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Synthesis and Conformational Study of the First Triply Bridged Calix[6]azatubes

Stéphane Le Gac,† Xianshun Zeng,† Olivia Reinaud,‡ and Ivan Jabin*,†

Faculté des Sciences et Techniques, URCOM, Université du Havre, 25 rue Philippe Lebon, BP 540, 76058 Le Havre Cedex, France, and Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques, UMR CNRS 8601, Université René Descartes, 45 rue des Saints Pères, 75270 Paris Cedex 06, France

ivan.jabin@univ-lehavre.fr

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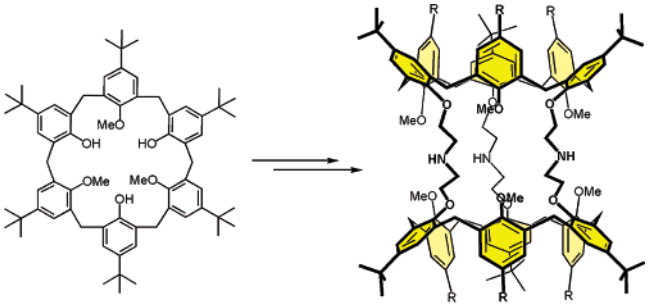

The first C_{3v}- and D_{3h}-symmetrical triply bridged calix[6]azatubes were prepared in good yields from the known 1,3,5-tris-methylated calix[6]arene through an efficient [1 + 1] macrocyclization reaction. A remarkably regioselective hexa *ipso*-nitration reaction led to a calix[6]azatube substituted at the wide rim in alternate position by *t*Bu and nitro groups. A ^{1}H NMR study showed that, whereas the parent bis-calix[6]arenes self-include their methoxy groups, thereby closing their inner tube, the nitro-substituted calix[6]azatube undergoes a conformational change with the expulsion of the methoxy groups, hence presenting a three-dimensional structure open for host−guest applications.

Introduction

Calixarenes are useful building blocks for the design of molecular receptors able to bind neutral or charged species.[1] In this regard, there is currently a growing interest in the preparation of larger polytopic receptors based on covalently linked multiple calixarene subunits.[2] Most of the studies have focused on bis-calix[4]arenes connected via the narrow (tail) or the wide rim (head). The bowl-shaped head-to-head bis-calix[4]arenes have led to molecular receptors for either metal ions,[3] ammonium ions,[4] or anions.[5] They have also been used as stopper units in rotaxanes.[6] In the case of tail-to-tail linkage, the bis-calix[4]arenes, providing two diverging cavities, have been used as tectons for polycap self-assembly.[7] However, because of the small size of their hydrophobic cavities, the two calix[4]arene moieties were mostly employed as platforms for the preorganization of a wider binding site situated in the spacer area. Thus, various selective ionophores have been reported.[8] Interestingly, when

* Phone: +332 32 74 43 99. Fax: +332 32 74 43 91.
† Université du Havre.
‡ Université René Descartes.

(1) For comprehensive reviews on calixarenes, see: (a) Gutsche, C. D. *Calixarenes Revisited, Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, UK, 1998. (b) Mandolini, L., Ungaro, R., Eds. *Calixarenes in Action*; Imperial College Press: London, 2000.

(2) Saadioui, M.; Böhmer, V. In *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, Holland, 2001; pp 130−154.

(3) Struck, O.; Chrisstoffels, L. A. J.; Lugtenberg, R. J. W.; Verboom, W.; van Hummel, G. J.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1997**, *62*, 2487−2493.

(4) (a) Lhotak, P.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 645−648. (b) Arduini, A.; Pochini, A.; Secchi, A. *Eur. J. Org. Chem.* **2000**, 2325−2334. (c) Hwang, G. T.; Kim, B. H. *Tetrahedron Lett.* **2000**, *41*, 5917−5921. (d) Araki, K.; Hayashida, H. *Tetrahedron Lett.* **2000**, *41*, 1209−1213. (e) Araki, K.; Watanabe, T.; Oda, M.; Hayashida, H.; Yasutake, M.; Shinmyozu, T. *Tetrahedron Lett.* **2001**, *41*, 7465−7468.

(5) Beer, P. D.; Gale, P. A.; Hesek, D. *Tetrahedron Lett.* **1995**, *36*, 767−770. Beer, P. D.; Cooper, J. B. *Chem. Commun.* **1998**, 129−130. Cooper, J. B.; Drew, M. G. B.; Beer, P. D. *J. Chem. Soc., Dalton Trans.* **2000**, 2721−2728. Stastny, V.; Lhotak, P.; Michlova, V.; Stibor, I.; Sykora, J. *Tetrahedron* **2002**, *58*, 7207−7211.

(6) Fischer, C.; Nieger, M.; Mogck, O.; Böhmer, V.; Ungaro, R.; Vögtle, F. *Eur. J. Org. Chem.* **1998**, 155−161.

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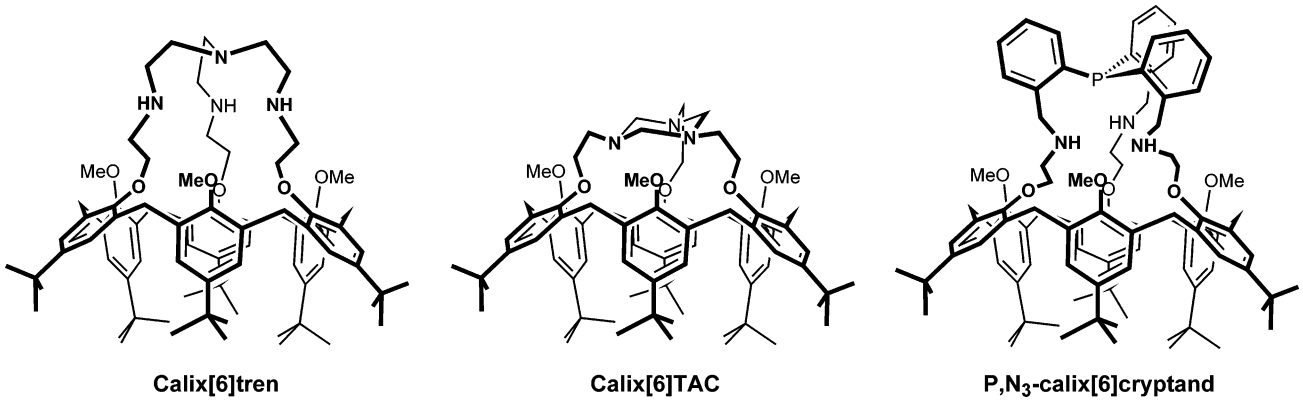


FIGURE 1. Calix[6]aza-cryptands.[16]

these bis-calix[4]arenes are rigidified by multiple ethylene bridges or are in the 1,3-alternate conformation, they possess a tubelike framework. These compounds have been used as potassium channel mimics[9] and as synthetic nanotubes for gaseous molecules[10] or metal ions,[11] respectively. In contrast, little is known about the chemistry of the larger bis-calix[6]arenes,[12] which are generally obtained in low yields. All tail-to-tail bis-calix[6]arene reported so-far are connected by one or two bridges at the most, and only three examples of capsulelike head-to-head double calix[6]arenes have been reported despite their interesting host properties toward ammoniums,[13] neutral guests,[14] or fullerenes.[15] This is attributable to the high flexibility of calix[6]arenes, which makes the control of their linkage particularly difficult. We have recently described a novel class of molecular receptors, the calix[6]aza-cryptands, which are based on a C_{3v}-symmetrical calix[6]arene core rigidified by a tripodal polyaza cap (Figure 1).[16,17] These receptors present remarkable host−guest properties toward neutral organic guests, ammoniums, and metal ions thanks to the aza-cryptand cap that provide an efficient donor binding site. One of our objectives is to extend this research to the design and study of calix[6]azatubes possessing a well defined inner tunnel able to interact with various guests. For this, we wanted to develop a synthetic strategy for the triple-linkage of two calix[6]arene moieties in a tail-to-tail fashion via an aza-cryptand spacer. As the previously reported calix[6]aza-cryptands, such rigidified multitopic receptors should possess versatile binding abilities and allosteric host properties are expected.[18] Moreover, they may constitute ideal tectons for the design of polyrotaxanes or for the self-assembly of organic nanotubes.[19] In this paper, we report the straightforward syntheses and NMR conformational studies of the first triply bridged calix[6]azatubes.

