Pergamon

Tetrahedron Letters 40 (1999) 6019–6023

TETRAHEDRON
LETTERS

A new biphenyl-20-crown-6-derived zinc(II) porphyrin dimer with a potentially heterotropic allostery

Yuji Kubo,[a,*,†] Yasuaki Murai,[a] Jun-ichi Yamanaka,[a] Sumio Tokita[a] and Yoshihiro Ishimaru[b]

[a]*Department of Applied Chemistry, Faculty of Engineering, Saitama University, 255 Shimo-ohkubo, Urawa, Saitama 338-8570, Japan*

[b]*Department of Functional Material Science, Faculty of Engineering, Saitama University, 255 Shimo-ohkubo, Urawa, Saitama 338-8570, Japan*

Received 11 March 1999; revised 7 June 1999; accepted 11 June 1999

Abstract

Synthesis of a new bis-porphyrinic system coupled with biphenyl-20-crown-6 as an allosteric spacer, **1**, is described; the incorporated rotatable biphenyl unit is capable of regulating the porphyrin center-to-center distance by an encapsulated metal ion in the crown-strapped cavity, so that the system displayed a potentially heterotropic allostery at the binding stage with a certain stereogenic α,ω-diamine guest, **2**. © 1999 Elsevier Science Ltd. All rights reserved.

Synthetic porphyrin dimers of many topologies have been widely studied as not only models of the photosynthetic reaction center[1] and light-harvesting complex,[2] but also as molecular catalysts.[3] Most notably, in the biomimetic approach using metalloporphyrins,[4] the dimers provide us with synthetically accessible means of constructing receptor models.[5] As our ongoing project aimed at the preparation of nanoscopic molecular devices, we have been strongly intrigued by the synthesis of bis-porphyrinic systems with a heterotropic allostery[6] because several functions ascribed to dimeric porphyrins could be fairly regulated by an external stimulus. The obtained insight might have important implications for the control of artificial porphyrin arrays[7] such as molecular-wires. However, to the best of our knowledge, the allosteric systems based on dimeric porphyrins which have been reported so far are limited in the utility of homotropic interactions.[8] Thus, with our strategy for producing the related heterotropic allosteric system, we decided to synthesize the title system **1** in which a biphenyl-20-crown-6 spacer was employed as a modulator. The main motivation is that the rotatable biphenyl unit could make the conformation of **1** to be variable and, consequently, the ditopic binding function due to the bis-porphyrins might be regulated by a metal ion encapsulated in the crown-strapped cavity. The intriguing result is described in this communication.

