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Solvent-manipulated Guest Binding and Signaling of a Fluorescent Resorcin[4]arene Cavitand with 1,3,2-Benzodiazaboryl D-π-A Conjugation Flaps

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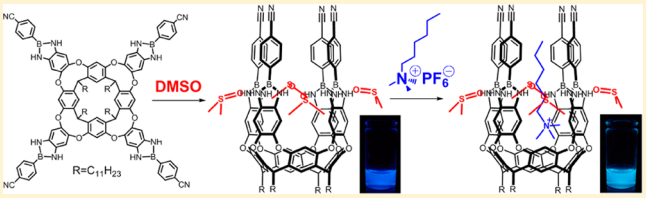
Supporting Information

ABSTRACT: The conformation of resorcin[4]arene cavitand system **1** was controlled by DMSO through a hydrogen bonding network between benzodiazaborole N*H*s of the cavitand flaps and DMSO molecules to stabilize the vase form. Subsequently, a guest-binding cavity of **1** was formed to accommodate tetraalkylammonium guest **3**, permitting the monitoring of the guest by the unaided eye as a result of a CH−π interaction between the benzodiazaborole π-donor group and the guest.



Much attention has been devoted to π-conjugated systems containing three-coordinate boryl substituents, in which the vacant p_z orbital of boron is conjugated to the π* orbitals of the adjacent π-framework.[1] The resultant unique optical and electronic properties of these compounds have motivated chemists to formulate organic materials for applications in nonlinear optical materials,[2] two-photon excited fluorescence materials,[3] luminescence,[4] and electron-transporting materials.[5] Despite their superior properties as organic materials, the use of boryl-functionalized π-systems in supramolecular chemistry has been limited to being used as chemosensors for detecting Lewis bases such as fluoride ion[6] and cyanide ion,[6d,7] in part because of the Lewis acid−base interactions in such π-systems based on the affinity of boron atoms. Because boronic acids are widely used in molecular-recognition events,[8] it is worthwhile to explore the possibility of using boron-containing π-conjugated molecules as artificial receptors in such events. With this objective, we recently synthesized resorcin[4]arene cavitand systems by incorporating a fluorescent 1,3,2-benzodiazaborole wall.[9] The resorcin[4]arene cavitand motif has been recognized as an excellent building block of artificial hosts.[10] The interplay of the benzodiazaborole segments based on conjugated three-coordinate organoboron[11] and cavitand led us to propose a new type of fluorescence receptor for detecting tetraalkylammonium guests that can be accommodated with the cavity. However, the role of benzodiazaborole with respect to fluorescence-signaling capability still remains unclear. Therefore, it is important to understand the functionality to design new chemosensors. In this paper, to study this phenomenon, we newly synthesized resorcin[4]arene cavitand **1** with D-π-A benzodiazaboryl walls by incorporating a CN group as an effective acceptor. Because the 1,3,2-benzodiazaborolyl group serves as a π-donor, the π-conjugation systems with acceptor groups will possess intramolecular charge transfer (ICT) characteristics,[12] which would help us to monitor the host−guest interaction between the benzodiazaborole wall of **1** and a guest accommodated with the cavitand cavity by spectrophotometry.

However, in the course of this study, we unexpectedly found that the benzodiazaborolyl D-π-A walls in **1** could act as a molecular "flap," capable of responding to a hydrogen-bond-acceptor solvent (DMSO). These conformational dynamics are attributable to a resorcin[4]arene cavitand that can be switched between two types of conformations: (i) closed "vase" and (ii) opened "kite."[10a−c] It was earlier reported that these conformations were controlled by chemical stimuli such as change in pH,[13] metal ion concentration,[14] solvent polarity,[15] and light.[16] In addition, only a few examples regarding DMSO-induced conformational regulation have been reported.[13a,17] Nevertheless, we have demonstrated here for the first time that fluorescent signaling based on host−guest interactions in a cavitand receptor is promoted by DMSO because of the hydrogen-donor ability of benzodiazaborole-N*H*. This paper also discusses the intriguing functionality of 1,3,2-benzodiazaborole from the viewpoint of conformational dynamics of the cavitand-type receptors as well as its fluorescent signaling.