(7) Castellano, R. K.; Rudkevich, D. M.; Rebek, J., Jr. *Proc. Natl. Acad. Sci. U.S.A.* **1997**, *94*, 7132−7137. Rebek, J., Jr. *Chem. Commun.* **2000**, 637−643. Martz, J.; Graf, E.; Hosseini, M. W.; De Cian, A.; Kyritsakas-Gruber, N. *C. R. Chimie* **2002**, *5*, 481−486. Xu, H.; Stampp, S. P.; Rudkevich, D. M. *Org. Lett.* **2003**, *5*, 4583−4586. See also for bis-calix[5]arene tectons: Garozzo, D.; Gattuso, G.; Kohnke, F. H.; Notti, A.; Pappalardo, S.; Parisi, M. F.; Pisagatti, I.; White, A. J. P.; Williams, D. J. *Org. Lett.* **2003**, *5*, 4025−4028.

(8) See ref 2. (a) Ohseto, F.; Shinkai, S. *Chem. Lett.* **1993**, 2045−2048. (b) Schmitt, P.; Beer, P. D.; Drew, M. G. B.; Sheen, P. D. *Tetrahedron Lett.* **1998**, *39*, 6383−6386. (c) Marchand, A. P.; Chong, H.-S.; Takhi, M.; Power, T. D. *Tetrahedron* **2000**, *56*, 3121−3126. (d) Chen, L.; Ju, H.; Zeng, X.; He, X.; Zhang, Z. *Anal. Chim. Acta* **2001**, *447*, 41−46. (e) Kumar, M.; Mahajan, R. K.; Sharma, V.; Singh, H.; Sharma, N.; Kaur, I. *Tetrahedron Lett.* **2001**, *42*, 5315−5318. (f) Budka, J.; Lhotak, P.; Stibor, I.; Michlova, V.; Sykora, J.; Cisarova, I. *Tetrahedron Lett.* **2002**, *43*, 2857−2861. (g) Webber, P. R. A.; Beer, P. D.; Chen, G. Z.; Felix, V.; Drew, M. G. B. *J. Am. Chem. Soc.* **2003**, *125*, 5774−5785. (h) Matthews, S. E.; Rees, N. H.; Felix, V.; Drew, M. G. B.; Beer, P. D. *Inorg. Chem.* **2003**, *42*, 729−734. (i) Mahajan, R. K.; Kaur, I.; Kumar, M. *Sensors Actuators B* **2003**, *91*, 26−31. (j) Kumar, M.; Sharma, V.; Babu, J. N. *Tetrahedron* **2003**, *59*, 3267−3273. (k) Nabeshima, T.; Saiki, T.; Sumitomo, K.; Akine, S. *Tetrahedron Lett.* **2004**, *45*, 4719−4722. (l) Nabeshima, T.; Saiki, T.; Sumitomo, K.; Akine, S. *Tetrahedron Lett.* **2004**, *45*, 6761−6763.

(9) Mattews, S. E.; Felix, V.; Drew, M. G. B.; Beer, P. D. *New J. Chem.* **2001**, *25*, 1355−1358. Mattews, S. E.; Schmitt, P.; Felix, V.; Drew, M. G. B.; Beer, P. D. *J. Am. Chem. Soc.* **2002**, *124*, 1341−1353. Webber, P. R. A.; Cowley, A.; Drew, M. G. B.; Beer, P. D. *Chem. Eur. J.* **2003**, *9*, 2439−2446.

(10) Zyryanov, G. V.; Rudkevich, D. M. *J. Am. Chem. Soc.* **2004**, *126*, 4264−4270.

(11) Ikeda, A.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1994**, 2375−2376. Kim, S. K.; Sim, W.; Vicens, J.; Kim, J. S. *Tetrahedron Lett.* **2003**, *44*, 805−809. For a 1,3-alternate trimeric thiacalix[4]crown tube, see also: Kim, S.; Lee, J. K.; Lee, S. H.; Lim, M. S.; Lee, S. W.; Sim, W.; Kim, J. S. *J. Org. Chem.* **2004**, *69*, 2877−2880.

(12) (a) Aleksiuk, O.; Biali, S. E. *J. Org. Chem.* **1996**, *61*, 5670−5673. (b) Bottino, A.; Cunsolo, F.; Piattelli, M.; Garozzo, D.; Neri, P. *J. Org. Chem.* **1999**, *64*, 8018−8020. (c) Li, J.-S.; Chen, Y.-Y.; Lu, X.-R. *Eur. J. Org. Chem.* **2000**, 485−490. (d) Zang, W.-C.; Zhu, Y.; Li, E.-C.; Liu, T.-J.; Huang, Z.-T. *Tetrahedron* **2000**, *56*, 3365−3371. (e) Santoyo-Gonzalez, F.; Torres-Pinedo, A.; Sanchéz-Ortega, A. *J. Org. Chem.* **2000**, *65*, 4409−4414.

(13) Arduini, A.; Ferdani, R.; Pochini, A.; Secchi, A. *Tetrahedron* **2000**, *56*, 8573−8577.

(14) Arimura, T.; Matsumoto, S.; Teshima, O.; Nagasaki, T.; Shinkai, S. *Tetrahedron Lett.* **1991**, *32*, 5111−5114.

(15) Wang, J.; Gutsche, C. D. *J. Am. Chem. Soc.* **1998**, *120*, 12226−12231.

