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ENCAPSULATION OF COFACIAL DIARYLACETYLENE DIMERS USING [*c*2]DAISY CHAIN ROTAXANE STRATEGY

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Abstract – [*c*2]Daisy chain rotaxanes are mechanically interlocked molecules that can cofacially assemble two π-conjugated molecules. In this study, we employed a rotaxane architecture to encapsulate diarylacetylene dimers modified with an electron-withdrawing or electron-donating substituent in two permethylated α-cyclodextrins. Solvent- and concentration-dependent ^{1}H nuclear magnetic resonance measurements indicated the selective formation of the cofacial dimers. These dimers were mechanically interlocked by condensation with 4-{2-[2-(2-hydroxyethoxy)ethoxy]ethoxy}-3,5-dimethylaniline to obtain the corresponding [*c*2]daisy chain rotaxanes (up to 68% yield). UV-visible absorption and fluorescence spectra revealed that the diarylacetylene substituents modulated the optical properties of the rotaxanes.

INTRODUCTION

The optical and electrical properties of π-conjugated molecules can be diversified through chemical modification with electron-withdrawing and electron-donating groups and physical control of intermolecular interactions and side chain arrangements.[1] Therefore, these compounds have been extensively investigated for the development of light-emitting and electronic devices.[2] In this context, through-space communication between cofacially oriented π-conjugated molecules continues to be one of the key issues in this research field. Recently, cyclophanes with a rigidly fixed dimer, wherein two π-conjugated molecular cores are cofacially oriented and covalently bonded, have exhibited unusual optical properties, which are contrary from those of monomeric π-conjugated molecular cores (Figure 1a).[3–6] These

cyclophane systems have been applied in the construction of molecular detectors[7–9] and mechanically responsive luminescent polymers.[10] Additionally, systems with noncovalently bonded cofacial π-conjugated dimers have been developed based on the construction of mechanically interlocked molecules (MIMs), such as [2]catenanes[11] and [3]rotaxanes[12,13] (Figure 1b). These MIM-based systems can exhibit switchable properties because the locations of their cores can be reversibly changed through external stimuli, such as the solvent, temperature, and pH.[14] In particular, cyclodextrin-based MIMs, which exhibit remarkable switching under a given stimulus, have been developed by several research groups.[15] Recently, we reported the efficient selective synthesis and optical properties of a [*c*2]daisy chain rotaxane system wherein the two cofacial diarylacetylene core molecules are insulated by two permethylated α-cyclodextrins (PM α-CDs).[16] Our strategy can be potentially used in the cofacially oriented aggregation of π-conjugated molecules and can contribute to the investigation of their physical properties. In the present study, we designed a monomer with a diarylacetylene core whose substituent (X group) is placed in close proximity to the PM α-CD in order to overcome the inhibition of face-to-face dimerization and demonstrated that insulated cofacial diarylacetylene dimers with substituents are efficiently formed from the corresponding monomers using the [*c*2]daisy chain rotaxane strategy (Figure 1c). This allows the synthesis of insulated cofacial π-conjugated dimers with substituents, which is difficult to achieve using conventional MIM methods. Further, we showed that the optical properties of insulated cofacial diarylacetylene dimers with substituents can be tuned by the electron-withdrawing or electron-donating substituent. These findings are expected to advance the MIM-based integration of π-conjugated molecules for optical and electrical applications.

