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Synthesis, Structure, and Fullerene-Complexing Property of Azacalix[6]aromatics

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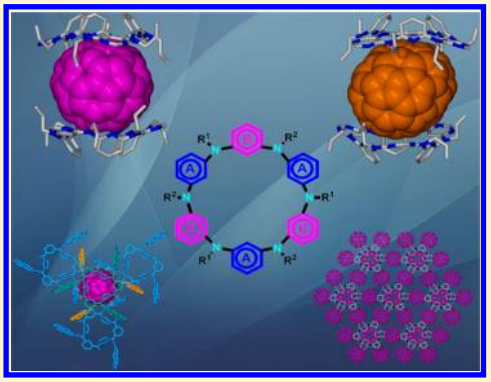
Supporting Information

ABSTRACT: Synthesis, structure, and fullerene-binding property of azacalix[6]aromatics were systematically studied. By means of [3 + 3] and [2 + 2 + 2] fragment coupling protocols, a number of azacalix[6]aromatics containing different combinations of benzene, pyridine, and pyrimidine rings and various substituents on the bridging nitrogen atoms were synthesized conveniently in moderate to good yields. The resulting macrocycles adopt in the solid state symmetric and heavily distorted 1,3,5-alternate conformations depending on the aromatic building units, whereas, in solution, they exist as a mixture of conformers that undergo rapid interchanges relative to the NMR time scale. All macrocycles were able to form 1:1 complexes with C_{60} and C_{70} in toluene with the association constants up to 7.28×10^4 M^{-1}. In the crystalline state, azacalix[6]aromatics form complexes with C_{60} and C_{70} with 2:1, 1:1, and 1:2 stoichiometric ratios between host and guest. Azacalix[6]aromatics interact with fullerene by forming mainly the sandwich structure in which C_{60} or C_{70} is sandwiched by two macrocycles. X-ray molecular structures revealed that multiple $\pi-\pi$ and CH$-\pi$ interactions between concave azacalix[6]aromatics and convex fullerenes C_{60} and C_{70} contribute a joint driving force to the formation of host–guest complexes.



INTRODUCTION

Because of their unique structures and interesting physiochemical properties, fullerenes have attracted great attention since their discovery. Along with the tremendous development of the study of chemical reactivity and modification of fullerenes, particularly C_{60}, in the hope of finding practical applications in the field of materials and biology, supramolecular fullerene chemistry, the study of noncovalent interactions between fullerenes with synthetic hosts or receptors, has also emerged as an important interdisciplinary subject.[1] Highly selective recognition and manipulation of fullerenes of varied sizes and geometries would provide not only efficient methods of separation and purification of ball-shaped fullerene isomers but also pave the ways to the fine fabrications and molecular self-assemblies of fullerene-based materials and devices in order to achieve the best performances of these distinctive carbon materials.

Since the milestone works of Atwood et al.[2] and Nakashima and Shinkai[3] in 1994 when they independently reported selective isolation of fullerenes C_{60} and C_{70} from fullerite using conventional ^{t}Bu-calix[8]arene, other macrocyclic host molecules, including calix[n]arenes and their derivatives,[4] calixresorcinarenes,[5] cyclotriveratrylenes (CTV),[6] crown ethers,[7] homooxacalix[3]arene,[8] and γ-cyclodextrin,[9] have been shown to form host–guest complexes with fullerenes due to the concave–convex complementarity. To increase the complexation capability and to improve possibly the selectivity, functionalized and cavity-confined receptors based on the aforementioned motifs have been developed. For example, Mendoza et al.[10] have devised a tripodal exTTF-CTV host that strongly binds C_{60} and C_{70} in chlorobenzene with an association constant log $K_{a(1:1)}$ of 5.3 and 6.3, respectively. While a double cancave host composed of two corannulene moieties behaves as a hydrocarbon "buckycatcher",[11] metalloporphyrin-derived macrocycles have been shown to exhibit strong and selective encapsulation of higher fullerenes.[12] Very recently, a cycloparaphenylene ring,[13] a member of a fascinating type of macrocycles, has been shown to bind C_{60} and C_{70} highly selectively.

Heteracalixaromatics, or heteroatom-bridged calixaromatics, are a new generation of macrocyclic host molecules.[14] In contrast to the methylene linkages in conventional calixarenes, heteroatoms such as nitrogen can adopt different electronic configurations and, more importantly, form various conjugation systems with their adjacent aromatic rings to give different bond lengths and angles.[15] As a result, heteracalixaromatics are able to self-regulate their conformational structures and to fine-tune their cavity sizes when interacting with guest species. In addition to this, the presence of different substituents on the

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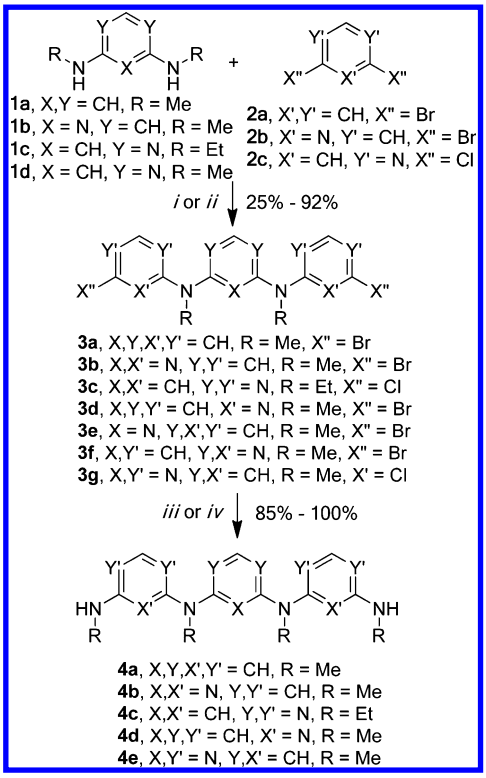
bridging nitrogen atoms would also play a role in tuning the cavity of heteracalixaromatics owing to their electronic and steric effects.[16] Because of the ease of introducing diverse aromatic moieties into the macrocyclic scaffolds, interplay between heteroatoms and aromatic rings allows the construction of molecular cavities of varied electronic features. For example, azacalix[4]pyridines are powerful and selective hosts for transition-metal ions[17] and for hydrogen bond donors,[18] whereas oxacalix[2]arene[2]triazines utilize their π-electron-deficient cleft to form complexes with anions of various geometries and shapes through cooperative anion$-\pi$ and lone-pair electrons$-\pi$ interactions.[19]

Although the past decade has witnessed tremendous development of heteracalixaromatics, the majority of the studies are concentrated on heteroatom-bridged calix[4](het)-arenes, the macrocycles that contain four (hetero)aromatic rings. The scarcity of research on larger macrocyclic homologues[20−22] may be partly due to the synthetic difficulty as almost all one-pot macrocyclic condensation reactions reported to date between aromatic dinucleophiles and dielectrophiles produce heteracalix[4]aromatics as the thermodynamically stable products.[14,20b,23] Only using the stepwise fragment coupling approaches, a few heteracalixaromatics containing more than five aromatic rings have been constructed.[21,22] On the other hand, it has been reported[22b] that larger heteracalixaromatics such as azacalix[n]pyridines (n = 5 −10) are powerful monomacrocyclic receptors to interact with fullerenes C_{60} and C_{70}, yielding 1:1 complexes in toluene with the association constants in the range of 2.6×10^4 to 1.3×10^5 M^{-1}. However, the nature of the interaction between these macrocycles and fullerenes remains unknown. It appears formidable and challenging to elucidate the effect of the interplay between bridging segments and aromatic rings on the molecular recognition property of heteracalixaromatics. As a continuation of the research program, our interests in developing the synthetic methods for large heteracalixaromatics and in understanding their structures and binding property led us to undertake the current work. We report herein in detail a systematic study of the synthesis, structure, and selective fullerene-binding property of a series of *N*-substituted azacalix-[6]aromatics containing varied combinations of benzene, pyridine, and pyrimidine rings.[24]

RESULTS AND DISCUSSION

Synthesis of Azacalix[6]aromatics. Retrosynthetically, azacalix[6]aromatics might be prepared by various methods. After considering the availability of starting materials and the shortest possible synthetic steps, a [3 + 3] fragment coupling approach[15a,b] was employed in the first place. As illustrated in Scheme 1, dielectrophilic linear trimeric fragments **3** were readily prepared from two directional arylation of aromatic diamines **1** with 1,3-dihalo-substituted aromatic reactants **2** in one-pot reaction fashion. It should be noted that the unreactive 1,3-dibromobenzene **2a** underwent the palladium-catalyzed cross-coupling reaction with 1,3-phenylene diamine **1a** or 2,6-diaminopyridine **1b** in refluxing 1,4-dioxane to give product **3a** or **3e**, respectively, in moderate chemical yields. In the case of reactive substrates, such as 2,6-dibromopyridine **2b** and 4,6-dichloropyrimidine **2c**, nucleophilic aromatic substitution reaction with dinucleophiles **1** proceeded effectively in the presence of NaH to afford the corresponding trimers **3** in the yields ranging from 69% to 92%. Further cross-coupling reaction of the resulting α,ω-dihalo-bearing linear trimers **3**

Scheme 1. Synthesis of α,ω-Dihalo Linear Trimers 3a−3g and α,ω-Diamino Linear Trimers 4a−4e[a]



[a]Conditions: *i*. $Pd_2(dba)_3$ (15 mol %), dppp (30 mol %), 1,4-dioxane, reflux; *ii*. NaH (4 equiv), THF, reflux; *iii*. CH_3NH_2 (5 equiv), CuI (10 mol %), L-proline (20 mol %), K_2CO_3, H_2O, DMSO, 100 °C; *iv*. $MeNH_2$ or $EtNH_2$ (5 equiv), H_2O in a sealed tube, 120 °C.

with methylamine under the catalysis of CuI in the presence of L-proline or simply nucleophilic aromatic substitution reaction of **3** with methylamine or ethylamine led to the formation of targeted diamine products **4** in excellent yields.

With all necessary dielectrophilic and dinucleophilic fragments in hand, synthesis of azacalix[6]aromatics was implemented. Under the standard conditions of Pd-catalyzed C−N bond-forming reaction,[15a,25] the [3 + 3] fragment coupling reactions between **3a** and **4a**, and between **3b** and **4b**, resulted in the formation of azacalix[6]arene **5a** in 23% yield and azacalix[6]pyridine **5b** in 31% yield. While azacalix-[3]arene[3]pyridine **5d** was obtained in a comparable yield (30%) from the similar [3 + 3] macrocyclization reaction from **4d** and **3e**, trimer **4e** underwent efficient cross-coupling reaction with trimer **3f** to furnish the formation of azacalix[3]-pyridine[3]pyrimidine **5e** in 73% yield[24] (Scheme 2). Without using any transition-metal catalysts, a [3 + 3] macrocyclic condensation reaction between **4c** and **3c** with the aid of NaH produced azacalix[6]pyrimidine **5c** in an acceptable yield (Scheme 3). It is worth addressing that azacalix[6]arene **5a** was isolated in only 2% yield from Pd-catalyzed macrocyclic oligimerization of 3-bromo-*N*-methylaniline,[26] while reaction between 2,6-dibromopyridine and 2,6-bis(methylamino)-pyridine gave azacalix[6]pyridine in 10% yield.[27]

The formation of azacalix[3]pyridine[3]pyrimidine **5e** in an exceedingly high yield from efficient macrocyclic cross-coupling reaction between trimer fragments **3f** and **4e** was fascinating. Although the exact reason is not clear at this stage, the thermodynamic stability may contribute a decisive driving

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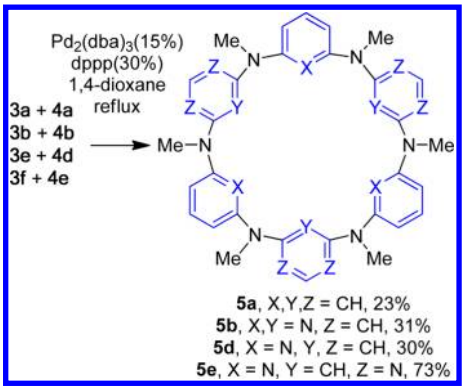
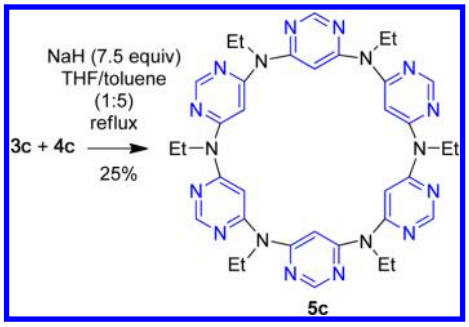
Scheme 2. Synthesis of Azacalix[6]aromatics 5a, 5b, 5d, and 5e