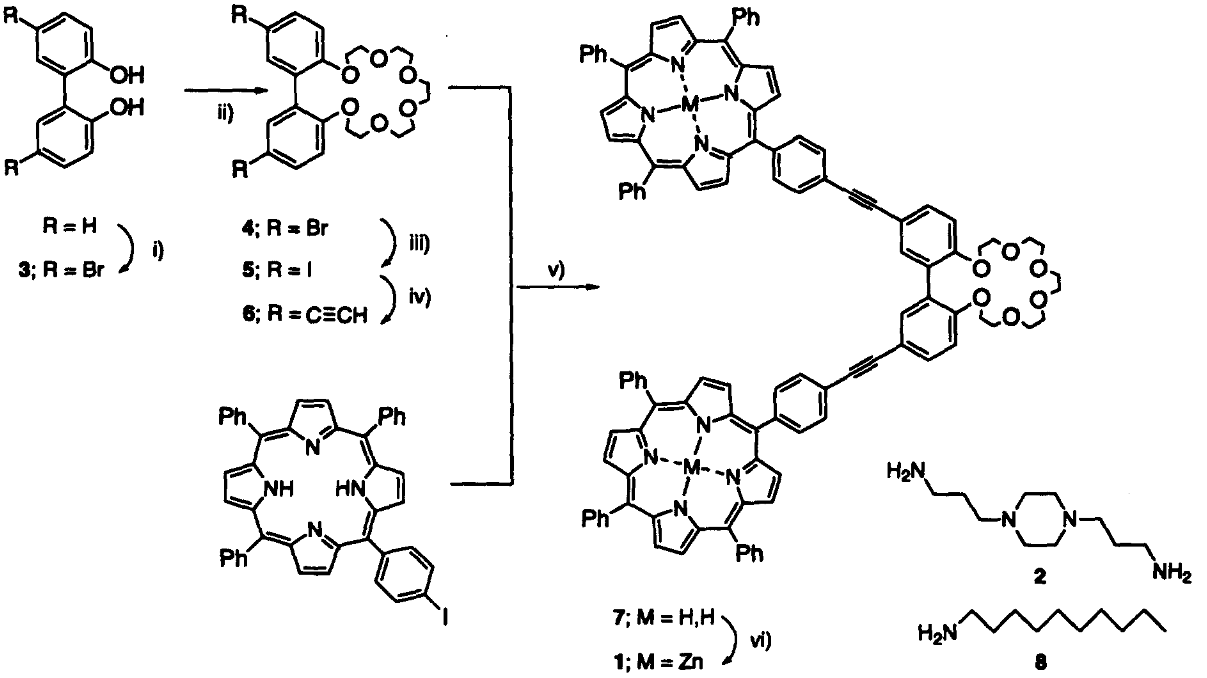
---

[*] Corresponding author. E-mail: yuji@apc.saitama-u.ac.jp

[†] PRESTO, Japan Science and Technology Corporation (JST).

PII: S0040-4039(99)01187-9

The synthetic path of target **1** is shown in Scheme 1. The starting material, 1,1′-bi-2-phenol, was allowed to react with 3 equiv. of Br_2 in dry $CHCl_3$ to give 5,5′-dibrominated product **3** in 97% yield,[9] followed by a Williamson synthesis with penta(ethyleneglycol) ditosylate, halogen exchange reaction, Pd-mediated coupling reaction with (trimethylsilyl)acetylene in the presence of CuI, and then deprotection to give **6**. The connection of 5-(4-iodephenyl)-10,15,20-triphenylporphyrin[10] to **6** by a copper-free cross-coupling reaction using $Pd(PPh_3)_4$, led to biphenyl-20-crown-6-derived free base porphyrin dimer **7** in 66% yield being transferred to target **1** in 64% yield under standard conditions using $Zn(AcO)_2 \cdot 2H_2O$. The assignment of this structure was sufficiently conducted by several spectral data[11] and in a UV/vis-detectable concentration at room temperature **1** did not participate in self-association.



Scheme 1. Reagents and conditions: (i) Br_2, dry $CHCl_3$, 97%; (ii) penta(ethyleneglycol) ditosylate, K_2CO_3, dry CH_3CN, reflux, 91%; (iii) KI, CuI, HMPA, 160°C, 64%; (iv) TMSA, $(PPh_3)_2PdCl_2$, CuI, dry $(i\text{-}Pr)_2NH$–dry DMF (5:1 v/v), 70°C, and then 1N KOH aq., CH_3OH, room temperature, 78%; (v) $(PPh_3)_4Pd$, dry DMF–dry NEt_3 (5:1 v/v), 50°C, 66%; (vi) $Zn(AcO)_2 \cdot 2H_2O$, CH_3OH–CH_2Cl_2, room temperature, 64%

The concave structure of **1** makes it possible to complex with a putative stereogenic α,ω-diamine guest. Indeed, the significant interaction between **1** and 1,4-bis(3-aminopropyl)piperazine **2** was obtained using a UV/vis titration in CH_2Cl_2–CH_3CN (9:1 v/v) as shown in Fig. 1. The Soret band of **1** bathochromically shifted from 423 to 429 nm after the addition of incremental amounts of **2**, the stoichiometric assessment by a Job plot[12] suggesting a 1:1 complex formation. The binding constant (K_a) could be estimated to be 7.9×10^5 M^{-1} using a nonlinear least-squares curve fitting plot. These findings are indicative of strong chelation within the bis-zinc(II) porphyrin cave of **1** as also supported by the ^1H NMR spectra in which the amino protons of **2** within **1** were drastically affected by the porphyrin system's magnetic anisotropy, shifting upfield by 5.7 ppm. Furthermore, the resonances arising from the methylene protons of **2** appeared at −2.06 and −1.62 ppm.