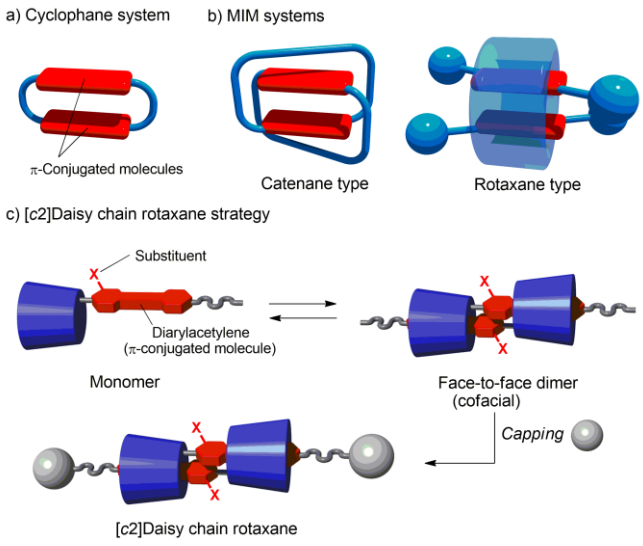


Figure 1. a) Cyclophane and b) MIM systems for the cofacial assembly of two π-conjugated molecules. c) Overview of the [*c*2]daisy chain rotaxane strategy, which is one of the MIM methods.

RESULTS AND DISCUSSION

Monomers **1b**–**d** were synthesized based on a substitution reaction between a PM α-CD monotosylate and halophenol derivative under basic conditions, followed by a Sonogashira cross-coupling reaction with an ethynylbenzene derivative bearing a terminal ester and hydrolysis of the ester moiety, as shown in Scheme S1. Good yields (up to 86% yield in three steps) were obtained under reaction conditions similar to those used for the synthesis of monomer **1a**.[16]

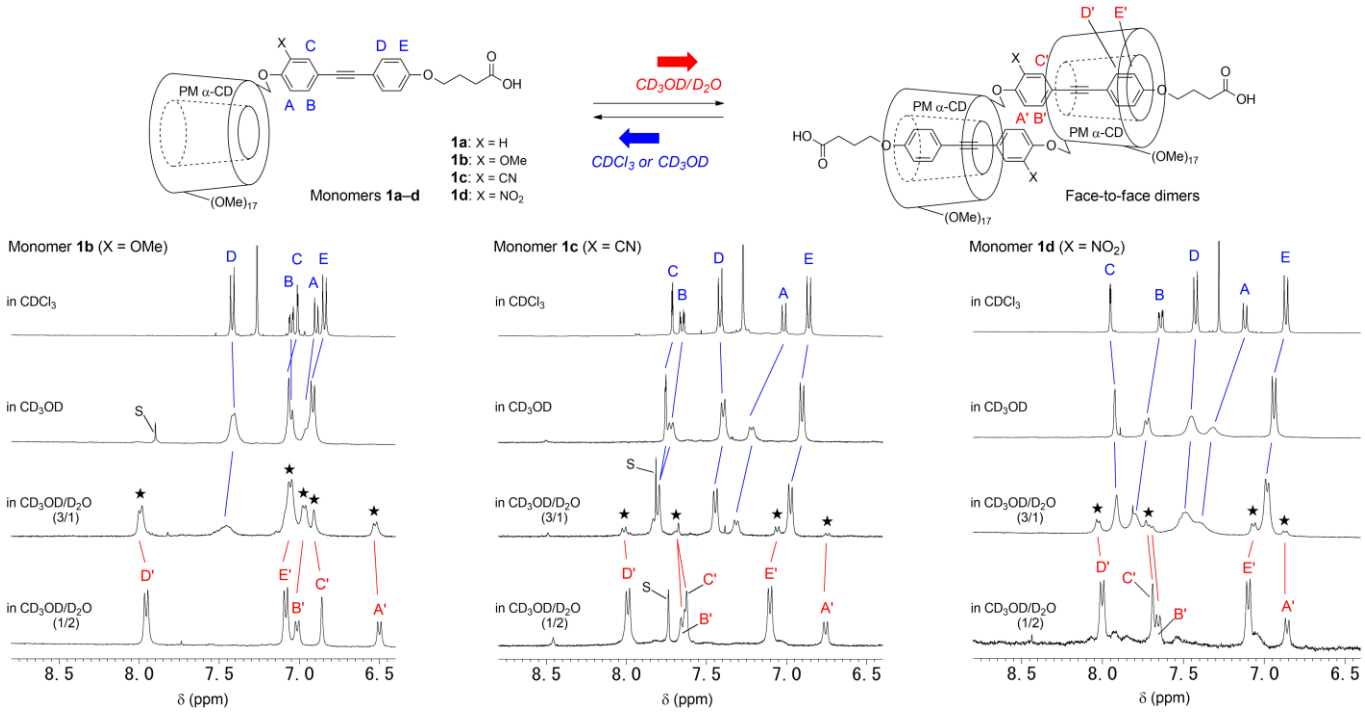


Figure 2. Partial ^{1}H NMR spectra of monomers **1b**–**d** in $CDCl_3$, CD_3OD, and CD_3OD/D_2O at 20 °C. Residual $CHCl_3$ peak is indicated by "S". Peaks of association complex are marked by stars.

