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Dynamic Rotational Oscillation of Cerium(IV) Bis(porphyrinate) and Its Control by Diamine Guest Binding with Positive Homotropic Allosterism

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We have synthesized a porphyrin oscillator (**1**) composed of cerium(IV) bis(porphyrinate) bearing four peripheral zinc(II) porphyrinates. The rotational oscillation frequency of the porphyrin was evaluated in solution with and without the presence of diamine guest **2** by variable temperature NMR spectroscopy. The results established that the rotational frequency can be controlled by added guest utilizing positive homotropic allosterism.

Introduction

The design of molecular machines, in which the dynamic motions are controlled by photo-, electro- (redox-), and host–guest-type interactions, has attracted growing attention.[1] Particular interest has recently been focused on rotating modules[2] because a typical biological molecular machine, ATP synthase, can directly convert chemical energy derived from the hydrolysis of ATP into mechanical rotational energy with extremely high efficiency.[3] In artificial systems, it was demonstrated that cerium(IV) bis(porphyrinate)s act as interesting rotating modules in which a sandwiched metal ion acts as the axis of rotation.[4–7] We are interested in the construction of artificial positive homotropic allosteric systems that contain cerium(IV) bis(porphyrinate)s as dynamic rotating modules.[8] We have recently found that the rotational oscillation frequency of cerium(IV) bis(porphyrinate)s is significantly accelerated when silver(I) ions are inserted into the cleft that is constructed by the two porphyrin rings.[7a] Herein, we report the synthesis of a new porphyrin oscillator composed of cerium(IV) bis(porphyrinate) bearing four peripheral zinc(II) porphyrinates by a convergent synthetic method. The influence of diamine guest binding on the rotational oscillation frequency of the porphyrin oscillator was evaluated in solution by variable temperature (VT) NMR spectroscopy.

Results and Discussion

Porphyrin oscillator compound **1**, which has four zinc(II) porphyrin rings around a cerium(IV) bis(porphyrinate), was newly designed.[9] Molecular model calculations (Insight II/Discover 3.0) allowed us to estimate that compound **1** has a molecular size of (6 × 6) nm as an extended form. In principle, there are two strategies, a divergent method and a convergent method, for the synthesis of compound **1**. The divergent method is more versatile because one can easily introduce various types of functional groups at a later time. It is important to carefully choose the reaction conditions for the bond formation reaction because cerium(IV) bis(porphyrinate) is unstable, especially in the presence of acids. Thus, we decided to use the divergent method, which includes an ether bond formation reaction that can easily proceed in basic media. For this reason, we first tried to synthesize cerium(IV) bis[bis(hydroxyphenyl)porphyrinate]. However, no reaction took place between free base bis(hydroxyphenyl)porphyrin and $Ce(acac)_3{\cdot}3H_2O$ when they were heated at reflux in 1,2,4-trichlorobenzene (Scheme S1).[4] As an alternative method, we next applied a convergent method to obtain desired compound **1** (Scheme 1).

In order to eliminate the undesired formation of the cerium(IV) bis(porphyrinate), a porphyrin trimer[10] bearing two Zn(II) porphyrinates at each end was employed. Simple treatment of a 1,2,4-trichlorobenzene solution of the porphyrin trimer in the presence of $Ce(acac)_3{\cdot}3H_2O$ heated at reflux and subsequent purification by silica gel column chromatography and size-exclusion chromatography (Biobeads SX-1) successfully afforded compound **1** in 10% yield from the corresponding porphyrin trimer as a purple solid (Scheme 1). Its molecular weight was confirmed by MALDI-TOF MS analysis (Figure S1). Compound **1** was soluble in common organic solvents such as chloroform, dichloromethane, benzene, and so forth.

