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Strong Binding Affinity of a Zinc–Porphyrin-Based Receptor for Halides through the Cooperative Effects of Quadruple C–H Hydrogen Bonds and Axial Ligation

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Abstract: A new type of host compound (**1**), tetraphenyl zinc–porphyrin (ZnTPP) that contains four triazole groups at the *ortho*-position of each phenyl group, has been synthesized and characterized by using ^{1}H, ^{13}C NMR, and MALDI-TOF-MS analyses. The host–guest complex formation between **1** and halides was investigated by using ^{1}H NMR spectroscopy in [D_6]DMSO. The triazole, benzyl, and phenylene proton signals were shifted upfield by the addition of halides in the form of tetrabutylammonium salts, which implies that the triazole protons in **1** are allocated very closely to the porphyrin ring and are directed toward the binding pocket over the porphyrin ring during the formation of hydrogen bonds. The UV/Vis absorption spectra showed that both the Soret and Q band absorptions of **1** underwent a strong redshift due to the addition of halides. Compound **1** exhibited surprisingly strong binding affinities for the halides, where the association constants for Cl^-, Br^-, and I^- binding were estimated to be larger than 10^8, 1.79×10^7, and $1.84\times10^5\,M^{-1}$, respectively. The UV/Vis absorption changes and the result of competitive titration using 4-*tert*-butylpyridine indicated that the cooperative effects of axial coordination and C–H···X hydrogen bond interactions resulted in the strong binding affinity of **1** to halides.

Keywords: cooperative binding · halides · host–guest systems · hydrogen bonds · porphyrins

Introduction

There has been considerable interest in the design of artificial anion-binding receptors because anions play very important roles in chemical and biological events.[1] Various types of artificial anion binding receptors with multiple hydrogen-binding donors have been designed and extensively explored their anion binding phenomena.[2] For example, indole- or pyrrole-based macrocyles and foldamers have exhibited strong binding affinities to anionic guests through multiple N–H···X hydrogen-bonding events.[3] In addition, C–H···X hydrogen bonding has been a highlighted topic in recent studies because this type of bonding is also very important in the recognition of biological anions.[4] However, only a few examples of C–H···X hydrogen bonding have been demonstrated in artificial receptors.[5] In pioneering work, Flood et al. recently reported that macrocyclic triazolophanes and triazole-based foldamers exhibit C–H···X hydrogen bonding interactions that are strong enough to form a stable host–guest complex.[6] In particular, macrocyclic triazolophane exhibited unexpectedly large association constants to anionic guests ($1.1\times10^7\,M^{-1}$ for Cl^- in CH_2Cl_2) due to the preorganized conformation of C–H hydrogen bonding donors in the shape-persistent host compound.[6d] However, flexible triazole oligomers have shown relatively weak binding affinities compared with those of the rigid triazolophane, indicating the importance of preorganization.[6h] Herein, we demonstrate the significantly strong anion binding affinity of a porphyrin-based receptor containing four triazole units despite its acyclic structure.

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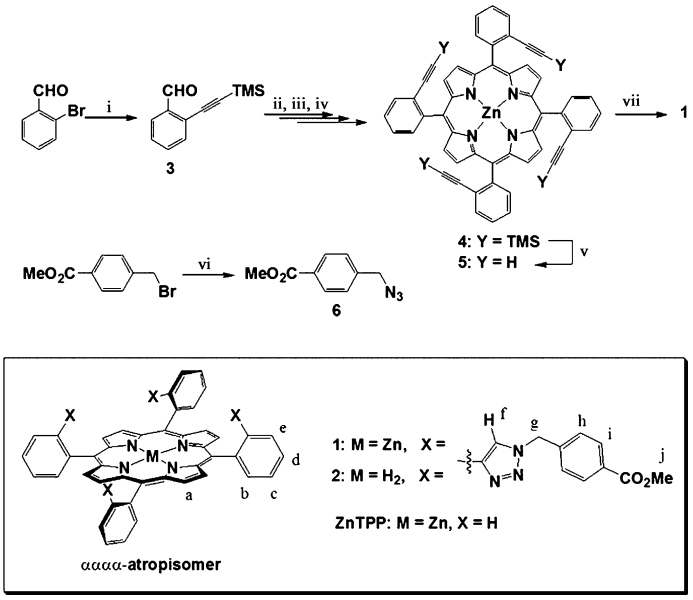
Results and Discussion