Resorcin[4]arene cavitand system **1** was synthesized by condensing octaaminocavitand **4**[9] with 4-cyanophenylboronic acid in a solid-state reaction in 36% yield. The UV/vis absorption and fluorescence spectra could be measured in a CH_2Cl_2 solution of **1** (10 μM), which showed absorption (λ_{max} = 329 nm) and fluorescence bands (λ_{max} = 473 nm, λ_{ex} = 329 nm) with a high quantum yield (Φ) of 0.63 against a *p*-terphenyl dye (Φ_R = 0.92)[18] (Supporting Information). A large Stokes shift of 144 nm allowed us to detect a blue light emission from the solution. Its specific properties were

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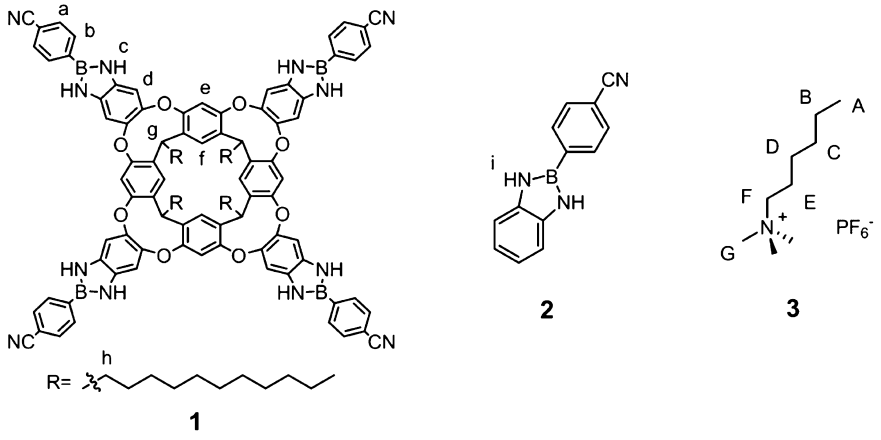
Chart 1. Chemical Structures of the Compounds 1 and 2 Investigated in This Study and Guest 3



attributed to the benzodiazaboryl walls of the cavitand. To further investigate, 2-(4-cyanophenyl)-1,3,2-benzodiazaborole **2** was synthesized as the model fluorophore (Chart 1).

Table 1 summarizes the absorption and fluorescence data of **2** in which toluene, AcOEt, CH_2Cl_2, DMSO, and MeCN were employed for the assessment. Although the observed changes in the absorption spectra were small—up to 8 nm on moving from toluene to MeCN—the fluorescence band was significantly shifted to a longer wavelength as the polarity of the solvent was increased. Thus, the change in the static dipole moments of the fluorophore ($\Delta\mu$) can be estimated to be 13.7 D by employing a Lippert-Mataga plot[19] in Figure S9 (Supporting Information). The value is almost congruent with that of *trans*-ethyl-*p*-(dimethylamino)cinnamate,[20] implying that compound **2** has an efficient D-π-A character when the benzodiazaborole group acts as an electron donor. On careful observation, we noted that λ_{max} values of both the UV/vis absorption and fluorescence spectra obtained in DMSO were slightly larger than those obtained in MeCN (higher polarity). Further, we noticed that the quantum yield of the fluorescence dramatically decreased in DMSO compared to other solvents used, the value being 0.053, presumably because of a facile nonradiative pathway. This suggests that DMSO could efficiently interact with **2**. This speculation was supported by ^{1}H NMR measurements (Figure S8 in Supporting Information); when CD_2Cl_2 was replaced with DMSO-d_6, the benzodiazaborole N*H* resonance was significantly low-field shifted by 2.46 ppm. We reasoned that diazaborole N*H* would act as a hydrogen donor, which plays an important role in the conformational dynamics of the cavitand (*vide infra*).

Table 1. Absorption and Fluorescence Data of 2

solvent	E_T	λ_{abs} (nm)	λ_{em} (nm)	Stokes shift (nm)	Stokes shift (cm^{-1})	Φ^a
Toluene	33.9	316	416	100	7607	0.94
AcOEt	38.1	316	437	121	8762	0.91
CH_2Cl_2	40.7	312	443	131	9478	1.0
DMSO	45.1	324	473	149	9723	0.053
MeCN	45.6	313	464	151	10397	0.77

[a]Values were determined against a *p*-terphenyl dye (Φ_R = 0.92). Conditions: [**2**] = 10 μM at 25 °C.