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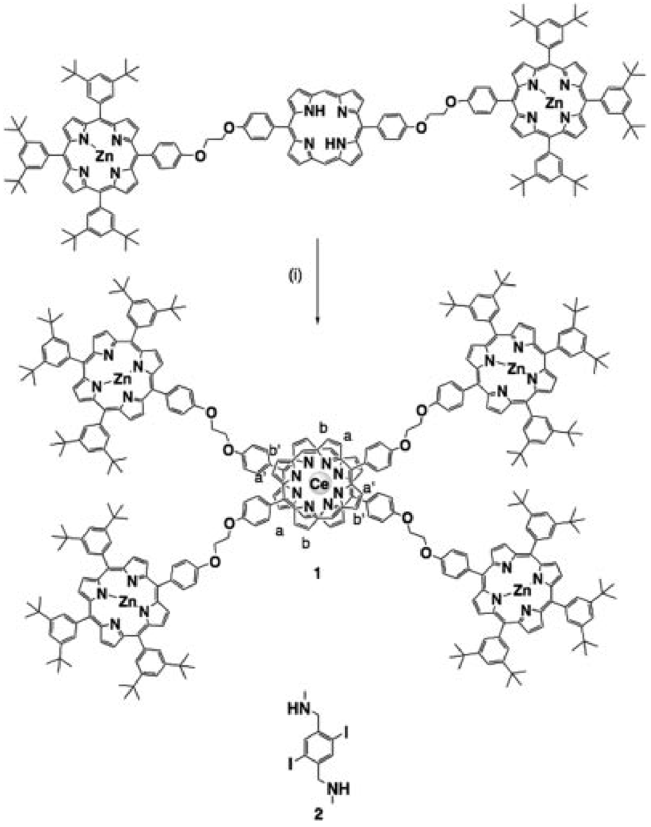

Scheme 1. Synthesis of compound **1** and chemical structure of diamine guest **2**: (i) Ce(acac)$_3$·3H$_2$O in 1,2,4-trichlorobenzene, reflux (10%).

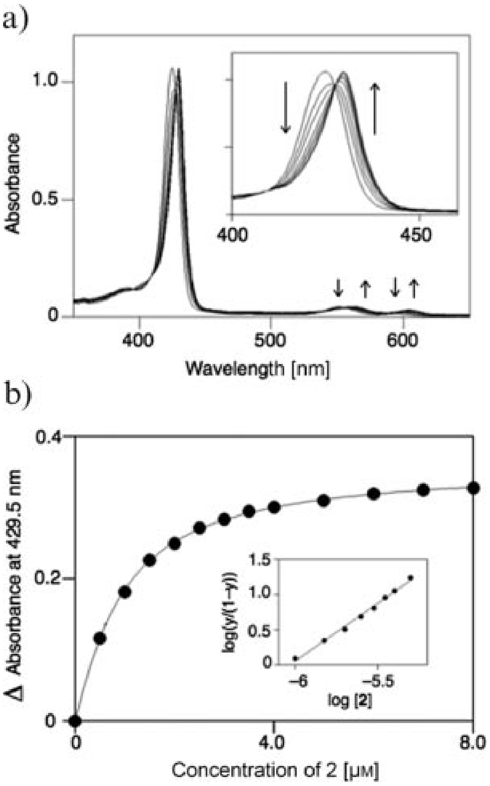

Figure 1. (A) Concentration dependence of UV/Vis spectra ([**1**] = 2.00 μM, [**2**] = 0.5–8 μM) in chloroform at 25 °C with 1-cm cell. (B) plots of absorbance at 429.5 nm for compound **1** against [**2**]. Inset of B shows the Hill plot. The solid lines in B represent theoretical curves.

The UV/Vis spectrum of compound **1** in chloroform shows Soret bands at 389.5 (shoulder) and 425.0 nm, and Q bands at 551 and 595 nm (Figure 1A). The similarity of the UV/Vis spectrum of compound **1** with the additive sum of zinc(II) tetrakis(4-*tert*-butylphenyl)porphyrinate (the Soret band appears at 424.0 nm) and cerium(IV) bis[5,15-bis(4-butoxyphenyl)porphyrinate] (the Soret band appears at 387.0 nm)[7a] implies that porphyrins in compound **1** do not interact with each other in an intramolecular manner. No emission band was observed for compound **1**, which indicates that excited energy could migrate from the peripheral four zinc(II) porphyrinates to the central cerium(IV) bis(porphyrinate). It is known that cerium(IV) bis(porphyrinate)s show no emission due to the nonradiative CT state that underlies its π* state.[4]