α,ω-Diamine binding affinity for a concave porphyrin dimer has been known to depend on the porphyrin center-to-center distance.[5c] Thus, we investigated to see if the rotatable biphenyl-20-crown-6

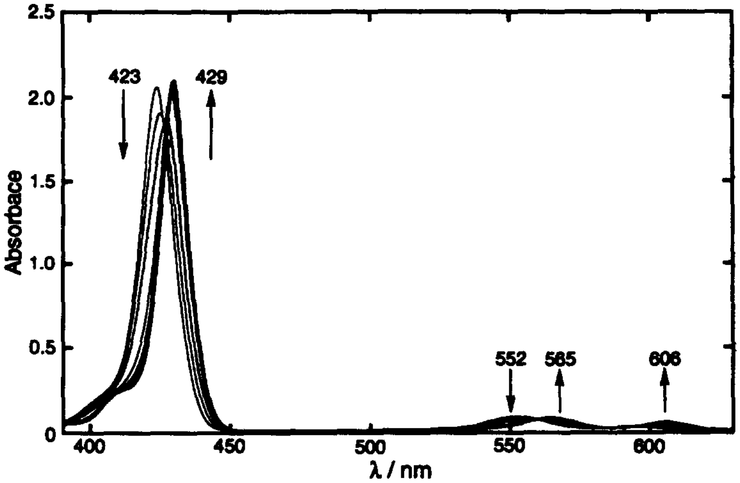


Figure 1. UV/vis spectral changes of **1** (2.0 μM) upon addition of α,ω-diamine **2** (0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0 μM) in CH_2Cl_2–CH_3CN (9:1 v/v) at 298 K

spacer could regulate the distance upon complexation with a suitable cation. In this context, Ba^{2+} as an effector (the diameter of which is 2.7 Å) was employed on the basis of the speculation that it could sufficiently bind to the allosteric spacer.[13] As expected, the addition of $Ba(ClO_4)_2$ caused a progressive decrease in the absorption intensity at 429 nm due to the **1**·**2** complex which suggested that Ba^{2+} is efficient in perturbation of the binding behavior between **1** and **2**; with 2 equiv. of Ba^{2+}, ca. 70% of the absorption intensity was apparently diminished (see Fig. 2). The control experiments using $LiClO_4$ under

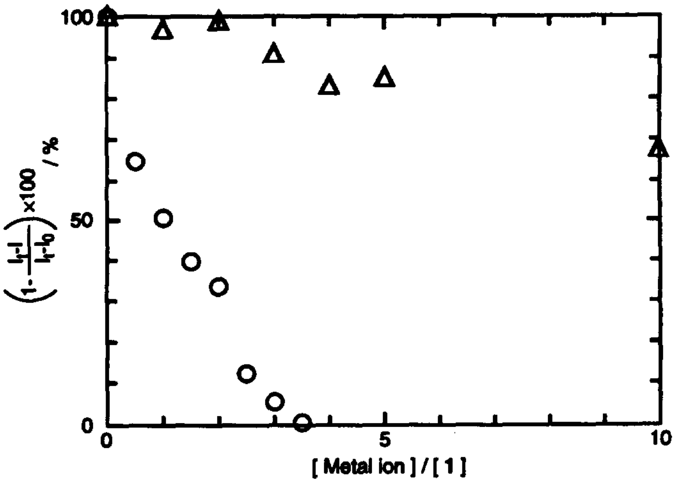


Figure 2. Decrease of the absorption intensity of **1**·**2** complex in the presence of metal perchlorate: Ba^{2+} (○), Li^+ (Δ); [**1**]=2.0 μM), [**2**]=4.0 μM), CH_2Cl_2–CH_3CN (9:1 v/v) at 298 K. I_0 is absorption intensity of **1** at 429 nm. I_t and I are the absorption intensities of **1**·**2** complex at 429 nm in the absence or in the presence of the metal ions

