, T. Imada, and S. Shinkai, *Supramol. Chem.*, in press. b) M. Takeuchi, T. Imada, and S. Shinkai, *Angew. Chem. Int. Ed.*, **37**, 2096 (1998).

9 a) A. Sugasaki, M. Ikeda, M. Takeuchi, and S. Shinkai, *Angew. Chem. Int. Ed.*, **39**, 3839 (2000). b) A. Sugasaki, M. Ikeda, M. Takeuchi, K. Koumoto, and S. Shinkai, *Tetrahedron*, **56**, 4717 (2000).

10 More reliable stoichiometry would be obtained from the Job plot, however the plot at ~10^{-3} mol dm^{-3} was difficult because of the solubility limitation.

11 K. A. Connors, "Binding Constants", Wiley, New York (1987).

12 In the low **2** concentration region (–3.00×10^{-4} mol dm^{-3}), it took several min to reach the equilibrium values. The plot was made from these equilibrated values.