

## Boron Macrocycles Having a Calix-Like Shape. Synthesis, Characterization, X-ray Analysis, and Inclusion Properties

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Received October 25, 2005

The syntheses, structure, and inclusion properties of trinuclear boron compounds having a calix-like shape are described. The compounds have been obtained via self-assembly reactions between salicylaldehyde derivatives and 3-aminophenylboronic acid, whereby the formation of three N → B coordination bonds favored the oligomerization. The products have high melting points (>370 °C), are stable to moisture, and have good solubility in organic solvents; the latter property is useful for host–guest recognition experiments. The structural analysis by X-ray diffraction revealed that diverse conformations are possible because of the presence of two different units of aromatic rims. A cone–cone (double-cone) conformation is observed for three of these compounds, while the remaining one has a cone–partial cone conformation. An analysis of the molecular packing showed that the molecules are stacked in columns in two different orientations in relation to the organization of the macrocycles when referred to the N–B bonds. The inclusion properties toward primary amines and ammonium chlorides were analyzed by titration experiments and monitored by UV spectroscopy, whereby association constants on the order of 10<sup>2</sup>–10<sup>3</sup> M<sup>-1</sup> were determined.

### Introduction

As a result of their good inclusion properties, calix-like compounds have become common hosts for a large variety of guest molecules during the past few years.<sup>1</sup> Among all calix[*n*]arenes reported until now, the tetrameric species (calix[4]arenes) have received more attention as molecular receptors.<sup>2,3</sup> The fact that they are the most favorable products in the cyclization reactions between para-substituted phenols and formaldehyde leads to enhanced applicability for

calix[4]arenes. Studies of larger calix[*n*]arenes (*n* = 6 and 8) have been less extended.<sup>4,5</sup> There are different methods to synthesize calixarenes; however, the preferred reaction pathway is via self-assembly of organic networks in one-pot reactions.<sup>6</sup> When longer routes are followed, the yields are diminished considerably.<sup>7</sup> One of the more recent developments in this area is the construction of calixarenes with heteroaromatic rings instead of phenol derivatives<sup>8</sup> or with the methylene bridges substituted by heteroatoms.<sup>9</sup> These modifications have been carried out with the aim to

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(1) Böhmer, V. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713–745.

(2) León, S.; Leigh, D. A.; Zerbetto, F. *Chem.—Eur. J.* **2002**, *8*, 4854–4866.

(3) Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713–1734 and references cited therein.

(4) Bottino, A.; Cunsolo, F.; Piattelli, M.; Garozzo, D.; Neri, P. *J. Org. Chem.* **1999**, *64*, 8018–8020.

(5) Leverd, P. C.; Rinaldo, D.; Nierlich, M. *Eur. J. Inorg. Chem.* **2001**, 2021–2025.

(6) Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, *103*, 3782–3792.

(7) Gopalsamuthiram, V.; Wulff, W. D. *J. Am. Chem. Soc.* **2004**, *126*, 13936–13937.

(8) Wang, M.-X.; Yang, H.-B. *J. Am. Chem. Soc.* **2004**, *126*, 15412–15422.

(9) Iki, N.; Kabuto, C.; Fukushima, T.; Kumagai, H.; Takeya, H.; Miyanari, S.; Miyashi, T.; Miyano, S. *Tetrahedron* **2000**, *56*, 1437–1443.

improve the inclusion properties by changing the conformation and size of the cavity. Nevertheless, as a consequence of the more difficult synthetic procedures and functionalization, the structures and recognition properties of these heterocalix[*n*]arenes have been less explored.

On the other hand, it has been shown that macrocyclic species can be easily formed by involving coordination chemistry.<sup>10,11</sup> In this respect, it is well-known that nitrogen atoms can form strong coordination bonds with boron atoms, which constitute a useful tool for the construction of macrocycles.<sup>12–15</sup> Recently, we described the synthesis of a boron–nitrogen calix[3]arene (**1a**) through a one-pot procedure;<sup>16</sup> this constitutes the first example of a calix-shaped structure, in which the formation of N → B coordination bonds play an important role in the cyclization reaction. As far as we know, no synthetic pathways are known so far to prepare calix[3]arenes from formaldehyde and phenol derivatives. Nonetheless, several examples of heterocalix[3]arenes have been described;<sup>17</sup> of these, aza- and oxacalix[3]arenes have been used as receptors for metal cations.<sup>18–20</sup> Some studies have also been focused on the recognition of ammonium salts,<sup>21,22</sup> which have been attributed in part to the C<sub>3</sub> symmetry present in both the host and guest molecules. Crystallographic studies of the host–guest complexes between the calix and ammonium molecules have shown that the cations are included in the calixarene cavity through N–H···π contacts.<sup>23</sup> NMR studies have demonstrated that the inclusion persists in solution.<sup>23</sup> Chiral recognition experiments between α-amino acid derivatives and homooxacalix[3]arenes have shown that the structural design of the host is very important for the recognition of the guest.<sup>24</sup>

Herein we describe the synthesis of a series of boronate derivatives having a 15-membered macrocyclic ring structure. X-ray diffraction analyses showed that in the solid state the preferred conformation for these structures is the *cone–cone* conformer in relationship to the calix[3]arene compounds.

- (10) Holliday, B. J.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 2022–2043.
- (11) Kusakawa, T.; Fujita, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 3142–3143.
- (12) Sugihara, Y.; Takakura, K.; Murafuji, T.; Miyatake, R.; Nakasuji, K.; Kato, M.; Yano, S. *J. Org. Chem.* **1996**, *61*, 6829–6834.
- (13) Weiss, A.; Barba, V.; Pritzkow, H.; Siebert, W. *J. Organomet. Chem.* **2003**, *680*, 294–300.
- (14) Christinat, N.; Scopelli, R.; Severin, K. *Chem. Commun.* **2004**, 1158–1159.
- (15) Höpfl, H. *Struct. Bonding*, **2002**, *103*, 1–56.
- (16) Barba, V.; Höpfl, H.; Farfán, N.; Santillan, R.; Beltran, H. I.; Zamudio-Rivera, L. S. *Chem. Commun.* **2004**, 2834–2835.
- (17) König, B.; Hechavarria-Fonseca, M. *Eur. J. Inorg. Chem.* **2000**, 2303.
- (18) Daitch, C. E.; Hampton, P. D.; Duesler, E. N.; Alam, T. M. *J. Am. Chem. Soc.* **1996**, *118*, 7769–7773.
- (19) Thuéry, P.; Nierlich, M.; Vicens, J.; Masci, B.; Takemura, H. *Eur. J. Inorg. Chem.* **2001**, 637–643.
- (20) Hampton, P. D.; Tong, W.; Duesler, E. N. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1127–1130.
- (21) Yamato, T.; Zhang, F.; Tsuzuki, H.; Miura, Y. *Eur. J. Org. Chem.* **2001**, 1069–1075.
- (22) Araki, K.; Inada, K.; Otsuka, H.; Shinkai, S. *Tetrahedron* **1993**, *49*, 9465–9478.
- (23) Leverd, P. C.; Berthault, P.; Lance, M.; Nierlich, M. *Eur. J. Org. Chem.* **2000**, 133–139.
- (24) Araki, K.; Inada, K.; Shinkai, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 72–74.