Solvent-dependent ^{1}H NMR measurements were performed to confirm the formation of the association complexes of monomers **1b**–**d** in various deuterated solvents. In $CDCl_3$ and CD_3OD, the peaks corresponding to a non-associated monomer were only observed in the absence of an associated species. In contrast, in CD_3OD/D_2O (3/1), new peaks (indicated by stars in Figure 2) appeared irrespective of the peaks of the non-associated monomer, indicating a partial formation of an association complex. These results differ from those of a previous study[16] wherein the peaks of the association complex of monomer **1a** appeared for CD_3OD and those of the non-associated monomer almost disappeared for CD_3OD/D_2O (3/1). These results suggest that the steric bulkiness of substituent X of the benzene ring attached to the PM α-CD significantly affects the association of monomers **1b**–**d**. Nevertheless, for all the monomers, the non-associated monomer almost disappeared in CD_3OD/D_2O (1/2), and a single association complex was completely formed. This indicates that as the volume ratio of D_2O in the CD_3OD/D_2O mixture increased,

the hydrophobic interaction between the diarylacetylene moiety and inner surface of the PM α-CD was enhanced, promoting the formation of the association complex.

Assuming that single association complexes were formed from monomers **1a**–**d**, the association numbers were calculated using the concentration-dependent ^{1}H NMR data[17] for CD_3OD and CD_3OD/D_2O (Table 1). The calculated association numbers strongly suggested the selective formation of associated dimers (face-to-face dimers) from monomers **1a**–**d** in aqueous solutions. In CD_3OD/D_2O (3/1), monomers **1b**–**d** had significantly smaller association constants (*K*) than monomer **1a**, indicating that dimerization was significantly inhibited by steric hindrance and/or electrostatic interactions between substituent X and the PM α-CD connected to another monomer unit. However, as the water content of the solvent increased, their association constants were enhanced by the increased hydrophobic interaction such that the association dimers could be selectively and efficiently formed from any monomer. In addition, the *K* of monomer **1b** bearing an electron-donating group was slightly larger than those of monomers (**1c** and **1d**) bearing an electron-withdrawing group. Although further investigation is required, these results suggest that dimerization may be affected by π-π interactions that can occur at partially overlapping sites between the diarylacetylene cores.

Table 1. Association numbers and association constants (*K*, M^{-1}) of monomers **1a**–**d** in various deuterated solvents[a,b]