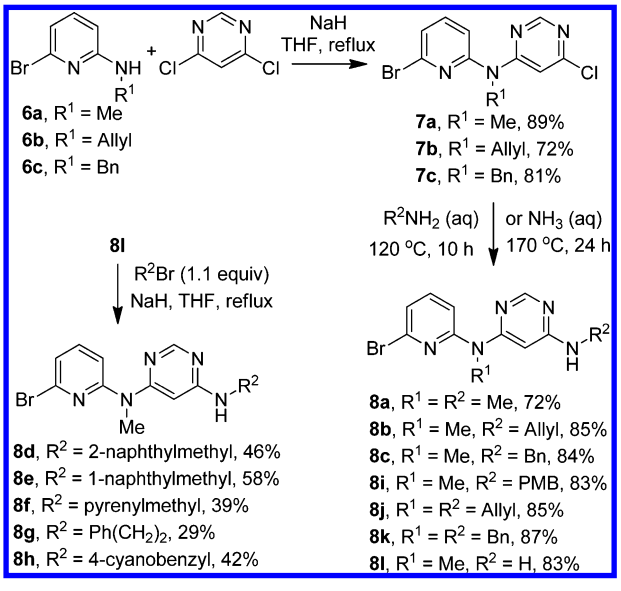


Scheme 3. Synthesis of Azacalix[6]pyrimidine 5c

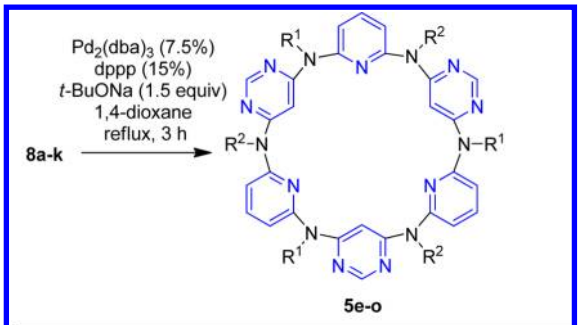


force. Nevertheless, the outcomes promoted us to test the synthesis of **5e** using smaller and simpler fragments. Under the identical catalytic conditions, the reaction of 4,6-diaminopyrimidine **1d** with equimolar 2,6-dibromopyridine **2b** proceeded effectively. The desired product **5e** was obtained in 37% yield along with the formation of larger macrocyclic homologues. To our delight, macrocyclic cross-coupling reaction of dimer **8a** itself, that was conveniently obtained starting from 2-amino-6-bromopyridine **6a** and **2c** (Scheme 4), yielded azacalix[3]pyridine[3]pyrimidine **5e** in 54% yield (Scheme 5). Taking advantage of the highly efficient macrocyclization reaction from

Scheme 4. Synthesis of Dimers 8a–8l



Scheme 5. Synthesis of Azacalix[3]pyridine[3]pyrimidines 5e–5o



Reactant	Product	R^1	R^2	Yield (%)
8a	**5e**	Me	Me	54
8b	**5f**	Me	Allyl	55
8c	**5g**	Me	Bn	52
8d	**5h**	Me	2-Naphthylmethyl	43
8e	**5i**	Me	1-Naphthylmethyl	46
8f	**5j**	Me	1-Pyrenylmethyl	35
8g	**5k**	Me	$Ph(CH_2)_2$	41
8h	**5l**	Me	4-cyanobenzyl	32
8i	**5m**	Me	PMB	46
8j	**5n**	Allyl	Allyl	46
8k	**5o**	Bn	Bn	61

a dimeric fragment, we then synthesized a number of azacalix[3]pyridine[3]pyrimidine derivatives **5**. As summarized in Scheme 5, all dimers containing diverse substituents on the bridging and terminal nitrogen atoms underwent desired macrocyclic head-to-tail cross-coupling reaction to afford products in good yields. It is worth addressing that the method provided a straightforward route to functional azacalix[3]pyridine[3]pyrimidines installed with either identical or two different substituents on the linking nitrogen atoms.

Structure of Azacalix[6]aromatics. All azacalix[6]aromatics synthesized are crystalline compounds, and recrystallization gave high-quality single crystals suitable for X-ray diffraction analysis. The X-ray molecular structures, which are illustrated in Figures 1–5 and Figures S27 and S28 (Supporting Information), allow us to understand the conformation of macrocycles in the solid state. It is interesting to note that, in comparison to the smaller macrocyclic homologues azacalix[4]aromatics that generally give similar 1,3-alternate conformations, azacalix[6]aromatics adopt varied conformations. More importantly, the conformational structures of azacalix[6]aromatics are strongly influenced by the nature of the aromatic rings.

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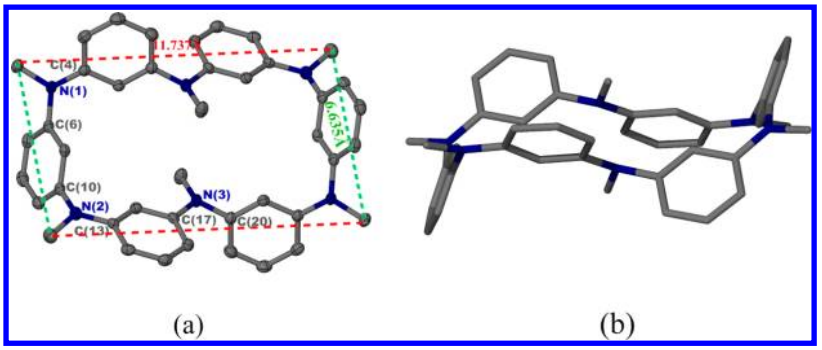

Figure 1. X-ray crystal structure of azacalix[6]arene **5a**: (a) top view and (b) side view. All hydrogen atoms are omitted for clarity. Selected bond lengths (Å): C(10)−N(2) 1.428, N(2)−C(13) 1.390, C(17)−N(3) 1.393, N(3)−C(20) 1.436, C(4)−N(1) 1.392, N(1)−C(6) 1.418.

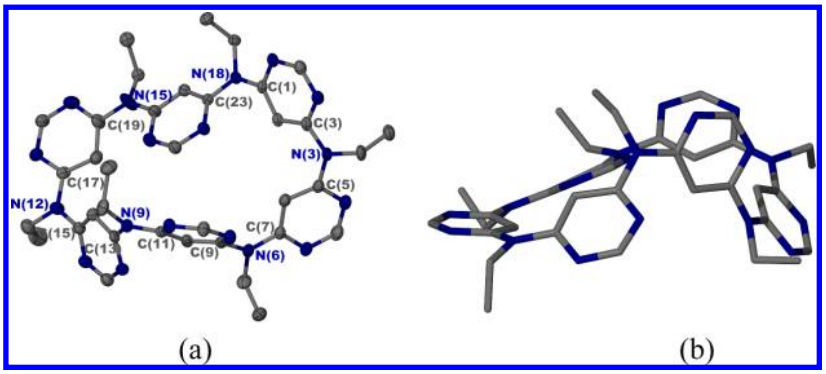

Figure 2. X-ray crystal structure of azacalix[6]pyrimidine **5c**: (a) top view and (b) side view. The disorders of C(31), C(32), C(33), C(34), N(12), N(15), and all hydrogen atoms are omitted for clarity. Selected bond lengths (Å): C(3)−N(3) 1.385, N(3)−C(5) 1.406, C(7)−N(6) 1.383, N(6)−C(9) 1.411, C(11)−N(9) 1.380, N(9)−C(13) 1.408, C(5)−N(12) 1.393, N(12)−C(17) 1.411, C(19)−N(15) 1.459, N(15)−C (21) 1.426, C(23)−N(18) 1.382, N(18)−C(1) 1.413.

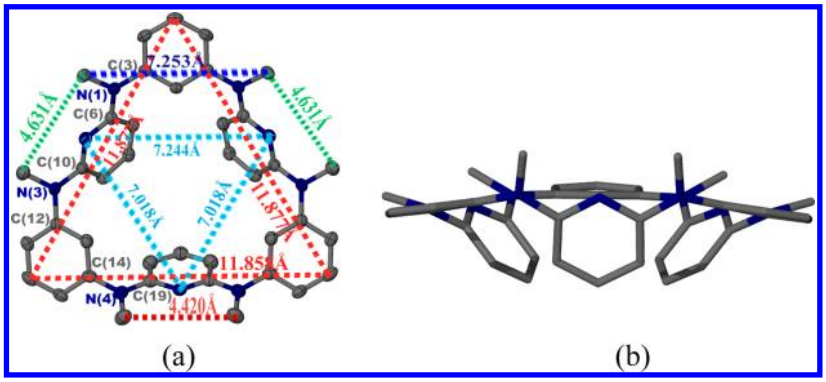

Figure 3. X-ray crystal structure of azacalix[3]arene[3]pyridine **5d**: (a) top view and (b) side view. All hydrogen atoms are omitted for clarity. Selected bond lengths (Å): C(3)−N(1) 1.425, N(1)−C(6) 1.396, C(10)−N(3) 1.415, N(3)−C(12) 1.413, C(14)−N(4) 1.422, N(4)−C(19) 1.389.

As shown in Figure 1, azacalix[6]arene **5a** adopts a 1,3,5-alternate conformation with a C_2 symmetry. Careful scrutiny of the bond lengths and bond angles of all bridging nitrogen atoms revealed that the macrocycle can be regarded as consisting of three different segments including conjugated *meta*-bis(methylamino)benzene and (methylamino)benzene, and isolated benzene. It was also worth noting that one of the methyl substituents on nitrogen of the conjugated *meta*-bis(methylamino)benzene is *s-cis*-configured while the other is *s-trans*-positioned. As a result, two *s-trans*-configured methyl groups are orientated inwardly to the cavity of the macrocyclic ring. In the case of azacalix[6]pyridine **5b** (Figure S27, Supporting Information) and azacalix[6]pyrimidine **5c** (Figure 2), macrocycles show heavily distorted 1,3,5-alternate conformations. Noticeably, one of the pyridine rings in **5b** and one of the pyrimidine rings in **5c** orientate inwardly to the macrocyclic cavity. The bond length between linking nitrogen atoms and carbon atoms of their adjacent pyridine rings in **5b** varies from 1.39 to 1.43 Å, while azacalix[6]pyrimidine **5c** gives $N_{bridge}-C_{pyrimidine}$ bond lengths in the range of 1.38−1.46 Å. Judged on the basis of the bond lengths and angles of the nitrogen linkages, different conjugation systems, such as aminopyridine, dipyrid-2-ylamine, and 2,6-diaminopyridine segments, were observed in azacalix[6]pyridine **5b**. However, macrocycle **5c** was mainly composed of aminopyrimidine units.

Being different from azacalix[6]arene **5a**, azacalix[6]pyridine **5b**, and azacalix[6]pyrimidine **5c**, azacalix[6]aromatics constituted by two different aromatic rings adopt a more symmetric

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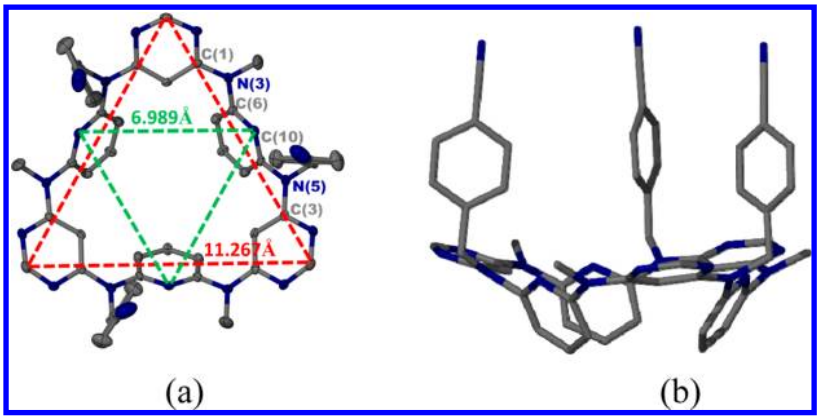

Figure 4. X-ray crystal structure of **5l**: (a) top view and (b) side view. Selected bond lengths (Å): C(1)−N(3) 1.368, N(3)−C(6) 1.417, C(10)−N(5) 1.415, N(5)−C(3) 1.376.