The ability to recognize primary amines and ammonium chlorides was evaluated by titration experiments that were monitored by UV spectroscopy. It is noteworthy to mention that the macrocycles possess C<sub>3</sub> symmetry in solution, which is also present in the ammonium chlorides; therefore, a good host–guest complementary relationship can be expected.

## Experimental Section

**Materials.** All reagents and solvents used were obtained from commercial suppliers and used without further purification. Ammonium chlorides were synthesized through the reaction of aqueous hydrochloric acid with the respective primary amine under stirring to room temperature in a CH<sub>2</sub>Cl<sub>2</sub> solution.

**Instrumentation.** The <sup>1</sup>H, <sup>13</sup>C, and <sup>11</sup>B NMR spectra were recorded at room temperature using a Varian Gemini 200 spectrophotometer. Tetramethylsilane (TMS; internal, <sup>1</sup>H, δ = 0.00 ppm, <sup>13</sup>C, δ = 0.0 ppm) and BF<sub>3</sub>·OEt<sub>2</sub> (external, <sup>11</sup>B, δ = 0.0 ppm) were used as standard references. 2D COSY, HMQC, and NOESY experiments were carried out for the unambiguous assignment of the <sup>1</sup>H and <sup>13</sup>C NMR spectra. Infrared spectra were recorded on a Bruker Vector 22 FT-IR spectrophotometer. Mass spectra were obtained with a JEOL JMS 700 equipment. Elemental analyses were carried out on a Perkin-Elmer series II 2400 instrument. Elemental analysis for carbon was not satisfactory. It is known that elemental analyses of boronic acid derivatives are particularly complicated because of the production of incombustible residues (e.g., boron carbide) and are, therefore, not always in the established limits of exactitude, especially with respect to carbon.<sup>25</sup> Therefore, only the values for hydrogen and nitrogen are indicated. Melting points were determined with a Büchi B-540 digital apparatus. The electronic absorption spectra were recorded at 25 °C on a Hewlett-Packard 8452A diode-array spectrophotometer.

**X-ray Crystallography.** X-ray diffraction studies were performed on a Bruker APEX diffractometer with a CCD area detector, Mo Kα radiation, λ = 0.71073 Å, and a graphite monochromator. Frames were collected at T = 100 K by ω rotation (Δ/ω = 0.3°) at 10 s/frame. The measured intensities were reduced to F<sup>2</sup>.<sup>26</sup> Structure solution, refinement, and data output were carried out with the *SHELXTL-NT* program package.<sup>27</sup> All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in geometrically calculated positions using a riding model. High R values are observed because of the disorder at the solvent molecule. Crystallographic data have been deposited at the Cambridge Crystallographic Data Center as CCDC Nos. 277869–277871 for **1b–d**, respectively. Copies of the data can be obtained free of charge upon application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (e-mail: deposit@ccdc.cam.ac.uk).

**UV/Vis Titrations.** Titrations were performed typically by adding aliquots of 0.25 or 0.5 M guest stock solutions to a (2–8) × 10<sup>−5</sup> M calixarene solution of the corresponding calixarene in chloroform for amines and in methanol for ammonium chlorides. The experimental data were fitted using a nonlinear least-squares regression calculated with the Microcal Origin 5 program. Several wavelengths of the electronic absorption spectra were used for the fitting, and the binding constants obtained were averaged.

**General Method for the Preparation of Boron Complexes 1b–d.** Compounds **1b–d** were synthesized from the reaction of 3

- (25) James, T. D.; Sandanayake, K. R. A. S.; Shinkai, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1910.
- (26) *SAIN-NT*, version 6.04; Bruker Analytical X-ray Systems: Karlsruhe, Germany, 2001.
- (27) *SHELXTL-NT*, version 6.10; Bruker Analytical X-ray Systems: Karlsruhe, Germany, 2000.

## Boron Macrocycles Having a Calix-Like Shape

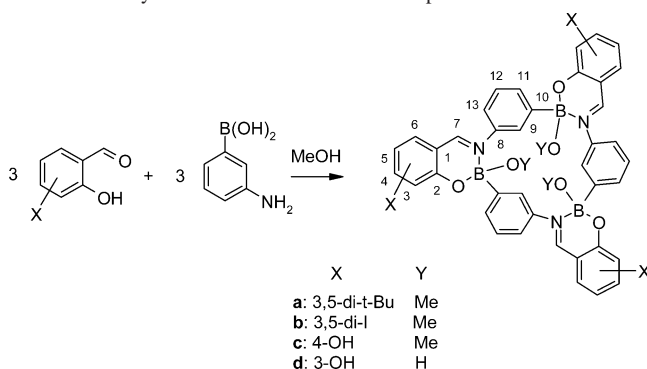
equiv of the salicylaldehyde derivative with 3 equiv of 3-aminophenylboronic acid in methanol. The reaction mixtures were refluxed for 30 min under stirring, except for compound **1d**, which precipitated after 15 min of stirring at room temperature. After that, the solvent and the water formed through the sextuple-condensation reaction were completely removed using a vacuum pump. The products were purified by recrystallization in solvent mixtures (1:3 ratio): MeOH/benzene for **1b**, MeOH/CH<sub>2</sub>Cl<sub>2</sub> for **1c**, and MeOH/MeCN for **1d**.

**Calix[3]arene 1b.** Compound **1b** was prepared from 0.15 g (0.968 mmol) of 3-aminophenylboronic acid and 0.36 g (0.968 mmol) of 3,5-diiodosalicylaldehyde. The product was obtained as an orange powder. Yield: 0.79 g (56%). Mp<sub>dec.</sub>: >370 °C. <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>, δ, ppm, *J*, Hz): 8.90 (s, 3H, H-7), 8.11 (d, <sup>4</sup>*J* = 2.0, 3H, H-4), 7.98 (d, <sup>4</sup>*J* = 2.0, 3H, H-6), 7.82 (s, 3H, H-9), 7.74 (d, <sup>3</sup>*J* = 7, 3H, H-13), 7.40–7.60 (m, 6H, H-12, H-11), 2.1 (s, 9H, OMe). <sup>13</sup>C NMR (50 MHz, DMSO-*d*<sub>6</sub>, δ, ppm): 161.1 (C-7), 160.3 (C-2), 147.9 (C-4), 144.6 (C-8), 140.7 (C-6), 133.3 (C-11), 128.6 (C-12), 126.9 (C-9), 122.6 (C-13), 120.4 (C-1), 88.6 (C-5), 80.7 (C-3), 40 (OMe). <sup>11</sup>B NMR (64 MHz, DMSO-*d*<sub>6</sub>, δ, ppm): +1.7 (*h*<sub>1/2</sub> = 2080 Hz). IR (KBr, cm<sup>-1</sup>):  $\bar{\nu}$  3059 (w), 2924 (w), 2373 (w), 2339 (w), 1619 (C=N, s), 1521 (w), 1439 (s), 1354 (m), 1308 (m), 1217 (m), 1186 (m), 1156 (w), 976 (w), 869 (w), 739 (w), 705 (w), 660 (w). FAB-MS: *m/z* (%) 1435 (M – OMe)<sup>+</sup>, 48), 1237 (50), 1167 (26), 535 (55), 479 (74), 449 (13), 374 (23), 309 (30), 294 (21), 219 (15), 191 (14), 154 (100), 136 (62), 94 (39), 93 (28), 63 (16). Elem anal. Calcd for C<sub>42</sub>H<sub>30</sub>B<sub>3</sub>N<sub>3</sub>O<sub>6</sub>I<sub>6</sub>: H, 2.04; N, 2.86. Found: H, 1.89; N, 2.73%.