Synthesis: A new type of host compound (**1**), tetraphenyl zinc–porphyrin (ZnTPP) containing four triazole groups at the *ortho*-position of each phenyl group, has been prepared and characterized by using ^{1}H, ^{13}C NMR, and MALDI-TOF-MS analyses. The synthesis procedure of **1** is summarized in Scheme 1. Briefly, a Sonogashira coupling reaction between 2-bromobenzaldehyde and TMS–acetylene was conducted to obtain **3**. Subsequently, an acid-catalyzed condensation reaction of **3** with pyrrole and a successive oxidation reaction were performed. The addition of zinc acetate to the reaction mixture introduced a zinc ion to the center of the porphyrin unit to obtain **4**. This reaction was followed by TMS deprotection to give **5**, which was used to react with methyl-4-(azidomethyl)benzoate (**7**) using a Cu^I-catalyzed alkyne-azide click reaction.[7] The formation of four different atropisomers was expected in the preparation of porphyrins.[8] However, a successful separation method for each atropisomer for **4** and **5** using conventional column



Scheme 1. Synthesis of **1**. Reagents and conditions: i) $[Pd(PPh_3)_2Cl_2]$, CuI, TMS–acetylene, Et_3N/THF, 50 °C, 16 h; ii) pyrrole, TFA, CH_2Cl_2, 25 °C, 12 h; iii) *p*-chloranil, 25 °C,4 h; iv) $Zn(OAc)_2$, CH_2Cl_2/MeOH, 25 °C, 1 h; v) tetrabutylammonium fluoride, CH_2Cl_2, 25 °C, 30 min; vi) NaN_3, acetone/H_2O, 25 °C, 30 min; vii) **6**, $CuSO_4{\cdot}5H_2O$, sodium ascorbate, THF/H_2O, 50 °C, 12 h.

chromatography could not be established. After the click reaction, the αααα-atropisomer (**1**) was perfectly separated as the major product from the reaction mixture using silica column chromatography.

MALDI-TOF-MS analysis: The host-guest complex formation between **1** and halides has been directly confirmed by MALDI-TOF-MS analysis (Figure 1). In negative ionization mode, the mass spectrum of **1** with tetrabutylammonium (TBA) I^- salt exhibited not only a molecular ion signal at 1538.04 Dalton but also a $[\mathbf{1}+I]^-$ signal at 1665.05 Dalton.

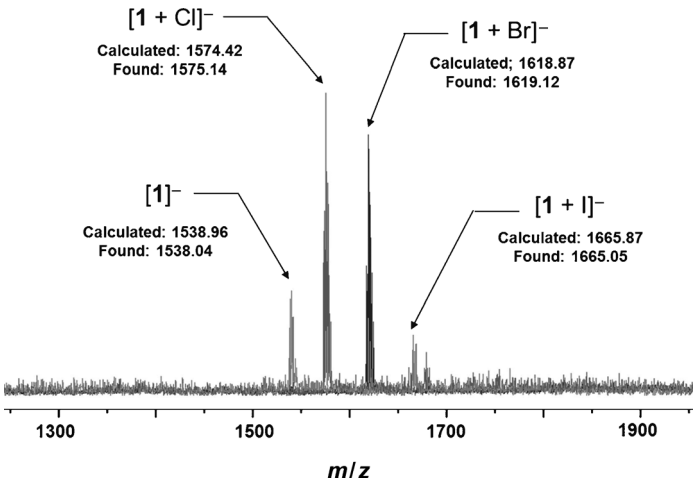


Figure 1. MALDI-TOF-MS spectra of **1** with halides.

For the mixture of **1** with Cl^- or Br^- salt, the major intense signals appeared at 1575.14 and 1619.12 Dalton, corresponding to molecular weight of the $[\mathbf{1}+Cl]^-$ and $[\mathbf{1}+Br]^-$, respectively, indicating the high stability of Cl^- or Br^- complex of **1**.

^{1}H NMR spectroscopy: ^{1}H NMR studies have been carried out in $[D]_6$DMSO. The triazole proton signals in **1** appeared at a quite strong upfield region (5.5 ppm) compared with those of the general triazoles, indicating that the triazole proton was located on the porphyrin ring and was influenced by the porphyrin ring current effect. Figure 2 shows

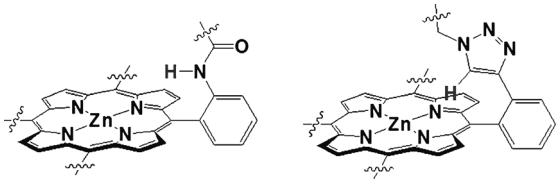


Figure 2. Simplified chemical structures of amido- or urea-type picket porphyrin and **1**.

