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Heterodimer of tetraaryl- and tetratosylurea calix[4]arenes: first single crystal X-ray analysis and guest encapsulation properties in $CDCl_3$

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Abstract—The first single crystal X-ray analysis of the heterodimer of tetraaryl- and tetratosylurea calix[4]arenes was reported, which revealed the real pattern of the hydrogen bonds. Moreover, the heterodimer showed good encapsulation abilities for some organic molecules in $CDCl_3$.

Self-assembled capsules[1] are of current interest in supramolecular chemistry for their potential applications in chemical, biologic, and material sciences. Calix[4]arenes have been used as useful building blocks for self-assembled capsules.[2] In particular, the dimeric capsules[3] formed by urea substituted calix[4]arenes on their wide rim in aprotic, apolar solvents are highly attractive. This has been established to have a seam of hydrogen bonds between the urea functions by ^{1}H NMR spectral methods[4] and single crystal X-ray analysis of homodimers.[5] It was found that generally two identical tetraurea calix[4]arenes can form homodimeric capsules, but different tetraurea calix[4]arenes result in heterodimeric capsules with statistical equilibrium.[4b]

In 1997, Rebek et al.[6] first reported that the heterodimer in an equimolar solution of tetraaryl- and tetratosylurea calix[4]arenes was formed exclusively in apolar solvent. This might be due to the increased acidity of the tosylurea and the aryl–aryl interactions of the tosyl groups of arylureas and tosylureas.[7] This result has been used to construct linear polymers,[7] and structurally uniform dendrimers.[8] Such heterodimers also showed encapsulation properties to benzene or camphor in *p*-xylene,[6,9] and chloroform in the absence or presence of other guests.[10] It is surprising to note that so far no single crystal analysis of the heterodimer is reported, although it might be useful to reveal such a structure and further find more practical applications in supramolecular chemistry.

Here we[11] report the single crystal X-ray structure of the heterodimer **1a**·**2a**. It not only confirms unambiguously the existence of such a hydrogen-bonded heterodimer in the crystalline state but also reveals the real pattern of the hydrogen bonds. Moreover, the heterodimer **1b**·**2b** shows good encapsulation abilities for *N*-methyl-2-pyrrolidone, cyclohexanone, cycloheptanone, and cyclohexanol in $CDCl_3$ (Fig. 1).

Single crystal of **1a**·**2a**[12] suitable for X-ray analysis was obtained by slow diffusion of *n*-pentane into an equimolar mixture of **1a** and **2a** in dichloromethane/benzene solution. As shown in Figure 2, the heterodimer is composed of two crystallographically independent calix[4]arenes, which are entangled via their urea residues. The arylurea unit forms a nearly planar system with the interplanar angles of 23.37°, 17.99°, 24.15°, and 23.69° between ring I (phenolic unit of the calixarene) and ring II (tolyl residue of the urea). Because of the tetrahedron shape of sulfur atom,[13] the tosylurea units

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Keywords: Dimeric capsule; Calix[4]arene; Self-assembly; X-ray analysis; Guest encapsulation.

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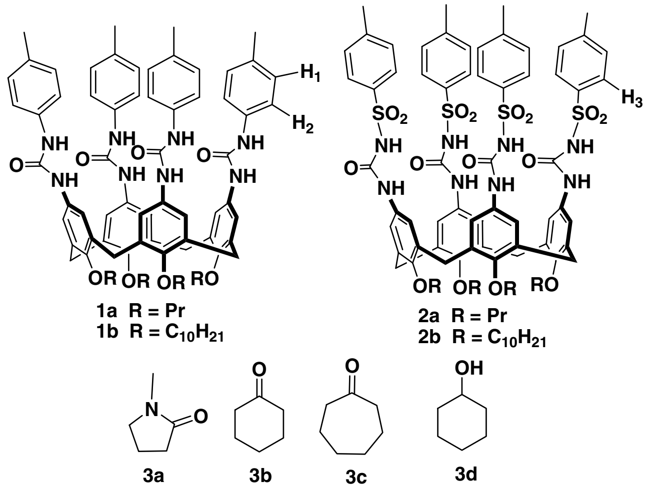

Figure 1. Chemical structures of tetraarylurea calix[4]arene **1**, tetratosylurea calix[4]arene **2** and the guests **3a**–**d** used in encapsulation studies.