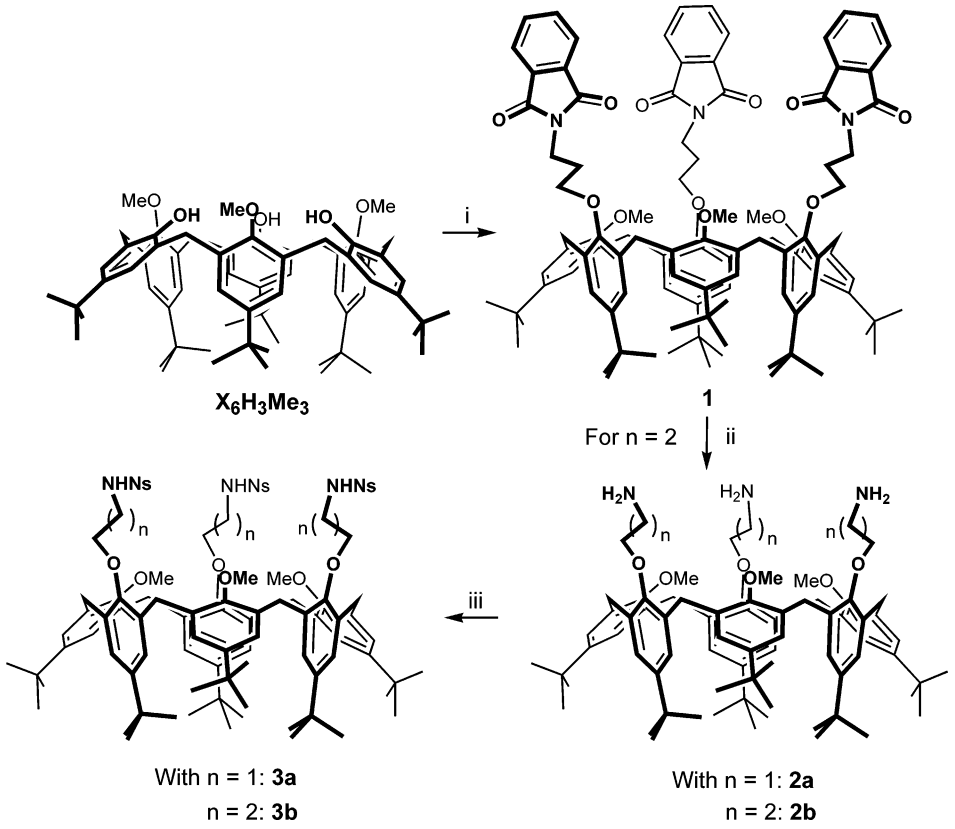
(16) For references on calix[6]tren, see: (a) Jabin, I.; Reinaud, O. *J. Org. Chem.* **2003**, *68*, 3416−3419. (b) Darbost, U.; Zeng, X.; Rager, M.-N.; Giorgi, M.; Jabin, I.; Reinaud, O. *Eur. J. Inorg. Chem.* **2004**, 4371−4374. For a reference on calix[6]TAC, see: (c) Darbost, U.; Giorgi, M.; Reinaud, O.; Jabin, I. *J. Org. Chem.* **2004**, *69*, 4879−4884. For a reference on PN_3-calix[6]cryptand, see: (d) Zeng, X.; Hucher, N.; Reinaud, O.; Jabin, I. *J. Org. Chem.* **2004**, *69*, 6886−6889.

(17) For leading references on the rigidification of calix[6]arenes by a metal ion, see: Blanchard, S.; Le Clainche, L.; Rager M.-N.; Chansou, B.; Tuchagues, J.-P.; Duprat, A. F.; Le Mest, Y.; Reinaud, O. *Angew. Chem., Int. Ed.* **1998**, *37*, 2732−2735. Sénèque, O.; Rager, M.-N.; Giorgi, M.; Reinaud, O. *J. Am. Chem. Soc.* **2000**, *122*, 6183−6189. Le Clainche, L.; Giorgi, M.; Reinaud, O. *Inorg. Chem.* **2000**, *39*, 3436−3437. Rondelez, Y.; Bertho, G.; Reinaud O. *Angew. Chem., Int. Ed.* **2002**, *41*, 1044−1046. Rondelez, Y.; Rager, M.-N.; Duprat, A. F.; Reinaud O. *J. Am. Chem. Soc.* **2002**, *124*, 1334−1340. Sénèque, O.; Giorgi, M.; Reinaud, O. *Supramol. Chem.* **2003**, *15*, 573−580. Sénèque, O.; Campion, M.; Douziech, B.; Giorgi, M.; Le Mest, Y.; Reinaud, O. *J. Chem. Soc., Dalton Trans.* **2003**, 4216−4218.

(18) Lehn, J.-M. *Supramolecular Chemistry, Concepts and Perspectives*; VCH: Weinheim, Germany, 1995.

(19) For a comprehensive review on organic nanotubes, see: Bong, D. T.; Clark, T. D.; Granja, J. R.; Ghadiri, M. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 988−1011.

SCHEME 1[a]



[a] Conditions: (i) *N*-(3-bromopropyl)phthalimide, NaH, THF, reflux, 82%; (ii) $NH_2NH_2{\cdot}H_2O$, EtOH, reflux, 98%; (iii) NsCl, TEA, CH_2Cl_2, rt, 95% (**3a**) and 88% (**3b**).

Results

Synthesis of D_3h- and C_3v-Symmetrical Calix[6]-azatubes. A general route for the syntheses of aza-bridged bis-calix[4]arenes consists of the connection of two diaminocalix[4]arene units with a bis-electrophile. In this regard, [2 + 2] condensation with various dialdehydes have been proved to be efficient.[20] However, such a strategy was inappropriate for the synthesis of bis-calix-[6]arenes connected by covalent bridges containing only one nitrogen atom per link. The synthesis of the previously reported calix[6]tren[16a] (Figure 1) was achieved via a [1 + 1] macrocyclization reaction between a 1,3,5-tris-tosylated calix[6]arene **4** and a tren unit bearing 2-nitrobenzenesulfonyl groups (i.e., nosyl groups = Ns). We decided to attempt the syntheses of the N_3-bis-calix[6]-arenes via a similar key step, i.e., by reacting synthon **4** with calix[6]tris-amines bearing Ns groups (**3a**,**b**) (Scheme 1). For this purpose, it was necessary to prepare the calix-[6]tris-amine **2b**, while the synthesis of the calix[6]tris-amine **2a** was previously reported through a straightforward pathway[16c] (77% overall yield) from the known symmetrically 1,3,5-tris-O-methylated calix[6]arene,[21] namely $X_6H_3Me_3$. The classical Gabriel two-step sequence was used for the preparation of the calix[6]tris-amine **2b**. First, $X_6H_3Me_3$ was reacted with a large excess of *N*-(3-bromopropyl)phthalimide in the presence of a strong base (NaH) giving the N-protected calix[6]tris-amine **1** in 82% yield after flash chromatography purification. A subsequent reaction with hydrazine afforded the required calix[6]tris-amine **2b** in high yield (98%). Thus, new synthon **2b** was obtained in a 80% overall yield from $X_6H_3Me_3$. Finally, reaction between calix[6]tris-amines **2a**,**b** and a slight excess of 2-nitrobenzenesulfonyl chloride (NsCl) in the presence of triethylamine (TEA) afforded the N-protected calix[6]tris-amines **3a**,**b** in good yields (95 and 88%, respectively) (Scheme 1).