**Calix[3]arene 1c.** Compound **1c** was prepared from 0.30 g (1.936 mmol) of 3-aminophenylboronic acid and 0.27 g (1.936 mmol) of 2,4-dihydroxysalicylaldehyde. The product was obtained as a lemon-yellow powder. Yield: 0.83 g (57%). Mp<sub>dec.</sub>: >370 °C. <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>, δ, ppm, *J*, Hz): 10.29 (s, 3H, OH<sub>arom</sub>), 8.79 (s, 3H, H-7), 8.18 (d, <sup>3</sup>*J* = 7.7, 3H, H-11), 7.73 (s, 3H, H-9), 7.67 (t, <sup>3</sup>*J* = 7.7, 3H, H-12), 7.45 (d, <sup>3</sup>*J* = 7.4, 3H, H-6), 7.40 (d, <sup>2</sup>*J* = 7.7, 3H, H-13), 6.41 (d, <sup>3</sup>*J* = 7.4, 3H, H-5), 6.30 (d, <sup>4</sup>*J* = 2.7, 3H, H-3), 3.16 (s, 9H, OMe). <sup>13</sup>C NMR (50 MHz, DMSO-*d*<sub>6</sub>, δ, ppm): 161.0 (C-7), 160.2 (C-2), 153.8 (C-4), 147.9 (C-8), 135.9 (C-6), 128.5 (C-12), 127.7 (C-11), 126.9 (C-9), 122.5 (C-13), 120.3 (C-1), 118.4 (C-5), 114.0 (C-3), 42.66 (OMe). <sup>11</sup>B NMR (64 MHz, DMSO-*d*<sub>6</sub>, δ): +2.3 (*h*<sub>1/2</sub> = 2427 Hz). IR (KBr, cm<sup>-1</sup>):  $\bar{\nu}$  3407 (s), 3059 (m), 2943 (m), 1623 (C=N, s), 1558 (m), 1499 (w), 1454 (s), 1375 (w), 1226 (m), 1130 (w), 1083 (w), 999 (w), 940 (w), 846 (w), 793 (w), 704 (w). FAB-MS: *m/z* (%) 727 (M – OMe)<sup>+</sup>, 20), 531 (40), 528 (25), 460 (25), 391 (20), 307 (20), 289 (13), 273 (20), 180 (20), 154 (100), 136 (68), 69 (23), 55 (24), 43 (17), 27 (40). Elem anal. Calcd for C<sub>42</sub>H<sub>36</sub>B<sub>3</sub>N<sub>3</sub>O<sub>9</sub>: H, 4.78; N, 5.53. Found: H, 4.86; N, 5.21%.

**Calix[3]arene 1d.** Compound **1d** was prepared from 0.30 g (1.936 mmol) of 3-aminophenylboronic acid and 0.27 g (1.936 mmol) of 2,3-dihydroxysalicylaldehyde. The product was obtained as an orange powder. Yield: 0.93 g (67%). Mp<sub>dec.</sub>: >370 °C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>, δ, ppm, *J*, Hz): 9.08 (s, 3H, Ar–OH), 9.02 (s, 3H, B–OH), 8.79 (s, 3H, H-7), 8.32 (t, <sup>4</sup>*J* = 2.4, 3H, H-9), 8.30 (dd, <sup>3</sup>*J* = 10.4, <sup>4</sup>*J* = 2.4, 3H, H-13), 8.13 (t, <sup>3</sup>*J* = 10.4, 3H, H-12), 8.08 (dd, <sup>3</sup>*J* = 10.4, <sup>4</sup>*J* = 2.4, 3H, H-11), 6.96–7.24 (m, 9H, H-4,6). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>, δ, ppm): 162.2 (C-7), 158.6 (C-2), 152.3 (C-3), 143.2 (C-8), 141.2 (C-5), 128.3 (C-6), 128.3 (C-12), 127.5 (C-11), 127.0 (C-9), 122.2 (C-13), 122.2 (C-4), 117.7 (C-1). <sup>11</sup>B NMR (64 MHz, DMSO-*d*<sub>6</sub>, δ, ppm): +2.0 (*h*<sub>1/2</sub> = 1847 Hz). IR (KBr, cm<sup>-1</sup>):  $\bar{\nu}$  3444 (s), 3405 (m), 1625 (C=N, s), 1572 (s), 1471 (s), 1378 (m), 1313 (m), 1280 (s), 1223 (s), 1169 (m), 1091 (w), 985 (m), 938 (w), 854 (w), 792 (w), 738

**Scheme 1.** Synthesis of Trimeric Boron Complexes **1a–d**



(w), 705 (w), 673 (w). FAB-MS: *m/z* (%) 717 ([M<sup>+</sup>], 42), 672 (78), 607 (10), 584 (10), 568 (32), 474 (2), 437 (40), 420 (30), 359 (62), 312 (92), 291 (57), 258 (50), 229 (40), 146 (100). Elem anal. Calcd for C<sub>39</sub>H<sub>30</sub>B<sub>3</sub>N<sub>3</sub>O<sub>9</sub>: H, 4.48; N, 5.86. Found: H, 4.87; N, 5.60%.

## Results and Discussion

**Synthesis.** The macrocyclic compounds **1b–d** have been prepared in moderate yields by one-step syntheses between the salicylaldehyde derivatives and 3-aminophenylboronic acid (Scheme 1). As described for **1a**,<sup>16</sup> reflux conditions were used for trimeric compound formation, except for compound **1d**, which precipitates almost immediately (15 min) after the reagents are mixed. All compounds are stable in the solid state and also in organic solvent solutions for several days at room temperature. For all three new compounds, high melting points have been measured (>370 °C), which is also characteristic for other macrocycles having a calix-like shape.

**Characterization.** Initially, the trimeric nature of these compounds was evidenced by fast atom bombardment mass spectrometry (FAB-MS), showing also that methanolysis reactions had occurred in the cases of compounds **1b** and **1c** when the B–OH groups were substituted by OMe groups. A peak corresponding to the molecular ion with the loss of one OMe group was observed for compounds **1b** and **1c**. Similar fragmentation patterns have been detected for the analogous compound **1a**<sup>16</sup> and are comparable with those of other boronate derivatives.<sup>28,29</sup> In accordance with this technique, in the case of compound **1d**, the solvolysis reaction did not take place, and the OH groups remained attached to the boron atoms. The reason that compound **1d** does not undergo methanolysis is attributed to the fact that the product precipitates at room temperature, in contrast to the reflux conditions used for the syntheses of **1b** and **1c**.