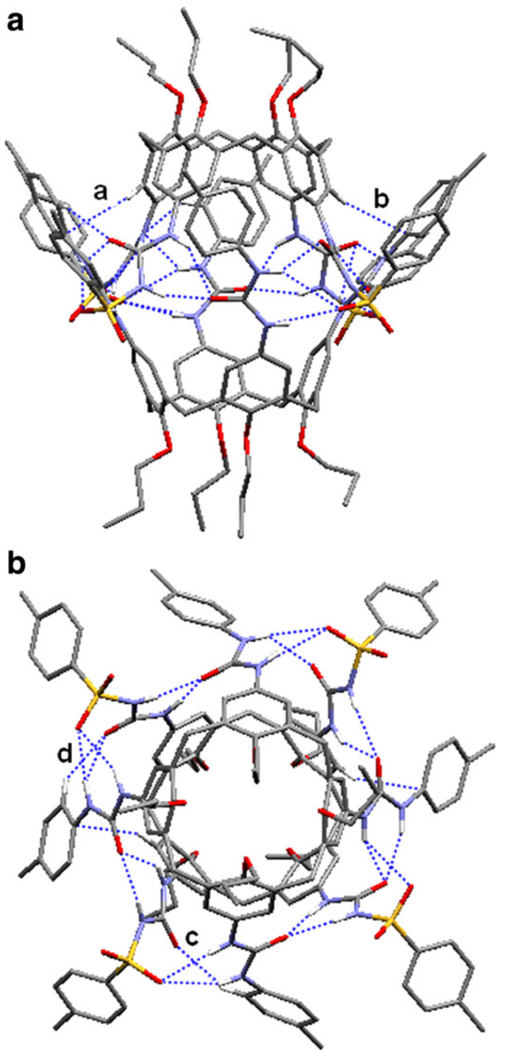

Figure 2. (a) Side view and (b) top view of crystal structure of the dimer **1a**·**2a**. Solvent molecules (dichloromethane and benzene) and hydrogen atoms are omitted for clarity.

have a big bend of 114.66°, 92.71°, 124.75°, and 102.65°. As a result, eight tolyl residues are toward one direction. The distances of H_1 to H_3 and H_2 to H_3 are 2.835 Å and 2.947 Å, respectively, which are consistent with results of the NOE contacts.[7] However, the distances of the tolyl groups of arylurea and tosylurea are too far to form the aryl–aryl interactions.[14] The distance between the planes through the methylene carbon atoms is 10.39 Å. This distance is longer than that in the homodimer, which indicates that the volume of this heterodimer is larger than that of the homodimer.

Figure 3 shows the belt of urea functions forming the hydrogen-bonding system, which holds together the heterodimer. This reveals a different intermolecular hydrogen bond pattern from those of the homodimers of tetraarylurea calix[4]arenes.[5a] In the crystal structure of **1a**·**2a**, there exist seven $\mathrm{S{=}O\cdots HN}$ hydrogen bonds and thirteen $\mathrm{C{=}O\cdots HN}$ hydrogen bonds, in which five three-center $\mathrm{C{=}O\cdots HN}$ hydrogen bonds, three two-center $\mathrm{C{=}O\cdots HN}$ hydrogen bonds, three $\mathrm{S{=}O\cdots HN}$ three-center hydrogen bonds and one $\mathrm{S{=}O\cdots HN}$ two-center hydrogen bonds were observed.