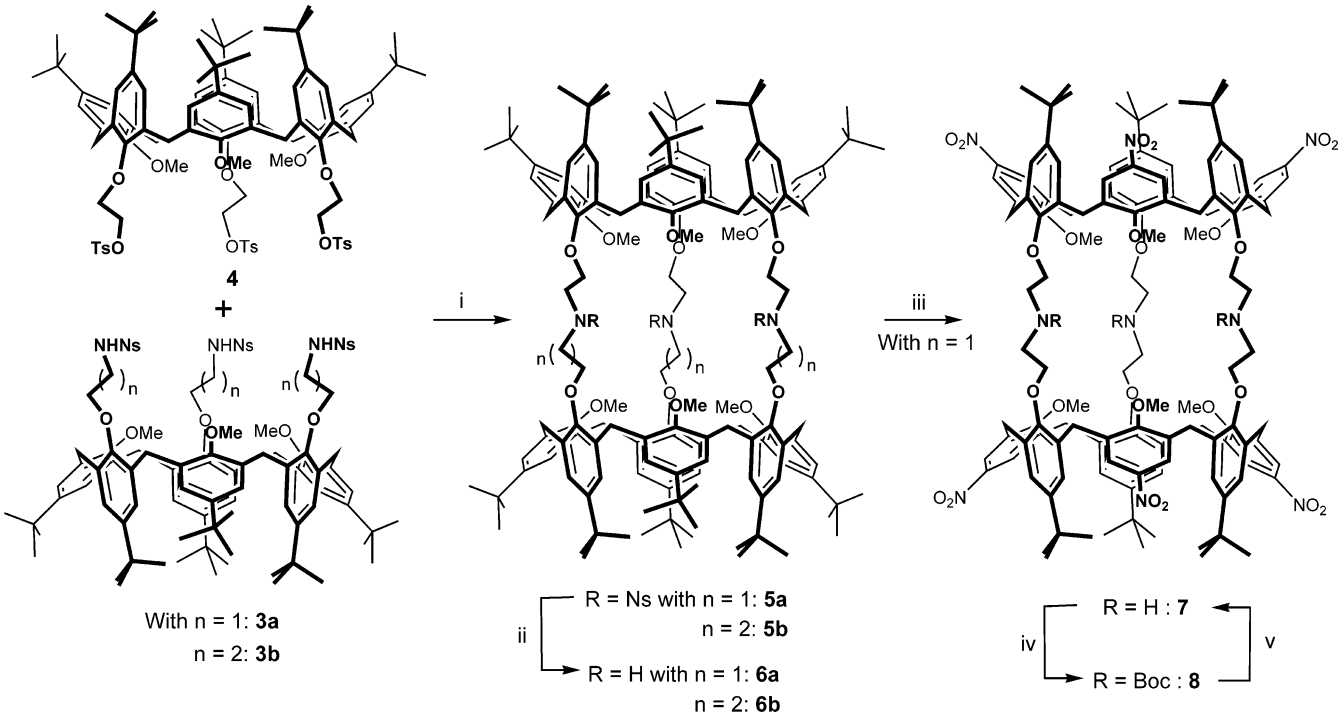
The ^{1}H NMR spectra of new compounds **1**, **2b**, and **3a**,**b**, recorded in $CDCl_3$, are all characteristic of a major flattened cone conformation with C_{3v} symmetry. All the signals were attributed through two-dimensional NMR experiments (HMQC, HMBC). In the cases of compounds **1** and **3a**,**b**, minor dissymmetrical conformers are observed (see Supporting Information) as it is often the case when the calix[6]arene core is substituted with bulky arms.[22] The axial and equatorial ArCH_2Ar protons of **1** and **3a**,**b** give differentiated doublets showing that the cone−cone interconversion is slower than the NMR time scale, thanks to the presence of large substituents on the nitrogenous arms. This stands in contrast to the more flexible **2b**, which presents a broad and unique signal

(20) See refs 4c and 8e,i,j.

(21) Janssen, R. G.; Verboom, W.; Reinhoudt, D. N.; Casnati, A.; Freriks, M.; Pochini, A.; Uggozoli, F.; Ungaro, R.; Nieto, P. M.; Carramolino, M.; Cuevas, F.; Prados, P.; de Mendoza, J. *Synthesis* **1993**, 380−386.

(22) In the cases of compounds **3a**,**b**, no coalescence was observed between the signals of the major and minor species over a 293−370 K temperature range (^{1}H NMR, 300 MHz, DMSO-d_6), suggesting that these two species are more likely diastereomers than conformers. For a review on the conformational properties of calix[6]arenes, see: Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713−1734.

SCHEME 2[a]



[a] Conditions: (i) K_2CO_3, Cs_2CO_3, DMF (anhydrous), 90 °C, 42% (**5a**) and 34% (**5b**); (ii) K_2CO_3, PhSH, DMF (anhydrous), 140 °C, 92% (**6a**) and 90% (**6b**); (iii) HNO_3/AcOH (1:1), CH_2Cl_2, 0 °C then rt; (iv) Boc_2O, TEA, CH_2Cl_2, 0 °C then rt, 35% (overall yield from **6a**); (v) TFA, CH_2Cl_2, rt, then CH_2Cl_2, NaOH, 99%.

for all the bridging methylene ArC*H*$_2$Ar protons.[23] In all cases, the methoxy groups are projected toward the inside of the cavity as indicated by their high-field resonances ($\delta_{OMe} = 2.09-2.40$ ppm), while their bulkier nitrogenous arms are rejected outside.

Key step [1 + 1] macrocyclization reactions between tris-tosylated calix[6]arene **4** and N-protected calix[6]tris-amines **3a**,**b** were conducted under basic conditions (Cs_2CO_3/K_2CO_3 mixture) in anhydrous DMF (Scheme 2). A study showed that the yields were highly dependent on the Cs_2CO_3/calix ratio, which suggests a role of template for the cesium cation. Thus, a 1:6:2 Cs_2CO_3/K_2CO_3/**3a**,**b** ratio led to the best yields of bis-calix[6]arene **5a**,**b** after flash chromatography purification (42 and 34%, respectively). In the course of our research toward the synthesis of novel calix[6]aza-cryptands, we tested different tripodal amines protected by Ns groups [i.e., $CH_3C(CH_2NHNs)_3$, *cis*-1,3,5-tris-NHNs-cyclohexane] under the same reaction conditions with the tris-tosylated calix[6]arene **4**, and only calix[6]tris-amines **3a**,**b** displayed such a high reactivity. This shows that the [1 + 1] macrocyclization requires the selection of a tripodal partner that fits perfectly from a geometrical point of view with **4**. Deprotection of the amino groups was performed by SNAr substitution of the Ns groups by thiophenate, giving the desired N_3-bis-calix[6]arenes **6a**,**b** in high yields (92 and 90%, respectively). It is noteworthy that these deprotection reactions have to be performed at an unusually high temperature (140 °C), which suggests that the approach of the Ns groups is sterically difficult.

We were also interested in evaluating the conformational impact of the nature of the wide rim substituents of the calix[6]azatubes. Hence, bis-calix[6]arene **6** was regioselectively nitrated[24] at 1,3,5,1′,3′,5′-positions, leading to compound **7**, which is the major calixarene-type product observed by ^{1}H NMR analysis of the crude material. Compound **7** was purified through a two-step protection−deprotection sequence, as its crystallization or chromatography remained unsuccessful in our hands. Thus, crude **7** was converted into its carbamate derivative **8**, which was isolated by flash chromatography on silica gel. The 35% overall yield from **6a** emphasizes the remarkable regioselectivity of the hexanitration process. Final deprotection of the amino groups with trifluoroacetic acid (TFA) led to pure compound **7**[25] in a quantitative yield (Scheme 2).

NMR Characterization and Conformational Study of the Calix[6]azatubes. The ^{1}H NMR spectra of bis-calix[6]arenes **5a**,**b**, **6a**,**b**, and **7** (see Figure 2a−c for the spectra corresponding to **6a**,**b** and **7**) reflect very simple D_{3h} (in the case of **5a**, **6a**, and **7**) or C_{3v} (in the case of **5b** and **6b**) symmetrical signatures.[26] In each case, all the

(23) A similar NMR fact was observed for compound **2a**. See ref 16c.

(24) Redon, S.; Li, Y.; Reinaud, O. *J. Org. Chem.* **2003**, *68*, 7004−7008.

(25) Compound **7** was characterized in parts (mass spectroscopy, mp, IR) through its salt derivative, namely, **7.3TFA**. We were unable to obtain reproducible elemental analyses of bis-calix[6]arenes **7** or **7.3TFA**, certainly because of their host−guest properties toward small molecules of the solvent. However, correct elemental analysis of the derivative **8** was successfully obtained (See Experimental Section).