simplified chemical structures of amido- or urea-type picket porphyrin and **1**. It is noteworthy that **1** has an additional C–C bond between the hydrogen-bond donating triazole C–H group and phenyl ring in ZnTPP when it compared with amido- or urea-type picket porphyrins. Considering the additional C–C bond, hydrogen-bonding donors in **1** are significantly closer to the porphyrin ring than other amido- or urea-type picket porphyrins. Furthermore, the C–H bonds in the triazole group should be directed into the porphyrin center due to the rigid chemical structure and bond angles. Those distinct structural characteristics have a strong influence on the chemical shift changes of **1** by the anionic guest bindings. As shown in Figure 3, the triazole, benzyl, and phenylene proton signals were shifted upfield by the addition of halides in the form of TBA salts. In particular, the triazole proton exhibited a very strong upfield shift (−0.94 ppm) due to the addition of Cl^-. To the best of our knowledge, such a strong upfield shift has never been observed in the process of hydrogen-bonding formation, even in various picket-type porphyrin receptors.[9]

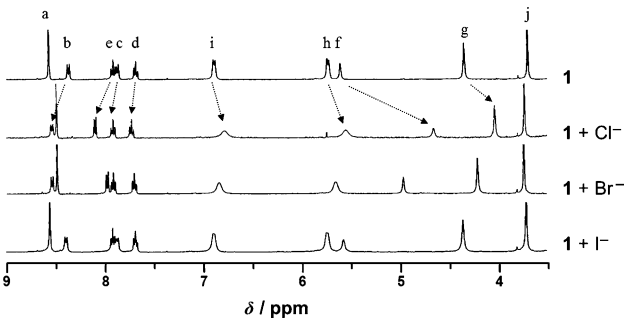


Figure 3. ^{1}H NMR spectra (400 MHz, $[D_6]$DMSO, 298 K) of **1** (1.6 mM) recorded upon addition of 10 equivalents of halides.

Two different effects can influence the triazole proton upon host–guest complex formation. First, the electron density of protons eventually decreases when the protons participate in hydrogen bonding; as such, a downfield shift can be observed due to the deshielding effect. Second, porphyrin ring current effects can lead to a shielding effect on triazole protons if they are directed toward the center of the porphyrin; our results from NMR experiments indicate that this is the predominant effect working in the triazole protons. Therefore, the strong upfield shift implies that the triazole protons in **1** are located very closely to the porphyrin ring and are directed toward the binding pocket over the porphyrin ring when they form hydrogen bonds. According to the increase in ionic radius, the upfield shift decreased because the distance from the porphyrin center to the triazole proton increased (Figure 3).

UV/Vis spectroscopy: The formation of a host–guest complex between **1** and halides was again investigated using UV/Vis spectroscopic analysis of the Soret and Q bands of the porphyrin in CH_2Cl_2, acetone, and DMSO. The UV/Vis absorption spectra showed that both the Soret and Q band absorptions of **1** underwent a strong redshift with clear isosbestic points due to the addition of halides (Figure 4a, Figure 5, and Supporting Information). The spectral changes of **1** took place in a symmetrical manner on the basis of isosbestic points (Figure 4a and Supporting Information). The continuous variation method (Job's plot) demonstrated that **1** and halides form 1:1 host–guest complexes.[10] The association constant for halides to **1** was determined by nonlinear curve-fitting analysis of the UV/Vis spectral changes using a commercially available HypSpec software. Interestingly, **1** exhibited surprisingly strong halide binding affinities, in which the association constants for Cl^-, Br^-, and I^- binding were estimated to be larger than 10^8, 1.79×10^7, and $1.84\times10^5\,M^{-1}$, respectively, in CH_2Cl_2 (Table 1). Notably, **1** has one order of magnitude greater binding affinities for all halides compared with the triazolophane values published by Flood et al. under the same conditions.[6d] Because the binding affinity of **1** to halides was unexpectedly high, the estimated association constant of **1** for Cl^- in CH_2Cl_2 is at the upper limit for accurate calculation. Hence, we again carried out the UV/Vis titration experiments in polar solvents, such as acetone and DMSO, which showed that **1** still has strong binding affinities for halides in polar solvents (results summarized in Table 1). Although the binding affinities decreased, the relative binding strength in polar solvents was still maintained. Considering the molecular structure of the host compound, **1** can provide only four C–H hydrogen-bonding donors for the formation of a host–guest complex. Also, **1** has a relatively flexible structure relative to the cyclic triazolophane. Therefore, the strong binding affinities for the anionic guests are clearly an abnormal aspect of **1** when only C–H···X hydrogen bonding is considered.