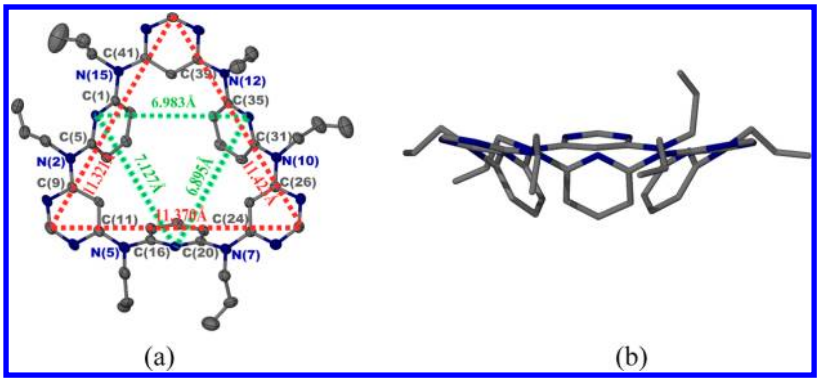

Figure 5. X-ray crystal structure of **5n**: (a) top view and (b) side view. Selected bond lengths (Å): C(1)−N(15) 1.416, N(15)−C(41) 1.378, C(2)−N(5) 1.422, N(2)−C(9) 1.376, C(11)−N(5) 1.383, N(5)−C(16) 1.414, C(20)−N(7) 1.418, N(7)−C(24) 1.386, C(26)−N(10) 1.396, N(10)−C(31) 1.406, C(35)−N(12) 1.414, N(12)−C(39) 1.394.

1,3,5-alternate conformation in the crystalline state. This has been exemplified convincingly by the X-ray single crystal and molecular structures of azacalix[3]arene[3]pyridine **5d** (Figure 3) and azacalix[3]pyridine[3]pyrimidines **5l** (Figure 4), **5n** (Figure 5), and **5o** (Figure S28, Supporting Information). A few interesting structural features are worth addressing. First of all, both azacalix[3]arene[3]pyridine and azacalix[3]pyridine-[3]pyrimidines have bowl-shaped structures. Apparently, three alternate benzene rings in **5d** or pyrimidine rings in **5l**, **5n**, and **5o** are procumbent, lying almost on the same plane defined by bridging nitrogen atoms. On the other hand, three alternate pyridine rings in all macrocycles tend to be perpendicular to the plane with dihedral angles of about 51−62°, forming a concavity. Second, bond lengths and angles of bridging nitrogen atoms observed in the X-ray molecular structures indicated interesting conjugation systems. In the case of azacalix[3]arene[3]pyridine **5d**, different conjugation systems, such as 2,6-diamonopyridine and aminopyridine segments, were observed while all benzene rings are relatively isolated. However, macrocycles **5l**, **5n**, and **5o** seemed to be composed of conjugated aminopyrimidine and partially conjugated aminopyridine and aminopyrimidine. In **5n**, there is also a conjugated diaminopyrimidine segment. It is apparent that bridging nitrogen atoms tend to conjugate with the more electron-deficient aromatic ring. Furthermore, cavity size varies depending on the aromatic components involved. For azacalix-[3]arene[3]pyridine **5d**, the average distances between the upper-rim carbon atoms of benzene rings and between the lower-rim nitrogen atoms of pyridine rings are around 11.87 and 7.17 Å, respectively. Azacalix[3]pyridine[3]pyrimidine rings appeared to have slightly shrinked cavities as the average distances between the upper-rim carbon atoms of pyrimidine rings and between the lower-rim nitrogen atoms of pyridine rings are around 11.32 and 7.00 Å, respectively. Finally, all six substituents directly connected to the bridging nitrogen atoms are cisoid-positioned. Noticeably, three 4-cyanophenyl groups in compound **5l** are orthogonal to the plane formed by bridging nitrogen atoms, yielding an expanded cavity, whereas six phenyl groups in compound **5o** turn around to the other direction. Such orientation of six *N*-benzyl groups is most probably due to the avoidance of repulsion among *N*-benzyl groups.

All macrocyclic compounds in solution may not be able to retain their conformational structures found in the crystalline state. This has been evidenced clearly by the observation of one single set of simple proton and carbon signals in their ^{1}H and ^{13}C NMR spectra, respectively, in $CDCl_3$ (see the Supporting Information). For example, the ^{1}H NMR spectrum of azacalix[6]pyrimidine **5c** exhibits, in addition to ethyl proton signals, two singlet peaks at 8.57 and 7.04 ppm corresponding to protons at 2- and 5-positions of pyrimidine, respectively. In its ^{13}C NMR spectrum, only five carbon signals were observed. Although all azacalix[6]aromatics may adopt a highly symmetric macrocyclic structure like azacalix[3]pyridine[3]-pyrimidines **5e**−**5o**, we accounted, however, the highly fluxional conformational structures in solution to the simplicity of ^{1}H and ^{13}C NMR spectra. It is most likely that different conformational structures undergo very rapid interconversions in solution at room temperature relative to the NMR time scale.

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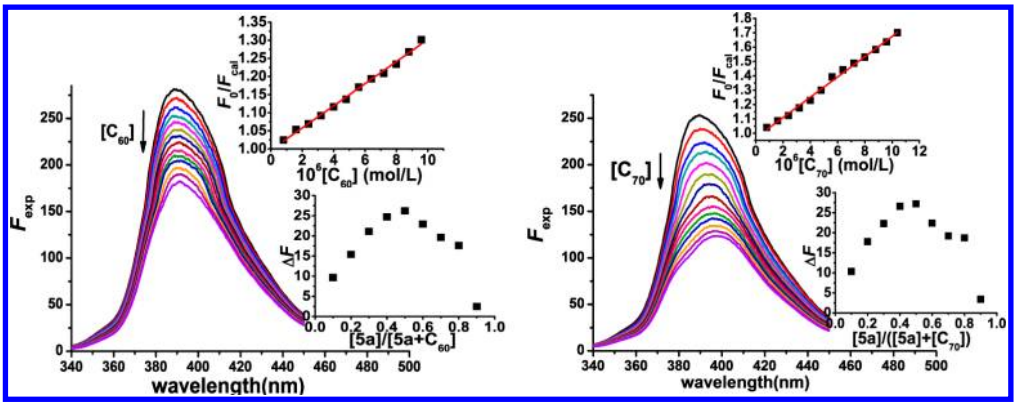

Figure 6. Fluorescence titration of azacalix[6]arene **5a** (λ_{ex} = 308 nm) with C_{60} (left) and C_{70} (right). Upper insertions are variations of fluorescence intensity F_o/F_{cal} of **5a** with increasing C_{60} and C_{70} concentrations, and lower insertions are Job's plot.

To shed light on the interplay between bridging units and aromatic rings assembled in macrocycles, the ^{1}H NMR spectra of azacalix[6]aromatics were investigated (Figure S1 and Table S1, Supporting Information). In comparison to the chemical shift of protons of parent benzene, pyridine, and pyrimidine, varied upfield shifts ($\Delta\delta$ = 0.18−1.19 ppm) of all protons of aromatic rings of compounds **5** were observed, substantiating the formation of conjugation between bridging nitrogen atoms with their adjacent aromatic rings. The $\Delta\delta$ values of azacalix[6]aromatics that contain two different aromatic rings were especially worth addressing. In the case of azacalix[3]-arene[3]pyridine **5d**, the benzene moiety showed $\Delta\delta$ of 0.18−0.44 ppm, while the pyridine ring gave $\Delta\delta$ in a range of 0.26−1.19 ppm. A much stronger shielding effect ($\Delta\delta$ = 0.58−0.87 ppm) on the pyrimidine ring than on the pyridine ring ($\Delta\delta$ = 0.21−0.60 ppm) was observed in **5e**−**5o**. The outcomes revealed convincingly the tendency of the linking nitrogen atom to form a stronger conjugation system with pyridine than with benzene in **5d**, and with pyrimidine than with pyridine in **5e**−**5o**. As a result, the π-electron density of pyridine was higher than that of benzene in **5d**, while the pyrimidine ring appeared electron-richer than the pyridine ring in **5e**−**5o**. It should also be noted that, in azacalix[3]pyridine[3]pyrimidine derivatives **5e**−**5o**, the substituents on the bridging nitrogen atoms also influenced the chemical shift of aromatic protons. Experience of the change of chemical shifts of pyrimidine ($\Delta\delta$ = 0.13 ppm) and pyridine ($\Delta\delta$ = 0.28 ppm) reflected a much stronger electronic effect of the substituents on the pyridine ring than that on the pyrimidine ring.

The formation of conjugation between aromatic rings and bridging nitrogen atoms was also evidenced by electronic spectroscopy (see the Supporting Information). In UV−visible spectra, macrocyclic compounds **5** gave maximum absorption bands in the regions of 297−333 nm, respectively, with the molar extinction coefficient (ε) ranging from 4.9 × 10^4 to 7.4 × 10^4 except *N*-pyrenylmethyl-substituted azacalix[3]pyridine[3]-pyrimidine **5j**, which gave characteristic absorption bands at 342 and 349 nm. The obvious red shift of absorption bands in all of the above cases revealed the presence of conjugation of the bridging nitrogen atoms with their adjacent aromatic rings, which is in agreement with the conclusion drawn from NMR spectroscopic data.

Fullerene-Recognition Property of Azacalix[6]-aromatics. The bowlic cavity of azacalix[6]aromatics render these macrocycles excellent receptors for ball-shaped fullerene guests on the basis of the principle of complementarity. To understand the capability of synthesized azacalix[6]aromatics in complexing fullerenes, interactions between synthetic hosts and C_{60} and C_{70} in toluene were investigated following an established fluorescence titration method.[28] As illustrated in Figure 6 and Figures S3−S26 in the Supporting Information, titration of macrocyclic host molecules **5a**−**5o** with C_{60} and C_{70} led to the gradual quenching of fluorescence emissions. The Job's plot experiments, inserted in Figure 6 and Figures S3−S26, indicated distinctly a 1:1 stoichiometry of the complex formed between an azacalix[6]aromatic receptor and a fullerene guest. On the basis of the fluorescence titration data, the association constants for the 1:1 complexes at room temperature in toluene between azacalix[6]aromatics and fullerenes were calculated using the Hyperquad 2000 program.[29]

As indicated by the results compiled in Table 1, all azacalix[6]aromatics synthesized showed expectedly strong binding ability toward fullerenes C_{60} and C_{70}. The association constants for 1:1 complexation between macrocyclic hosts and fullerenes C_{60} and C_{70} ranged from 3.05× 10^4 to 7.28 × 10^4 M^{-1} in toluene at room temperature. To the best of our knowledge, as monomacrocyclic species, azacalix[6]aromatics are very powerful fullerene-complexing host molecules. Depending on the nature of aromatic rings and of, to a less degree, *N*-substituents, azacalix[6]aromatics displayed different capability and selectivity in forming fullerene complexes. For example, when complexing with C_{60}, azacalix[6]pyridine **5b** gave a larger K_a (6.62 × 10^4 M^{-1}) than other azacalix[6]-aromatics (entries 1−5, Table 1). Azacalix[3]arene[3]pyridine **5d** acted as the strongest receptor toward C_{70} in comparison to its macrocyclic analogues (entries 1−5, Table 1). Variation of *N*-methyl group to *N*-arylmethyl and *N*-allyl groups in azacalix[3]pyridine[3]pyrimidine derivatives **5e**−**5o** led to the enhancement of C_{60}-binding power (entries 5−15, Table 1), with macrocycle **5j** being the strongest host (entry, 10, Table 1). Introduction of groups other than methyl into the bridging nitrogen atoms of azacalix[3]pyridine[3]pyrimidines **5e**−**5o** caused, on the contrary, a slight decrease of interaction with C_{70} in most cases (entries 5−15, Table 1). Although not remarkable, selectivity in forming complexes with C_{60} and C_{70} was observed for some azacalix[6]aromatics. For instance, azacalix[6]arene **5a** was found to bind C_{70} (K_a = 7.06 × 10^4 M^{-1}) more than 2-fold stronger than to bind C_{60} (3.05 × 10^4 M^{-1}) (entry 1, Table 1).