The use of NMR spectroscopic analysis is the most convenient method to monitor the conformational preferences of the cavitand.[10a] We thus investigated how the conformation of **1** would be affected by varying the content of DMSO-d_6 in CD_2Cl_2. Figure 1 shows the ^{1}H NMR spectra of **1** upon varying

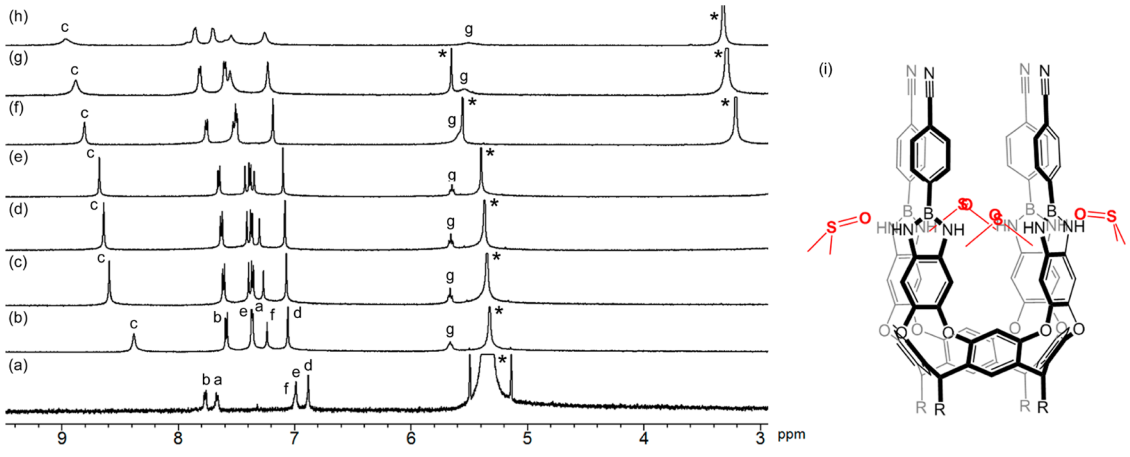


Figure 1. ^{1}H NMR spectra of **1** at 25 °C; (a) CD_2Cl_2 (85 μM), (b) CD_2Cl_2:DMSO-d_6 99:1 v/v (2 mM), (c) CD_2Cl_2:DMSO-d_6 95:5 v/v (2 mM), (d) CD_2Cl_2:DMSO-d_6 90:10 v/v (2 mM), (e) CD_2Cl_2:DMSO-d_6 85:15 v/v (2 mM), (f) CD_2Cl_2:DMSO-d_6 50:50 v/v (2 mM), (g) CD_2Cl_2:DMSO-d_6 25:75 v/v (2 mM), (h) DMSO-d_6 (2 mM). Signals with an asterisk (*) represent residual solvent peaks. (i) A plausible structure of DMSO-interacted **1**.

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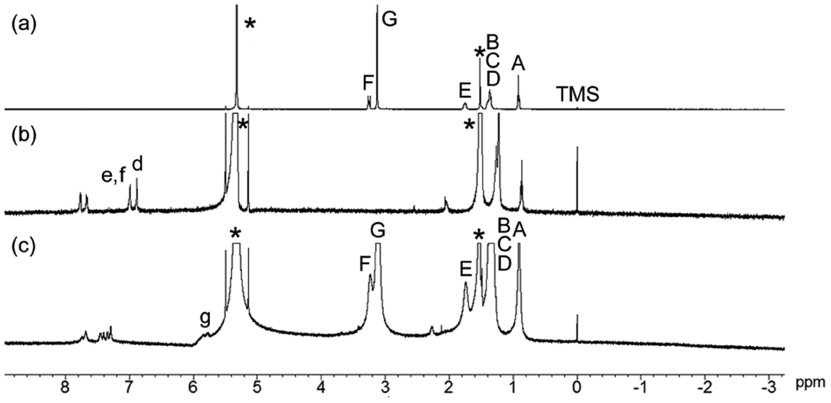

Figure 2. ^{1}H NMR spectra in CD_2Cl_2 at 25 °C. (a) **3** (2 mM), (b) **1** (85 μM), (c) **1** (85 μM) plus **3** (850 μM). Signals with an asterisk (*) represent residual solvent peaks.