On the other hand, zinc–porphyrin contains a Lewis acidic site (Zn^{2+}) for the binding of a lone pair of electrons. Therefore, it is also possible that the lone pair electrons of

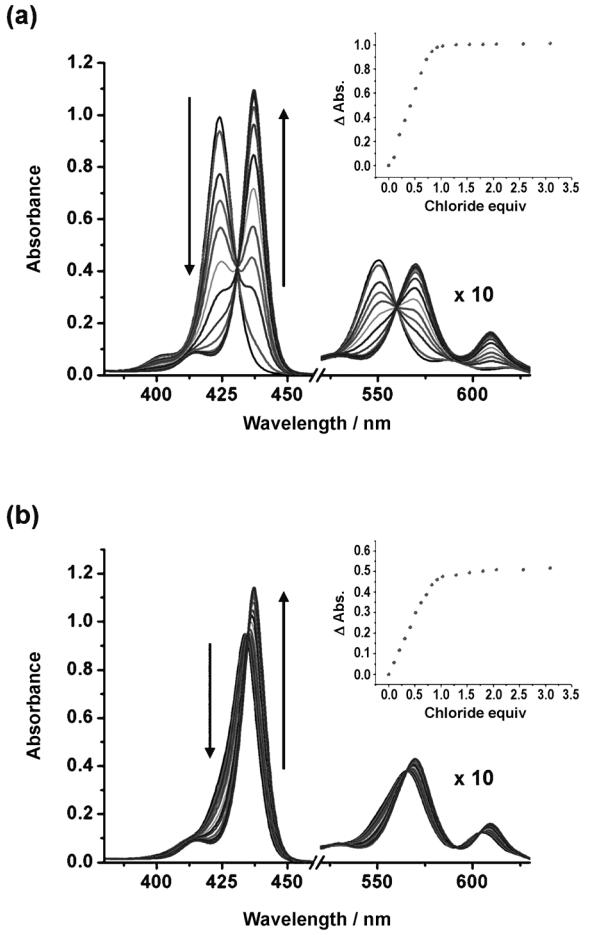


Figure 4. Spectroscopic titration of a) **1** (2.3 μM) with Cl^- and b) **1** containing 300 equivalents of TBP with Cl^-. Inset: Spectroscopic titration curves of Cl^-. Measured in CH_2Cl_2 at 298 K.

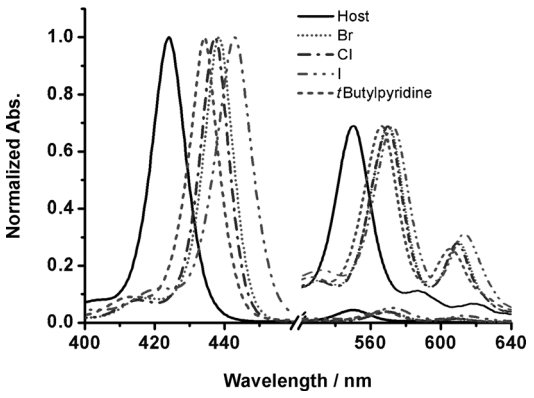


Figure 5. Normalized absorption spectra of **1** and various host–guest complexes.

halides could take part in coordination to the zinc ion. As mentioned above, the strong redshifts of the Soret and Q band absorptions of **1** were observed due to the addition of halide. Such strong absorption shifts cannot be achieved by simple C–H···X hydrogen-bond formation. It is known that

Table 1. Association constants K and ΔG for the complex formation of **1** with various anionic guests at 298 K.[a]

Solvent	Guest	K [M^{-1}]	ΔG [kJ mol^{-1}]
CH_2Cl_2	Cl^-	$>10^8$	>-45.6
	Br^-	1.79×10^7	-41.4
	I^-	1.84×10^5	-30.0
	TBP[b]	1.08×10^4	-23.0
acetone	Cl^-	3.53×10^6	-37.4
	Br^-	1.92×10^5	-30.1
	I^-	3.21×10^3	-20.0
DMSO	Cl^-	2.22×10^4	-24.8
	Br^-	4.09×10^2	-14.9
	I^-	12	-6.2

[a] Estimated errors $<5\%$. [b] TBP = *tert*-butylpyridine.

a very weak interaction exists between halides and ZnTPP in CH_2Cl_2, where the association constants in CH_2Cl_2 were about 290 and 17 M^{-1} for Cl^- and Br^-, respectively.[11] Nappa and Valentine reported the relationship between the redshift value and the axial ligation of various ligands and proposed that the charge donation ability is related to the electronegativity and polarizability of the ligand.[11] Therefore, the order of redshifts due to halide ligation would be $Cl^- < Br^- < I^-$. A large amount of halide was used to determine the redshift values due to the very low binding affinity, where the literature redshift values for ZnTPP were 770 and 850 cm^{-1} for Cl^- and Br^- ligation, respectively. Moreover, the ZnTPP redshift value due to I^- ligation was not determined due to the lack of binding affinity. Throughout the halide titration experiments with **1**, all halides exhibited a sufficiently strong affinity to successfully determine their redshift values with minimum amounts of guest addition, which were determined to be 750, 830, and 990 cm^{-1} for Cl^-, Br^-, and I^-, respectively (Figure 5). The order of redshift and the values for Cl^- and Br^- binding agree well with the those from the experiments of Nappa and Valentine.[11] Although the Lewis acidic zinc ion in the porphyrin center had weak interactions with halides, such strong coordination of I^- to the porphyrin zinc ion has not been reported. Therefore, to the best of our knowledge, this is the first examination of halide ligation to a zinc ion with the aid of C–H···X hydrogen bonds.