The distances and angles of the hydrogen bonds are summarized in Table 1. Compared with the homodimer of the tetraarylurea calix[4]arene,[5a] it was found that the lengths of the hydrogen bonds of the heterodimer **1a**·**2a** are shorter than those of the homodimers. Moreover, three-center hydrogen bonds are generally weaker than two-center hydrogen bonds due to the negative cooperativity.[15] These results imply that the hydrogen bonds of the heterodimer are stronger than those of the homodimer. Besides the conventional H-bonds, a pair of intermolecular $\mathrm{CH}\cdots\pi$ interactions with the distances of 2.832 Å (a) and 2.832 Å (b), and a pair of $\mathrm{CH}\cdots\mathrm{O}$ interactions between the two calix[4]arenes with distances of 2.618 Å (c) and 2.553 Å (d) were also observed

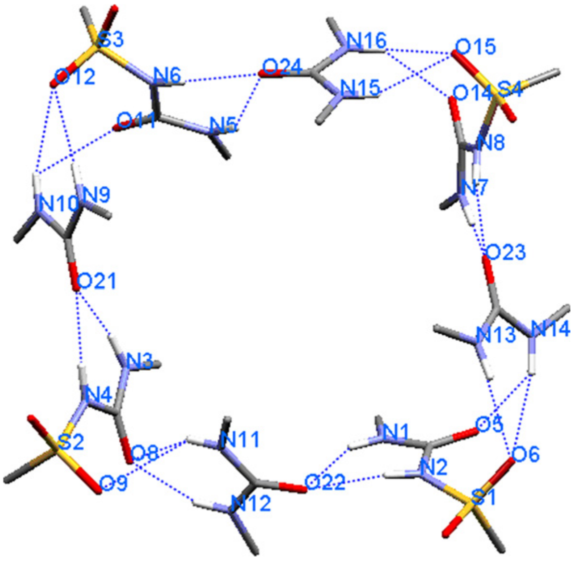

Figure 3. The belt of hydrogen bonds in **1a**·**2a**. Solvent molecules and hydrogen atoms are omitted for clarity. Hydrogen bonds are indicated by dotted lines.

Table 1. The distances of N···O and the angles of NH···O of the belt of hydrogen bonds in the crystal

Distance of N···O (Å)	Angle of NH···O (°)	Distance of N···O (Å)	Angle of NH···O (°)
N(1)O(22)	N(1)O(22)	N(2)O(22)	N(2)O(22)
2.858	153.92	2.856	141.80
N(3)O(21)	N(3)O(21)	N(4)O(21)	N(4)O(21)
2.933	151.08	2.751	155.24
N(5)O(24)	N(5)O(24)	N(6)O(24)	N(6)O(24)
2.903	143.96	2.755	147.02
N(7)O(23)	N(7)O(23)	N(8)O(23)	N(8)O(23)
3.096	147.47	2.735	159.04
N(9)O(12)	N(9)O(12)	N(10)O(11)	N(10)O(11)
3.042	170.58	2.965	110.47
N(10)O(12)	N(10)O(12)	N(11)O(8)	N(11)O(8)
3.345	149.32	3.476	145.25
N(11)O(9)	N(11)O(9)	N(12)O(8)	N(12)O(8)
3.148	122.26	2.906	150.59
N(13)O(6)	N(13)O(6)	N(14)O(5)	N(14)O(5)
3.023	166.40	2.973	128.59
N(14)O(6)	N(14)O(6)	N(15)O(15)	N(15)O(15)
3.418	143.70	2.972	152.97
N(16)O(14)	N(16)O(14)	N(16)O(15)	N(16)O(15)
2.899	135.41	3.428	142.68

(Fig. 2). These non-covalent interactions may play an important role in formation of the heterodimer, but they do not exist in the homodimer.[5a]

Furthermore, we also studied the encapsulation properties of such a heterodimer to some organic guests in $CDCl_3$. We used **1b** and **2b** as hosts because of the poor solubility of **1a** and **2a** in $CDCl_3$. In general, such heterodimers cannot encapsulate other guests in chloroform because chloroform is an excellent guest.[10] But we found that the heterodimer **1b·2b** could encapsulate guests **3a–d** in $CDCl_3$. Moreover, it was also found that the heterodimer shows better encapsulation abilities than the homodimers.