(26) In the case of the bis-calixarene **8**, its ^{1}H NMR spectrum, recorded at room temperature in $CDCl_3$, reflects an unsymmetrical calixarene structure. However, a variable-temperature ^{1}H NMR study has shown that **8** displayed a D_{3h} symmetrical signature at 330 K (See Supporting Information). The loss of symmetry at room temperature may be due to a different *Z*/*E* stereochemistry adopted by one of the Boc groups compared to the other two. It is noteworthy that a similar NMR fact was also observed on a closely related structure, i.e., a PN_3-calix[6]arene N-protected by Boc groups (See ref 16d).

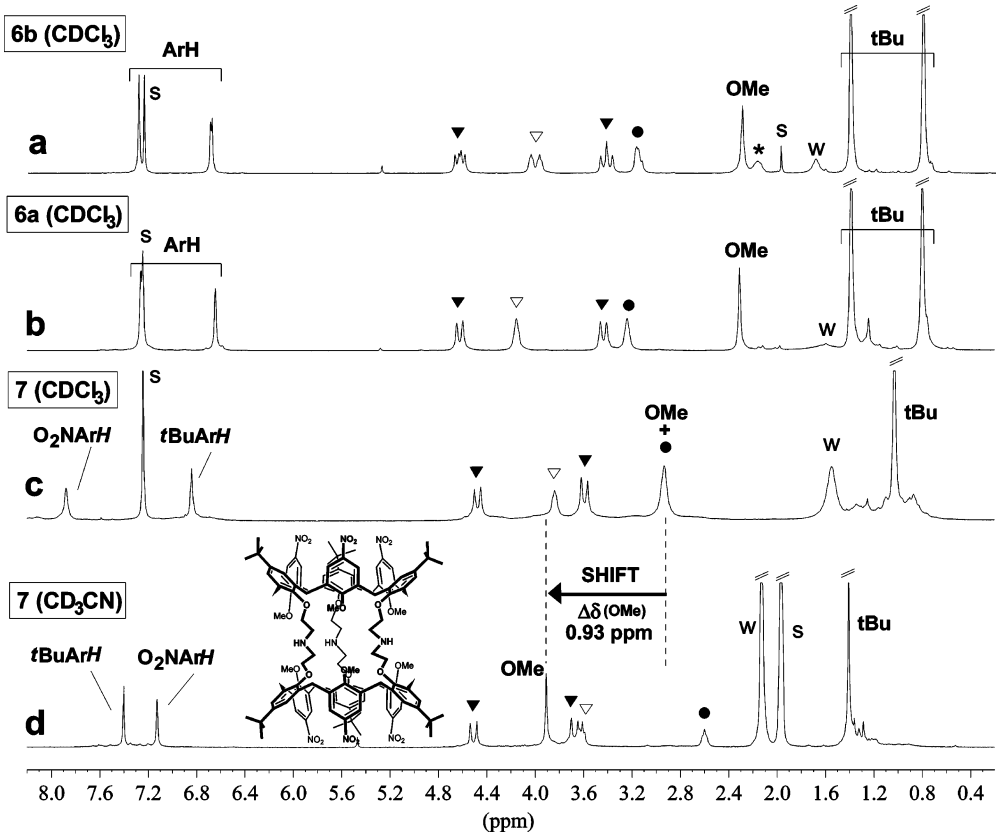


FIGURE 2. ^{1}H NMR spectra (300 MHz) recorded at 313 K of (a) bis-calix[6]arene **6b** in $CDCl_3$; (b) bis-calix[6]arene **6a** in $CDCl_3$; (c) bis-calix[6]arene **7** in $CDCl_3$; (d) bis-calixarene **7** in CD_3CN. ▼, $ArCH_2$; ▽, CH_2O; ●, CH_2N; *, CH_2CH_2N. Residual solvent and water are labeled S and W, respectively.

signals were assigned through two-dimensional NMR spectroscopy (HMQC and HMBC). First evidence for the formation of dimeric species was obtained by mass spectroscopy and ^{1}H NMR spectra of compounds **5a**,**b** and **6b**.[27] Indeed, integrations of the signals belonging to the Ns groups of **5a**,**b** compared to those of the calixarene cores showed a 1:2 Ns/calixarene ratio. Bis-calix[6]arenes **5b** and **6b** display spectra with two sets of signals corresponding to the two unequivalent calixarene cores. All compounds (**5a**,**b**, **6a**,**b**, and **7**) present well-defined doublets for their $ArCH_2Ar$ protons, in agreement with the inhibition of the cone−cone interconversion. The large splits between the Ar*H* signals of the same calixarene core ($\Delta\delta_{ArH} = 0.60$, 0.61, and 1.03 ppm in the case of **6a**,**b** and **7**, respectively) indicate that the calixarene structures adopt a pinched cone conformation. The aromatic walls lie alternatively in *in* and *out* positions relative to the cavity with the methoxy groups of the anisole units projected toward the inside of the cavity ($\delta_{OMe} = 2.29$, 2.28, and 2.97 ppm in the case of **6a**,**b** and **7**, respectively). A similar alternate conformation has been previously reported on a closely related self-assembled dimer[28] and on a covalent head-to-head double calix[6]arene,[13] both deriving from $X_6H_3Me_3$. In both cases, it was shown that the permanent filling of the cavity by the methoxy groups of the anisole moieties prevents guest inclusion. Therefore, some interesting NMR data should be emphasized in the case of the bis-calix[6]arenes **6a**,**b**, **7**:

(i) The addition of an increasing amount of CD_3CN into a solution of **7** in $CDCl_3$ led to a progressive high-field shift of its O_2NArH and CH_2N signals and a downfield shift of its OMe, *t*Bu, and *t*BuAr*H* signals. When the spectrum of **7** was recorded in pure CD_3CN (Figure 2d), the methoxy groups were observed at a normal resonance ($\delta_{OMe} = 3.90$), showing that they were completely rejected from the hydrophobic cavity. In contrast, such a conformational change was not observed with the bis-calix[6]arenes **6a**,**b** upon the addition of CD_3CN.

(ii) A variable-temperature ^{1}H NMR study in $CDCl_3$ showed that the spectra of compounds **6a**,**b** were barely affected in the whole temperature range (223−330 K), while broad and ill-defined spectra were observed for bis-calix[6]arene **7** below 260 K.

(iii) Two-dimensional NOESY spectra of compound **7** either in $CDCl_3$ or in CD_3CN revealed strong interactions between the O_2NArH and *t*BuAr*H* protons, confirming that **7** adopts a classical pinched cone conformation in both solvents (See Supporting Information).

All these NMR observations indicate that, in contrast to compounds **6a**,**b**, the calixarene framework of **7** can switch from one alternate conformation to the other, the MeO groups adopting either an *in* or an *out* position (which correspond to the structures displayed in Scheme 2 and in Figure 2d, respectively). Indeed, the reduced bulkiness of the nitro substituents compared to the *t*Bu groups stands in favor of their *in* position and explains

(27) In addition, elemental analyses were compatible with the formation of the dimeric species (See Experimental Section).

(28) Rincon, A. M.; Prados, P.; de Mendoza, J. *Eur. J. Org. Chem.* **2002**, 640−644.

the conformational flip of the aromatic walls of **7** in CD_3CN, with possible inclusion of solvent molecules. It also shows that the flexibility of the *whole* calix[6]azatube skeleton is highly dependent on the nature of the wide rim substituents and that *ipso*-nitration provides an efficient way to the opening of the calix[6]azatubes.