The IR spectra for compounds **1b–d** show bands at  $\nu$  1619, 1623, and 1625 cm<sup>-1</sup>, respectively, which correspond to the asymmetric stretching of the C=N groups, thus giving evidence that the condensation between the amine and aldehyde groups has occurred. The spectrum of compound

(28) Barba, V.; Vázquez, J.; López, F.; Santillan, R.; Farfán, N. *J. Organomet. Chem.* **2005**, *690*, 2351–2357.

(29) Barba, V.; Gallegos, E.; Santillan, R.; Farfán, N. *J. Organomet. Chem.* **2001**, *622*, 259–264.

**Table 1.** Crystallographic Data for Compounds **1b–d**

	<b>1b</b>	<b>1c</b>	<b>1d</b>
empirical formula	C <sub>42</sub> H <sub>30</sub> B <sub>3</sub> N <sub>3</sub> O <sub>6</sub> I <sub>6</sub> ·3C <sub>6</sub> H <sub>6</sub>	C <sub>42</sub> H <sub>36</sub> B <sub>3</sub> N <sub>3</sub> O <sub>9</sub> ·2CH <sub>2</sub> Cl <sub>2</sub> ·H <sub>2</sub> O	C <sub>39</sub> H <sub>30</sub> B <sub>3</sub> N <sub>3</sub> O <sub>9</sub> ·4H <sub>2</sub> O
fw	1700.84	947.04	781.09
cryst size [mm <sup>3</sup> ]	0.20 × 0.20 × 0.10	0.30 × 0.24 × 0.20	0.22 × 0.20 × 0.16
cryst syst	trigonal	monoclinic	monoclinic
space group	P3	P2 <sub>1</sub> /n	P2 <sub>1</sub> /n
unit cell dimensions			
<i>a</i> [Å]	15.4284(11)	17.4628(18)	17.408 (3)
<i>b</i> [Å]	15.4284(11)	16.8118(17)	12.442(2)
<i>c</i> [Å]	15.8947 (16)	17.5255(17)	18.370(3)
β [deg]	90 (γ = 120°)	117.275(2)	95.361(4)
V [Å <sup>3</sup> ]	3276.6(5)	4573.1(8)	4573.1(8)
Z	2	4	4
ρ <sub>calcd</sub> [g/cm <sup>3</sup> ]	1.724	1.376	1.310
μ [mm <sup>-1</sup> ]	2.892	0.319	0.098
collected rflns	25633	18439	18160
independent rflns ( <i>R</i> <sub>int</sub> )	2865 (0.089)	6220 (0.047)	2728 (0.096)
no. of param	237	609	529
<i>R</i> <sub>1</sub> [ <i>I</i> > 2σ( <i>I</i> )]	0.082	0.098	0.097
w <i>R</i> <sub>2</sub> (all data)	0.181	0.245	0.283
GOF	1.175	1.096	1.083

**1d** shows a strong band at  $\nu$  3494 cm<sup>-1</sup>, which is attributed to the hydroxyl group attached to the boron atom.

As a consequence of the C<sub>3</sub> symmetry of the molecules in solution, only a single set of signals was observed in the NMR spectra. For instance, the <sup>1</sup>H NMR spectra show a single signal for the hydrogen corresponding to the –HC=N– group at  $\delta$  8.90, 8.79, and 8.79 ppm for **1b–d**, respectively. In the <sup>13</sup>C NMR spectra, the signal corresponding to the –HC=N– group was observed at  $\delta$  161.7, 161.0, and 162.2 ppm for **1b–d**, respectively, with these shift displacements being characteristic for imines coordinated to a boron atom.<sup>16,28,29</sup> The chemical shifts of the remaining signals in the <sup>1</sup>H and <sup>13</sup>C NMR spectra are very similar for the three compounds and also with compound **1a** previously reported,<sup>16</sup> except for the positions in wherein different substituents are localized. A fast dynamic equilibrium between the two conformations normally observed in calix-[3]arenes<sup>22</sup> is excluded because of the rigid nature of the six-membered rings that connect the aromatic moieties.<sup>16</sup>

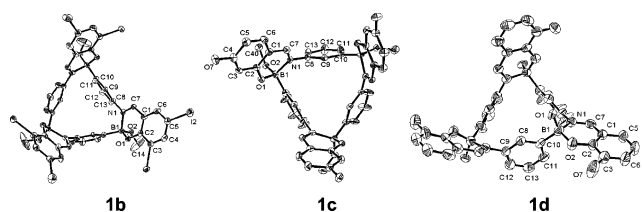
The formation of N → B coordinative bonds is evident from the <sup>11</sup>B NMR spectra, wherein the signals were found in the range of  $\delta$  1.7 and 2.3 ppm; these chemical shifts are typical for species with tetracoordinative boron atoms and are in agreement with the previous results.<sup>16,28,29</sup> Only a broad single signal was observed for each compound, this being again an indication of the symmetric nature of the molecules in solution.

**X-ray Analysis.** More details on the structures of compounds **1b–d** were obtained from X-ray crystallographic analyses. The most relevant crystallographic data are described in Table 1, and the molecular structures for **1b–d** are shown in Figure 1. Selected geometric parameters are shown in Table 2 and compared with those of compound **1a**. It is evident that the formation of the macrocycles is induced by the presence of three N → B coordinative bonds, which have average distances of 1.647(18), 1.618(8), and 1.595(15) Å for **1b–d**, respectively. For compound **1a** in the 1:5 calix/C<sub>6</sub>H<sub>6</sub> clathrate form,<sup>16</sup> a similar N–B distance bond has been determined [1.631(6) Å]. The O–B distances within the six-membered C<sub>3</sub>BNO heterocycles are larger

**Table 2.** Comparison between Selected Bond Lengths (Å) and Bond and Torsion Angles (deg) for Compounds **1a–d**<sup>a</sup>