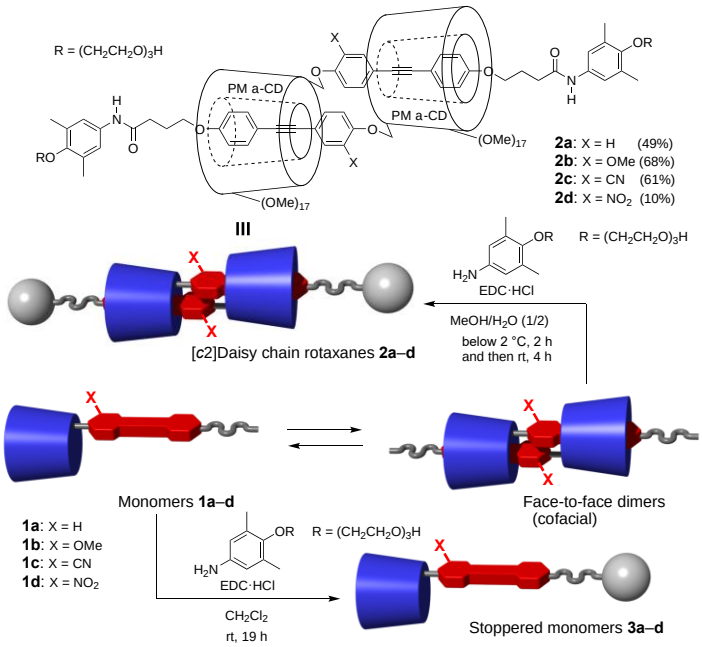
Monomer	CD_3OD	CD_3OD/D_2O (3/1)	CD_3OD/D_2O (1/2)
1a (X = H)	1.9 ± 0.1 (45 ± 2)	2.2 ± 0.3 (11500 ± 600)	—[d]
1b (X = OMe)	—[c]	2.0 ± 0.1 (311 ± 7)	—[d]
1c (X = CN)	—[c]	1.9 ± 0.02 (94 ± 2)	1.9 ± 0.1 (24000 ± 800)
1d (X = NO_2)	—[c]	2.0 ± 0.03 (63 ± 1)	2.1 ± 0.01 (15900 ± 300)

[a] ^{1}H NMR spectra were measured three times in the monomer concentration range of 1.4–10 mM. [b] Values in parentheses are association constants (*K*). [c] Values were not calculated because only the non-associated monomer was observed. [d] Values were not calculated because the non-associated monomer almost disappeared.

The differences between the chemical shifts of the diarylacetylene protons in $CDCl_3$ and CD_3OD/D_2O (1/2) before and after complexation were calculated. For all monomers, the protons of the alkyl-bearing benzene (protons D and E) were significantly shifted downfield, whereas that of the X-substituted benzene (proton A) were shifted upfield (Table S1). These downfield and upfield shifts, which were common to monomers **1a**–**d**, can be explained by the deshielding effect due to the approaching glycosidic oxygen atoms of the

PM α-CD cavity and the shielding effect due to the proximity of the benzene ring directly connected to the PM α-CD, respectively. This indicates that the dimers were formed in a face-to-face orientation in aqueous solutions, as shown in Figure 2, and that the dimer structures were hardly affected by the steric hindrance of the substituents.

The face-to-face dimers were capped by a condensation reaction with water-soluble reagents, i.e., 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl) and 4-{2-[2-(2-hydroxyethoxy)-ethoxy]ethoxy}-3,5-dimethylaniline, in MeOH/H_2O (1/2) to form [*c*2]daisy chain rotaxanes **2a**–**d** (Scheme 1). No trimeric or larger oligomeric daisy chain rotaxanes were detected via mass spectrometry. However, a low yield (10%) was obtained for rotaxane **2d** because monomer **1d** possessed a lower solubility in MeOH/H_2O (1/2) compared to the other monomers. Stoppered monomers **3a**–**d** were also prepared individually as reference compounds via the same condensation reaction in CH_2Cl_2.



Scheme 1. Synthesis of [*c*2]daisy chain rotaxanes **2a**–**d** and stoppered monomers **3a**–**d**

The UV–visible absorption spectra of rotaxanes **2a**–**d** and reference stoppered monomers **3a**–**d** in various solvents are shown in Figure 3. The shifts (<2 nm) in the absorption peaks (λ_{max}) of rotaxanes **2a**–**d** in various solvents were smaller than those (<10 nm) of the corresponding stoppered monomers **3a**–**d** (Table S2). This smaller shift suggests that the solvation effect on the diarylacetylene core was suppressed owing to insulation by the PM α-CD. In contrast, the λ_{max} and absorption edge of the rotaxanes were similar to those of the corresponding stoppered monomers, indicating that the conjugation in the diarylacetylene core was not affected by the construction of the [*c*2]daisy chain rotaxane. In addition, the absorption spectra of