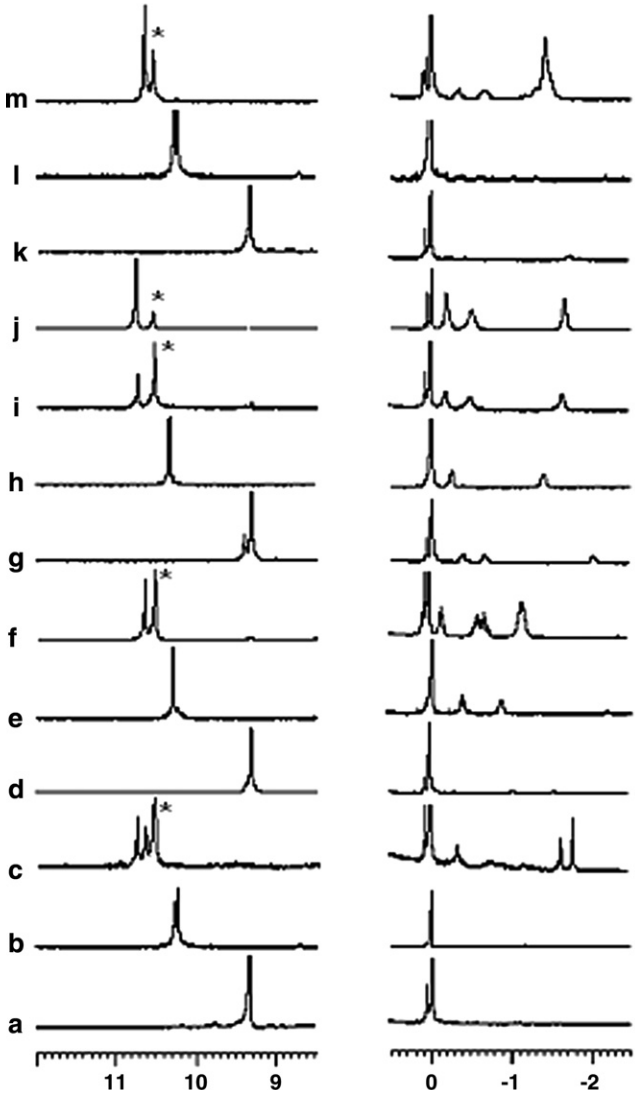

Figure 4. Partial ^1H NMR spectra (300 MHz, $CDCl_3$, 298 K) of (a) **1b** + **3a**; (b) **2b** + **3a**; (c) **1b** + **2b** + **3a**; (d) **1b** + **3b**; (e) **2b** + **3b**; (f) **1b** + **2b** + **3b**; (g) **1b** + **3c**; (h) **2b** + **3c**; (i) **1b** + **2b** + **3c**; (j) **1b** + **2b** + **3c**, after 2 days; (k) **1b** + **3d**; (l) **2b** + **3d**; (m) **1b** + **2b** + **3d**. Guests are excess. The NH signal of complex **1b·2b** containing $CDCl_3$ is indicated by star.

As shown in Figure 4, no obvious or poor encapsulation occurred when **1b**, and guests or **2b** and guests were mixed. But when **1b**, **2b** and guests were mixed, the region of −3–0 ppm showed the proton signals of encapsulated guests, while new NH signals of ureas appeared at 10–11 ppm. In the ^1H NMR spectrum of the complex **1b·2b** in the presence of **3a** (Fig. 4c), a double resonance pattern of the NH signals was observed, which implied that symmetry of the heterodimer was lost after encapsulation of guest **3a**.[7] For guest **3c**, the NH signals of the encapsulated dimer became stronger after two days (Fig. 4j), which indicated that guest exchange was kinetically stable. Moreover, it was also found that chloroform-*d* could not be completely replaced by **3a** (Fig. 4c) and **3b** (Fig. 4f), but it could be almost completely replaced by **3c** (Fig. 4j) and **3d** (Fig. 4m).[10] These observations suggested that the cavity of the heterodimer **1b·2b** is more suitable to guests **3**, especially bigger guests **3c** and **3d**, than chloroform.

