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Toward Long-Distance Mechanical Communication: Studies on a Ternary Complex Interconnected by a Bridging Rotary Module

Hiroyuki Kai, Shinji Nara, Kazushi Kinbara,* and Takuzo Aida*

Department of Chemistry and Biotechnology, School of Engineering and Center for NanoBio Integration, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

Received March 5, 2008; E-mail: kinbara@macro.t.u-tokyo.ac.jp; aida@macro.t.u-tokyo.ac.jp

In biological signal transduction systems, an external stimulus acquired by a receptor is converted into a mechanical motion, which is transmitted intermolecularly over a long distance via a physical interconnection. For example, in a vision system, a light-triggered configurational change of retinal is transmitted to rhodopsin.[1] Then, G-protein, located away from retinal, senses this configurational change. Despite a rapid progress in the field of synthetic molecular machines,[2,3] it is still a big challenge to design molecularly interconnected systems allowing for the transmission of mechanical motions to a remote place.[3b] Here we report a signal transmission system (Figure 1) consisting of three different movable components; a photochromic "signaling" unit (**1**; green), a chiral "scissoring" unit (**3***; red),[4] and an intermediately "bridging" unit (**2**; blue/purple). These components are mechanically interconnected with one another by the connection with bidentate coordination bonds, so that a configurational change of **1**, induced by UV or visible light, is transmitted over a long distance to **3*** through an angular motion of **2**.

Signaling unit **1** is a pyridine-appended dithienylethene derivative, which is known as a superb photochromic molecule, whose open and closed forms ($\mathbf{1}^{\mathrm{open}}$, $\mathbf{1}^{\mathrm{closed}}$), photochemically generated, do not interconvert thermally (Figure 1).[5] Upon irradiation with UV (λ = 350 ± 10 nm, 7 min) and visible (λ = 546 ± 10 nm, 24 min) lights in toluene at 20 °C, compound **1** isomerized between $\mathbf{1}^{\mathrm{open}}$ and $\mathbf{1}^{\mathrm{closed}}$ to furnish molar ratios [$\mathbf{1}^{\mathrm{open}}$]/[$\mathbf{1}^{\mathrm{closed}}$] of 3/97 and 92/8 at the photostationary states, respectively (Scheme 1). Scissoring component **3*** involves a chiral tetrasubstituted ferrocene core bearing two pyridyl groups, capable of accommodating the zinc porphyrin handles of bridging module **2**. Two free-base porphyrin units in **3*** are intended to monitor the conformational change of **3*** by means of circular dichroism (CD) spectroscopy.[3] Bridging module **2** is a biaryl derivative bearing four zinc porphyrin handles, where two of them (ZnP$^{\mathrm{short}}$) are shortly connected to the biaryl core, while the other two (ZnP$^{\mathrm{long}}$) are attached via an ethynylene spacer to the core. Due to a very small energetic barrier for the axial rotation,[6] **2** as well as **3***[3] can serve as a friction-free rotary module.

Compounds **1**−**3** were synthesized according to methods similar to those reported in the literature[3] and unambiguously characterized (see Supporting Information). For spectral understanding of the complexation, we also synthesized reference compounds **4**−**7** (Figure 2; see Supporting Information), which are expected to spectroscopically imitate four possible binding modes of **2**. Electronic absorption spectroscopy of **2** in toluene at 20 °C displayed two sets of Soret and Q bands at 421/545 and 441/605 nm, which are assigned to ZnP$^{\mathrm{short}}$ and ZnP$^{\mathrm{long}}$, respectively, by reference to the spectral features of **4** and **5** (see Supporting Information, Figure S3). When **2** was mixed in toluene with $\mathbf{1}^{\mathrm{open}}$ and an enantiomer of **3*** at a molar ratio [$\mathbf{1}^{\mathrm{open}}$]:[**2**]:[**3***] of 10.0:1.0:1.0, the two sets of zinc porphyrin Soret/Q bands were red-shifted to 426.5/560 and 443/622.5 nm, suggesting that all the zinc porphyrin handles of **2** in the ternary mixture accommodate an axial ligand (see Supporting Information, Figure S4). The ternary mixture showed clear Cotton effects in a visible absorption region from 400 to 460 nm. Of interest, the CD spectrum (Figure 3b) is much more intense than that of chiral **3*** (Figure 3a) and extended to a longer wavelength region involving the Soret bands of the zinc porphyrin handles. These observations indicate that compound **2** adopts a twisted chiral geometry upon complexation with chiral **3*** (Figure 1). The notable enhancement of the CD band at the free-base porphyrin Soret band (411 nm) indicates that the conformation of the ferrocene moiety of **3*** is fixed as a result of the complexation with **2**.[3b]