To understand the interactions between azacalix[6]aromatics and fullerenes at the molecular level by revealing the host−guest structures, single crystals of the complexes between

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Table 1. Association Constants for the 1:1 Complexation of Azacalix[6]aromatics 5a−5o with Fullerenes C_{60} and C_{70} at 298 K in Toluene[a]

entry	macrocyclic host	K_a (1:1 complexation with C_{60})	K_a (1:1 complexation with C_{70})
1	**5a**	$(3.05 \pm 0.06) \times 10^4$	$(7.06 \pm 0.15) \times 10^4$
2[b]	**5b**	$(6.62 \pm 0.22) \times 10^4$	$(6.24 \pm 0.19) \times 10^4$
3	**5c**	$(4.44 \pm 0.13) \times 10^4$	$(6.96 \pm 0.19) \times 10^4$
4	**5d**	$(5.22 \pm 0.11) \times 10^4$	$(7.27 \pm 0.02) \times 10^4$
5[c]	**5e**	$(4.93 \pm 0.10) \times 10^4$	$(6.66 \pm 0.17) \times 10^4$
6	**5f**	$(6.36 \pm 0.09) \times 10^4$	$(6.52 \pm 0.15) \times 10^4$
7	**5g**	$(5.86 \pm 0.11) \times 10^4$	$(5.86 \pm 0.18) \times 10^4$
8	**5h**	$(6.56 \pm 0.15) \times 10^4$	$(6.08 \pm 0.16) \times 10^4$
9	**5i**	$(5.70 \pm 0.11) \times 10^4$	$(5.79 \pm 0.11) \times 10^4$
10	**5j**	$(7.28 \pm 0.21) \times 10^4$	$(6.56 \pm 0.20) \times 10^4$
11	**5k**	$(5.59 \pm 0.15) \times 10^4$	$(6.26 \pm 0.14) \times 10^4$
12	**5l**	$(6.28 \pm 0.15) \times 10^4$	$(6.55 \pm 0.11) \times 10^4$
13	**5m**	$(6.26 \pm 0.14) \times 10^4$	$(5.92 \pm 0.11) \times 10^4$
14	**5n**	$(6.29 \pm 0.07) \times 10^4$	$(6.72 \pm 0.10) \times 10^4$
15	**5o**	$(6.15 \pm 0.09) \times 10^4$	$(6.25 \pm 0.12) \times 10^4$

[a]Association constants were calculated on the fluorescence titration data with the Hyperquad 2000 program. [b]Data was taken from ref 22b. [c]Data was taken from ref 24.

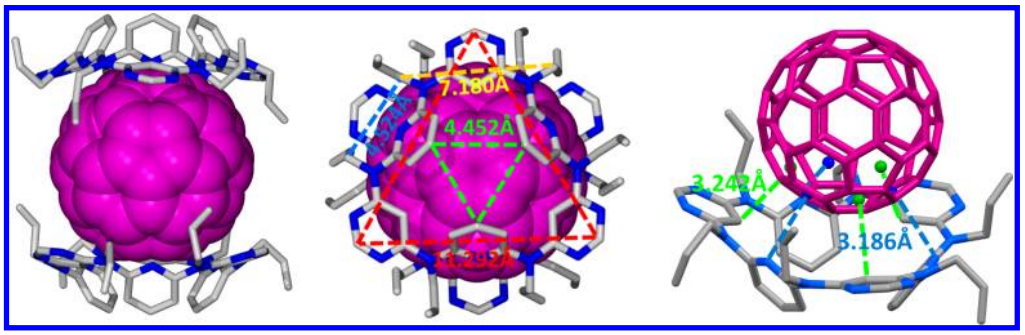

Figure 7. X-ray crystal structure of [$\mathbf{5n}_2$·C_{60}]: (a) side view, (b) top view, and (c) $\pi-\pi$ interaction between C_{60} and one host molecule. All hydrogen atoms are omitted for clarity. The green and cyan balls indicate the centroids of six-membered and five-membered rings of C_{60}, respectively.

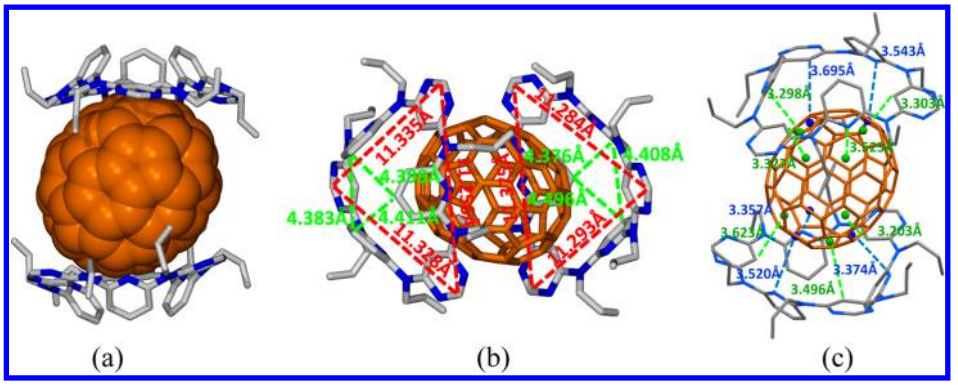

Figure 8. X-ray crystal structure of [$\mathbf{5n}_2$·C_{70}]: (a, b) side views and (c) $\pi-\pi$ interaction between C_{70} and one host molecule. All hydrogen atoms are omitted for clarity. The green and cyan balls indicate the centroids of six-membered and five-membered rings of C_{70}, respectively.

macrocycles **5** and fullerenes were prepared carefully by controlled slow mutual diffusion of fullerene solution in toluene and macrocycle solution in chloroform at ambient temperature. To our delight, high-quality single crystals of the complexes of **5d**, **5f**, **5j**, and **5n** with C_{60} and of **5n** with C_{70} were obtained, and their molecular structures were determined unambiguously by X-ray diffraction analysis. Very interestingly, as X-ray crystallography unveils, complexes of varied host−guest stoichiometric ratios were obtained depending on the structures of macrocyclic hosts. For example, while interaction of methylazacalix[3]arene[3]pyridine **5d** with C_{60} gave a [**5d**·$(C_{60})_2$] complex, *N*-pyrenyl-substituted azacalix[3]pyridine[3]-pyrimidine **5j** complexed with C_{60} to afford [**5j**·C_{60}] complex. In other cases, the 2:1 complexes between other azacalix[3]-pyridine[3]pyrimidine derivatives **5f**, **5n** and fullerenes C_{60} and C_{70} crystallized from the host−guest interactions.

Although complexes of different stoichiometries resulted from crystallization, one noteworthy common feature of almost all complexes is the formation of nearly identical capsule-like structures in which a fullerene guest such as C_{60} or C_{70} is sandwiched by two interdigitated azacalix[6]aromatics hosts. This has been well-illustrated by the X-ray molecular structures

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of [$\mathbf{5n}_2$·C_{60}], [$\mathbf{5n}_2$·C_{70}], [$\mathbf{5f}_2$·C_{60}], and [$\mathbf{5d}$·$(C_{60})_2$], which are depicted in Figures 7−9 and Figure S29 (Supporting Information), respectively.

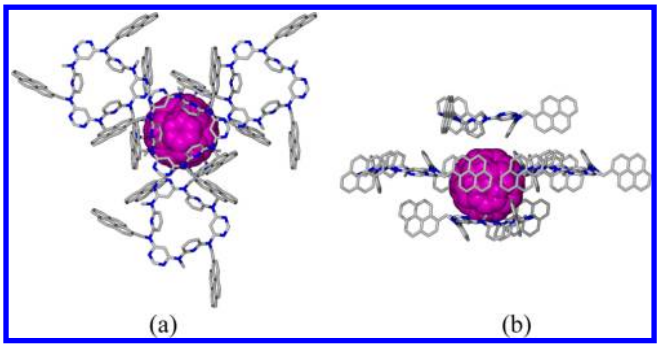

Figure 9. X-ray crystal structure of [$\mathbf{5f}$·C_{60}]: (a) top view, (b) side view. All hydrogen atoms are omitted for clarity.

Some interesting points are worth addressing. Taking the structure of [$\mathbf{5n}_2$·C_{60}] as a representive example (Figure 7), the macrocyclic host in the complex adopts a highly symmetric 1,3,5-altenate conformation with the upper-rim interatomic distances being 11.29 and 4.45 Å in order to achieve maximum contact with the convex of the buckball C_{60}. Each pyrimidine ring of azacalix[3]pyridine[3]pyrimidine interacts with the six-membered ring of the included C_{60}, while each pyridine ring points toward the five-membered ring of the complexed C_{60}. The distances of the lower-rim carbon atom of the pyrimidine ring to the plane of and the centroid of the six-membered ring of C_{60} are 3.22 and 3.24 Å, respectively. The pyridine nitrogen atom is located above the five-membered ring of C_{60} with a distance to the plane and the centroid being 3.18 and 3.19 Å, respectively. All distances are shorter than the sum of van der Waals radii, indicating strong and multiple $\pi-\pi$ interactions between azacalix[3]pyridine[3]pyrimidines and the sandwiched C_{60}. In addition, three alternating methylene units directly connected to the bridging nitrogens also interact with the included C_{60} through weak CH$-\pi$ interactions, as their distances to the nearest C_{60} carbon atoms are around 3.51 Å. Apart from the macrocyclic scaffold, substituents on the bridging nitrogen atoms provide further noncovalent binding sites to interact with fullerene guest, contributing extra driving force to stabilize host−guest complexes. For instance, as evidenced by the distance of the β-carbon atom of the *N*-allyl group to the nearest carbon atom of C_{60}, which equals 3.49 Å, three ethenyl groups form weak $\pi-\pi$ interactions with C_{60} in complex [$\mathbf{5n}_2$·C_{60}].

As C_{70} has a lower symmetric structure than C_{60}, formation of [$\mathbf{5n}_2$·C_{70}] complex along with its X-ray structure determination were significant.[30] It is the first supramolecular structure of a heteracalixaromatics-C_{70} complex reported to date, allowing elucidation of molecular details of noncovalent bond interactions between heteracalixaromatics and C_{70}. Being different from high symmetric [$\mathbf{5n}_2$·C_{60}] in the space group $R\bar{3}$, [$\mathbf{5n}_2$·C_{70}] crystallizes in a triclinic symmetry of $P\bar{1}$. The sandwiched C_{70} reclines between two macrocycle hosts and interacts with them in strikingly different modes. One of the macrocycles uses its pyrimidines and pyridines to interact with the six- and the five-membered rings of C_{70}, respectively. The average distance of the pyridine nitrogen atoms to the planes of their nearest five-membered ring of C_{70} is 3.33 Å, while the average distance between the lower-rim carbon atoms of pyrimidine rings and the planes of their nearest six-membered ring of C_{70} is 3.30 Å. On the other hand, the contacts of the five-membered rings of the C_{70} with one pyrimidine and one pyridine of the other macrocycle were observed. During the meantime, the remaining four aromatic rings of the macrocycle interact with the six-membered ring of the C_{70}. The average distances of the pyridine nitrogen atoms and the lower-rim carbon atoms of pyrimidine rings to their nearest aromatic ring of C_{70} are in the range of 3.19−3.32 Å (Figure 8). In addition to the multiple $\pi-\pi$ interactions between the concave of the host and the convex of the guest, *N*-allyl groups appeared important. The three *cis*-orientated 1,3,5-alternating allyl substituents not only created an expanding concave of heteracalix[6]aromatics **5n**, which fits more favorably the curvature of C_{70}, but also interacted nicely with C_{70} by means of weak $\pi-\pi$ interactions between the alkene moieties and C_{70} as the β-carbon atom of the allyl group is positioned to the nearest carbon atom of C_{70} with a mean distance of 3.43 Å. The outcomes of the aforementioned molecular structures indicate the versatility of azacalix[6]aromatics in forming macrocycle−fullerene complexes. Even with nearly similar 1,3,5-alternate conformations, they are able to fine-tune the concave structure to achieve maximum contacts with fullerenes of different symmetry.