rotaxanes (**2c** and **2d**) and the corresponding stoppered monomers (**3c** and **3d**), which possess donor and acceptor moieties, showed additional weak absorption shoulder attributed to the intramolecular charge transfer at longer wavelength than about 330 nm. Rotaxane **2** possesses two diarylacetylene molecules, hence the absorption coefficient is expected to be twice that of the corresponding stoppered monomer **3**. As expected, when substituent X was electron-donating, the absorption coefficient of rotaxane **2b** was twice that of the corresponding stoppered monomer **3b**. However, the absorption coefficients (at shorter wavelength than about 330 nm) were almost equal when substituent X was electron-withdrawing, and as a result, it appears that the light absorption by the monomeric diarylacetylene core of the rotaxanes (**2c** and **2d**) was half that of the corresponding stoppered monomers (**3c** and **3d**). In contrast, intensities of the absorption shoulder (>330 nm) of rotaxanes (**2c** and **2d**) were twice than those of the corresponding stoppered monomers (**3c** and **3d**). Therefore, these results indicate that monomeric absorption of the cofacial diarylacetylene dimer was affected by the forced proximity of the two donor-acceptor units (diarylacetylene cores) in the rotaxanes (**2c** and **2d**), while absorption ascribed to intramolecular charge transfer was not affected.

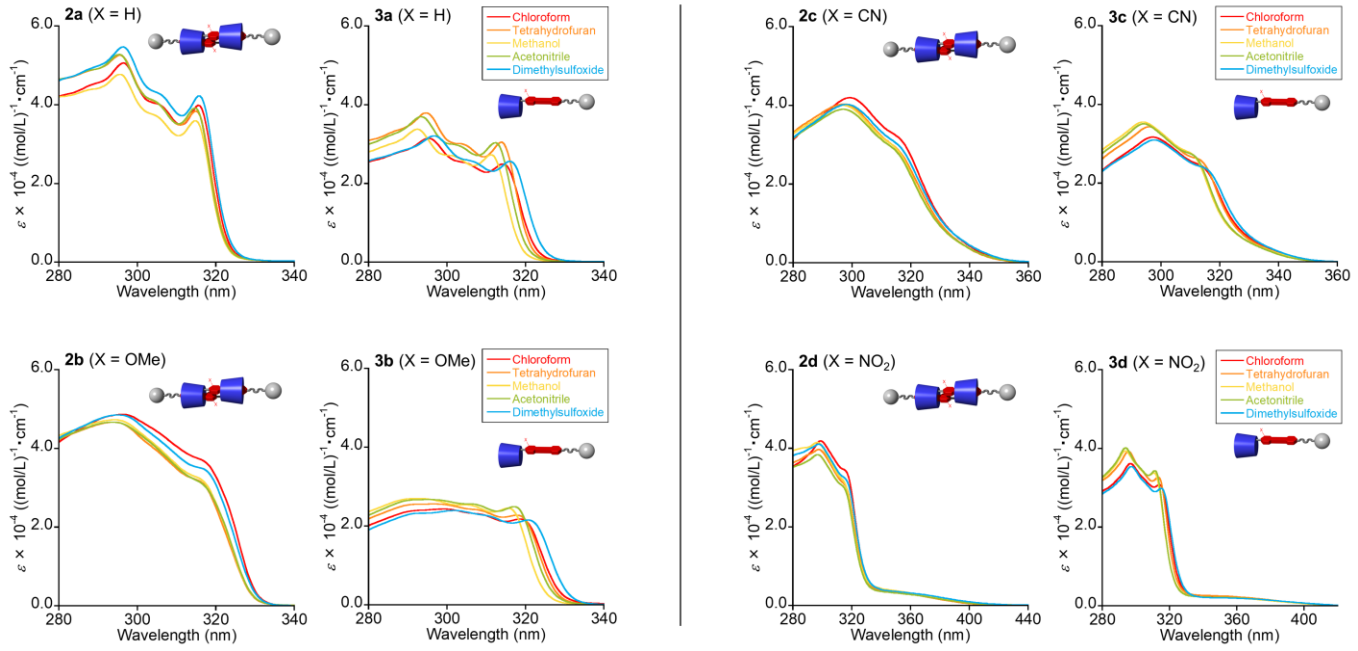


Figure 3. UV–visible absorption spectra of rotaxanes **2a**–**d** and stoppered monomers **3a**–**d**. Conditions: [**2**] = 1.3×10^{-5}–1.7×10^{-5} M, [**3**] = 3.2×10^{-5}–4.0×10^{-5} M.