similar conditions indicated no such significant allosteric effect, possibly supporting an argument that the event was not affected by ClO_4^-. The ^1H NMR analysis after solid [$Ba(ClO_4)_2$]–liquid [2.0 mM of **1** in $CDCl_3$–CD_3CN (9:1 v/v)] two-phase solvent extraction revealed that the ratio of the complexation between **1** and **2** was reduced to ca. 50% when **2** (2.0 mM) was added to the solution. In contrast, the K_a value of the porphyrin dimer–monoamine (**1**·**8**) is 4.1×10^4 M^{-1}, which is similar to that of Zn(II) tetraphenylporphyrin–**8** complex and diminishes affinity by a factor of 19 compared to the **1**·**2** complex.

Thus, in the condition of Fig. 2 no significant complexation with **8** could be detected. From these results, the allostery obtained in the binding stage between **1** and **2** can be interpreted on the basis of the ditopic interaction of the α,ω-diamine. The preliminary results of the negative heterotropic allostery might be speculated by performing a molecular mechanics calculation. The energy-minimization (ESFF force field) with the Quasi Newton–Raphson algorithm was performed using InsightII/Discover Release 3.0.0 (Version 97.0) of MSI on a Silicon Graphics COMTEC 4D O2 workstation. Fig. 3 shows the effector-free Zn(II) porphyrin dimer **1** in which the phenyl substituents on the porphyrin units are omitted to simplify the calculation. The porphyrin center-to-center distance is ca. 21 Å, being longer than the diamine N–N distance in **2** of 12 Å. As a result, the presence of **2** should induce a conformational change of **1** to bind **2** during the two porphyrins. It is interesting to note that, upon the complexation, the center-to-center distance reduces to 16 Å and then the value of the dihedral angle between the phenyl rings of the spacer (biphenyl unit) is smaller by 12°. Based on the calculation, it may be reasonable to consider that the binding of an appropriate metal ion to the biphenyl-derived crown ether unit could block the diamine-induced conformation change. Although additional mechanistic studies concerning the obtained allosteric effect are currently underway in our laboratory, it is worth remarking that the adroit use of the rotatable biphenyl unit allows a small cation to regulate the function of the porphyrin dimer. Furthermore, an alternative function involving chiral induction[14] by an external stimulus can emerge from the biphenyl unit. Taken together, the versatile properties might provide potent tools for an effective approach to porphyrin-based molecular architecture of nano-size technology.

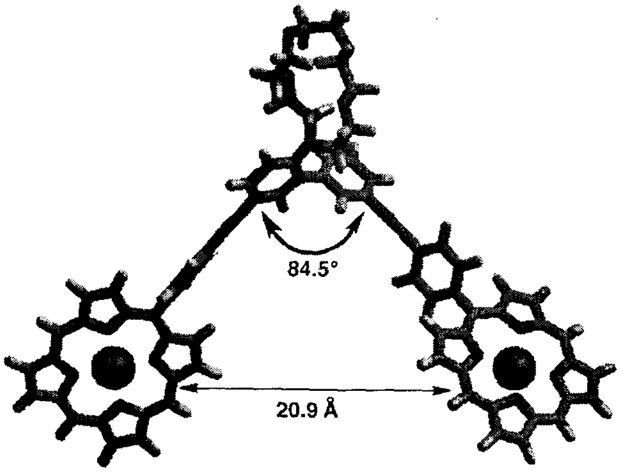


Figure 3. An energy-minimized structure of porphyrin dimeric system **1**

Acknowledgements

We thank Mr. S. Kawabata (Shimadzu Co. Ltd.,) for measuring the MALDI-TOF MS spectrum.