As an exception, the 1:1 complex [$\mathbf{5j}$·C_{60}] formed between *N*-pyrenylmethyl substituted azacalix[3]pyridine[3]pyrimidine **5j** and C_{60} did not involve the sandwiched structure as that observed in other heteracalix[6]aromatics−fullerene complexes. Instead, as indicated by the short interatomic distances in Figure 9, the bottom of the C_{60} guest molecule remains in close contact with the macrocyclic surface of one azacalix[3]pyridine-[3]pyrimidine **5j** through the aforementioned multiple $\pi-\pi$ and CH$-\pi$ interactions. Out of our expectation, none of the three 1,3,5-alternating pyrenes substituted on the bridging nitrogen atoms interacts with the same macrocycle ring-complexed C_{60}. The complexed C_{60} was actually surrounded by three other pyrenes of three neighboring azacalix[3]pyridine-[3]primidines. Furthermore, the top of the complexed C_{60} forms a short contact with the upper-rim carbon atoms of pyridine rings of another azacalix[3]pyridine[3]pyrimidine molecule. If we examined the host molecule in the crystal structure, it is very clear that each *N*-pyrenylmethyl-substituted azacalix[3]pyridine[3]primidine **5j** interacts with five C_{60} molecules using its concave, upper-rim pyridine C−H and three pyrene moieties. Remarkably, the molecular packing gives rise to the array of regular hexagram channels with diameters of their incircles being around 7.80 Å (Figures S33 and S34, Supporting Information). Being an electron-rich aromatic system, pyrene exhibits a beneficial effect in forming a complex with fullerenes. In the formation of 1:1 complex [$\mathbf{5j}$·C_{60}], the designedly introduced pyrene moieties in **5j** did not cooperatively participate in the interactions with the same macrocycle ring-complexed C_{60}. It is most probably the bulkiness of pyrenylmethyl groups that prohibits the favorable all-*cis*-orientation that is a prerequisite for cooperative interactions.

In the case of [$\mathbf{5d}$·$(C_{60})_2$], the only complex having a 1:2 ratio between host and guest, the same sandwiched complexation patter was also observed (Figure S29, Supporting Information). Interestingly, each sandwiched C_{60} was contacted by six C_{60} molecules in a hexagonal manner with the shortest distance between peripheral C_{60} molecules being 3.28 Å and the distance between peripheral C_{60} and the sandwiched C_{60}

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molecules being 3.29 Å (Figure S32, Supporting Information). In other words, in the crystalline state of [**5d**·(C_{60})$_2$], C_{60} molecules assemble into layers that are separated by macrocyclic hosts that form sandwich complexes with hexagonally arranged C_{60} (Figure S32).

As revealed convincingly by the X-ray molecular structures, multiple $\pi-\pi$ interactions are the dominant noncovalent bond interactions between concave azacalix[6]aromatics and convex fullerenes. Both the CH$-\pi$ and the $\pi-\pi$ interactions between substituents on the bridging nitrogen atoms and fullerenes also contribute to the formation of host−guest complexes. The details of the structures of azacalix[6]aromatics−fullerene complexes in solution are hard to know at this stage. Nevertheless, it is the multiple $\pi-\pi$ and CH$-\pi$ interactions between sterically complementary concave and convex that contribute a joint driving force to promote the formation of azacalix[6]aromatics−fullerene complexes in solution. It is most probably that all azacalix[6]aromatics **5**, irrespective of their compositions, adopt nearly identical 1,3,5-altenate conformations to form similar 1:1 complexes with C_{60} or C_{70} in solution; the association constants, therefore, have the same order of magnitude (see Table 1). Slight variations of association constants shown in Table 1 reflect most likely the different electronic effect that resulted from the interplay between varied aromatic rings and the bridging nitrogen atoms. The effect of *N*-substituents on host−guest binding appeared subtle. Although there is no correlation between binding and *N*-substituent, introduction of *N*-pyrenylmethyl has a beneficial effect to enhance the interaction with C_{60} (see entry 10, Table 1).

CONCLUSION

In summary, using [3 + 3] and [2 + 2 + 2] fragment coupling approaches, we have synthesized a number of azacalix[6]-aromatics containing different combinations of benzene, pyridine, and pyrimidine rings and various substituents on bridging nitrogen atoms. In the solid state, they form symmetric to heavily distorted 1,3,5-alternate conformers depending on the nature of aromatic building units, whereas, in solution, they exist probably as a mixture of conformers that undergo rapid interchanges relative to the NMR time scale. By means of fluorescence titration, all macrocycles synthesized were found to form 1:1 complexes with C_{60} and C_{70} in toluene with the association constants in the range of 3.05×10^4 to 7.28×10^4 M^{-1}. Crystallization gave complexes of a 2:1, 1:1, or 1:2 stoichiometric ratio between host and guest. X-ray crystallography revealed in all cases that multiple $\pi-\pi$ and CH$-\pi$ interactions between concave azacalix[6]aromatics and convex fullerenes C_{60} and C_{70} contribute a joint driving force to the formation of host−guest complexes. The outcomes of the study would provide guidelines for the future design and fabrication of heteracalixaromatics that are powerful and selective receptors in the recognition of diverse fullerenes.

EXPERIMENTAL SECTION

General Information. Compounds **1a**,[15a] **1b**,[22b] **1c**,[31] **1d**,[24] **3b**,[22b] **3d**,[15a] **3f-3g**,[24] **4b**,[22b] **4e**,[24] **5b**,[22b] **5e**,[24] and **6a**[22b] were prepared following the reported procedures. All new products were characterized by means of spectroscopic data and microanalysis. Fluorescence titration of azacalix[6]aromatics with fullerenes C_{60} and C_{70} was conducted according to the literature.[22b,28] Single crystals of the complexes between azacalix[6]aromatics and fullerenes C_{60} and C_{70} were cultivated by slow mutual diffusion of fullerene solution in toluene and macrocycle solution in chloroform at ambient temperature.

Preparation of 3a. Under argon protection, a mixture of **1a** (680 mg, 5 mmol) and *m*-dibromobenzene **2a** (2.95 g, 12.5 mmol), $Pd_2(dba)_3$ (690 mg, 0.75 mmol), dppp (615 mg, 1.5 mmol), and sodium *t*-butoxide (1.44 g, 15 mmol) in anhydrous 1,4-dioxane (100 mL) was refluxed for 10 h. The reaction mixture was cooled down to room temperature and filtered through a Celite pad. The filtrate was concentrated under vacuum. The residue was dissolved in dichloromethane (100 mL) and washed with brine (3 × 25 mL). The aqueous phase was re-extracted with dichloromethane (3 × 20 mL), and the combined organic phase was dried over anhydrous $MgSO_4$. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate (v:v = 8:1) as the mobile phase to give product **3a** (876 mg, 39%) as a white powder: mp 85−86 °C; IR (KBr) ν 1593, 1576, 1556, 1483, 1352 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (t, J = 7.8 Hz, 1H), 7.12−7.06 (m, 4H), 6.98 (d, J = 8.1 Hz, 2H), 6.86 (d, J = 7.5 Hz, 2H), 6.78 (s, 2H), 6.75 (d, J = 1.8 Hz, 1H), 3.27 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 149.3, 130.4, 130.3, 123.1, 123.0, 121.3, 117.2, 116.9, 116.5, 40.2; MS (CI) m/z (%) 448 $[M + 4]^+$ (58), 446 $[M + 2]^+$ (100), 444 $[M]^+$ (51), 365 $[M - Br]^+$ (51). Anal. Calcd. for $C_{20}H_{18}Br_2N_2$: C, 53.84; H, 4.07; N, 6.28. Found: C, 53.69; H, 4.11; N, 6.20.

Preparation of 3c. To a solution of 4,6-di(ethylamino)pyrimidine **1c** (1.66 g, 10 mmol) in dry THF (60 mL) at room temperature was added NaH (0.96 g, 40 mmol) slowly, and the mixture was heated to reflux. After 10 h, 4,6-dichloropyrimidine **2c** (5.96 g, 40 mmol) was added to the mixture slowly, and the reaction mixture was refluxed for another 6 h. The reaction mixture was then cooled down to room temperature, and water (1 mL) was added slowly. The solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane (200 mL). The organic solution was washed with brine (3 × 50 mL) and dried over anhydrous $MgSO_4$. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate (v:v = 8:1) as the mobile phase to give pure **3c** (2.71 g, 70%) as a colorless solid: mp 157−158 °C; IR (KBr) ν 1598, 1550, 1442, 1005 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.71 (s, 2H), 7.38 (s, 1H), 7.31 (s, 2H), 4.30 (q, J = 7.2 Hz, 4H), 3.33 (t, J = 6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 161.1, 161.0, 158.4, 158.3, 108.4, 104.2, 42.8, 13.0; MS (CI) m/z (%) 419 $[M + 29]^+$ (22), 392 $[M + 2]^+$ (35), 391 $[M + 1]^+$ (100), 390 $[M]^+$(15). Anal. Calcd. for $C_{16}H_{16}Cl_2N_8$: C, 49.12; H, 4.12; N, 28.64. Found: C, 48.90; H, 4.16; N, 28.67.

Preparation of 3e. Compound **3e** was prepared from 2,6-bis(methylamino)pyridine **1b** (685 mg, 5 mmol) following a similar procedure as that for the synthesis of **3a**. The product was obtained as a white solid (876 mg, 39%): mp 97−98 °C. IR (KBr) ν 3062, 1571, 1456, 1338, 1157 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (s, 2H), 7.21−7.06 (m, 7H), 5.96 (d, J = 8.1 Hz, 2H), 3.35 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 148.3, 138.3, 130.3, 128.6, 127.3, 124.1, 122.5, 98.9, 38.0; MS (CI) m/z (%) 449 $[M + 2]^+$ (7), 447 $[M]^+$ (11), 445 $[M - 2]^+$ (5). Anal. Calcd. for $C_{19}H_{17}Br_2N_3$: C, 51.03; H, 3.83; N, 9.40. Found: C, 50.86; H, 3.82; N, 9.06.

Preparation of 4a. A mixture of **3a** (2.23 g, 5 mmol), methylamine aqueous solution (25−30%) (3 mL), CuI (0.95 g, 0.5 mmol), L-proline (0.115 g, 1 mmol), and K_2CO_3 (2.07 g, 15 mmol) in DMSO (15 mL) was stirred in a sealed tube at 100 °C for 24 h. After the mixture was cooled to room temperature, the mixture was partitioned between ethyl acetate (50 mL) and water (50 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (2 × 25 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate (v:v = 2:1) as the mobile phase to give pure **4a** as a red oil (1.74 g, 100%): IR (KBr) ν 1593, 1576, 1556, 1483, 1352 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (t, J = 8.1 Hz, 1H), 7.08 (t. J = 8.1 Hz, 2H), 6.73 (t, J = 2.1 Hz, 1H), 6.61 (dd, J = 8.1, 2.1 Hz, 2H), 6.39 (dd, J = 8.1, 1.8 Hz, 2H), 6.30 (s, 2H), 6.23 (dd, J = 8.1, 1.5 Hz, 2H), 3.26 (s, 6H), 2.79 (s, 6H); ^{13}C NMR (75 MHz,

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$CDCl_3$) δ 150.2, 150.1, 149.9, 129.8, 129.4, 113.5, 112.9, 110.1, 105.9, 104.9, 40.2, 30.9; MS (CI) m/z (%) 375 $[M + 29]^+$ (18), 347 $[M]^+$ (100). Anal. Calcd. for $C_{22}H_{26}N_4$: C, 76.27; H, 7.56; N, 16.17. Found: C, 76.31; H, 7.51; N, 16.15.