To confirm again the axial ligation interaction, halides were titrated to **2**, **1** without Zn^{2+}. In these experiments there was no evidence of halide bindings to **2** even in CH_2Cl_2 using both UV/Vis and ^1H NMR spectroscopy, indicating that the axial ligation interaction is significantly important for the halide bindings. Considering the affinity of oligotriazoles to halides and extremely strong binding affinity for halides to **1**, it is unexpected result that **2** does not have any affinity to anionic species. Such unusual behavior by **2** can be explained by a repulsive interaction between the electron-rich free-base porphyrin and anionic guests. As mentioned above, when considering the chemical structure of **1** it is important to note that the C–H bonds in triazole groups are directed into center of porphyrin. Therefore, if anionic guests associate with **1** through hydrogen bonding, anions should be located at the porphyrin center. Therefore, the quadruple C–H···X hydrogen bonding enables the strong coordination interaction of halides onto Lewis acidic Zn^{2+}. However, **2** has a basic site at the center of the porphyrin, which may cause electronic repulsion to anionic species; therefore, **2** cannot accommodate anionic guests. Accordingly, it was concluded that the cooperative effects of axial coordination and C–H···X hydrogen bonding interactions resulted in the strong binding affinity of **1** to halides.

Competitive binding experiments: To verify the strong binding affinity of **1** to Cl^- and Br^- in CH_2Cl_2, we carried out competitive binding experiments using 4-*tert*-butylpyridine (TBP) and I^- as competitive ligands (Table 2). The addition of TBP to **1** resulted in a redshift of the Soret absorption band to 540 cm^{-1}, which also agrees with the redshift value of ZnTPP (530 cm^{-1}) by axial ligation of pyridine in CH_2Cl_2 (Figure 5), where the binding constant of **1** to TBP was estimated to be 1.08×10^4 M^{-1}. Halides were again titrated to **1** in the presence of 300 equivalents of TBP. As a result, the Soret band of **1** was further redshifted due to the addition of halides, even I^- (Figure 4b and the Supporting Information). On the other hand, the absorption bands of **1** exhibited slight blue shift by addition of Cl^- and Br^- when 300 equivalent amounts of I^- existed in the solution. All halides showed a decreased binding affinity to **1**, indicating that the TBP and I^- successfully worked as competitive ligands. Using Hypspec software, nonlinear curve fitting analysis was again carried out to estimate the binding affinities of Cl^- and Br^-. From the competitive binding experiments, we could again confirm that the binding constants of **1** to Cl^- and Br^- are greater than 10^8 and 10^7, respectively.

Table 2. Results of competitive binding experiments at 298 K in CH_2Cl_2[a].

Guest	K_{app} [M^{-1}][b]	K [M^{-1}][c]	K_{app} [M^{-1}][d]	K [M^{-1}][c]
Cl^-	1.00×10^8	$>10^8$	8.71×10^5	1.35×10^8
Br^-	1.90×10^6	1.51×10^7	6.46×10^4	1.03×10^7
I^-	4.72×10^4	4.43×10^5	–	–

[a] Estimated errors $<5\%$. [b] Apparent association constants of halides to **1** in the presence of 300 equivalents of TBP. [c] Estimated association constants of **1** to halides by nonlinear curve fitting. [d] Apparent association constants of halides to **1** in the presence of 300 equivalents of I^-.

Computer modeling: Structural optimization of host–guest complexes was carried out using a CAChe 7.5 PM5 semiempirical calculation (Figure 6). The results indicate that all protons in triazole units are directed to the center of the porphyrin unit and create optimum cavity for the formation of hydrogen bonding with halides. Because the triazole C–H is directed toward to the center of the porphyrin, all halides become very close to the metal center. Interestingly, in the energy-minimized structure of **1**, all triazole groups have tilted conformation with same direction for the formation of C–H···X hydrogen bonding. This observation may provide another interesting aspect that **1** may create chiral space