When the ternary mixture was irradiated with UV light (λ = 350 ± 10 nm) for the purpose of isomerizing $\mathbf{1}^{\mathrm{open}}$ into $\mathbf{1}^{\mathrm{closed}}$, the CD band at the zinc porphyrin Soret band of **2** (447.5 nm) was gradually enhanced and reached a plateau in 4 min, while that of **3*** at 410 nm decreased synchronously (Figure 4a,b, see also Supporting Information, Figure S5a). On the other hand, upon exposure of the resulting mixture to visible light (λ = 546 ± 10 nm) to allow the isomerization of $\mathbf{1}^{\mathrm{closed}}$ back to $\mathbf{1}^{\mathrm{open}}$, a backward CD spectral change took place and subsided in 17 min (see Supporting Information; Figure S5b). We also confirmed that these CD spectral changes are synchronous to a change in the mole fraction of $\mathbf{1}^{\mathrm{open}}$ ([$\mathbf{1}^{\mathrm{open}}$]/([$\mathbf{1}^{\mathrm{open}}$] + [$\mathbf{1}^{\mathrm{closed}}$])) in the ternary

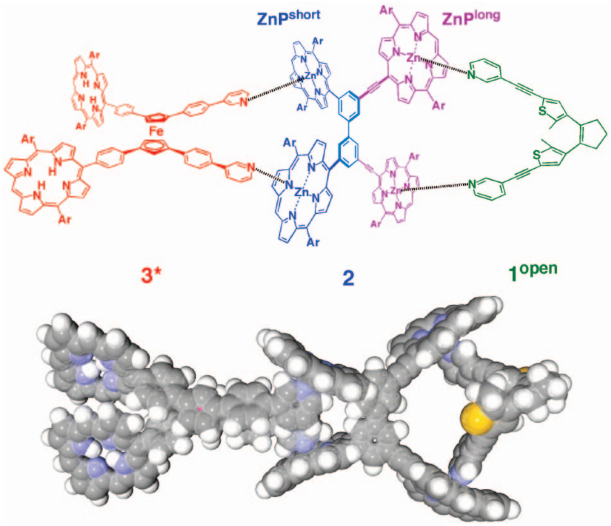
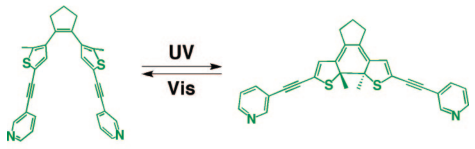


Figure 1. Schematic illustration of the expected ternary complex of $\mathbf{1}^{\mathrm{open}}$, **2**, and **3*** (Ar: 3,5-dioctyloxyphenyl).

Scheme 1. Isomerization of Photochromic Module **1**



$\mathbf{1}^{\mathrm{open}}$ $\mathbf{1}^{\mathrm{closed}}$

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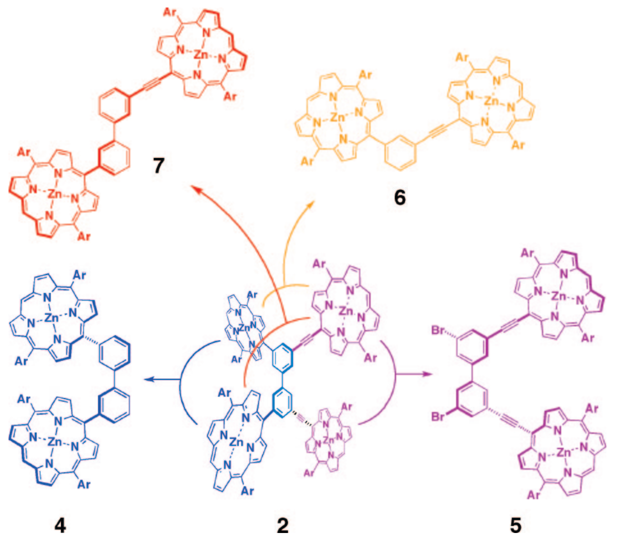

Figure 2. Structures of reference compounds **4**−**7** for imitating four possible binding modes of bridging **2**.