Preparation of 4c. An autoclave equipped with a magnetic stir bar was charged with **3c** (1.95 g, 5 mmol) and 5 mL of ethylamine aqueous solution (55−60%). Then it was heated at 120 °C for 10 h. After the mixture was cooled to room temperature, dichloromethane (100 mL) was added, and the organic phase was washed with brine (3 × 50 mL). The aqueous phase was re-extracted with dichloromethane (3 × 20 mL), and the combined organic phase was dried over anhydrous $MgSO_4$. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate (v:v = 2:1) as the mobile phase to give pure **4c** (2.0 g, 99%) as a white solid: mp 200−201 °C; IR (KBr) ν 3258, 1622, 1566, 1449 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.33 (s, 2H), 7.07 (s, 1H), 6.17 (s, 2H), 4.87 (s, br, 2H), 4.20 (q, J = 6.9 Hz, 4H), 3.36−3.27 (m, 4H), 1.29−1.23 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 161.44, 161.38, 158.1, 158.0, 99.9, 91.0, 42.3, 36.3, 14.6, 13.4; MS (CI) m/z (%) 437 $[M + 29]^+$ (35), 409 $[M + 1]^+$(100), 408 $[M]^+$(18), 379 $[M - C_2H_5]^+$ (28). Anal. Calcd. for $C_{20}H_{28}N_{10}$: C, 58.80; H, 6.91; N, 34.29. Found: C, 58.32; H, 6.89; N, 34.49.

Preparation of 4d. Compound **4d** was prepared from **3d** (2.25 g, 5 mmol) following a similar procedure as that for the synthesis of **4a**. The product was obtained as a brown oil (1.74 g, 100%): IR (KBr) ν 3428, 1577, 1466, 1407, 1121 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31 (t, J = 8.1 Hz, 1H), 7.21−7.16 (m, 3H), 7.03 (dd, J = 8.1, 2.1 Hz, 2H), 5.96 (d, J = 8.1 Hz, 2H), 5.76 (d, J = 7.8 Hz, 2H), 4.32 (s, br, 2H), 3.42 (s, 6H), 2.88 (d, J = 5.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 157.9, 148.0, 138.4, 129.7, 123.3, 121.7, 98.1, 94.5, 37.9, 29.2; MS (CI) m/z (%) 377 $[M + 29]^+$ (100), 349 $[M + 1]^+$ (100). Anal. Calcd for $C_{20}H_{24}N_6$: C, 68.94; H, 6.94; N, 24.12. Found: C, 68.78; H, 6.82; N, 24.01.

General Procedure for the Synthesis of 2-Amino-6-bromopyridines 6b and 6c. An autoclave equipped with a magnetic stir bar was charged with 2,6-dibromopyridine (94.8 g, 400 mmol) and excess amine as solvent (150 mL for **6b**, 100 mL for **6c**). It was then heated at 150 °C for 5 h. After cooling to room temperature, the solvent was removed under reduced pressure, and the residue was dissolved in ether acetate (400 mL). The organic solution was washed with brine (3 × 150 mL), and the organic phase was dried over anhydrous Na_2SO_4. After removal of solvent, the residue was chromatographed on a silica gel column using a mixture of petroleum ether and ethyl acetate (v:v = 20:1) as the mobile phase to give pure product.

6b. Compound **6b** was obtained as an orange oil (70.60 g, 83%): IR (KBr) ν 3303, 1605, 1594, 1528, 1450, 918, 770 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, J = 8.0 Hz, 1H), 6.67 (d, J = 7.6 Hz, 1H), 6.25 (d, J = 8.0 Hz, 1H), 5.84 (m, 1H), 5.32−5.16 (m, 2H), 5.14−5.08 (m, 1H), 3.86 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 140.2, 139.7, 134.4, 116.4, 115.9, 104.6, 44.7. HRMS (FTMS-ESI) calcd. for $C_8H_9BrN_2$: $[M + H]^+$ 213.00274. Found: 213.00270.

6c. Compound **6c** was obtained as a white solid (47.62 g, 48%): mp 80−81 °C; IR (KBr) ν 3286, 1597, 1431, 1094, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.23 (m, 5H), 7.19 (t, J = 7.8 Hz, 1H), 6.74 (d, J = 7.3 Hz, 1H), 6.25 (d, J = 8.2 Hz, 1H), 5.38 (br. s, 1H), 4.48 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 140.3, 139.7, 138.5, 128.8, 127.5, 127.4, 116.2, 104.7, 46.4; MS (APCI) m/z 263 $[M + H]^+$. Anal. Calcd. for $C_{12}H_{11}BrN_2$: C, 54.77; H, 4.21; N, 10.65. Found: C, 54.89; H, 4.22; N, 10.76.

General Procedure for the Synthesis of Dimers 7a−7c. To a solution of 2-amino-6-bromopyridine **6a−6c** (30 mmol) in dry THF (60 mL) at room temperature was added NaH (1.44 g, 60 mmol) slowly, and the mixture was heated to reflux. After 10 h, 4,6-dichloropyrimidine (8.94 g, 60 mmol) was added slowly, and the reaction mixture was refluxed for another 6 h. The reaction mixture was then cooled down to room temperature, and water (1 mL) was added slowly. The solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane (200 mL). The organic solution was washed with brine (3 × 50 mL) and dried over anhydrous $MgSO_4$. After removal of solvent, the residue was chromatographed on a silica gel column using a mixture of petroleum ether and ethyl acetate (v:v = 10:1) as the mobile phase to give pure products.

7a. Compound **7a** was obtained as a white solid (8.01 g, 89%): mp 112−114 °C; IR (KBr) ν 1588, 1574, 1557, 1523, 1489, 1435, 1376, 1162, 1113, 1098, 979, 943 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.36−7.32 (m, 2H), 7.00 (s, 1H), 3.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 160.4, 158.1, 155.5, 140.3, 140.0, 124.7, 117.2, 105.7, 36.2; MS (APCI) m/z 280 $[M + H]^+$. Anal. Calcd. for $C_{17}H_{16}BrN_5$: C, 55.15; H, 4.36; N, 18.92. Found:C, 54.95; H, 4.37; N, 18.52.

7b. Compound **7b** was obtained as a white solid (8.31 g, 72%): mp 69−70 °C; IR (KBr) ν 1585, 1557, 1463, 1432, 1412, 1392, 1334, 1232, 1101 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 0.8 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H), 7.31 (d, J = 7.2 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 6.97 (d, J = 0.8 Hz, 1H), 5.97−5.88 (m, 1H), 5.20−5.15 (m, 2H), 4.77 (dt, J = 4.8 Hz, J = 1.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 160.5, 158.2, 154.8, 140.3, 140.2, 132.4, 124.9, 117.5, 117.3, 106.2, 50.9; MS (APCI) m/z 325 $[M + H]^+$. Anal. Calcd. for $C_{12}H_{10}BrClN_4$: C, 44.27; H, 3.10; N, 17.21. Found: C, 44.66; H, 3.14; N, 17.09.

7c. Compound **7c** was obtained as a white solid (11.24 g, 81%): mp 135−136 °C; IR (KBr) ν 1562, 1523, 1430, 1223, 1100, 977, 929 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.40−7.18 (m, 7H), 6.99 (s, 1H), 4.53 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 160.5, 158.3, 154.8, 140.5, 140.3, 136.9, 128.8, 127.6, 127.3, 125.1, 117.4, 106.3, 51.7; MS (APCI) m/z 375 $[M + H]^+$. Anal. Calcd. for $C_{16}H_{12}BrClN_4$: C, 51.16; H, 3.22; N, 14.91. Found: C, 51.20; H, 3.24; N, 14.97.

General Procedure for the Synthesis of Dimers 8a−8c and 8i−l. An autoclave equipped with a magnetic stir bar was charged with **7a−7c** (10 mmol), water (10 mL), and amines (20 mmol) or aqueous methylamine (33%, 1.88 mL, 20 mmol) or 15 mL of aqueous ammonia solution (25−28%). It was then heated at 120 °C for 10 h (or at 170 °C for 24 h in the case of synthesis of **8l**). After the mixture was cooled to room temperature, dichloromethane (50 mL) was added, and the organic phase was washed with brine (3 × 50 mL). The aqueous phase was re-extracted with dichloromethane (3 × 20 mL), and the combined organic phase was dried over anhydrous $MgSO_4$. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate (v:v = 1:1) as the mobile phase to give products. For **8l**, a mixture DCM and ethyl acetate (v:v = 1:1) was used.

8a. Compound **8a** was obtained as a white solid (2.12 g, 72%): mp 115−116 °C; IR (KBr) ν 3246, 3112, 3007, 1614, 1439, 1300, 1152, 798, 783 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.40 (t, J = 8.0 Hz, 1H), 7.35 (d, J = 7.2 Hz, 1H), 7.10 (d, J = 7.2 Hz, 1H), 5.99 (s, 1H), 5.46 (br. s, 1H), 3.53 (s, 3H), 2.86 (d, J = 5.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 161.8, 157.4, 156.5, 139.4, 122.0, 115.9, 86.2, 35.6, 28.4; MS (ESI) m/z (%) 294 $[M + H]^+$ (100), 296 $[M + 3]^+$ (94). Anal. Calcd. for $C_{11}H_{12}BrN_5$: C, 44.92; H, 4.11; N, 23.81. Found: C, 44.99; H, 4.11; N, 23.51.

8b. Compound **8b** was obtained as a white solid (2.72 g, 85%): mp 132−133 °C; IR (KBr) ν 3227, 3103, 3005, 1606, 1574, 1554, 1478, 1441, 1163, 798, 786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.13 (d, J = 7.6 Hz, 1H), 6.03 (s, 1H), 5.94−5.85 (m, 1H), 5.27 (dd, J_1 = 17 Hz, J_2 = 1.4 Hz, 1H), 5.20−5.17 (m, 2H), 3.89 (t, J = 5.6 Hz, 2H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 161.9, 157.7, 156.6, 139.6, 139.1, 134.0, 122.1, 116.8, 115.9, 87.1, 44.1, 35.6; MS (APCI) m/z 320 $[M + H]^+$. Anal. Calcd. for $C_{13}H_{14}BrN_5$: C, 48.76; H, 4.41; N, 21.87. Found: C, 48.65; H, 4.30; N, 21.69.

8c. Compound **8c** was obtained as a white solid (3.08 g, 84%): mp 145−147 °C; IR (KBr) ν 3209, 2987, 1602, 1569, 1423, 1409, 1277, 1118, 1096, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.37−7.27 (m, 6H), 7.19 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 5.98 (s, 1H,) 5.40 (br.s, 1H), 4.46 (d, J = 6.0 Hz, 2H), 3.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 161.9, 157.8, 156.5, 139.6, 139.1, 138.0, 128.9, 127.7, 127.4, 122.1, 115.8, 87.2, 45.8, 35.5; MS

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(APCI) m/z 370 $[M + H]^+$. Anal. Calcd. for $C_{17}H_{16}BrN_5$: C, 55.15; H, 4.36; N, 18.92. Found: C, 54.95; H, 4.37; N, 18.52.

8i. Compound **8i** was obtained as a white solid (3.30 g, 83%): mp 162−163 °C; IR (KBr) ν 3212, 1600, 1570, 1512, 1424, 1246, 792 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.24−7.21 (m, 3H), 7.11 (d, J = 6.8 Hz, 1H), 6.87 (dt, J_1 = 8.8 Hz, J_2 = 2.6 Hz, 2H), 5.98 (d, J = 0.8 Hz, 1H), 5.36 (br.s, 1H), 4.39 (d, J = 5.6 Hz, 2H), 3.80 (s, 3H), 3.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 161.9, 159.2, 157.6, 156.5, 139.6, 139.1, 129.9, 128.7, 122.1, 115.8, 114.3, 87.2, 55.4, 45.3, 35.6; MS (APCI) m/z 400 $[M + H]^+$. Anal. Calcd. for $C_{18}H_{18}BrN_5O$: C, 54.01; H, 4.53; N, 17.50. Found: C, 54.01; H, 4.52; N, 17.29.

8j. Compound **8j** was obtained as a white solid (2.94 g, 85%): mp 68−69 °C; IR (KBr) ν 3231, 3104, 3078, 3004, 1602, 1571, 1551, 1435, 1328, 1220, 1164, 1136, 931, 918, 781 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.44 (t, J = 7.8 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.13 (d, J = 7.6 Hz, 1H), 6.05 (s, 1H), 5.99−5.84 (m, 2H), 5.26−5.12 (m, 5H), 4.76 (d, J = 5.2 Hz, 2H), 3.87 (t, J = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 161.5, 157.8, 155.8, 139.6, 139.3, 134.0, 133.7, 122.3, 116.8, 116.6, 116.1, 87.5, 50.2, 44.2; MS (APCI) m/z 346 $[M + H]^+$. Anal. Calcd. for $C_{15}H_{16}BrN_5$: C, 52.04; H, 4.66; N, 20.23. Found: C, 52.04; H, 4.66; N, 20.01.