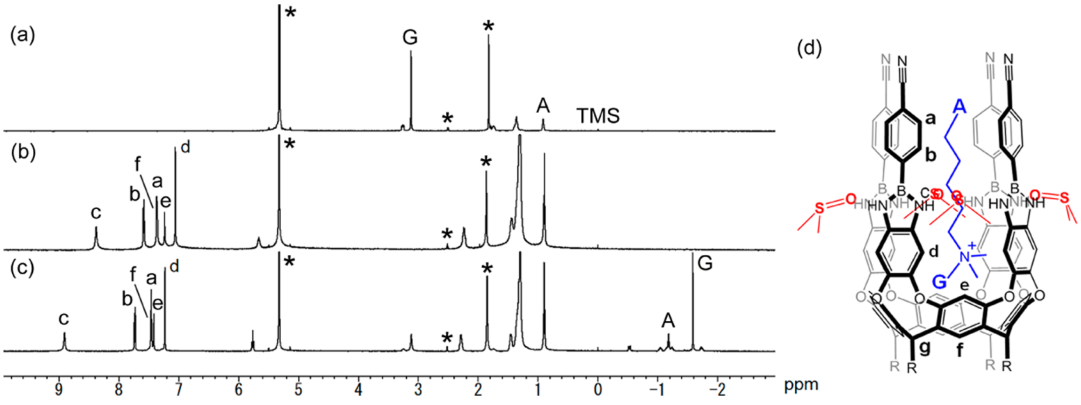

Figure 3. ^{1}H NMR spectra in CD_2Cl_2:DMSO-d_6 (99:1 v/v) at 25 °C. (a) **3** (2 mM), (b) **1** (2 mM), (c) **1** (2 mM) plus **3** (2 mM). (d) Plausible complex structure of DMSO-interacted **1** and **3** where counterion of **3** are omitted for clarity.

the content of DMSO-d_6 in CD_2Cl_2. Because of the low solubility in CD_2Cl_2, its NMR measurement in CD_2Cl_2 was carried out using a low concentration of **1** (85 μM). As inferred from Figure 1a, although aromatic resonances were observed in **1**, there were no detectable signals arising from the methine protons, possibly because of a slow exchange rate in vase/kite equilibration on the NMR time scale.[21] This means that the entropically unfavorable vase conformer was destabilized in CD_2Cl_2.

In contrast, in a CD_2Cl_2 solution with 1% vol DMSO-d_6, the solubility of **1** was remarkably improved and the ^{1}H NMR spectrum ([**1**] = 2 mM) at 25 °C suggested that **1** mostly assumed a vase conformation despite somewhat broadened signals (Figure 1b); the signal attributed to the methine proton was detectable at 5.66 ppm. The proton resonance for diazaborole N*H* was also observed as a singlet at 8.38 ppm. Interestingly, increase in the fraction of DMSO-d_6 up to 15% (v/v) in CD_2Cl_2 provided a set of well-defined spectral peaks assignable to the vase form (Figure 1c, d, e). This result indicates that the addition of incremental amounts of DMSO-d_6 into a CD_2Cl_2 solution of **1** promoted the stabilization of the vase conformation. Taking into account a lower shift for diazaborole N*H* proton, DMSO could participate in hydrogen bonding interactions with the two donors of the diazaborole N*H*s at the corner of the cavitand walls to complete the seam of a hydrogen bond network, the plausible structure being depicted in Figure 1i. However, the ^{1}H NMR spectra broadened when the content of DMSO was ≥50% (Figure 1f, g, h), indicative of the bulk environment where the polarity of DMSO governed the conformation dynamics. The observation of broadened and higher-field-shifted methine resonances allowed us to assume that an exchange equilibrium with the alternate kite conformations may be involved under the conditions.[17] Taken together, we proposed that the cavitand with 1,3,2-benzodiazaborole flips could stabilize a vase-like geometry influenced by a network of DMSO-mediated hydrogen bonds along its upper rim.