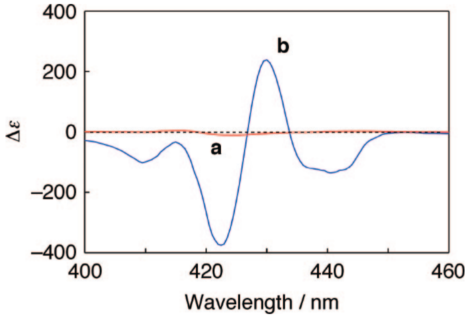

Figure 3. Circular dichroism (CD) spectra of (a) **3*** (3.8 μM) and (b) a ternary mixture of $\mathbf{1^{open}}$, **2**, and **3*** ([**3***] = 2.2 μM, [**3***]/[**2**]/[$\mathbf{1^{open}}$] = 1.0/1.0/10.0) in toluene at 20 °C.

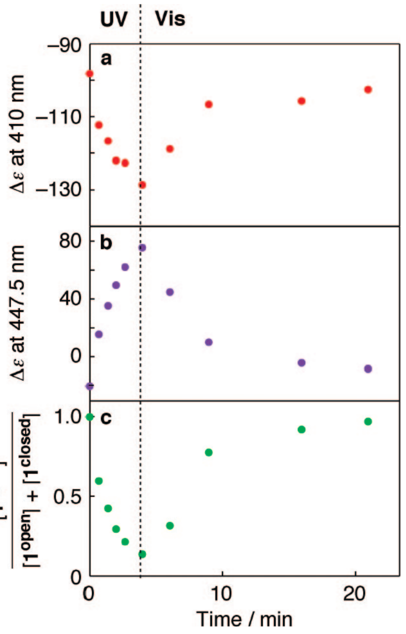

Figure 4. Circular dichroism (CD) intensity changes at 20 °C of a ternary mixture of **1**, **2**, and **3*** ([**2**] = 2.2 μM, [**3***]/[**2**]/[**1**] = 1.0/1.0/10.0) in toluene at (a) 410 nm for **3*** and (b) 447.5 nm for **2**, as a function of (c) the extent of isomerization of **1** upon irradiation with UV (λ = 350 ± 10 nm, 4 min) and visible (λ = 546 ± 10 nm, 17 min) lights.

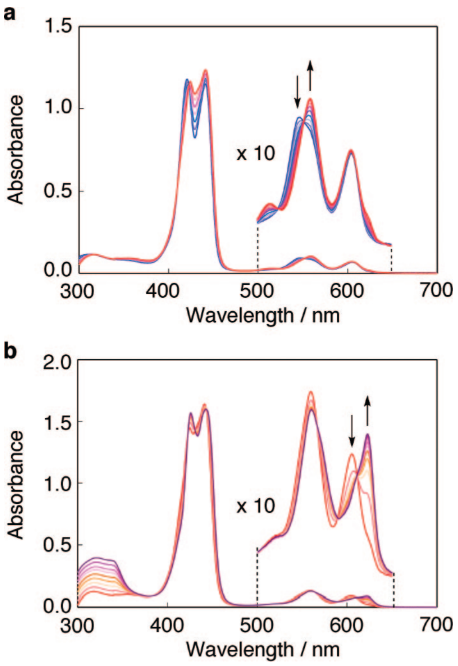

Figure 5. Absorption spectral changes upon titration of (a) **2** (1.5 μM) with **3*** (0−0.9 equiv) and (b) a binary mixture of **2** and **3*** ([**2**] = 2.2 μM, [**2**]/[**3***] = 1.0) with $\mathbf{1^{open}}$ (0−10.0 equiv) in toluene at 20 °C.

mixture (Figure 4c).[7] Therefore, three components **1**, **2**, and **3*** are mechanically interconnected. In sharp contrast, when bridging **2** was absent, neither CD enhancement of **1** nor light-induced CD spectral change resulted for a mixture **1** and **3*** (13:1) (see Supporting Information, Figure S6). These results clearly demonstrate that scissoring **3*** is able to communicate with photochromic **1** but only in the presence of bridging **2** (Figure 1).