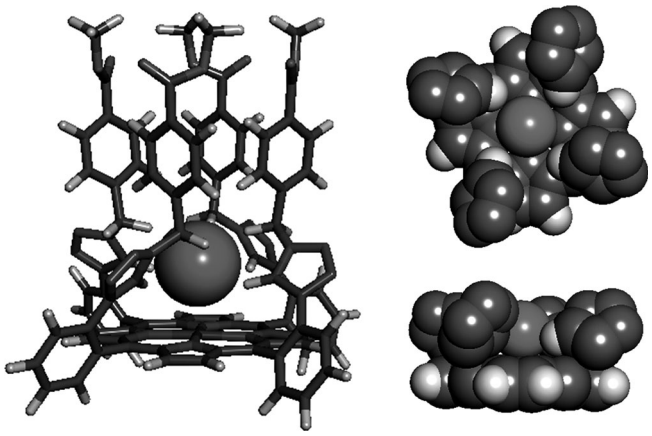


Figure 6. The energy-minimized molecular structure of **1** with Cl^- and omission of other functionalities except porphyrin and triazoles.

when it forms host–guest complexes with halides. Therefore, we are going to investigate the control of chiral space using chiral guest or introduction of chiral substituent in a further study.

Conclusion

We designed a new type of porphyrin-based host compound containing four triazole groups. While this new host compound does not have a shape-persistent macrocyclic structure of triazole groups, the cooperative effects of axial coordination and quadruple C−H···X hydrogen bonds resulted in extremely high halide binding affinities. Moreover, we were the first to examine halide ligation to zinc ions with the aid of C−H···X hydrogen bonds. Thus, the present work may allow future investigation of new physicochemical aspects of metalloporphyrins associated with axial ligation of halides. In addition, new ideas for receptor design can be proposed based on a combination of multiple binding motifs.

Experimental Section

Measurements: Electronic-absorption spectra were recorded on a JASCO V-660 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Advance DPX 400 spectrometer at 25°C in $CDCl_3$ and [D_6]DMSO. MALDI-TOF-MS was performed on an Applied Biosystems 4700 proteomics analyzer with α-cyano-4-hydroxycinnamic acid as the matrix.

Synthesis of 3: 2-Bromobenzaldehyde (10.22 g, 55.22 mmol), CuI (0.526 g, 2.76 mmol), and [$Pd(PPh_3)_2Cl_2$] (3.88 g, 5.52 mmol) were mixed in a Schlenk flask. The flask was degassed three times under high vacuum and back-filled with N_2. Dried THF (70.0 mL), Et_3N (30.0 mL), and trimethylsilylacetylene (11.47 mL, 82.83 mmol) were added. The reaction mixture was stirred for 16 h at 50°C and then filtered through Celite. The filtrate was concentrated and then purified using column chromatography with 2% ethyl acetate/hexane to produce **3** as a colorless oil (10.0 g, 90%): ^1H NMR (400 MHz, $CDCl_3$, 25°C): $\delta = 10.55$ (s, 1H), 7.90 (d, $J = 8$ Hz, 1H), 7.58–7.51 (m, 2H), 7.43 (t, $J = 6$ Hz, 1H), 0.27 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): $\delta = 191.99$, 136.30, 133.81, 133.63, 128.96, 127.00, 102.55, 100.19 ppm.

Synthesis of 4: TFA (2.0 mL, 25.96 mmol) was added to a mixture solution of **3** (4.0 g, 19.77 mmol) and pyrrole (1.31 g, 19.77 mmol) in CH_2Cl_2 (1.0 L) and stirred for 12 h at 25°C. Then, *p*-chloranil (7.29 g, 29.66 mmol) was added, and the reaction mixture was further stirred for 4 h. The reaction mixture was concentrated to a volume of 200 mL and then chromatographed in silica gel with CH_2Cl_2. Without further purification, the product was dissolved in 10% MeOH/CH_2Cl_2 containing Zn(OAc)$_2$ (4.34 g, 19.77 mmol) and then stirred for 1 h at 25°C. The reaction mixture was purified using column chromatography with 30% CH_2Cl_2/hexane to produce a mixture of atropisomers of **4** as a reddish–purple solid (0.79 g, 15%): MALDI-TOF-MS: *m/z* calcd for $C_{64}H_{60}N_4Si_4Zn$: 1062.94 $[M]^+$; found: 1063.08.

Synthesis of 5: Tetrabutylammonium fluoride (5.0 mL, 1 M in THF) was added to a solution of **4** (0.79 g, 0.74 mmol) in CH_2Cl_2 (100 mL) and stirred for 30 min at 25°C, then the solvent was removed under reduced pressure. The residue was purified using column chromatography with 50% CH_2Cl_2/hexane as the eluent. Recrystallization from the CH_2Cl_2/hexane gave a mixture of the atropisomers of **5** as a purple solid (0.55 g, 95%): MALDI-TOF-MS: *m/z* calcd for $C_{52}H_{28}N_4Zn$: 774.22 $[M]^+$; found 774.52.