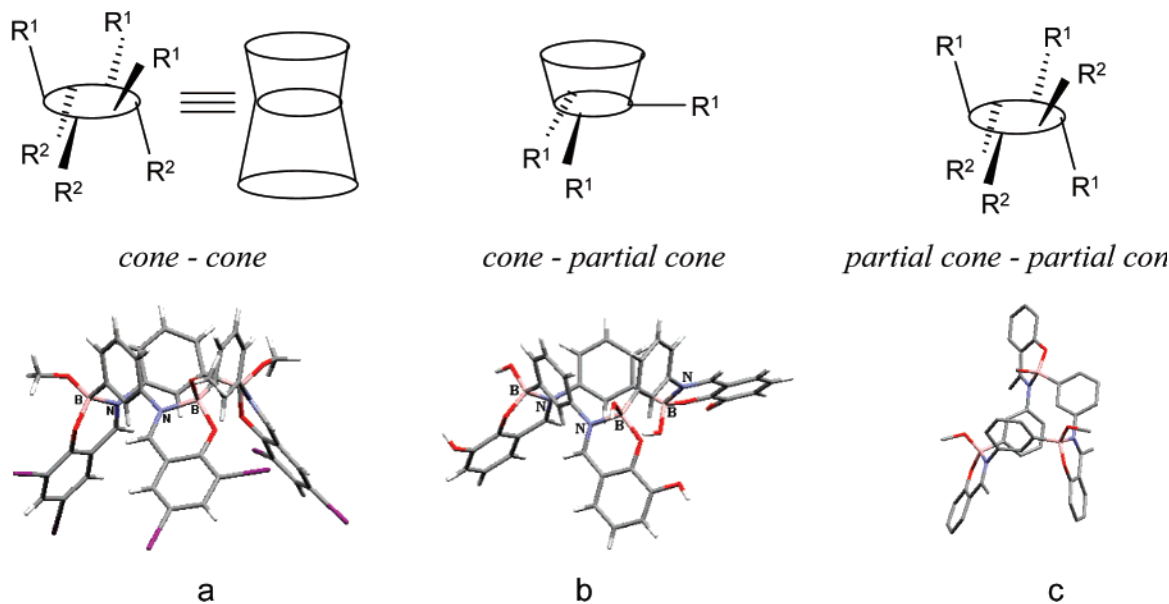
	<b>1a</b> <sup>b</sup>	<b>1b</b>	<b>1c</b>	<b>1d</b>
Bond Lengths (Å)				
N–B	1.631(6)	1.647(18)	1.618(8)	1.595(15)
O1–B	1.487(6)	1.477(18)	1.503(8)	1.477(14)
O2–B	1.426(6)	1.413(17)	1.443(8)	1.420(14)
C–B	1.601(6)	1.590(19)	1.599(9)	1.592(17)
N–C <sub>iminic</sub>	1.305(6)	1.268(15)	1.305(7)	1.305(13)
Bond Angles (deg)				
O2–B–N	104.9(4)	102.5(11)	104.5(5)	106.1(9)
O1–B–N	108.9(4)	104.5(10)	110.3(4)	108.1(9)
C–B–N	110.1(4)	108.5(10)	111.0(4)	109.9(9)
O2–B–O1	113.7(4)	113.3(10)	111.2(4)	110.9(9)
O1–B–C	107.9(4)	110.4(11)	107.1(5)	109.5(9)
O2–B–C	111.1(4)	112.4(12)	111.9(5)	112.0(9)
Torsion Angles (deg)				
C8–N1–B1–C10	40.8(4)	37.3(15)	40.6(4)	42.7(9)
C7–N1–B1–O1	–23.3(4)	–24.7(15)	–21.0(5)	–15.7(9)

<sup>a</sup> Average values are described. <sup>b</sup> The values were taken for complex **1a** (1:5 calix/C<sub>6</sub>H<sub>6</sub> clathrate complex).<sup>16</sup>

**Figure 1.** Perspective views of the molecular structures of compounds **1b–d**.

when compared to those of the OMe groups because of the higher annular tension in six-membered rings. As a consequence of the annular tension within the six-membered heterocycle ring, the conformation is not planar, placing the boron atom out of the mean plane by approximately 0.85 Å.

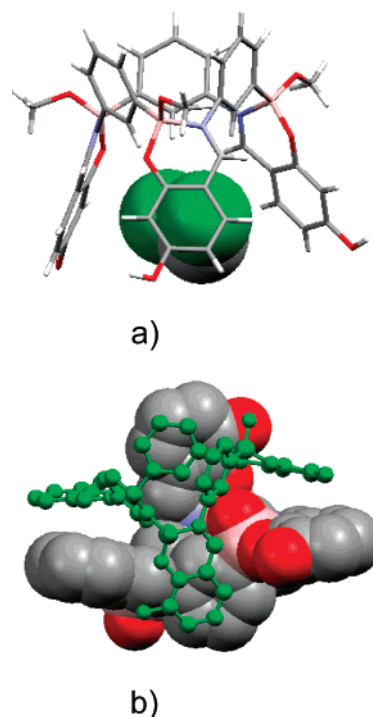
Because of the existence of two different types of aromatic rings attached to the 15-membered macrocycle, these molecules can have a series of different conformers. Three different arrangements have been observed so far experimentally by X-ray diffraction considering the disposition of the aromatic rings: (i) Compounds **1a–c** have a *cone–cone* conformation that can be considered as a double calixarene;



**Figure 2.** Conformations observed for B–N compounds: (a) double-*cone* conformer for compounds **1a–c**; (b) *cone–partial cone* conformer for compound **1d**; (c) *partial cone–partial cone* conformer for compound **2**. Top: schematic representations. Bottom: figures obtained from by X-ray diffraction analysis.

all three OMe groups are pointing outward of the calix shape (Figure 2a), with the relative configuration for boron atoms being *RRR* or *SSS*. (ii) In the case of compound **1d**, the upper aromatic rings of the condensed arylboronic acid fragments are oriented in the same direction (cone shape), while the aromatic rings of the salicylidene moieties (only two) are in a *cis* disposition, with one of them pointing outward from the calix and, at the same time, one OH group oriented toward the center of the calix (Figure 2b). The relative configuration for boron atoms is *RRS* or *SSR*. This arrangement can be considered as a *cone–partial cone* conformation. (iii) The existence of a *partial cone–partial cone* conformation is also possible, and in this case, one pair of neighboring aromatic rings has changed their orientation (Figure 2c). This conformation was found for compound **2**, which was derived from 2-hydroxyacetophenone and 3-aminophenylboronic acid.<sup>29</sup> The relative configuration for boron atoms in this case is *RRR* or *SSS*.

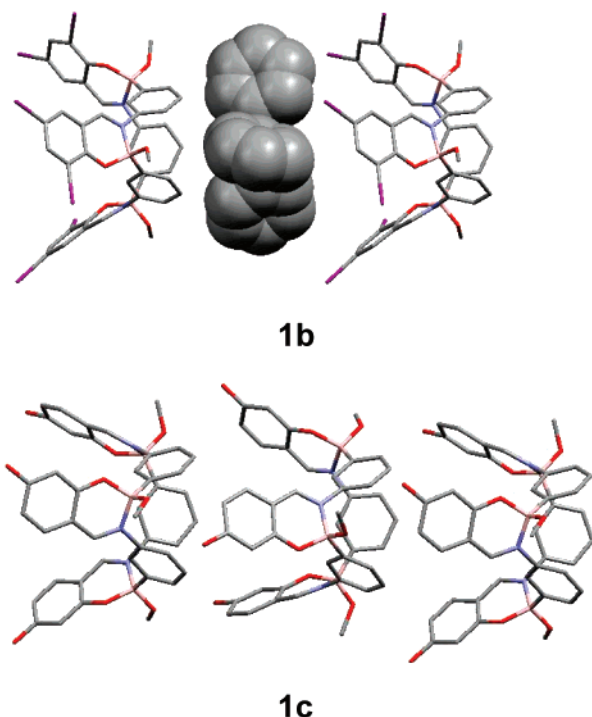
In the compounds having the double-*cone* conformation (**1a–c**), the cavity is surrounded only by aromatic rings so that it can be considered to be of hydrophobic nature. The volumes of the cavities are 192 and 172 Å<sup>3</sup> for **1b** and **1c**, respectively,<sup>30</sup> thus being larger when compared to that of compound **1a** (160 Å<sup>3</sup>).<sup>16</sup> The latter differences should mainly be due to the substitution of the salicylidene moieties. As has been shown by the inclusion experiments with different solvent molecules, such as benzene, THF, and AcOMe, in the case of compound **1a**,<sup>16</sup> it is possible to trap guest molecules in the interior of these complexes. In the solid state, compound **1c** shows a behavior similar to that of compound **1a**, having a dichloromethane molecule included in its interior (Figure 3a). Until now, the guest inclusion has only been carried out in the cone formed by the salicylidene