Conclusion

In conclusion, a new calix[6]tris-amine synthon **2b** was prepared in high yield through an efficient two-step sequence from the known $X_6H_3Me_3$. Efficient key step [1 + 1] macrocyclization reactions between the *N*-Ns calix[6]tris-amines **3a**,**b** and the tris-tosylated calix[6]arene **4** led to the first C_{3v}- and D_{3h}-symmetrical triply bridged bis-calix[6]arenes **5a**,**b** and **6a**,**b**. The dimeric nature of the double calix[6]arenes was evidenced by NMR analyses. *ipso*-Nitration of **6a** led to its hexanitro D_{3h}-symmetrical derivative, calix[6]azatube **7**, with a remarkable selectivity. In contrast to compounds **5** and **6**, a ^{1}H NMR study showed that **7** can present an open tubelike cavity with its MeO groups rejected away from the C_3 axis. This unique conformational property of calix[6]azatube **7** is very promising for host−guest applications that are now under investigation in our laboratories.

Experimental Section

5,11,17,23,29,35-Hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-tris(3-(1,3-dioxoisoindolin-2-yl)propoxy)calix[6]arene 1. $X_6Me_3H_3$ (5.08 g, 5.00 mmol) and *N*-(3-bromopropyl)-phthalimide (13.40 g, 49.98 mmol) were added successively to a solution of NaH (60% in oil, 1.80 g, 45.00 mmol) in anhydrous THF (250 mL). The reaction mixture was refluxed for 15 h. After removal of the solvent under reduced pressure, the resulting residue was dissolved with CH_2Cl_2 (100 mL), and water (100 mL) was added. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (50 mL × 2). The organic phases were combined, washed with water (50 mL × 2), and dried with $MgSO_4$. After filtration and removal of the solvent under reduced pressure, the crude residue was purified by column chromatography (CH_2Cl_2/acetone; 19:1), giving the amino-protected calixarene **1** (6.46 g, 82%) as a white solid. Mp: 230−232 °C. IR (KBr): ν 3703 to 3115, 1711 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.76 (s, 27 H, *t*Bu), 1.38 (s, 27H, *t*Bu), 2.09 (s, 9H, OCH_3), 2.30 (t, 6H, J = 7 Hz, CH_2CH_2N), 3.38 (d, 6H, J = 15 Hz, ArCH_{eq}), 3.90−4.05 (m, 12H, OCH_2 + NCH_2), 4.54 (d, 6H, J = 15 Hz, ArCH_{ax}), 6.60 (s, 6H, ArH_{calix}), 7.24 (s, 6H, ArH_{calix}), 7.71 (dd, 6H, J_1 = 3 Hz, J_2 = 5 Hz, ArH_{arm}), 7.86 (dd, 6H, J_1 = 3 Hz, J_2 = 5 Hz, ArH_{arm}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.6, 31.1, 31.6, 33.9, 34.2, 35.7, 60.0, 70.7, 123.3, 123.4, 127.9, 132.2, 133.0, 133.6, 133.8, 145.6, 157.8, 154.4, 168.3. Anal. Calcd for $C_{102}H_{117}N_3O_{12}\cdot 2H_2O$: C, 76.81; H, 7.52; N, 2.63. Found: C, 76.51; H, 7.52; N, 2.41.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-tris(3-amino-propoxy)calix[6]arene 2b. Hydrazine monohydrate (13.30 mL, 273.65 mmol) was added to a solution of compound **1** (7.65 g, 4.85 mmol) in ethanol (200 mL). The reaction mixture was refluxed for 12 h and then cooled to room temperature. Water (300 mL) was added, and the resulting precipitate was extracted into CH_2Cl_2 (50 mL × 4). The organic phases were combined and dried with $MgSO_4$. After filtration, removal of the solvent under reduced pressure afforded pure calix[6]tris-amine **2b** (5.64 g, 98%) as a white solid. Mp: 177−178 °C. IR (KBr): ν 3698 to 3099, 1482, 1202 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 320 K): δ 0.90 (s, 27H, *t*Bu), 1.38 (s, 27H, *t*Bu), 1.96 (t, 6H, J = 6 Hz, CH_2CH_2N), 2.40 (s_b, 9H, OCH_3), 2.99 (t, 6H, J = 6 Hz, CH_2N), 3.80−4.20 (s_b, 12H, ArCH_{eq} + ArCH_{ax}), 3.93 (t, 6H, J = 6 Hz, OCH_2), 6.75 (s, 6H, ArH), 7.26 (s, 6H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.9, 31.2, 31.6, 33.9(8), 34.0(4), 34.2, 39.6, 60.1, 70.8, 124.0, 127.7, 133.1, 133.5, 145.6, 145.8, 152.0, 154.3. Anal. Calcd for $C_{78}H_{111}N_3O_6\cdot H_2O\cdot CH_2Cl_2$: C, 73.57; H, 8.99; N, 3.26. Found: C, 73.75; H, 9.01; N, 3.07.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-tris(2-(2-nitro-benzenesulfonamide)ethoxy)calix[6]arene 3a. At 0 °C, 2-nitro-benzenesulfonyl chloride (0.70 g, 3.16 mmol) was added in small portions to a solution of calix[6]tris-amine **2a** (1.10 g, 0.96 mmol) and TEA (0.56 mL, 3.98 mmol) in anhydrous CH_2Cl_2 (20 mL). After 16 h at room temperature, the reaction mixture was diluted with CH_2Cl_2 (80 mL) and washed with water (20 mL) and the aqueous layer was extracted with CH_2Cl_2 (20 mL × 3). After evaporation of the solvent, ethanol (5 mL) was added at 0 °C on the crude product and the resulting solid was isolated by filtration, yielding compound **3a** (1.55 g, 95%) as a pale yellow solid. Mp: 227−228 °C. IR (KBr): ν 3690 to 3125, 1543, 1362, 1171 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.76 (s, 27H, *t*Bu), 1.33 (s, 27H, *t*Bu), 2.21 (s, 9H, OMe), 3.21 (d, J = 15 Hz, 6H, ArCH_{eq}), 3.68 (q, J = 5 Hz, 6H, CH_2N), 3.99 (s_b, 6H, CH_2O), 4.26 (d, J = 15 Hz, 6H, ArCH_{ax}), 6.37 (t, J = 6 Hz, 3H, NH), 6.60 (s, 6H, ArH_{calix}), 7.14 (s, 6H, ArH_{calix}), 7.49 (t, J = 7 Hz, 3H, ArH_{arm}), 7.65−7.80 (m, 6H, ArH_{arm}), 8.19 (d, J = 7 Hz, 3H, ArH_{arm}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.4, 31.0, 31.6, 33.9, 34.2, 44.4, 60.0, 70.3, 123.8, 125.9, 127.7, 130.6, 132.7, 132.8, 133.3, 133.4, 134.0, 145.9, 146.2, 148.0, 150.6, 154.0. Anal. Calcd for $C_{93}H_{114}N_6O_{18}S_3\cdot 3H_2O$: C, 63.68; H, 6.90; N, 4.79. Found: C, 63.58; H, 6.62; N, 4.62.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-tris(3-(2-nitro-benzenesulfonamide)propoxy)-calix[6]arene 3b. The calix[6]tris-amine **2b** (2.37 g, 2.00 mmol) was reacted as **2a** in the case of the preparation of **3a**. Crude compound was purified by precipitation in acetonitrile, and the resulting solid was isolated by filtration, yielding compound **3b** (3.06 g, 88%) as a pale yellow solid. Mp: 206 °C (dec). IR (KBr): ν 3700 to 3130, 1543, 1363, 1170 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.77 (s, 27H, *t*Bu), 1.37 (s, 27H, *t*Bu), 2.08 (s_b, 6H, CH_2CH_2N), 2.13 (s, 9H, OMe), 3.34 (d, J = 15 Hz, 6H, ArCH_{eq}), 3.50 (q, J = 6 Hz, 6H, CH_2N), 3.98 (s_b, 6H, CH_2O), 4.38 (d, J = 15 Hz, 6H, ArCH_{ax}), 5.88 (t, J = 6 Hz, 3H, NH), 6.61 (s, 6H, ArH_{calix}), 7.22 (s, 6H, ArH_{calix}), 7.55−7.75 (m, 9H), 8.12 (d, J = 8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.5, 30.2, 31.0, 31.6, 33.9, 34.2, 41.9, 60.1, 70.2, 123.7, 125.4, 128.0, 130.8, 132.8, 133.3(6), 133.4(4), 133.4(7), 145.9(5), 145.9(9), 147.9, 151.2, 154.2. Anal. Calcd for $C_{96}H_{120}N_6O_{18}S_3$: C, 66.18; H, 6.94; N, 4.82. Found: C, 66.07; H, 7.01; N, 4.68.