The next stage was to examine how DMSO would influence host–guest interactions of **1** with hexyltrimethylammonium hexafluorophosphate **3**. In CD_2Cl_2, taking into account a low concentration of **1** (85 μM) for the measurement, an excess of **3** (10 equiv) was added to the solution of **1** (Figure 2). However, there were no detectable signals at >0 ppm and no change of signals for **3**, indicative of no guest-encapsulation as a result of the destabilization of the vase conformer in CD_2Cl_2.[22]

On the other hand, in CD_2Cl_2/DMSO-d_6 (99:1 v/v), where a vase conformation was stabilized with 70 equiv of DMSO, the addition of 1 equiv. of **3** into a solution of **1** allowed us to detect proton signals assignable to the encapsulated **3** at >0 ppm (Figure 3). A full assignment of the signals was accomplished by ^{1}H–^{1}H COSY experiments (Figure S11 in Supporting Information). The most intense peak at −1.59 ppm was ascribable to $N(CH_3)_3$ protons (H^G), and the value of the upfield shift compared to that of the free guest ($\Delta\delta$ = 4.71 ppm) was indicative of binding within the shielding aromatic cavity of **1**. Further evidence for the host–guest complexation came from the 2D NOESY measurement (Figure S12 in Supporting Information). NOE cross-peaks were obtained

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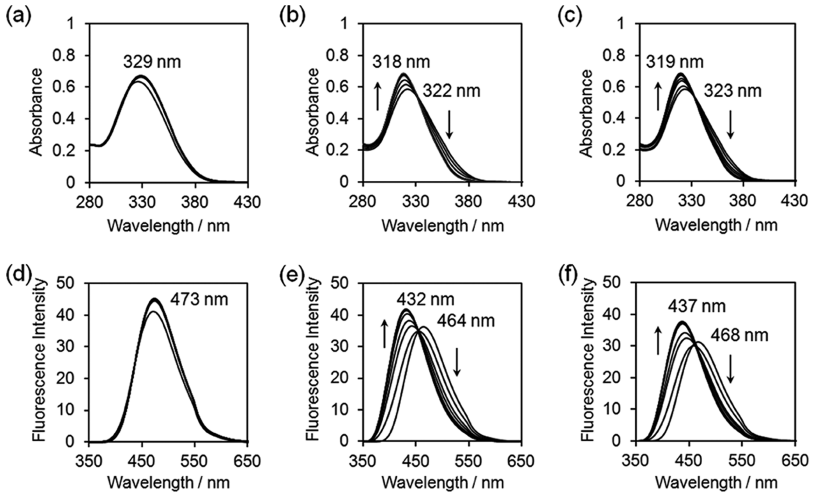

Figure 4. Change in (a, b, c) UV/vis absorption and (d, e, f) fluorescence spectra of **1** upon the addition of incremental amounts of **3** in CH_2Cl_2 (a, d), CH_2Cl_2/DMSO (99:1 v/v) (b, e), and CH_2Cl_2/DMSO (95:5 v/v) (c, f) at 25 °C. [**1**] = 10 μM, [**4**] = 0−100 μM. The values of λ_{ex} are 329 nm for (d), 331 nm for (e), and 332 nm for (f).

between not only H^f and H^G but also between H^d and H^G. This indicates that CH_3-N^+ of the guest is adjacent to the benzodiazaborole segment of the cavitand wall. Taking into account the electron-donor character of benzodiazaborole, significant CH-π interactions were presumed to be the driving force for complexation. Indeed, lower field-shifted aromatic (H^d, H^e, and H^f) and diazaborole N*H* resonances (H^c) (Figure 3c) strongly supported our speculation. Such interactions could affect the optical properties of the diazaborole flap in **1** to induce an optical response (*vide infra*). In this way, DMSO is thought to allosterically mediate host−guest interactions of **1** with **3**.