Upon the addition of diamine **2** to a solution of compound **1** (2.00 μM) in chloroform at 25 °C, the Soret band of compound **1** shifted from 425.0 nm to 429.5 nm with clear isosbestic points (Figure 1A). The plot of absorbance at 429.5 nm against the molar concentration of **2** was firstly analyzed with the Hill equation. The Hill plot for diamine guest **2** provides evidence with n_H (Hill coefficient) = 1.6, which indicates that the binding to compound **1** takes place cooperatively. We thus analyzed the binding isotherm with a nonlinear least-squares method by assuming the stepwise formation of 1:1 and 1:2 complexes. The association constants thus obtained are $K_1 = (1.6 \pm 0.1) \times 10^6\ \text{M}^{-1}$, $K_2 = (7.4 \pm 0.4) \times 10^5\ \text{M}^{-1}$, which satisfy the prerequisite for positive homotropic allosterism, $K_2 > 0.25K_1$. These association constants and Hill coefficient n_H obtained for diamine guest **2** are sufficiently high to evaluate the temperature dependence by VT NMR spectroscopy: owing to the allosteric effect, one can judge that only the 1:2 complex is the object of the VT NMR spectroscopic measurements and that the contribution from the 1:1 complex can be neglected (Figure 1).

In order to estimate the rotational oscillation frequency of compound **1** ([**1**] = 0.5 mM) in CD$_2$Cl$_2$ solution, VT ^{1}H NMR spectroscopic analysis was performed. As shown in Figure 2, four doublets assignable to the pyrrole β-protons [δ = 8.53 (a), 8.62 (a′), 8.88 (b), and 8.97 (b′) ppm; Scheme 1] were observed at 0 °C. With increasing temperature, the exchangeable peaks b/b′ broadened and coalesced at 10 °C (T_c). The exchange rate was evaluated to be 120 s^{-1} [$\Delta G^{\ddagger}$ (283 K) = 14 kcal mol^{-1}] at 10 °C by using the Gutowsky and Holm equation.[11] This value is almost comparable to those previously reported for simple mononuclear cerium(IV) bis(porphyrinate)s.[5,6,7a] The result supports the view that the dynamic motion observed in the VT NMR spectra can be ascribed to the rotational oscillation frequency of the cerium(IV) bis(porphyrinate) moiety of compound **1**. Remarkably, upon addition of diamine guest **2** to the CDCl$_2$CDCl$_2$ solution of compound **1** ([**1**] = 0.1 mM, [**2**]/[**1**] = 2), the coalescence temperature (T_c) of the pyrrole β-protons [δ = 8.59 (b) and 8.53 (b′) ppm] increased to 60 °C with an exchange rate of 80 s^{-1} [$\Delta G^{\ddagger}$ (333 K) = 17 kcal mol^{-1}]. The difference indicates that cooperative binding of two molecules of **2** slows down the oscillation frequency of the central metal axis in the central cerium(IV) bis(porphyrinate) of compound **1**.

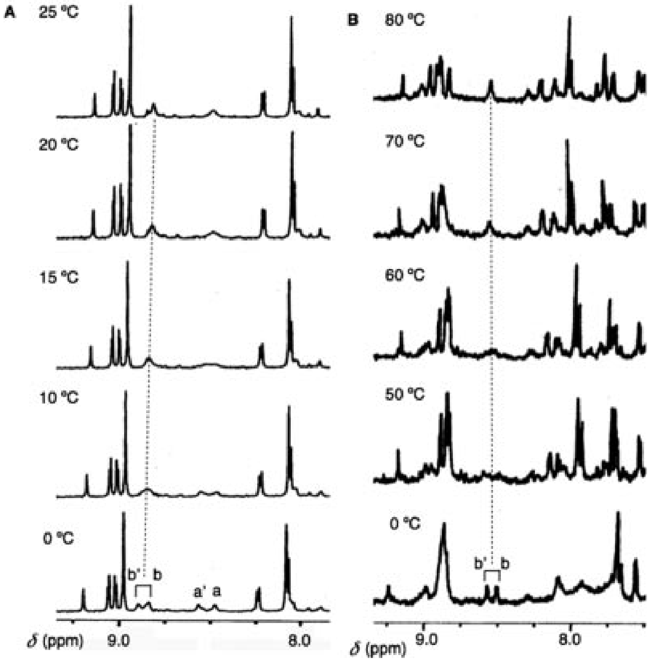

Figure 2. VT ^1H NMR spectra of (A) compound **1** ([**1**] = 0.5 mM) in CD_2Cl_2 and (B) compound **1** ([**1**] = 0.1 mM) in $CDCl_2CDCl_2$ in the presence of diamine guest **2** ([**2**]/[**1**] = 2).