Protected Bis-calix[6]arene 5a. A solution of calix[6]arene derivative **3a** (63 mg, 0.037 mmol) in anhydrous DMF (1.4 mL) and a solution of tris-tosylated calix[6]arene **4** (60 mg, 0.037 mmol) in anhydrous DMF (1.4 mL) were successively added to a mixture of K_2CO_3 (15 mg, 0.11 mmol) and Cs_2CO_3 (6 mg, 0.018 mmol). After 2 days at 90 °C, the DMF was removed under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 and washed with water, and the aqueous layer was extracted twice with CH_2Cl_2. After evaporation of the solvent, the crude compound was purified by flash chromatography on silica gel (CH_2Cl_2/cyclohexane; 4:1), yielding bis-calix[6]arene **5a** (43 mg, 42%) as a white solid. Mp: 271 °C (dec). IR (KBr): ν 3700 to 3140, 1545, 1482, 1361, 1169 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.76 (s, 54H, *t*Bu), 1.41 (s, 54H, *t*Bu), 2.22 (s, 18H, OMe), 3.25 (d, J = 15 Hz, 12H, ArCH_{eq}), 4.17 (s_b, 24H, OCH_2CH_2N), 4.44 (d, J = 15 Hz, 12H, ArCH_{ax}), 6.57 (s, 12H, ArH_{calix}), 7.23 (s, 12H, ArH_{calix}), 7.38−7.56 (m, 9H, ArH_{arm}), 8.14 (d, J = 7 Hz, 3H, ArH_{arm}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.9, 31.1, 31.7, 33.9, 34.3, 48.6, 60.6, 70.6, 123.5, 123.7, 128.3, 131.5, 131.6, 132.8, 133.1, 133.5, 134.6, 145.8(6), 145.9(4), 147.9, 151.0, 154.8. Anal. Calcd for $C_{168}H_{210}N_6O_{24}S_3\cdot 3H_2O$: C, 70.86; H, 7.65; N, 2.95. Found: C, 70.47; H, 7.59; N, 2.81.

Protected Bis-calix[6]arene 5b. The calix[6]arene derivative **3b** (45 mg, 0.026 mmol) was reacted as **3a** in the case of the preparation of **5a**. Crude compound was purified by flash chromatography on silica gel (CH_2Cl_2/cyclohexane; 4:1), yielding bis-calix[6]arene **5b** (25 mg, 34%) as a white solid. Mp: 259 °C (dec). IR (KBr): ν 3700 to 3130, 1548, 1482, 1363, 1168 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 0.75 (s, 27H, *t*Bu), 0.78 (s, 27H, *t*Bu), 1.39 (s, 54H, *t*Bu), 2.13 (s, 9H, OMe), 2.28 (s_b, 15H, OMe + CH_2CH$_2$N), 3.29 (d, $J \approx 17$ Hz, 6H, ArCH_{eq}), 3.35 (d, $J \approx 17$ Hz, 6H, ArCH_{eq}), 3.83−4.05 (m, 18H, OCH_2 + CH_2N), 4.17 (s_b, 6H, CH_2O), 4.44 (d, $J = 15$ Hz, 6H, ArCH_{ax}), 4.52 (d, $J = 15$ Hz, 6H, ArCH_{ax}), 6.61 (s, 6H, ArH_{calix}), 6.66 (s, 6H, ArH_{calix}), 7.24 (s, 6H, ArH_{calix}), 7.26 (s, 6H, ArH_{calix}), 7.45−7.55 (m, 9H, ArH_{arm}), 7.96−8.04 (m, 3H, ArH_{arm}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.9, 29.5, 29.8, 31.0(3), 31.0(7), 31.7, 34.0, 34.2(5), 34.2(7), 47.2(8), 47.3(1),60.2, 60.6, 69.6, 71.0, 123.5, 123.6, 124.2, 128.0, 128.1, 130.6, 131.6, 132.8, 133.0, 133.3, 133.5, 133.7, 145.7, 145.8, 145.9, 146.0, 148.2, 151.2, 151.4, 154.3, 154.5. Anal. Calcd for $C_{171}H_{216}N_6O_{24}S_3 \cdot 5H_2O$: C, 70.20; H, 7.79; N, 2.87. Found: C, 69.91; H, 7.58; N, 2.79.

***N*$_3$-Bis-calix[6]arene 6a.** A solution of bis-calix[6]arene **5a** (300 mg, 0.107 mmol), K_2CO_3 (519 mg, 3.76 mmol), and PhSH (0.39 mL, 3.80 mmol) in anhydrous DMF (10 mL) was stirred for 2 h at 140 °C. After removal of the DMF under reduced pressure, the residue was dissolved in CH_2Cl_2 and washed with an aqueous solution of NaOH (1 M) and the aqueous layer was extracted twice with CH_2Cl_2. The organic phases were combined, and the solvent was removed under reduced pressure. Upon the addition of acetonitrile on the residue, pure bis-calix-[6]arene **6a** (221 mg, 92%) was obtained as a white solid. Mp: 259 °C (dec). IR (KBr): ν 3690 to 3130, 1481, 1202 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 0.80 (s, 54H, *t*Bu), 1.40 (s, 54H, *t*Bu), 2.29 (s, 18H, OMe), 3.25 (s_b, 12H, CH_2N), 3.45 (d, $J = 15$ Hz, 12H, ArCH_{eq}), 4.18 (s_b, 12H, CH_2O), 4.63 (d, $J = 15$ Hz, 12H, ArCH_{ax}), 6.65 (s, 12H, ArH), 7.28 (s, 12H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.2, 31.2, 31.7, 33.9, 34.2, 50.3, 60.7, 72.4, 123.6, 128.2, 133.1, 133.9, 145.6, 145.7, 152.2, 154.8. ESI-MS (MeOH/HCOOH): *m/z* (%) 1119.9 (100), calcd for $[M + 2H]^{2+}$ 1119.8; 746.9 (11), calcd for $[M + 3H]^{3+}$ 746.9. Anal. Calcd for $C_{150}H_{201}N_3O_{12} \cdot 4H_2O$: C, 77.98; H, 9.12; N, 1.82. Found: C, 77.71; H, 8.82; N, 1.82.