The fluorescence spectra of the rotaxanes (**2b** and **2c**) and the corresponding stoppered monomers (**3b** and **3c**) in various solvents at low concentrations are shown in Figure 4. Rotaxane **2b** and stoppered monomer **3b**, wherein substituent X was the electron-donating methoxy group, exhibited only monomer emission. Further, the shift (<3 nm) in the emission peaks (λ_{max}) of rotaxane **2b** in various solvents was smaller than

that (<8 nm) of the corresponding stoppered monomer **3b** (Table S3). On the other hand, both rotaxane **2c** and stoppered monomer **3c**, wherein substituent X was electron-withdrawing cyano group, exhibited strong emission at longer wavelengths and the shift (<10 nm) in the emission peaks (λ_{max}) of rotaxane **2c** in various solvents was smaller than that (<18 nm) of the corresponding stoppered monomer **3c** (Table S3). The shift values of **2c** and **3c** were larger and correlated with the dielectric constant of the solvent, in contrast to those of the unsubstituted compounds (**2a** and **3a**) and the compounds (**2b** and **3b**) with electron-donating methoxy group. The maximum fluorescence wavelengths of the compounds (**2c** and **3c**) with electron-withdrawing cyano group tended to be red-shifted in solvents with high dielectric constants. These weak solvatochromic behaviors indicated that the emission of **2c** and **3c** were ascribed from intramolecular charge transfer.

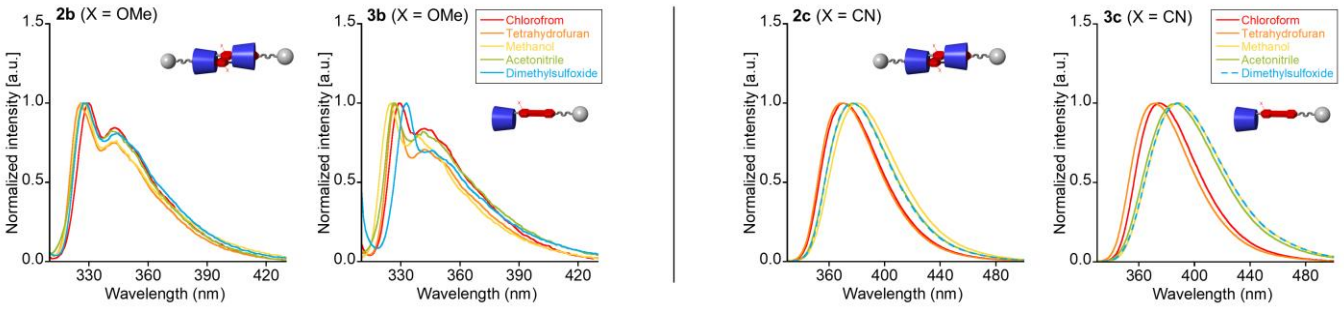


Figure 4. Fluorescence spectra of rotaxanes (**2b** and **2c**) and stoppered monomers (**3b** and **3c**) in various solvents. Conditions: [**2**] = 6.5×10^{-7}–8.0×10^{-7} M, [**3**] = 1.6×10^{-6}–2.0×10^{-6} M, excitation at the maximum absorption wavelength.

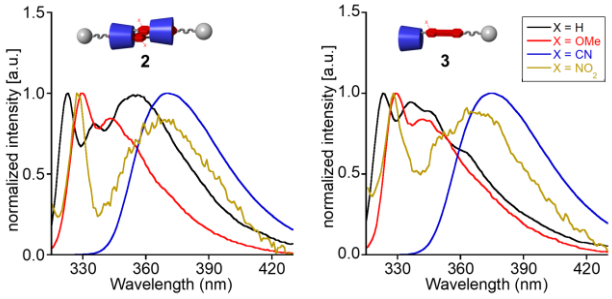


Figure 5. Fluorescence spectra of rotaxanes **2a**–**d** and stoppered monomers **3a**–**d** in $CHCl_3$. Conditions: [**2**] = 2.6×10^{-7}–8.0×10^{-7} M, [**3**] = 1.5×10^{-6}–2.0×10^{-6} M, excitation at the maximum absorption wavelength.