Conclusions

In conclusion, we have successfully synthesized porphyrin hexamer **1**, which can be regarded as an artificial molecular oscillator, from a convergent synthetic method. The rotational oscillation frequency of compound **1** in solution was estimated by VT ^1H NMR spectroscopy, which established that the rotational oscillation frequency can be controlled by diamine guest binding. This is the first experimental evidence that the cooperative binding of guest molecules slows down the oscillation frequency of the central metal axis in cerium(IV) bis(porphyrinate); the change in torque of the rotational axis is likely to be one origin of the cooperative binding, which results in unique positive homotropic allosterism.

Experimental Section

General: All starting materials and solvents were purchased from Tokyo Kasei Chemicals or Wako Chemicals and used as received. ^1H NMR spectra were recorded with a Bruker DRX 600 spectrometer. Chemical shifts are reported in ppm downfield from tetramethylsilane as the internal standard. Mass spectroscopic data were obtained with a Perseptive Voyager RP MALDI-TOF spectrometer. UV/Vis spectra were recorded with a Shimadzu UV-2500 PC. Compound **2** was synthesized according to the method reported previously.[12]

Compound 1: To a stirred solution of the corresponding porphyrin trimer (15 mg, 5.8 µmol) in 1,2,4-trichlorobenzene (1 mL), Ce(acac)$_3$·3H_2O (8.5 mg, 3 equiv.) was added. The mixture was heated at reflux for 5 h under a nitrogen atmosphere. After cooling to room temperature, the solvent was removed in vacuo. The residue was purified by column chromatography (silica, chloroform/methanol 100:1, twice) and size-exclusion chromatography (Biobeads SX-1, chloroform, twice) to yield compound **1** as a purple solid (1.5 mg, 10%). TLC (chloroform/methanol 100:1): R_f = 0.3. ^1H NMR (600 MHz, CD_2Cl_2, 0 °C): δ = 9.84 (d, J = 7.7 Hz, 2 H, Ar-H), 9.24 (s, 4 H, *meso*-H), 9.10 (d, J = 4.4 Hz, 8 H, Ar-H), 9.06 (d, J = 4.4 Hz, 8 H, Ar-H), 9.02 (s, 4 H, Ar-H), 8.97 (d, J = 3.8 Hz, 4 H, pyrrole-β-H), 8.88 (d, J = 3.8 Hz, 4 H, pyrrole-β-H), 8.62 (d, J = 3.8 Hz, 4 H, pyrrole-β-H), 8.53 (d, J = 3.8 Hz, 4 H, pyrrole-β-H), 8.28 (d, J = 7.8 Hz, 8 H, Ar-H), 8.12 (m, 16 H, Ar-H), 8.11 (m, 8 H, Ar-H), 7.83 (m, 8 H + 2 H, pyrrole-β-H + Ar-H), 7.70 (m, 8 H, pyrrole-β-H), 7.57 (m, 8 H, pyrrole-β-H), 7.53 (m, 8 H, pyrrole-β-H), 7.10 (d, J = 7.5 Hz, 2 H, Ar-H), 6.56 (d, J = 7.5 Hz, 2 H, Ar-H), 4.89 (m, 8 H, OCH_2), 4.20 (m, 8 H, OCH_2), 1.59 (s, 144 H, *tert*-butyl-H), 1.52 (s, 72 H, *tert*-butyl-H) ppm. MALDI-TOF MS: m/z = 5353.85 $[M + H]^+$.

Supporting Information (see footnote on the first page of this article): Divergent method for the synthesis of compound **1** and ^1H NMR and MALDI-TOF MS spectra of compound **1**.

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