In order to investigate if components **1**−**3*** indeed form a ternary assembly (Figure 1), we carried out ^{1}H DOSY spectroscopy at 27 °C, where a 1:1:1 mixture of **1**, **2**, and *rac*-**3***, as expected, showed a smaller diffusion constant ($\log_{10}[D/\text{m}^2\ \text{s}^{-1}] = -9.75$) than individual monomeric components and even 1:1 binary mixtures *rac*-**3***/**2** and **1**/**2** (see Supporting Information, Figures S7−S9).[8] Then, for further structural understanding, some selected binary mixtures were investigated spectroscopically. Of interest, when **2** was titrated with **3***, only the absorption bands of $\text{ZnP}^{\text{short}}$ were red-shifted with clear isosbestic points at 422.5 and 552 nm, while those of ZnP^{long} remained substantially unchanged until the molar ratio [**3***]/[**2**] reached 0.9 (Figure 5a). In conformity with this observation, when the titration was followed by ^{1}H NMR spectroscopy, the signals due to the meso-substituents of $\text{ZnP}^{\text{short}}$ showed an upfield shift, but those of ZnP^{long} remained almost unchanged (see Supporting Information, Figure S10). Thus, the short ZnP handles of **2** selectively accommodate an axial ligand. The site-selective complexation between **2** and **3***, thus observed, indicates that the pyridyl groups of **3*** coordinate very tightly to the short handles of **2**. Although the K_{assoc} value of **3*** with **2** was unable to evaluate spectroscopically due to the concomitant occurrence of a secondary complexation at [**3***]/[**2**] > 1, model studies with reference compounds **4**−**7** (Figure 2) allowed us to conclude that the K_{assoc} value of **3*** with **4** carrying only $\text{ZnP}^{\text{short}}$ handles (4×10^7 M^{-1}) is indeed greater than those of **3*** with **6** (9×10^5 M^{-1}) and **7** (4×10^6 M^{-1}, see Supporting Information, Figures S11−S13). Due to a spectral interference by the free-base porphyrin (P_{Fb}) units in **3***, the K_{assoc} value of **3*** with **5** was again unavailable. So, we titrated **5** with a modified version of **3*** without P_{Fb} and confirmed that the K_{assoc} value (1×10^7 M^{-1}) of **5**/**3*** is again smaller than that of **4**/**3*** (see Supporting Information, Figure S14).

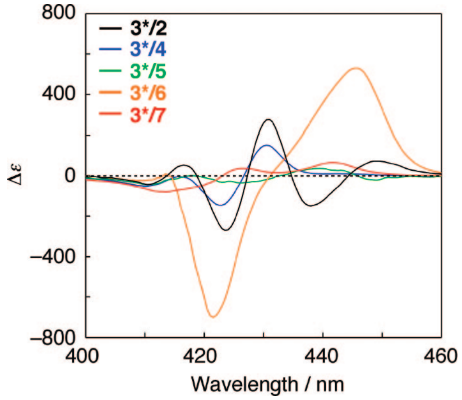

Figure 6. Circular dichroism (CD) spectra in toluene at 20 °C of binary mixtures **3*/2** (black; [**2**] = 2.2 μM, [**3***]/[**2**] = 1.0), **3*/4** (blue; [**4**] = 4.6 μM, [**3***]/[**4**] = 1.9), **3*/5** (green; [**5**] = 1.0 μM, [**3***]/[**5**] = 1.7), **3*/6** (orange; [**6**] = 1.8 μM, [**3***]/[**6**] = 3.0), and **3*/7** (red; [**7**] = 2.4 μM, [**3***]/[**7**] = 2.2).

For spectral characterization of the ternary mixture, binary complex **2/3*** (1:1) was titrated with **1**$^{\mathbf{open}}$, where the absorption bands of the ligand-free ZnP$^{\text{long}}$ handles of **2** became red-shifted (Figure 5b). Noteworthy, this spectral change displayed clear isosbestic points at 443 and 610.5 nm. Together with the ^{1}H DOSY experiments (vide ante), such a stepwise spectral change indicates the formation of a single heterotropic complex from **1**$^{\mathbf{open}}$ and binary complex **2/3***. The K_{assoc} value observed for the complexation of **2/3*** with **1**$^{\mathbf{open}}$ (4×10^5 M^{-1}; see Supporting Information, Figure S15a) was reasonably small compared with that of **4** (alternative to **2**) with **3*** (4×10^7 M^{-1}).