The fluorescence spectra of the rotaxanes and stoppered monomers in chloroform are shown in Figure 5. Rotaxane **2a** exhibited evident excimer emission (λ_{max} = 355 nm) with monomer emission (λ_{max} = 323, 335

nm), as reported previously.[16] In contrast, the substituted rotaxane **2b** with electron-donating groups exhibited only monomer emission, similar to the corresponding stoppered monomer **3b**. Furthermore, the substituted rotaxanes (**2c** and **2d**) with electron-withdrawing groups exhibited emission derived from intramolecular charge transfer at longer wavelength, similar to the corresponding stoppered monomers (**3c** and **3d**). In addition, the nitro-substituted compounds (**2d** and **3d**) exhibited very weak emission owing to the fluorescence quenching effect of the nitro group. These results indicate the unfavorable formation of the excimer due to the electronic and/or steric effects of the incorporated substituent X.

In conclusion, substituted diarylacetylene dimers were efficiently encapsulated in the PM α-CDs using the [*c*2]daisy chain rotaxane strategy. The unfavorable formation of cofacial dimers due to steric hindrance of the substituent was overcome by introducing the substituent at the appropriate position in the diarylacetylene cores and by using the optimal methanol/water ratio of the solvent. For all the monomers, the cofacial dimer was selectively formed over the self-inclusion complex and other cyclic or linear daisy chain oligomers in MeOH/H_2O (1/2). The solvent-dependent ^{1}H NMR measurements of the monomers indicated that the benzene rings directly connected to the PM α-CDs were partially stacked, whereas those bearing the alkyl chain were preferentially positioned inside the PM α-CD cavities. The optical properties of the encapsulated cofacial diarylacetylene dimers were electronically and/or sterically affected by the incorporated substituents. The absorption and emission derived from intramolecular charge transfer were observed when substituent X was electron-withdrawing. On the other hand, the monomeric absorption coefficients of [*c*2]daisy chain rotaxanes (**2c** and **2d**) with electron-withdrawing groups were lower than the expected values calculated from those of the reference stoppered monomers (**3c** and **3d**). This result indicates that the monomeric absorption of the cofacial diarylacetylene dimer was affected by the forced proximity of the two donor-acceptor units (diarylacetylene cores) in the rotaxanes. These findings were obtained exclusively through our [*c*2]daisy chain rotaxane strategy, which maintains the distance between two π-conjugated molecules and isolates the dimer from the external environment, indicating that through-space communication between two diarylacetylene cores can be controlled by introducing appropriate substituents into the cores. These optical properties are expected to be further modified by chemical transformation through substitution.

EXPERIMENTAL

General Procedure for Synthesis of [*c*2]Daisy Chain Rotaxane 2

Monomer **1** (0.070 mmol) and 4-{2-[2-(2-hydroxyethoxy)ethoxy]ethoxy}-3,5-dimethylaniline (0.42 mmol) were dissolved in MeOH/H_2O (1/2) (10 mL). After the solution was cooled below 2 °C, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl) (0.42 mmol) was added. The reaction mixture was stirred below 2 °C for 2 h and then stirred at room temperature for an additional 4 h. The

reaction mixture was acidified with dilute HCl aq., diluted with EtOAc, and washed with brine. The organic layer was separated and dried over $MgSO_4$. The solvent was removed *in vacuo*, and the residue was purified via column chromatography on silica gel (EtOAc/MeOH (4/1)), yielding [*c*2]daisy chain rotaxane **2** as a formed solid (**2a**: 49%; **2b**: 68%; **2c**: 61%; **2d**: 10%).

The data that support the findings of this study are available in the Supporting Information.

ACKNOWLEDGEMENTS

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