8k. Compound **8k** was obtained as a white solid (1.94 g, 87%): mp 155−156 °C; IR (KBr) ν 3211, 1603, 1589, 1419, 1217, 1190 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.53−7.18 (m, 11H), 7.14 (d, J = 7.6 Hz, 2H), 7.10 (d, J = 8.0 Hz, 1H), 5.96 (s, 1H), 5.79 (br.s, 1H), 5.38 (s, 2H), 4.39 (d, J = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 161.7, 157.9, 155.8, 139.7, 139.3, 138.3, 128.9, 128.6, 127.6, 127.4, 127.2, 127.0, 122.4, 116.1, 87.8, 51.0, 45.8; MS (APCI) m/z 446 $[M + H]^+$. Anal. Calcd. for $C_{23}H_{20}BrN_5$: C, 61.89; H, 4.52; N, 15.69. Found: C, 61.66; H, 4.22; N, 15.63.

8l. Compound **8l** was obtained as a white solid (1.43 g, 83%): mp 185−186 °C; IR (KBr) ν 3198, 1664, 1604, 1579, 1533, 1439, 784 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.48 (t, J = 8.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H), 6.10 (d, J = 0.8 Hz, 1H), 4.80 (br.s, 2H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 162.1, 157.9, 156.4, 139.7, 139.3, 122.6, 116.5, 88.3, 35.7; MS (APCI) m/z 280 $[M + H]^+$. Anal. Calcd. for $C_{10}H_{10}BrN_5$: C, 42.88; H, 3.60; N, 25.00. Found: C, 42.90; H, 3.73; N, 24.73.

General Procedure for the Synthesis of Dimers 8d−8h. To a solution of **8l** (1.40 g, 5 mmol) in dry THF (50 mL) at room temperature was added NaH (180 mg, 7.5 mmol) slowly, and the mixture was heated to reflux. After 10 h, arylmethylene bromide (5.5 mmol) was added to the mixture slowly, and the reaction mixture was refluxed for another 3 h. The reaction mixture was then cooled down to room temperature, and water (0.5 mL) was added slowly. The solvent was removed under reduced pressure, and the residue was dissolved in dichloromethane (50 mL). The organic solution was washed with brine (3 × 20 mL) and dried over with anhydrous $MgSO_4$. After removal of solvent, the residue was chromatographed on a silica gel column using a mixture of petroleum ether and ethyl acetate (v:v = 1:1) as the mobile phase to give pure products.

8d. Compound **8d** was obtained as a white solid (960 mg, 46%): mp 153−155 °C; IR (KBr) ν 3222, 3094, 2990, 1600, 1569, 1423, 1406, 1323, 1117, 983 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.85−7.77 (m, 3H), 7.73 (s, 1H), 7.51−7.46 (m, 1H) 7.43 (dd, J = 8.6 Hz, J = 1.8 Hz, 1H), 7.03−6.96 (m, 3H), 5.98 (s, 1H), 5.58 (br.s, 1H), 4.62 (d, J = 5.6 Hz, 2H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 161.9, 157.9, 156.4, 139.6, 139.0, 135.5, 133.5, 132.9, 128.8, 127.8, 126.5, 126.1, 125.8, 125.3, 122.1, 115.6, 87.5, 46.0, 35.5; MS (APCI) m/z 420 $[M + H]^+$. Anal. Calcd. for $C_{21}H_{18}BrN_5$: C, 60.01; H, 4.32; N, 16.66. Found: C, 60.12; H, 4.36; N, 16.31.

8e. Compound **8e** was obtained as a white solid (1.21g, 58%): mp 154−155 °C; IR (KBr) ν 3220, 1600, 1570, 1472, 1421, 1397 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.26−8.20 (m, 3H), 7.91−7.89 (m, 1H), 7.83 (d, J = 8.0 Hz, 1H) 7.56−7.42 (m, 4H), 7.31 (t, J = 7.8 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 7.6 Hz, 1H), 6.03 (s, 1H), 5.42 (br.s, 1H), 4.91 (d, J = 5.2 Hz, 2H), 3.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 161.8, 157.8, 156.4, 139.6, 139.1, 134.0, 133.1, 131.4, 129.0, 128.6, 126.7, 126.1, 126.0, 125.5, 123.3, 122.2, 115.9, 87.3, 43.8, 35.6; MS (APCI) m/z 420 $[M + H]^+$. Anal. Calcd. for $C_{21}H_{18}BrN_5$: C, 60.01; H, 4.32; N, 16.66. Found: C, 59.60; H, 4.38; N, 16.77.

8f. Compound **8f** was obtained as a white solid (863 mg, 35%): mp 192−193 °C; IR (KBr) ν 3212, 1598, 1567, 1423, 845 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.01−8.00 (m, 1H), 8.15−8.12 (m, 2H), 8.09−8.00 (m, 4H), 7.16−7.09 (m, 2H), 6.94 (dd, J_1 = 7.0 Hz, J_2 = 1.0 Hz, 1H), 6.08 (d, J = 0.8 Hz, 1H), 5.35 (br.s, 1H), 5.17 (d, J = 4.8 Hz, 2H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 162.0, 157.8, 156.5, 139.6, 138.9, 131.4, 131.3, 130.89, 130.86, 128.9, 128.3, 127.6, 127.4, 126.4, 126.2, 125.5, 125.4, 125.2, 124.91, 124.88, 122.5, 122.0, 115.6, 87.6, 44.0, 35.5; MS (APCI) m/z 494 $[M + H]^+$. Anal. Calcd. for $C_{27}H_{20}BrN_5$: C, 65.59; H, 4.08; N, 14.17. Found: C, 65.45; H, 4.07; N, 13.97.

8g. Compound **8g** was obtained as a white solid (785 mg, 35%): mp 97−98 °C; IR (KBr) ν 3247, 1601, 1576, 1553, 1478, 1430, 1409, 1163, 796 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.45 (t, J = 7.8 Hz, 1H), 7.36−7.30 (m, 3H), 7.24−7.20 (m, 3H), 7.14 (d, J = 7.2 Hz, 1H), 6.02 (s, 1H), 4.87 (br.s, 1H), 3.54−3.51 (m, 5H),2.92 (d, J = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 161.9, 157.7, 156.6, 139.6, 139.2, 138.7, 128.9, 128.8, 126.7, 122.1, 115.9, 87.1, 42.8, 35.64, 35.56; MS (APCI) m/z 384 $[M + H]^+$. Anal. Calcd. for $C_{18}H_{18}BrN_5$: C, 56.26; H, 4.72; N, 18.22. Found: C, 56.20; H, 4.78; N, 18.21.

8h. Compound **8h** was obtained as a white solid (630 mg, 35%): mp 142−143 °C; IR (KBr) ν 3222, 2227, 1601, 1570, 1425, 1409 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.28(s, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.43−7.38 (m, 3H), 7.21 (d, J = 7.6 Hz, 1H), 7.13 (d, J = 7.2 Hz,1H), 6.04 (s, 1H), 5.53 (br.s, 1H), 4.58 (d, J = 5.6 Hz, 2H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 161.7, 157.8, 156.4, 144.1, 139.6, 139.3, 132.6, 127.8, 122.5, 118.8, 115.8, 111.4, 87.4, 45.1, 35.7; MS (APCI) m/z 395 $[M + H]^+$. Anal. Calcd. for $C_{18}H_{15}BrN_6$: C, 54.70; H, 3.83; N, 21.26. Found: C, 54.63; H, 3.86; N, 21.33.

General Procedure for the Synthesis of Methylazacalix[6]-aromatics 5a and 5d. Under argon protection, a mixture of **3a** (1 mmol) and **4a** (1 mmol) or a mixture **3e** (1 mmol) and **4d** (1 mmol), $Pd_2(dba)_3$ (138 mg, 0.15 mmol), dppp (123 mg, 0.3 mmol), and sodium *t*-butoxide (288 mg, 3 mmol) in anhydrous 1,4-dioxane (200 mL) was refluxed for 24 h. The reaction mixture was cooled down to room temperature and filtered through a Celite pad. The filtrate was concentrated under vacuum, and the residue was dissolved in dichloromethane (100 mL) and washed with brine (3 × 25 mL). The aqueous phase was re-extracted with dichloromethane (3 × 20 mL), and the combined organic phase was dried over anhydrous $MgSO_4$. After removal of solvent, the residue was chromatographed on a silica gel column using a mixture of petroleum ether and ethyl acetate (v:v = 1:1) as the mobile phase to give the products.

5a. Compound **5a** was obtained as a white solid (144 mg, 23%): mp > 300 °C; IR (KBr) ν 3074, 1589, 1572, 1487, 1115 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.13 (t, J = 7.8 Hz, 6H), 6.63 (t, J = 1.8 Hz, 6H), 6.57 (dd, J = 8.1 Hz, J = 2.1 Hz, 12H), 3.21 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.5, 129.7, 113.02, 113.00, 40.2; MS (MALDI-TOF) m/z 631 $[M + H]^+$. Anal. Calcd. for $C_{42}H_{42}N_6$: C, 79.97; H, 6.71; N, 13.32. Found: C, 79.62; H, 6.74; N, 13.13. Slow evaporation of the solvent from a mixture of CH_2Cl_2 and acetone gave a single crystal suitable for X-ray diffraction analysis.

5d. Compound **5d** was obtained as a colorless block (191 mg, 30%): mp 296−297 °C; IR (KBr) ν 1594, 1575, 1558, 1455, 1158 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38 (t, J = 7.8 Hz, 3H), 7.18 (s, 3H), 7.03 (t, J = 7.8 Hz, 3H), 6.92 (dd, J_1 = 8.1 Hz, J_2 =1.8 Hz, 6H), 6.05 (d, J = 8.1 Hz, 6H), 3.43 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 148.4, 136.8, 130.5, 122.0, 119.0, 101.3, 37.8; MS (MALDI-TOF) m/z 634 $[M + H]^+$. Anal. Calcd. for $C_{39}H_{39}N_9$: C, 73.91; H, 6.20; N, 19.89. Found: C, 73.72; H, 6.19; N, 19.77. Slow evaporation of the solvent from a mixture of CH_2Cl_2 and methanol gave a single crystal suitable for X-ray diffraction analysis.

Preparation of Ethylazacalix[6]pyrimidine 5c. To a solution of **4c** (390 mg, 1 mmol) in dry THF (30 mL) at room temperature was added NaH (180 mg, 7.5 mmol) slowly, and the mixture was heated to

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reflux. After 12 h, the dry toluene (150 mL) and **3c** (408 mg, 1 mmol) were added, and the resulting mixture was refluxed for another 48 h. The reaction mixture was then cooled down to room temperature, and water (1 mL) was added slowly. The solvent was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 (200 mL). The organic solution was washed with brine (3 × 50 mL) and dried over anhydrous $MgSO_4$. After removal of solvent, the residue was chromatographed on a silica gel column using a mixture of petroleum ether and ethyl acetate (v:v = 1:1) as the mobile phase to give pure **5c** (182 mg, 25%) as a white solid: mp 279−280 °C; IR (KBr) ν 1574, 1537, 1470, 1407, 1209 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.55 (s, 6H), 7.02 (s, 6H), 4.22 (q, J = 6.9 Hz, 12H), 1.29 (t, J = 6.9 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6, 158.2, 100.1, 43.0, 13.3; MS (MALDI-TOF) m/z 727 $[M + H]^+$. Anal. Calcd for $C_{36}H_{42}N_{18}$: C, 59.49; H, 5.82; N, 34.69. Found: C, 59.35; H, 5.78; N, 34.83. Slow evaporation of the solvent from a mixture of petroleum ether and ethyl acetate gave a single crystal suitable for X-ray diffraction analysis.