**Figure 3.** (a) Molecular view of the host–guest **1c**/CH<sub>2</sub>Cl<sub>2</sub> system, found in the solid state. (b) Self-assembly of two molecules of compound **1d** in the solid state, leading to a dimeric organization.

moieties, which has been attributed to the bigger cavities in this part of the molecules. When the double-*cone* conformation is not favored, inclusion of guest molecules in the solid state has not been observed; however, other very interesting arrangements are possible; e.g., for compound **1d**, a self-assembly occurs between neighboring molecules through  $\pi$ – $\pi$  interactions (ca. 3.96 Å) between aromatic salicylaldehyde moieties, giving rise to dimeric structures as depicted in Figure 3b. Similar assemblies have been observed for calix[4]arenes, when crystallized in the absence of guest molecules.<sup>31,32</sup>

(30) The diameter is defined by the circles that circumscribe the three carbon atoms located on the top of the upper rings and the three carbon atoms located on the bottom of the five-carbon substituent of the lower rings.

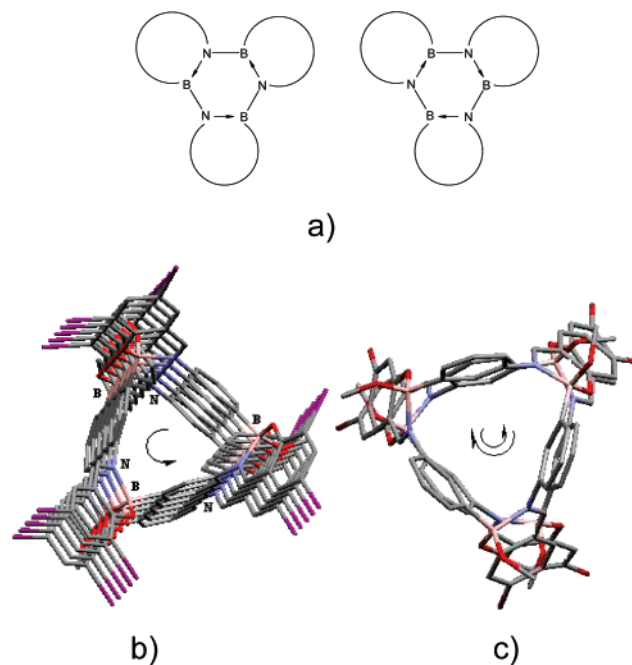


**Figure 4.** Fragments of the molecular packing arrangements found in the crystal lattice of compounds **1b** and **1c**, showing the *head–tail* orientation observed. In the case of compound **1b**, benzene molecules are present between two calix molecules.

The molecular packing showed that the molecules with double-cone conformation are stacked in columns, leading to channels along the *a* axis (Figure 4). Within the columns, the molecules are ordered in a *head–tail* disposition, with a separation of 2.92 Å in the case of **1c** and 8.2 Å in compound **1b**.<sup>33</sup> The difference is attributed to the fact that, in the crystal lattice of compound **1b**, benzene molecules are separating neighboring complex molecules, while solvent molecules were not found between the trimeric molecules in the case of **1c** (Figure 4). See the Supporting Information for more details.

Within the columns, the macrocyclic rings can have two different orientations in relation to the direction of the N → B coordination bonds (Figure 5a). Therefore, two arrangements have been found: (i) For compounds **1a** and **1b**, the N–B bonds in all macrocycles within each column are oriented in the same direction (Figure 5b). (ii) In the case of compound **1c**, the macrocycles have alternating dispositions between each other in this respect (Figure 5c). Both isomers shown in Figure 5a are conformationally locked and then chiral because of the rigidity of the structure. As a consequence, the arrangement shown in Figure 5b comprises just one enantiomer in each column, whereas that in Figure 5c comprises alternating enantiomers within each column.

The above results showed that self-assembly of the starting materials allows the formation of trimeric compounds in all three cases, wherein the macrocyclic arrangement is sup-



**Figure 5.** Part of the molecular packing arrangements found in complexes **1b** and **1c**: (a) schematic representation of the two possibilities for the orientation of the N → B coordination bonds; (b) stacking arrangement found for **1b** showing the presence of only one orientation; (c) stacking arrangement found for **1c** showing the presence of both orientations.

ported by three N → B coordination bonds. Although direct evidence for the conformation of the macrocycles is unclear, we are still working with analogous systems in order to describe the driving forces that predict this behavior.

**Inclusion Properties.** The inclusion abilities of the calix-[3]arenes **1a–d** were analyzed toward a set of primary amines and ammonium cations, which were chosen on the basis of their shapes and sizes. Thus, methyl-, propyl-, heptyl-, and benzylamines were selected as representatives of different-sized guest molecules. Additionally, propyl-, hexyl-, and benzylammonium chlorides were evaluated in order to compare their recognition toward neutral and cationic species. Studies were carried out at room temperature in chloroform for the free amines and in methanol for the ammonium cations.

The ability of compounds **1a–d** to encapsulate neutral and cationic amines was evaluated by titration experiments that were monitored by UV spectroscopy. For that, solutions of the amines or ammonium chlorides were added step by step to the calixarenes **1a–d** dissolved in the same solvent. During the titration, the UV spectra showed important absorption changes as an indication of the receptor–substrate interactions. Figure 6 shows the absorption changes observed during the titration of a  $8 \times 10^{-5}$  M solution of **1c** in chloroform and with a  $10^{-2}$  M solution of methylamine in the same solvent.

Among the alkylamines tested, propylamine gave the higher association constants, indicating a good interaction with the receptors (Table 3), which can be attributed to a host–guest size complementary relationship. In the case of

(31) Akdas, H.; Bringel, L.; Graf, E.; Hosseini, M. W.; Mislin, G.; Pansanel, J.; Cian, A. D.; Fischer, J. *Tetrahedron Lett.* **1998**, *39*, 2311–2314.

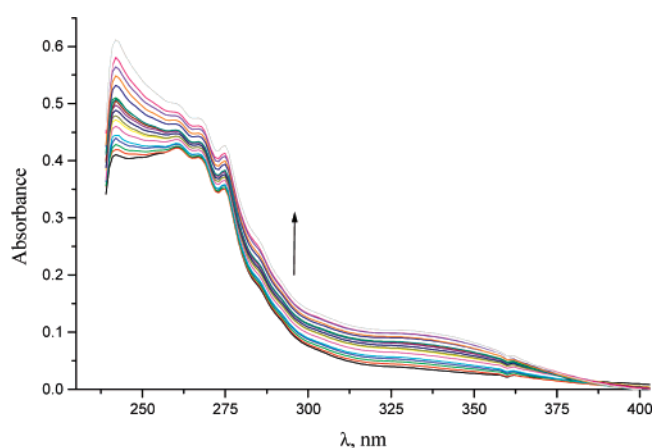
(32) Atwood, J. L.; Barbour, L. J.; Jerga, A. *Science* **2002**, *296*, 2367–2369.