In summary, we have described the first single crystal structure of the heterodimer of tetraaryl- and tetratosylurea calix[4]arenes and revealed the real pattern of hydrogen bonds. Moreover, we have also found that the heterodimer of **1b** and **2b** could encapsulate some organic guests in chloroform, but the homodimers did not work. The results presented here will provide us further opportunities to develop new functional heterodimers, such as heterodimeric capsules of inherently chiral calix[4]arenes,[16] which are in progress.

Acknowledgments

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11. Compounds **1a**,[17] **1b**,[17] **2b**[7] were synthesized according to the literatures. *Synthesis of* **2a**: To a solution of the tetraamino calix[4]arene (0.30 g, 0.46 mmol) in dry CH_2Cl_2 (50 mL) under N_2 was added *p*-toluenesulfonyl isocyanate (0.70 mL, 4.60 mmol). The reaction mixture was stirred at room temperature for 4 h, and then concentrated in vacuo. The resulting solid was triturated with MeOH, filtered, and dried in vacuo to give the product **2a** as a white power (0.61 g, 92.4%). Mp >300 °C. ^{1}H NMR (300 MHz, DMSO-d_6, 298 K): δ 10.21 (br s, 4H), 8.42 (s, 4H), 7.82 (d, $J = 8.1$ Hz, 8H), 7.42 (d, $J = 8.0$ Hz, 8H), 6.61 (s, 8H), 4.20 (d, $J = 12.6$ Hz, 4H), 3.68 (t, $J = 6.9$ Hz, 8H), 3.00 (d, $J = 12.6$ Hz, 4H), 2.40 (s, 12H), 1.81 (q, $J = 7.2$ Hz, 8H), 0.90 (t, $J = 6.9$ Hz, 12H) ppm. ^{13}C NMR (75 MHz, DMSO-d_6, 298 K): δ 179.9, 152.0, 149.0, 143.7, 141.8, 137.2, 131.7, 127.4, 119.0, 76.4, 30.3, 22.7, 21.0, 10.1 ppm. MALDI-TOF MS: m/z 1464.2 $(M+Na)^+$. Elemental Anal. Calcd for $C_{72}H_{80}N_8O_{16}S_4$: C, 59.98; H, 5.59; N, 7.77. Found: C, 60.02; H, 5.56; N, 7.86.
12. *Crystal data for complex* **1a·2a**: $C_{343}H_{379}Cl_8N_{32}O_{48}S_8$, $M_w = 6257.88$, crystal size: $0.28 \times 0.24 \times 0.08$ mm^3, crystal system: triclinic, space group: $P(-1)$, $a = 18.244(3)$ Å, $b = 21.954(4)$ Å, $c = 24.082(5)$ Å, $\alpha = 98.506(9)°$, $\beta = 107.685(10)°$, $\gamma = 107.411(11)°$, $U = 8461(3)$ Å^3, $Z = 4$, $T = 113(2)$ K, $\mu = 0.190$ mm^{-1}, 66,805 reflections measured, 32,325 unique ($R_{int} = 0.0700$), $R_1 = 0.1449$, $wR_2 = 0.3823$. CCDC637268 contains the supplementary crystallographic data for **1a·2a**. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk.
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14. The centroid–centroid distances of the tolyl groups of arylurea and tosylurea are 6.443, 7.845, 6.261, 7.270, 5.923, 7.686, 5.619, and 7.671 Å, respectively.
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