It is interesting to note that the guest signaling of **1** was significantly mediated by DMSO. Indeed, **1** showed almost no response to the guest in the UV/vis absorption and fluorescence spectra in CH_2Cl_2 (Figures 4a and 4d), which can be interpreted based on the fact that **1** cannot adopt the closed vase form under the conditions. On the other hand, when we set up conditions comprising a CH_2Cl_2 solution containing 1% vol DMSO, a hypsochromic shift of 4 nm was measured in the UV/vis absorption spectrum on adding **3** into the solution (Figure 4b). The fluorescence response was remarkable; a considerable short-wavelength shift of 32 nm was detected with increasing fluorescence intensity (Figure 4e). For the assessment, a nonlinear curve-fitting procedure carried out under the assumption of a 1:1 stoichiometric complex formation reproduced the fluorescence titrations data wherein the high association constant K_a was estimated to be 1.44×10^7 M^{-1} for **3** (Figure S13 in Supporting Information). The optical response of **3** in CH_2Cl_2/DMSO (95:5 v/v) (Figure 4c and f) is the same as that observed in CH_2Cl_2 solution with 1% vol DMSO. These results implied that DMSO should have a significant effect toward guest signaling. Taken together, benzodiazaborole plays a significant role not only in conformational dynamics but also in optical signaling; in the latter, the benzodiazaborole group acts as an electron donor in the fluorophore moiety on the cavitand wall, and therefore, significant CH−π interactions between the benzodiazaborole and guest encapsulated in the cavity diminish the strength of the dipole moment of the D-π-A conjugated wall to induce an optical response.

In conclusion, we fully evaluated the functionality of benzodiazaborole for host−guest interactions based on cavitand receptors as follows: (1) the hydrogen bonding donor capability of benzodiazaborole NH was proven to be feasible to stabilize a cavitand vase conformation through a seam of hydrogen-bonding networks with DMSO, resulting in the formation of a cavity for guest accommodation; (2) π-donor characteristics of benzodiazaborole allows for participation in CH−π interactions with electron-deficient guests to induce a significant response in the emission, permitting the monitoring of the guest by the unaided eye. We believe that the results obtained in this study will pave the way for designing new chemosensor systems based on cavitands and other receptor skeletons.

EXPERIMENTAL SECTION

General. ^1H and ^{13}C NMR spectra were recorded on a magnetic resonance spectrometer at 500 and 125 MHz, respectively. Chemical shifts (δ) are reported downfield from the internal standard Me_4Si. Mass spectrometry data of **1** and **2** were taken by using a MALDI-TOF mass spectrometer and a FAB mass spectrometer, respectively. Dithranol and distilled THF were used as a matrix and solvent for MALDI-TOF mass spectrometry and 3-nitrobenzyl alcoholwas used as a matrix for FAB mass spectrometry. The absorption spectra and fluorescence spectra were measured using a spectrophotometer and a spectrofluorometer, respectively. Elemental analyses were performed on an elemental analyzer.

Material. Reagents used for the synthesis were commercially available and used as supplied. Hexyltrimethylammonium ion as bromide salt purchased from a chemical supplier was exchanged to the corresponding hexafluorophosphate salt **3** using KPF_6.

Synthesis of Tetra(2-(4-cyanophenyl)-1,3,2-diazaborole)-appended Cavitand ***1****.* The octaaminocavitand precursor (**4**·nHCl) (487.7 mg, 0.270 mmol) dissolved in EtOH/H_2O (1:1 v/v) (200 mL) was basified with 1N NaOH aqueous solution. The product was extracted with CH_2Cl_2 (180 mL × 2), dried with Na_2SO_4, and evaporated under reduced pressure. Drying in vacuo for 1 h afforded a brown solid. This solid (377.7 mg) and 4-cyanophenylboronic acid **5** (153.1 mg, 1.04 mmol) were coground in a mortar and the resultant solid was stirred with zirconia balls (φ = 1.25 mm) under 60 Pa for 37 h at 140 °C. Dry-acetone/CH_2Cl_2 (1:1 v/v) was then added to the reaction mixture and the solution was then filtrated to remove insoluble impurities and zirconia balls. A solid was obtained by removal of solvent in vacuum. The solid was dissolved in a small