References

1. Wasielewski, M. R. *Chem. Rev.* **1992**, *92*, 435–461; Harriman, A.; Sauvage, J.-P. *Chem. Soc. Rev.* **1996**, 41–48.
2. Martensson, J.; Sandros, K.; Wennerström, O. *J. Phys. Org. Chem.* **1994**, *7*, 534–544; Chambron, J.-C.; Heitz, V.; Sauvage, J.-P.; Pierre, J.-L.; Zurita, D. *Tetrahedron Lett.* **1995**, *36*, 9321–9324; Kawabata, S.; Yamazaki, I.; Nishimura, Y.; Osuka, A. *J. Chem. Soc., Perkin Trans. 2* **1997**, 479–483.

3. Karaman, R.; Almarsson, Ö.; Blaskō, A.; Bruice, T. C. *J. Org. Chem.* **1992**, *57*, 2169–2173; Colman, J. P.; Wagenknecht, P. S.; Hutchison, J. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1537–1554, and references cited therein.
4. Ogoshi, H.; Mizutani, T. In *Comprehensive Supramolecular Chemistry*; Murakami, Y., Ed.; Pergamon Press: New York, 1996; Vol. 4, pp. 337–385.
5. (a) Danks, I. P.; Lane, T. G.; Sutherland, I. O.; Yap, M. *Tetrahedron* **1992**, *48*, 7679–7688; (b) Crossley, M. J.; Mackay, L. G.; Try, A. C. *J. Chem. Soc., Chem. Commun.* **1995**, 1925–1927; (c) Hayashi, T.; Nonoguchi, M.; Aya, T.; Ogoshi, H. *Tetrahedron Lett.* **1997**, *38*, 1603–1606; (d) Liu, H.; Huang, J.; Tian, X.; Jiao, X.; Luo, G.; Ji, L. *Chem. Commun.* **1997**, 1575–1576.
6. Host–guest complexation with a heterotropic allostery: review, see: Nabeshima, T. *Coord. Chem. Rev.* **1996**, *148*, 151–169; recent topics, see: Ohkanda, J.; Shibui, H.; Katoh, A. *Chem. Commun.* **1998**, 375–376; Beer, P. D.; Dent, S. W.; *Chem. Commun.* **1998**, 825–826; Nabeshima, T.; Takahashi, T.; Hanami, T.; Kikuchi, A.; Kawabe, T.; Yano, Y. *J. Org. Chem.* **1998**, *63*, 3802–3803; Haino, T.; Katsutani, Y.; Akii, H.; Fukazawa, Y. *Tetrahedron Lett.* **1998**, *39*, 8133–8136; Ikeda, A.; Suzuki, Y.; Yoshimura, M.; Shinkai, S. *Tetrahedron* **1998**, *54*, 2497–2508.
7. Mackay, L. G.; Wylie, R. S.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1994**, *116*, 3141–3142; Burrell, A. K.; Officer, D. L.; Reid, D. C. W. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 900–902; Wagner, R. W.; Lindsey, J. S.; Seth, J.; Palaniappan, V.; Bocian, D. F. *J. Am. Chem. Soc.* **1996**, *118*, 3996–3997; Tour, J. M. *Chem. Rev.* **1996**, *96*, 537–553; Tsuchiya, S. *J. Am. Chem. Soc.* **1999**, *121*, 48–53; self-assembling porphyrin arrays, see: Sessler, J. L.; Wang, B.; Harriman, A. *J. Am. Chem. Soc.* **1995**, *117*, 704–714; Funatsu, K.; Kimura, A.; Imamura, T.; Sasaki, Y. *Chem. Lett.