Synthesis of 6: NaN_3 (1.14 g, 17.46 mmol) was added to a stirred solution of methyl 4-(bromomethyl)benzoate (2.0 g, 8.73 mmol) in a 40.0 mL acetone/H_2O mixture (3:1). The resulting suspension was stirred for 30 min at 25°C, and the reaction mixture was evaporated. The residue was purified using column chromatography with 50% CH_2Cl_2/hexane to produce **6** as a white solid (1.6 g, 99%): ^1H NMR (400 MHz, $CDCl_3$, 25°C): $\delta =$ 8.05 (d, $J = 8$ Hz, 2H), 7.49 (d, $J = 8$ Hz, 2H), 4.41 (s, 2H), 3.92 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25°C): $\delta = 166.72$, 140.49, 130.21, 128.02, 54.37, 52.30 ppm.

Synthesis of 1: $CuSO_4 \cdot 5H_2O$ (0.16 g, 0.65 mmol) and sodium ascorbate (0.13 g, 0.65 mmol) were added to a mixture of **5** (0.1 g, 0.13 mmol) and **6** (0.13 g, 0.65 mmol) in 20 mL THF/H_2O (1:1). The reaction mixture was stirred for 12 h at 50°C, and then the organic layer was separated, dried over $MgSO_4$, and filtered. After evaporation of the solvent under reduced pressure, the residue was purified using column chromatography with 70% ethyl acetate/CH_2Cl_2 and the second fraction was collected and evaporated to dryness. The residue was recrystallized from CH_2Cl_2/hexane to produce **1** as a purple solid (0.1 g, 51%): ^1H NMR (400 MHz, [D_6]DMSO, 25°C): $\delta = 8.57$ (s, $J = 8$ H), 8.37 (d, $J = 8$ Hz, 4H), 7,93–7.86 (m, 8H), 7.78 (t, $J = 6$ Hz, 4H), 6.89 (d, $J = 8$ Hz, 8H), 5.74 (d, $J = 8$ Hz, 8H), 5.62 (s, 4H), 4.36 (s, 8H), 3.72 ppm (s, 12H); ^{13}C NMR (100 MHz, [D_6]DMSO, 25°C): $\delta = 165.40$, 149.30, 146.50, 140.12, 139.97, 134.76, 132.85, 131.40, 128.59, 128.43, 127.24, 126.16, 126.02, 123.03, 118.66, 52.12, 50.92 ppm; MALDI-TOF-MS: *m/z* calcd for $C_{88}H_{64}N_{16}O_8Zn$: 1538.96 $[M]^+$; found: 1538.04.

Synthesis of 2: Trifluoroacetic acid (1 mL) was added to a solution of **1** (50 mg, 0.03 mmol) in CH_2Cl_2 (10 mL), and stirred for 30 min. The reaction mixture was poured into water, and then extracted with CH_2Cl_2. After the evaporation of solvent, compound **2** was obtained as purple solid with quantitative yield. ^1H NMR (400 MHz, $CDCl_3$, 25°C): $\delta = 8.68$ (s, 8H), 8.48 (d, $J = 8$ Hz, 4H), 7.92 (t, $J = 7$ Hz, 8H), 7.75 (d, $J = 7$ Hz, 4H), 7.64 (t, $J = 8$, 4H), 6.21 (d, $J = 8$ Hz, 8H), 5.32 (s, 4H), 5.14 (d, $J = 8$, 4H), 4.13 (s, 8H), 3.63 (s, 12H), −2.60 ppm (s, 2H); MALDI-TOF-MS: *m/z* calcd for $C_{88}H_{66}N_{16}O_8$: 1476.58 $[M+H]^+$; found: 1477.08.

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[1] a) C. Miller, *Nature* **2006**, *440*, 484; b) R. Dutzler, E. B. Campbell, R. Mackinnon, *Science* **2003**, *300*, 108; c) R. Dutzler, E. B. Campbell, M. Cadene, B. T. Chait, R. Mackinnon, *Nature* **2002**, *415*, 287.

[2] a) P. A. Gale, *Chem. Commun.* **2011**, *47*, 82; b) S.-O. Kang, J. M. Llinares, V. W. Day, K. Bowman-James, *Chem. Soc. Rev.* **2010**, *39*, 3980; c) B. P. Hay, *Chem. Soc. Rev.* **2010**, *39*, 3700; d) V. Amendola, L. Fabbrizzi, L. Mosca, *Chem. Soc. Rev.* **2010**, *39*, 3889; e) V. Amendola, D. Esteban-Gomez, L. Fabbrizzi, M. Licchelli, *Acc. Chem. Res.* **2006**, *39*, 343; f) S. E. Matthews, P. D. Beer, *Supramol. Chem.* **2005**, *17*, 411.