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amount of dry-acetone/CH_2Cl_2 (1:1 v/v) and the addition of MeCN to the solution produced a precipitate. The reprecipitation procedure was repeated several times until the resultant supernatant solution became colorless. In this way, the entitled compound was obtained as a beige solid (175.3 mg, 36%). ^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6 (95:5 v/v)) δ (ppm) 8.41 (s, 8H), 7.43 (d, 8H, J = 8.0 Hz), 7.38 (s, 4H), 7.20 (d, 8H, J = 8.0 Hz), 7.17 (s, 4H), 7.07 (s, 8H), 5.68 (t, 4H, J = 7.7 Hz), 2.21 (quart, 8H, J = 7.6 Hz), 1.44−1.28 (m, 72H, $(CH_2)_9CH_3$), 0.89 (t, 12H, J = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$/DMSO-d_6 (95:5 v/v)) δ 156.1, 145.7, 134.7, 134.1, 133.1, 133.1, 130.6, 123.5, 118.3, 117.1, 112.1, 105.7, 33.2, 32.6, 31.8, 29.7, 29.6, 29.3, 28.1, 22.6, 14.1; MALDI-TOF-MS m/z = 1966.09 $[M + H]^+$, 1988.08 $[M + Na]^+$ (Matrix: dithranol); Elemental Anal. Calcd for $C_{124}H_{136}B_4N_{12}O_8$: C, 75.76; H, 6.97; N, 8.55. Found: C, 75.31; H, 7.06; N, 8.27%.

Synthesis of 2-(4-Cyanophenyl)-1,3,2-benzodiazaborole **2**. A mixture of *o*-phenylenediamine (73.6 mg, 0.681 mmol) and 4-cyanophenylboronic acid **5** (100.0 mg, 0.681 mmol) was ground in a mortar and the resultant solid was stirred with zirconia balls (φ = 1.25 mm) under a N_2 atmosphere for 72 h at 50 °C. To the reaction mixture was added CH_2Cl_2 and the resultant solution was filtrated to remove unreacted **5** and zirconia balls. The solution was concentrated using a rotary evaporator and the addition of hexane to obtain **2** as a yellow solid (56.4 mg, 38%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.82 (d, 2H, J = 8.1 Hz), 7.71 (d, 2H, J = 8.2 Hz), 7.16 (dd, 2H, J = 5.6 Hz, 3.3 Hz), 7.01 (dd, 2H, J = 5.8 Hz, 3.2 Hz), 6.87 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.9, 133.4, 131.6, 120.0, 118,9 113.1, 111.6; FAB-MS m/z = 219 $[M]^+$ (Matrix: 3-nitrobenzyl alcohol); Elemental Anal. Calcd for $C_{13}H_{10}BN_3$: C, 71.28; H, 4.60; N, 19.18. Found: C, 71.02; H, 4.62; N, 18.96%.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectroscopicand analytical data for new compounds of **1** and **2**, and host−guest complexation of **1** with **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(21) In order to get insight into the conformational exchange, we carried out VT ^{1}H NMR measurement of **1** (2 mM) in THF-d_8 ranging from 25 to −50 °C (Figure S10 in Supporting Information). At 25 °C, a broad signal resonating at 5.22 ppm was detected (Figure S10a in Supporting Information). However, upon cooling to −50 °C, the broad signal was found to split into two separate signals at 5.74 and 4.41 ppm. 2D ^{1}H−^{1}H COSY NMR measurement of **1** in THF-d_8 at −50 °C where cross peaks have been observed between each of the signals and methylene protons (H^h) allowed us to assign the peaks to methine protons. On the basis of a coalescence temperature, T_c, of 0 °C and $\Delta\mu$ = 664 Hz, the $\Delta G^{\ddagger}$ for the conformational exchange is calculated to be 12.0 kcal mol^{-1}, being almost consistent with that of cavitand with four quinoxaline flaps.[10b] Further, at −50 °C, the detection of plural signals resonating at around 9 ppm suggests that two types of kite conformers with C_{2v} symmetry may be involved in the solution (Figure S10d in Supporting Information). From these results, we consider that the cavitand can adopt vase and kite conformers where the signals at 5.74 ppm and at 4.41 ppm are assignable to methine protons of a vase conformer and kite conformer, respectively.
(22) On careful observation, we found that the low-field region (5.5−8 ppm) in Figure 2c shows not only that the aromatic resonances (H^d, H^e, and H^f) of **1** shifted lower by 0.41−0.47 ppm but also that new signals that may be assigned to methane protons (H^g) appeared at 5.78 ppm. This may indicate that the addition of an excess of **3** could affect the vase/kite conformational equilibrium. This perturbation may also be responsible for a slight change in the UV/vis and florescence spectra upon the addition of **3** to a CH_2Cl_2 solution of **1** (*vide infra*; Figure 4a and d).

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