***N*$_3$-Bis-calix[6]arene 6b.** The protected bis-calix[6]arene **5b** (77 mg, 0.027 mmol) was reacted as **5a** in the case of the preparation of **6a**. Thus, pure bis-calix[6]arene **6b** (56 mg, 90%) was obtained as a white solid. Mp: 259 °C (dec). IR (KBr): ν 3660 to 3110, 1482, 1202 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 0.80 (s, 27H, *t*Bu), 0.81 (s, 27H, *t*Bu), 1.41 (s, 54H, *t*Bu), 2.15−2.25 (s_b, 6H, CH_2CH$_2$N), 2.28 (s, 18H, OMe), 3.18 (s_b, 12H, CH_2N), 3.41 (d, $J \approx 15$ Hz, 6H, ArCH_{eq}), 3.46 (d, $J = 15$ Hz, 6H, ArCH_{eq}), 3.97 (s_b, 6H, CH_2O), 4.05 (s_b, 6H, CH_2O), 4.64 (d, $J = 15$ Hz, 6H, ArCH_{ax}), 4.67 (d, $J = 15$ Hz, 6H, ArCH_{ax}), 6.68 (s, 6H, ArH), 6.69 (s, 6H, ArH), 7.30 (s, 12H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.4, 29.5, 31.1, 31.6(6), 31.7(4), 33.9, 34.2, 48.7, 50.8, 60.1(7), 60.2(4), 70.7, 72.4, 123.4, 123.6, 127.9, 128.0, 133.1(9), 133.2(3), 133.8, 145.4(9), 145.5(3), 145.5(7), 145.7, 151.3, 151.5, 154.5(8), 154.6(3). Anal. Calcd for $C_{153}H_{207}N_3O_{12} \cdot 5H_2O$: C, 77.53; H, 9.23; N, 1.77. Found: C, 77.14; H, 9.01; N, 1.74.

***N*$_3$-Bis-calix[6]arene 7.** Trifluoroacetic acid (0.2 mL) was slowly added to a solution of bis-calix[6]arene **8** (52 mg, 0.021 mmol) in dry CH_2Cl_2 (0.5 mL). The mixture was stirred 2 h at room temperature and then concentrated to dryness under reduced pressure. The residue was dissolved in CH_2Cl_2 (2 mL) and washed with a solution of aqueous NaOH (1 M, 0.5 mL) and then with water (2 × 0.5 mL). The organic layer was filtered on Celite and concentrated under reduced pressure, yielding bis-calix[6]arene **7** (45 mg, 99%) as a beige solid. ^1H NMR (300 MHz, $CDCl_3$): δ 1.01 (s, 54H, *t*Bu), 2.87 (s_b, 18H, OMe), 2.97 (s_b, 12H, CH_2N), 3.61 (d, 12H, $J = 15$ Hz, ArCH_{eq}), 3.88 (s_b, 12H, CH_2O), 4.49 (d, $J = 15$ Hz, 12H, ArCH_{ax}), 6.82 (s, 12H, ArH), 7.93 (s, 12H, ArH). ^{13}C NMR (75 MHz, CD_3-CN): δ 31.1, 31.6, 34.9, 49.6, 61.3, 74.6, 122.3, 129.3, 132.7, 136.7, 144.7, 148.1, 155.0, 161.2. Complementary analyses were performed on the salt derivative of **7**, namely, **7.3TFA**. This latter was obtained from the addition of trifluoroacetic acid (10 μL, 0.135 mmol) to a solution of bis-calix[6]arene **7** (32 mg, 0.0147 mmol) in $CHCl_3$ (0.25 mL). After 30 min of stirring at room temperature, ether (2 mL) was added. The resulting precipitate was isolated by centrifugation and washed with ether (2 × 1 mL), yielding bis-calix[6]arene **7.3TFA** (27 mg, 73%) as a beige solid. Mp: 195 °C (dec). ^1H NMR (300 MHz, CD_3CN): δ 1.42 (s, 54H, *t*Bu), 3.50 (s_b, 12H, CH_2N), 3.78 (d, $J = 16$ Hz, 12H, ArCH_{eq}), 3.87 (s, 18H, OMe), 4.24 (s_b, 12H, CH_2O), 4.37 (d, $J = 16$ Hz, 12H, ArCH_{ax}), 6.91 (s, 12H, ArH), 7.50 (s, 12H, ArH), 8.32 (s_b, 3H, $^+NH_2$), 8.79 (s_b, 3H, $^+NH_2$). IR (KBr): ν 3700 to 3150, 1682, 1524, 1347, 1202 cm^{-1}. ESI-MS (MeOH): *m/z* (%) 1086.8 (100), calcd for $[M + 2H]^{2+}$ 1086.5; 724.8 (33), calcd for $[M + 3H]^{3+}$ 724.7.

***N*$_3$-Bis-calix[6]arene 8.** The glassware must be dried before use. At 0 °C, a 1:1 (v/v) mixture of fuming nitric acid and glacial acetic acid (1.1 mL) was slowly added to a solution of **6a** (75 mg, 0.0335 mmol) in anhydrous CH_2Cl_2 (10 mL). After 4 h of stirring at room temperature, the reaction mixture was carefully poured at 0 °C into 25 mL of 3% aqueous NH_4OH. The aqueous layer was extracted with CH_2Cl_2 (3 × 4 mL), and the combined organic layers were washed with 5 mL of an aqueous solution of NaOH (1 M). The aqueous layer was extracted with CH_2Cl_2 (5 mL), and the organic phases were combined and concentrated under reduced pressure. The crude mixture was dissolved in anhydrous CH_2Cl_2 (3 mL), and triethylamine (37 μL, 0.268 mmol) was added, followed, at 0 °C, by the addition of diterbutyl carbonate (44 mg, 0.20 mmol). After 14 h of stirring at room temperature, the reaction mixture was concentrated under reduced pressure and purified by flash chromatography on silica gel (CH_2Cl_2/ethyl acetate; 97:3), yielding bis-calix[6]arene **8** (29 mg, 35%) as a brown solid. Mp: 210 °C (dec). IR (KBr): ν 3698 to 3126, 1698, 1525, 1469, 1346 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 330 K): δ 0.86 (s, 54H, *t*Bu), 1.41 (s, 27H, Boc*t*Bu), 2.55−2.85 (m, 18H, OMe), 3.55−3.75 (m, 12H, ArCH_{eq}), 3.85−4.15 (m, 24H, CH_2N + CH_2O), 4.55 (d, $J = 14$ Hz, 12H, ArCH_{ax}), 6.68 (s, 12H, ArH), 8.26 (s, 12H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): complex spectrum characteristic of a dissymmetrical species (See Supporting Information). Anal. Calcd for $C_{141}H_{171}N_9O_{30} \cdot H_2O$: C, 68.01; H, 7.00; N, 5.06. Found: C, 67.71; H, 7.02; N, 4.74.

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Supporting Information Available: ^1H NMR spectra of **1**, **2b**, **3a**,**b**, **5a**,**b**, **7.3TFA**, and **8**; ^{13}C NMR and HMQC spectra of **1**, **2b**, **3a**,**b**, **5a**,**b**, **6a**,**b**, **7**, and **8**; HMBC spectra of **3a**,**b**, **5a**,**b**, **6a**,**b**, **7**, and **8**; two-dimensional NOESY spectra of **7** in CD_3CN and $CDCl_3$; and General experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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