[3] a) S. P. Mahanta, B. S. Kumar, P. K. Panda, *Chem. Commun.* **2011**, *47*, 4496; b) P. A. Gale, *Acc. Chem. Res.* **2011**, *44*, 216; Y. Haketa, H. Maeda, *Chem. Eur. J.* **2011**, *17*, 1485; c) C.-H. Lee, H. Yoon, P. Kim, S. Cho, D. Kim, W.-D. Jang, *Chem. Commun.* **2011**, *47*, 4246; d) C.-H. Lee, H. Yoon, W.-D. Jang, *Chem. Eur. J.* **2009**, *15*, 9972; e) P. A. Gale, *Chem. Commun.* **2008**, 4525; f) J. M. Suk, K.-S. Jeong, *J. Am. Chem. Soc.* **2008**, *130*, 11868; g) K. J. Chang, D. Moon, M. S. Lah, K. S. Jeong, *Angew. Chem.* **2005**, *117*, 8140; *Angew. Chem. Int. Ed.* **2005**, *44*, 7926; h) K.-J. Chang, B.-N. Kang, M.-H. Lee, K.-S. Jeong, *J. Am. Chem. Soc.* **2005**, *127*, 12214.

[4] G. R. Desiraju, T. Steiner, *The Weak Hydrogen Bond: In Structural Chemistry and Biology*, Oxford University Press, Oxford, **1999**.

[5] a) M. L. Chabinyc, J. I. Brauman, *J. Am. Chem. Soc.* **2000**, *122*, 8739; b) B. P. Hay, V. S. Bryantsev, *Chem. Commun.* **2008**, 2417; c) G. Harakas, T. Vu, C. B. Knobler, M. F. Hawthorne, *J. Am. Chem. Soc.* **1998**, *120*, 6405.

[6] a) Y. Hua, R. O. Ramabhadran, E. O. Uduehi, J. A. Karty, K. Raghavachari, A. H. Flood, *Chem. Eur. J.* **2011**, *17*, 312; b) Y. Hua, A. H. Flood, *J. Am. Chem. Soc.* **2010**, *132*, 12838; c) S. Lee, Y. Hua, H. Park, A. H. Flood, *Org. Lett.* **2010**, *12*, 2100; d) Y. Hua, A. H. Flood, *Chem. Soc. Rev.* **2010**, *39*, 1262; e) I. Bandyopadhyay, K. Raghavachari, A. H. Flood, *ChemPhysChem* **2009**, *10*, 2535; f) J. L. Sessler, J. Cai, H.-Y. Gong, X. Yang, J. F. Arambula, B. P. Hay, *J. Am. Chem. Soc.* **2010**, *132*, 14058; g) Y. Li, A. H. Flood, *J. Am. Chem. Soc.* **2008**, *130*, 12111; h) Y. Li, A. H. Flood, *Angew. Chem.* **2008**, *120*, 2689; *Angew. Chem. Int. Ed.* **2008**, *47*, 2649.

[7] V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem.* **2002**, *114*, 2708; *Angew. Chem. Int. Ed.* **2002**, *41*, 2596.

[8] a) E. Rose, A. Cardon-Pilotaz, M. Quelquejeu, N. Bernard, A. Kossanyi, B. Desmazieres, *J. Org. Chem.* **1995**, *60*, 3919; b) P. Maillard, S. Vilain, C. Huel, M. Momenteau, *J. Org. Chem.* **1994**, *59*, 2887; c) J. S. Lindsey, *J. Org. Chem.* **1980**, *45*, 5215.

[9] a) J.-D. Lee, Y.-H. Kim, H.-I. Hong, *J. Org. Chem.* **2010**, *75*, 7588; b) D. P. Cormode, M. G. B. Drew, R. Jagessar, P. D. Beer, *Dalton Trans.* **2008**, 6732; c) K. Calderon-Kawasaki, S. Kularatne, Y. H. Li, B. C. Noll, W. R. Scheidt, D. H. Burns, *J. Org. Chem.* **2007**, *72*, 9081; d) D. P. Cormode, S. S. Murray, A. R. Cowley, P. D. Beer, *Dalton Trans.* **2006**, 5135; e) D. H. Burns, K. Calderon-Kawasaki, S. Kularatne, *J. Org. Chem.* **2005**, *70*, 2803; f) Y.-H. Kim, J.-I. Hong, *Angew. Chem.* **2002**, *114*, 3071; *Angew. Chem. Int. Ed.* **2002**, *41*, 2947; g) Y.-H. Kim, J.-I. Hong, *Tetrahedron Lett.* **2000**, *41*, 4419.

[10] K. A. Connors, *Binding Constants: The Measurement of Molecular Complex Stability*, Wiley, New York, **1987**, p. 24.

[11] M. Nappa, J. S. Valentine, *J. Am. Chem. Soc.* **1978**, *100*, 5075.

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