CD spectral titration of **2** with **3*** resulted in the appearance of intense Cotton effects at the Soret bands of both noncoordinated ZnP$^{\text{long}}$ and coordinated ZnP$^{\text{short}}$ handles of **2** (see Supporting Information, Figure S16). Noteworthy, the CD spectral pattern at [**3***]/[**2**] = 1.0 (black curve, Figure 6) was analogous to that of the heterotropic **1**$^{\mathbf{open}}$**/2/3*** ternary complex (Figure 3b). Nevertheless, at a closer look, titration of binary complex **2/3*** with **1**$^{\mathbf{open}}$ gave rise to a CD spectral change at the Soret band of ZnP$^{\text{long}}$ (441 nm), as a possible consequence of the complexation of **1**$^{\mathbf{open}}$ with the long handles of **3***-bound **2** (see Supporting Information, Figure S17). CD spectral features of reference **4**−**7** upon complexation with **3*** are likely informative of the mode of ternary complexation. While they considerably differ from one another (Figure 6), we found that the one observed for **4/3*** (blue curve) quite resembles that of the ternary complex. Considering that reference **4** possesses only ZnP$^{\text{short}}$, it is now obvious that bridging module **2** in the heterotropic ternary complex uses its short ZnP handles to bind **3***, while the remaining long handles are used for grasping **1**$^{\mathbf{open}}$ on the other side (Figure 1). Use of closed isomer **1**$^{\mathbf{closed}}$ instead of **1**$^{\mathbf{open}}$ resulted in almost identical absorption[9] and CD spectral features (see Supporting Information, Figures S15b and S18), indicating the same mode of heterotropic binding of **1**$^{\mathbf{closed}}$ and **3*** mediated by **2**. This is essential for photoisomerizing **1** to mechanically communicate with **3***.

In conclusion, we succeeded in the construction of a heterotropic ternary complex, using a photochromic component (**1**) on one end, a scissoring component (**3***) on the other, and a bridging component (**2**) in the middle (Figure 1). The three components are connected together with bidentate coordination bonds and therefore mechanically interconnected. Upon photoirradiation, **1** undergoes an opening/closing motion, which gives rise to a rotary motion of **2** and a synchronous scissoring motion of **3*** on the other end. The system involves certain dissociation/association dynamics. However, considering the large K_{assoc} values, the dissociation events must occur much more slowly than the isomerization of the photochromic component and rotary motions of the ferrocene and biaryl moieties.[3,6] Thus, the light-induced motion of **1** can be transmitted to **3*** before the ternary complex dissociates. In this context, the heterotropic ternary complex illustrated in Figure 1 can be regarded as a prototype of "molecular reacher" and may be extended to polymeric systems of larger size regimes that could allow remote manipulation of molecular events.

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Supporting Information Available: Synthesis of **1**$^{\mathbf{open}}$−**7**, absorption spectra of **2** and reference compounds **4** and **5**. Absorption and CD spectral titrations of **4**−**7** with **3*** (**19*** for **5**), and their curve fitting profiles for evaluation of K_{assoc} values. Absorption spectral titration of **3*/2** with **1**$^{\mathbf{closed}}$. ^{1}H NMR spectra of **2**, *rac*-**3*/2** and *rac*-**3*/2/1**$^{\mathbf{open}}$, and ^{1}H DOSY spectra of **1**$^{\mathbf{open}}$−*rac*-**3***, **1**$^{\mathbf{open}}$**/2**, *rac*-**3*/2**, and *rac*-**3*/2/1**$^{\mathbf{open}}$. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) Determined by HPLC.
(8) Values of $\log_{10}D$ (D: diffusion constant in m^2 s^{-1}) were evaluated as follows: **1**$^{\mathbf{open}}$ = −9.15, **2** = −9.65, *rac*-**3*** = −9.51, *rac*-**3*/2** = −9.68, **1**$^{\mathbf{open}}$**/2** = −9.63, *rac*-**3*/2/1**$^{\mathbf{open}}$ = −9.75.
(9) Assuming the formation of a heterotropic ternary complex, the K_{assoc} value of **3*/2** with **1**$^{\mathbf{closed}}$ was evaluated as 2×10^5 M^{-1} (see Supporting Information, Figure S15b).

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