* **1995**, 765–766, and references cited therein; Chi, X.; Guerin, A. J.; Haycock, R. A.; Hunter, C. A.; Sarson, L. D. *J. Chem. Soc., Chem. Commun.* **1995**, 2567–2569; Miyaji, H.; Kobuke, Y.; Kondo, J. *Chem. Lett.* **1996**, 497–498; Kuroda, Y.; Kato, Y.; Ogoshi, H. *Chem. Commun.* **1997**, 469–470; Kuroda, Y.; Kawashima, A.; Hayashi, Y.; Ogoshi, H. *J. Am. Chem. Soc.* **1997**, *119*, 4929–4933; Johnston, M. R.; Gunter, M. J.; Warrener, R. N. *Chem. Commun.* **1998**, 2739–2740.
8. Hunter, A. C.; Meah, M. N.; Sanders, J. K. M. *J. Chem. Soc., Chem. Commun.* **1988**, 694–696; Hunter, C. A.; Leighton, P.; Sanders, J. K. M. *J. Chem. Soc., Perkin Trans. 1* **1989**, 547–552; Takeuchi, M.; Imada, T.; Shinkai, S. *J. Am. Chem. Soc.* **1996**, *118*, 10658–10659; Takeuchi, M.; Imada, T.; Shinkai, S. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2096–2099.
9. Runeberg, J. *Acta Chem. Scand.* **1958**, *12*, 188–192.
10. Syrbu, S. A.; Semikin, A. S.; Berezin, B. D. *Khim. Geterotsikl. Soedin.* **1990**, *11*, 1507–1509.
11. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 3.49–3.58 (m, 12H, -OCH_2-), 3.72 (t, 4H, -OCH_2CH_2OAr), 4.15–4.26 (m, 4H, -CH_2OAr), 7.23 (d, J=8.5 Hz, 2H, biphenylH), 7.57 (d, J=2.0 Hz, 2H, biphenylH), 7.67–7.70 (m, 2H, biphenylH), 7.70–7.85 (m, 18H, ArH), 7.91 (d, J=7.8 Hz, 4H, ArH), 8.16–8.20 (m, 16H, ArH), 8.76–8.86 (m, 16H, pyrroleH); ^{13}C NMR (100.7 MHz, DMSO-d_6): δ (ppm) 68.42 (m), 69.21, 70.14, 70.32, 70.48, 88.52, 90.68, 113.16, 114.48, 119.61, 120.64, 120.74, 122.12, 122.43, 126.82, 127.71, 127.86, 129.68, 131.85, 132.03, 132.76, 132.86, 134.38, 134.73, 142.88, 143.05, 149.50, 149.55, 151.25, 157.10, 159.32; MASS (MALDI-TOF): *m/z* 1789 $[M]^+$, 1613 $[M-C_8H_{16}O_4]^+$, 1569 $[M-C_{10}H_{20}O_5]^+$; elemental analysis: calcd for $C_{114}H_{80}N_8O_6Zn_2\cdot H_2O$: C, 75.79; H, 4.58; N, 6.20; found: C, 75.87; H, 4.49; N, 6.13.
12. Job, P. *Ann. Chim. Ser.* **1928**, *9*, 113–134.
13. It is known that 5,5′-dimethyl-1,1′-biphenyl-20-crown-6 has exhibited a remarkable affinity for K^+ (K_a=1.7×10^6 M^{-1}); Koenig, K. E., Lein, G. M.; Stuckler, P.; Kaneda, T.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 3553–3566. However, $KClO_4$ as a putative effector in this stage is insoluble in the CH_2Cl_2–CH_3CN (9:1 v/v) system.
14. Mizutani, T.; Takagi, H.; Hara, O.; Horiguchi, T.; Ogoshi, H. *Tetrahedron Lett.* **1997**, *38*, 1991–1994.