(33) At the supramolecular level, the distances between the host molecules were measured from the center of the circles described in ref 30.

**Table 3.** Binding Constants for the Inclusion of Different Amines and Ammonium Chlorides within Compounds **1a–d**<sup>a</sup>

calixarene	guest, K (M <sup>-1</sup> )						
	CHCl <sub>3</sub>				CH <sub>3</sub> OH		
	methylamine	propylamine	heptylamine	benzylamine	propylammonium	heptylammonium	benzylammonium
<b>1a</b>	<i>b</i>	256 ± 47 (305, 380, and 398 nm)	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>
<b>1b</b>	<i>c</i>	<i>c</i>	<i>c</i>	<i>c</i>	$K_{11} = 1368 \pm 284$ , <sup>d</sup> $K_{12} = 608 \pm 127$ (M <sup>-2</sup> ) (316 and 336 nm)	$K_{11} = 3156 \pm 111$ <sup>e</sup> (228 and 473 nm)	$K_{13} = 5.7 \times 10^9$ $\pm 3.13 \times 10^8$ (M <sup>-3</sup> ) <sup>f</sup> (316, 336, and 358 nm)
<b>1c</b>	411 ± 31 (250, 325, and 350 nm)	2828 ± 329 (300, 330, and 350 nm)	769 ± 94 (264, 300, 315, 330, and 350 nm)	3520 ± 390 (285, 302, 325, and 350 nm)	1762 ± 147 (239, 337, 378, and 424 nm)	1032 ± 74 (237 and 420 nm)	927 ± 103 (277, 311, 375, and 424 nm)
<b>1d</b>	<i>c</i>	797 ± 107 (248 and 254 nm)	406 ± 85 (262, 272, 295, and 311 nm)	<i>b</i>	1454 ± 180 (215, 225, and 270 nm)	<i>b</i>	<i>b</i>

<sup>a</sup> Binding constants correspond to average values calculated using different wavelengths, which are shown in parenthesis for each case. <sup>b</sup> No interaction was detected. <sup>c</sup> Not tested. <sup>d</sup> Complex with a 1:2 calixarene/propylammonium stoichiometry. <sup>e</sup> Complex with a 1:2 calixarene/heptylammonium stoichiometry; a very small  $K_{12}$  value was observed. <sup>f</sup> Complex with a 1:3 calixarene/benzylammonium stoichiometry;  $K_{11} = K_{12} = 0$ .

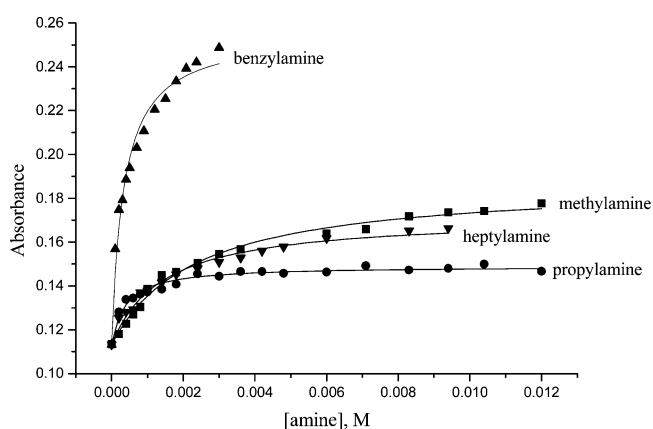


**Figure 6.** Changes of the UV absorption spectra during the titration of calixarene **1c** ( $8 \times 10^{-5}$  M) with different quantities of methylamine solutions [ $(0-1.2) \times 10^{-2}$  M]. The experiments were carried out in chloroform. The arrow indicates the spectral changes occurring in response to an increasing concentration of methylamine.

the **1c**/benzylamine complex, the higher association constant observed could be attributed to  $\pi-\pi$  interactions between the guest and salicylidene moieties, which should be stronger than the C–H $\cdots\pi$  interactions that probably occur with the aliphatic amines. It is important to remark that the titration of *p*-nitrophenol (as a model molecule with a  $pK_a$  of 7.18, which is close to that of the monomeric unit of calixarene **1c** with a  $pK_a = 7.12$ )<sup>34</sup> with propylamine in a chloroform solution did not show evidence of a possible interaction; therefore, the binding between the OH groups present in compounds **1c** and **1d** was discarded. This fact suggests that the observed and quantified effect corresponds to the guest inclusion as a result of N–H $\cdots\pi$  interactions and the hydrophobic effect of the calixarene cavity.

The absorptions recorded at different wavelengths were plotted versus the guest concentration and analyzed using

(34) The  $pK_a$  values were determined using the program *Advanced Chemistry Development Inc.*, version 3; ACD/Labs: Toronto, Ontario, Canada, 1994–1997.



**Figure 7.** Titration plots for the titration of calixarene **1c** with primary amines recorded at  $\lambda = 330$  nm in chloroform. The solid lines are the fitting curves in accordance with eq 1.

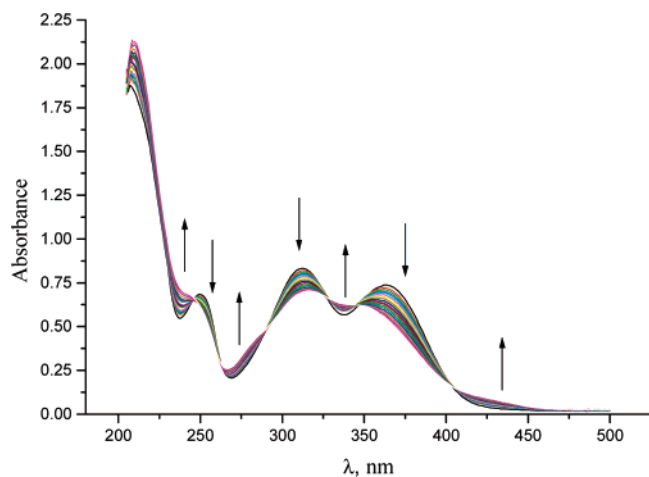
eq 1,<sup>35</sup> which assumes a 1:1 complex ratio ( $[guest] \gg [calixarene]$ ).  $A_{obs}$  is the observed absorbance,  $A_0$  is the

$$A_{obs} = (A_0 + A_{\infty}K[G]_T)/(1 + K[G]_T) \quad (1)$$

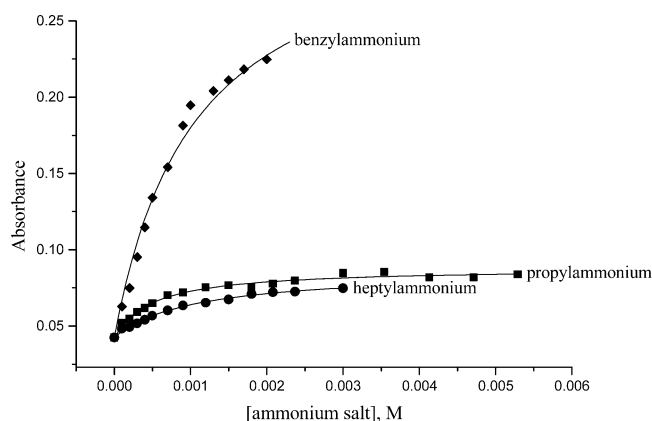
absorbance of the calixarene,  $A_{\infty}$  is the maximum absorbance induced by the presence of a given guest,  $[G]_T$  is the total concentration of the guest, and  $K$  is the binding constant of the host–guest supramolecular entity. As a representative example, Figure 7 shows the titration plots obtained for the inclusion experiment of compound **1c** with the primary amines.