General Procedure for the Synthesis of Azacalix[3]pyridine-[3]pyrimidines 5e−5o. Under argon protection, a mixture of **8a−8k** (2 mmol) and $Pd_2(dba)_3$ (138 mg, 0.15 mmol), dppp (123 mg, 0.3 mmol), and sodium *t*-butoxide (288 mg, 3 mmol) in anhydrous 1,4-dioxane (200 mL) was refluxed for 3 h. The reaction mixture was cooled down to room temperature and filtered through a Celite pad. The filtrate was concentrated under vacuum, and the residue was dissolved in dichloromethane (100 mL) and washed with brine (3 × 25 mL). The aqueous phase was re-extracted with dichloromethane (3 × 20 mL), and the combined organic phase was dried over anhydrous $MgSO_4$. After removal of solvent, the residue was chromatographed on a silica gel column using a mixture of petroleum ether and ethyl acetate (v:v = 1:1) as the mobile phase to give products **5e−5o**.

5e. Compound **5e** was obtained as colorless needles (229 mg, 54%): mp > 300 °C; IR (KBr) ν 1601, 1565, 1525, 1429 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, J = 0.6 Hz, 3H), 7.38 (t, J = 8.1 Hz, 3H), 6.77 (d, J = 8.1 Hz, 6H), 6.47 (s, 3H), 3.57 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 158.8, 156.2, 137.8, 111.6, 92.3, 34.9; MS (MALDI-TOF) m/z 662 $[M + Na]^+$, 640 $[M + H]^+$. Anal. Calcd. for $C_{33}H_{33}N_{15}$: C, 61.96; H, 5.20; N, 32.84. Found: C, 61.99; H, 5.20; N, 32.80.

5f. Compound **5f** was obtained as a colorless block (263 mg, 55%): mp > 300 °C; IR (KBr) ν 1600, 1566, 1523, 1471, 1425, 1224, 1157 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 3H), 7.40 (t, 3H, J = 7.8 Hz), 6.80−6.77 (m, 6H), 6.49 (s, 3H), 6.01−5.91 (m, 3H), 5.16 (dd, 3H, J_1 = 17.2 Hz, J_2 = 1.6 Hz), 5.06 (dd, 3H, J = 10.2 Hz, J = 1.4 Hz), 5.82 (d, 6H, J = 5.6 Hz), 3.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 161.8, 159.1, 156.2, 155.4, 137.7, 134.4, 116.6, 111.8, 111.6, 92.9, 49.4, 34.8; MS (MALDI-TOF) m/z 719 $[M + H]^+$. Anal. Calcd. for $C_{39}H_{39}N_{15}$: C, 65.25; H, 5.48; N, 29.27. Found: C, 65.23; H, 5.54; N, 29.16.

5g. Compound **5g** was obtained as a white solid (301 mg, 52%): mp 161−162 °C; IR (KBr) ν 1600, 1566, 1526, 1437, 1220, 1158 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 3H), 7.37−7.32 (m, 9H), 7.23−7.16 (m, 9H), 6.74 (d, 3H, J = 8.0 Hz), 6.69 (d, 3H, J = 7.6 Hz), 6.51 (s, 3H), 5.43 (s, 6H), 3.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 162.0, 159.1, 156.2, 155.5, 139.0, 137.8, 128.3, 127.9, 126.9, 111.9, 111.6, 93.1, 50.3, 34.8; MS (MALDI-TOF) m/z 869 $[M + H]^+$. Anal. Calcd. for $C_{51}H_{45}N_{15}$: C, 70.57; H, 5.23; N, 24.2. Found: C, 70.44; H, 5.32; N, 23.88.

5h. Compound **5h** was obtained as a white solid (292 mg, 43%): mp 168−169 °C; IR (KBr) ν 3054, 1600, 1565, 1526, 1429, 1400, 1220 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 3H), 7.79−7.70 (m, 12H), 7.55 (dd, 3H, J = 8.4 Hz, J = 1.6 Hz), 7.43−7.38 (m, 6H), 7.34 (t, 3H, 8.0 Hz), 6.77−6.74 (m, 6H), 6.57 (s, 3H), 5.60 (s, 6H), 3.51 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 162.1, 159.1, 156.3, 155.5, 137.8, 136.6, 133.4, 132.7, 127.9, 127.7, 127.6, 126.8, 126.3, 125.9, 125.5, 112.1, 111.7, 93.0, 50.5, 34.8; MS (MALDI-TOF) m/z 1019 $[M + H]^+$. Anal. Calcd. for $C_{63}H_{51}$ shyN_{15}: C, 74.32; H, 5.05; N, 20.63. Found: C, 74.08; H, 5.04; N, 20.59.

5i. Compound **5i** was obtained as a white solid (312 mg, 46%): mp 268−269 °C; IR (KBr) ν 3046, 1599, 1567, 1525, 1474, 1437, 1397, 1221 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 3H), 8.17 (d, 3H, J = 8.0 Hz), 7.83 (d, 3H, J = 8.0 Hz), 7.69 (d, 3H, J = 7.6 Hz), 7.54−7.46 (m, 6H), 7.37 (d, 3H, J = 6.4 Hz), 7.32−7.27 (m, 6H), 6.79 (d, 3H, J = 7.6 Hz), 6.75 (d, 3H, J = 8.0 Hz,), 6.56 (s, 3H), 5.95 (s, 6H), 3.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 159.0, 156.2, 155.1, 138.2, 133.8, 133.7, 131.3, 128.8, 127.5, 126.1, 125.7, 125.3, 124.7, 123.3, 112.9, 112.1, 92.2, 18.2, 34.9; MS (MALDI-TOF) m/z 1019 $[M + H]^+$. Anal. Calcd. for $C_{63}H_{51}N_{15}$: C, 74.32; H, 5.05; N, 20.63. Found: C, 73.93; H, 5.10; N, 20.25.

5j. Compound **5j** was obtained as a white powder (290 mg, 35%): mp 226−227 °C; IR (KBr) ν 3037, 1599, 1566, 1526, 1436, 1220, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 3H), 8.46 (d, 3H, J = 8.8 Hz), 8.16 (m, 6H), 8.10 (d, 3H, J = 9.2 Hz), 8.02−7.95 (m, 15H), 7.16 (t, 3H, J = 7.8 Hz), 6.71 (d, 3H, J = 8.0 Hz), 6.65 (d, 3H, J = 8.0 Hz,), 6.51 (s, 3H), 6.20 (s, 6H), 3.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 162.1, 158.8, 156.3, 155.0, 138.2, 132.0, 131.4, 130.9, 130.5, 128.7, 127.6, 127.4, 127.1, 126.1, 125.9, 125.14, 125.07, 124.95, 124.9, 124.6, 123.0, 113.1, 112.0, 92.4, 48.4, 35.0; MS (MALDI-TOF), *neg* m/z 1238 $[M - H]^-$. Anal. Calcd for $C_{81}H_{57}N_{15}$: C, 78.43; H, 4.63; N, 16.94. Found: C, 78.17; H, 4.70; N, 16.75.

5k. Compound **5k** was obtained as a white solid (249 mg, 41%): mp 280−282 °C; IR (KBr) ν 3030, 2956, 1601, 1566, 1526, 1477, 1435, 1419, 1265, 1233, 1187, 1161, 982 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 3H), 7.41 (t, 3H, J = 8.0 Hz), 7.30−7.17 (m, 15H), 6.79 (d, 3H, J = 8.0 Hz), 6.71 (d, 3H, J = 8.0 Hz,), 6.52 (s, 3H), 4.44 (t, 6H, J = 7.6 Hz), 3.66 (s, 9H), 3.04 (t, 6H, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 161.9, 159.2, 156.2, 155.8, 139.5, 137.4, 129.0, 128.4, 126.2, 111.7, 111.3, 93.0, 49.0, 35.2, 34.7; MS (MALDI-TOF) m/z 910 $[M + H]^+$. Anal. Calcd. for $C_{54}H_{51}N_{15}$: C, 71.27; H, 5.65; N, 23.09. Found: C, 70.95; H, 5.79; N, 22.75.

5l. Compound **5l** was obtained as a colorless block (201 mg, 32%): mp 182−184 °C; IR (KBr) ν 2940, 2227, 1601, 1567, 1527, 1440, 1220, 1166, 983, 964 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 3H),7.54−7.42 (m, 15H), 6.81−6.79 (m, 6H), 6.57 (s, 3H), 5.47 (s, 6H), 3.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 161.7, 159.2, 156.3, 155.2, 144.8, 137.9, 132.2, 128.4, 118.9, 111.9, 111.6, 110.8, 92.9, 50.0, 34.7; MS (MALDI-TOF) m/z 943 $[M + H]^+$. Anal. Calcd. for $C_{54}H_{42}N_{18}$: C, 68.78; H, 4.49; N, 26.74. Found: C, 68.78; H, 4.57; N, 26.46. Slow diffusion of benzene into CCl_4 solution gave a single crystal suitable for X-ray diffraction analysis.

5m. Compound **5m** was obtained as a white powder (294 mg, 46%): mp 151−152 °C; IR (KBr) ν 2948, 2936, 2834,1600, 1565, 1525, 1512, 1436, 1425, 1396, 1246, 1218, 1160 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, 3H, J = 0.8 Hz), 7.35−7.30 (m, 9H), 6.77−6.72 (m, 9H), 6.68 (d, 3H, J = 7.6 Hz), 6.47 (s, 3H), 6.36 (s, 6H), 3.73 (s, 9H), 3.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 161.9, 159.0, 158.6, 156.1, 155.5, 137.8, 131.0, 129.4, 113.6, 112.0, 111.6, 93.2, 55.3, 49.7, 34.9; MS (MALDI-TOF) m/z 958 $[M + H]^+$. Anal. Calcd. for $C_{54}H_{51}N_{15}O_3$: C, 67.70; H, 5.37; N, 21.93.Found: C, 67.92; H, 5.49; N, 21.69.

5n. Compound **5n** was obtained as a colorless block (244 mg, 46%): mp 282−283 °C; IR (KBr) ν 1598, 1567, 1525, 1475, 1444, 1421, 1212, 1157 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 3H), 7.43 (t, 3H, 8.0 Hz), 6.80(d, 6H, J = 8.0 Hz), 6.52 (s, 3H), 6.00−5.90 (m, 3H), 5.13 (dd, 6H, J = 17.0 Hz, J = 1.4 Hz), 5.05 (dd, J = 10.2 Hz, J = 1.4 Hz), 4.79 (d, 12H, J = 4 Hz), 3.73 (s, 9H), 3.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 159.3, 155.5, 137.7, 134.4, 116.6, 111.9, 93.2, 49.3; MS (MALDI-TOF) m/z 796 $[M + H]^+$. Anal. Calcd for $C_{45}H_{45}N_{15}$: C, 67.90; H, 5.70; N, 26.40. Found: C, 67.64; H, 5.60; N, 26.24. Slow evaporation of the solvent from a mixture of petroleum ether and ethyl acetate gave a single crystal suitable for X-ray diffraction analysis.

5o. Compound **5o** was obtained as a white powder (244 mg, 61%): mp 268−269 °C; IR (KBr) ν 3033, 1598, 1565, 1525, 1474, 1440, 1278, 1206, 1162 cm^{-1}; ^1H NMR (400 MHz, d6-DMSO) δ 8.45 (s, 3H), 7.69 (t, 3H, J = 7.6 Hz), 7.18−7.09 (m, 36H), 6.48 (s, 3H), 5.30 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 159.4, 138.8, 137.5, 128.3, 127.7, 126.9, 111.9, 93.4, 50.1; MS (MALDI-TOF) m/z 1096 $[M + H]^+$. Anal. Calcd for $C_{69}H_{57}N_{15}$: C, 75.59; H, 5.24; N, 19.16. Found: C, 75.19; H, 5.31; N, 19.16. Slow evaporation of the solvent

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from a mixture of petroleum ether and ethyl acetate gave a single crystal suitable for X-ray diffraction analysis.

■ ASSOCIATED CONTENT

Supporting Information

Fluorescence titration; X-ray crystallographic files of **5a**−**5d**, **5l**, **5n**, **5o**, [**5d**·$(C_{60})_2$], [**5f**$_2$·C_{60}], [**5j**·C_{60}], [**5n**$_2$·C_{60}], and [**5n**$_2$·C_{70}]; UV−vis spectra of **5a**−**5o**; and ^{1}H and ^{13}C NMR spectra of new products. 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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