As expected, the boracalix[3]arenes **1a–d** also showed recognition toward ammonium salts wherein the  $C_3$  symmetry of the ammonium salts could provide a better inclusion of the guest through the simultaneous formation of N–H $\cdots\pi$  interactions. Figure 8 depicts the absorption changes during the titration of **1c** with heptylammonium chloride in methanol, and Figure 9 shows the titration plots

(35) Schneider, H.-J.; Yatsimirsky, A. *Principles and Methods in Supramolecular Chemistry*; John Wiley & Sons: England, 2000; p 142.



**Figure 8.** Changes of the absorption spectra during the titration of calixarene **1c** ( $2.4 \times 10^{-5}$  M) with different quantities of heptylammonium hydrochloride [ $(0-1.2) \times 10^{-2}$  M]. The experiments were carried out in methanol. The arrow indicates the spectral changes occurring in response to an increasing concentration of heptylammonium hydrochloride.

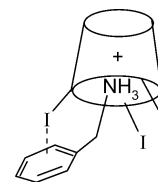


**Figure 9.** Titration plots for the titration of calixarene **1c** with ammonium chlorides recorded at  $\lambda = 424$  nm in methanol. The solid lines are the fitting curves in accordance with eq 1.

of the same host with ammonium chlorides. The average binding constants calculated for the different guests are listed in Table 3. As can be noticed, calix **1a** has no interaction toward the ammonium salt, which is contrary to the results previously observed,<sup>16</sup> wherein relatively small changes in the chemical shifts were determined by  $^1\text{H}$  NMR analysis (ca.  $\Delta\delta$  0.2 ppm). This different behavior has been attributed, in part, to the different methods and solvents used: chloroform in the case of  $^1\text{H}$  NMR<sup>16</sup> and methanol for the UV/vis determination. It has been observed that the use of polar solvents for the calix[4]arenes toward ammonium cation recognition leads to decreases in the association constant values, even when the same technique of analysis is used.<sup>36</sup>

In the case of compounds **1c** and **1d**, the analyses showed that the host–guest complexes are formed in a 1:1 ratio, as it was observed also for the recognition of the free amines. Nonetheless, the largest association constants for the complexation of ammonium salts are obtained with calix[3]arene **1b**. In fact, in the case of host **1b**, the analysis of the titration plots showed that the binding constants were different

**Chart 1.** Schematic Representation of the Calix **1b**/Benzylammonium Inclusion Complex



depending on the wavelength, thus indicating a more complex association scheme for this case. For that reason, the experimental data were analyzed by using eq 2.<sup>35</sup>  $A_{\text{obs}}$  is

$$A_{\text{obs}} = \{A_0 + A_{11}K_{11}[G]_{\text{T}} + A_{12}K_{11}K_{12}[G]_{\text{T}}^2\}[H]_{\text{T}} / (1 + K_{11}[G]_{\text{T}} + K_{11}K_{12}[G]_{\text{T}}^2) \quad (2)$$

the observed absorbance,  $A_0$ ,  $A_{11}$ , and  $A_{12}$  are the absorbances of the free host (calixarene) and its 1:1 and 1:2 respective complexes,  $K_{11}$  and  $K_{12}$  are the corresponding stepwise formation constants, and  $[G]_{\text{T}}$  and  $[H]_{\text{T}}$  are the total concentrations of the guest and host, respectively.

Thus, both complexes were considered: the 1:1 and 1:2 host–guest ratios. With this method, better wavelength-independent binding constant relationships were observed for **1b**/propylammonium and **1b**/heptylammonium complexes.

Furthermore, the experimental data for the **1b**/benzylammonium complex suggested a strong cooperative effect, forming a 1:3 calixarene/benzylammonium complex. The 1:3 stoichiometry was confirmed by continuous-variation (Job) plots.<sup>37</sup> The fitting curve in accordance with eq 3 shows a good agreement with the experimental points (see the Supporting Information).

$$A_{\text{obs}} = (A_0 + A_{\infty}K_{13}[G]_{\text{T}}^3) / (1 + K_{13}[G]_{\text{T}}^3) \quad (3)$$

The high selectivity could be hypothesized as being due to the existence of a cooperative effect between the calix shape and the iodine groups present in the lower rims, which can increase the recognition factor through  $\text{I} \cdots \pi$  interactions, as depicted in Chart 1. As a consequence of the three iodine atoms present in the molecule, three aromatic units can be incorporated into the host, which is in accordance with the stoichiometry observed. It is well-known that iodine can form charge-transfer complexes through  $\text{I} \cdots \pi$  interactions.<sup>38</sup>

## Conclusion

We have developed both an efficient and a convenient one-pot approach to the synthesis of heterocalix[3]arenes. It was noticed that the presence of different substituents on the aromatic ring base of salicylaldehyde has no influence on the reaction course. In all three cases, trimeric compounds were obtained. These macrocycles are stabilized through the formation of three  $\text{N} \rightarrow \text{B}$  coordination bonds, which allow easy self-assembly of the counterpart materials. The presence of two different aromatic fragments gives rise to different

(36) Arduini, A.; Pochini, A.; Secchi, A. *Eur. J. Org. Chem.* **2000**, 2325–2334.

(37) Connors, K. A. *Binding Constants. The Measurement of Molecular Complex Stability*; John Wiley & Sons: New York, 1987; p 24.

(38) Bühler, R. E. *J. Phys. Chem.* **1972**, 76, 3220–3228.



### ***Boron Macrocycles Having a Calix-Like Shape***

conformers, of which the *double-cone*, the *cone-partial cone*, and the *partial cone-partial cone* conformations have been detected experimentally in the solid state by X-ray diffraction analysis. These new macrocycles have a cavity large enough for the inclusion of primary amines as well as ammonium chloride derivatives. Furthermore, as was observed for the **1b**/benzylammonium complex, the cooperative effect between the calix shape and  $I\cdots\pi$  interactions can help to increase the host-guest recognition.

Further investigation on exploring other synthetic strategies to improve the yields is ongoing in our group. Studies also are now in progress to understand the factors that influence

the nature of the conformation of the macrocycles as well as to identify more details of the host-guest molecular interactions.

**Acknowledgment.** Financial support of CONACyT and Programa de Ingeniería Molecular-IMP are gratefully acknowledged.

**Supporting Information Available:** Additional X-ray figures, titration plots, and crystallographic data (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

IC051850O