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Unsymmetrical N and/or O-bridged calixarene derivatives: synthesis, structure and encapsulation of solvent molecules in the solid state

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ABSTRACT

Eight unsymmetrical N and/or O-bridged calixarene derivatives were obtained by **1** (naphthalene-2,7-diol), **2** (bis(4-hydroxyphenyl)methanone), **3** (4,4′-methylenedianiline), **4** (3,3′-methylenedianiline), **5** (4,4′-oxydianiline) and **6** (4,4′-(perfluoropropane-2,2-diyl)dianiline) reacting with fragment **a** (4,4′-bis(-dichloro-*s*-triazinyloxy)propane-2,2-diyldibenzene) and **b** (*N*,*N*′-bis(dichloro-*s*-triazinyl)-4,4′-methylenedianiline) under very mild reaction conditions via efficient fragment coupling strategy. We also obtained the crystal structure of **1a** (tetraoxocalix[2](propane-2,2-diyldibenzene,naphthalene)[2]triazine) which can form a molecular capsule by two dimers with C–H···N and C–H···O quadruple hydrogen bonds, and it has the encapsulation ability toward solvent molecules.

Proficiency in the art of design and synthesis of novel and functional macrocyclic host molecules is a fundamental target of the modern supramolecular chemistry. Along with the rapid development of supramolecular chemistry, it is apparent that oxa-[1] and azacalixarenes[2] have become the star molecules getting on the stage of the macrocyclic host–guest chemistry due to their facile synthesis and the interesting supramolecular properties that nitrogen and oxygen can bring to the host molecules. Hitherto, there is much compelling work in this area, especially from groups such as Wang,[1b–f,2c–g,3,5a–c] Chen,[1m,n,2m,n,5e] Katz,[1g,h,2l] Chambers,[1a] Dehaen,[1i,j] and Siri.[2i–k] And preliminarily, heterocalixaromatics have exhibited potential recognition to various guest species.[3]

In our previous work, we have developed a one-pot approach toward cavity-size tunable oxacalixarene derivatives.[4] However, for the synthesis of unsymmetrical heterocalixaromatics,[5] the fragment coupling[1b] is more ideal than the one-pot approach due to the appealing advantages in the straightforward introduction of different heteroatoms and substituents into the bridging positions.[2d] In a continuation of our efforts, herein we reported a convenient fragment coupling strategy for the synthesis of novel unsymmetrical N and/or O-bridged calixarene derivatives under very mild conditions from simple and easily available starting materials. We also obtained the crystal structure of **1a** which can form a molecular capsule by two dimers with C–H···N and C–H···O quadruple hydrogen bonds, and it has the encapsulation ability toward solvent molecules.

We began our investigation with 4,4′-(propane-2,2-diyl) diphenol (3.42 g, 15 mmol) as the nucleophilic reagent reacting with cyanuric chloride (5.54 g, 30 mmol) in the presence of diisopropylethylamine (DIPEA) (4.84 g, 37.5 mmol) using tetrahydrofuran (THF) (100 ml) (Scheme 1). To avoid the production of di- or trisubstitution chlorine, ice bath was used.[6] Molecular fragment **a** (4,4′-bis(dichloro-*s*-triazinyloxy)propane-2,2-diyldibenzene) was obtained in a 48% yield. The yield can be elevated slightly when a large excess amount of cyanuric chloride was used.[1b]

With fragment **a** in hand, the synthesis of **1a** was then attempted under different conditions. As shown in Table 1, both the base and the solvent were employed. When the reaction was conducted with the base DIPEA, the use of 1,4-dioxane, DMF, and CH_3CN all gave only a trace amount of the desired product **1a** (entries 3–5), and the use of THF only gave 17% yield (entry 2), whereas acetone acted as an effective solvent to promote the formation of **1a** in a 66% yield (entry 1). And then, change of the base from inorganic base (Na_2CO_3 and K_2CO_3) to organic base (Et_3N), no expected product was observed (entries 6–8). So the combination of DIPEA with acetone was the optimization condition for the synthesis of **1a**.

With the optimization condition, a series of diphenols and aromatic diamines were investigated for the synthesis of the unsymmetrical heterocalixaromatic derivatives. In the beginning, as illustrated in Scheme 2, naphthalene-2,7-diol (**1**) (160 mg, 1 mmol) reacted with **a** (524 mg, 1 mmol) in acetone (80 ml), with the addition of DIPEA (322.5 mg, 2.5 mmol) as the acid scavenger to afford **1a** in a 70% yield. As the result of the introduction of the naphthalene with fluorescence effect and electron-rich conjugate surfaces into the molecule, it was expected that the conformation of the host molecule could demonstrate interesting effects.

In succession, treatment of bis(4-hydroxyphenyl)methanone (**2**) (214 mg, 1 mmol) with molecular fragment **a** (524 mg, 1 mmol) in the same conditions led to the formation of **2a** in a 61% yield

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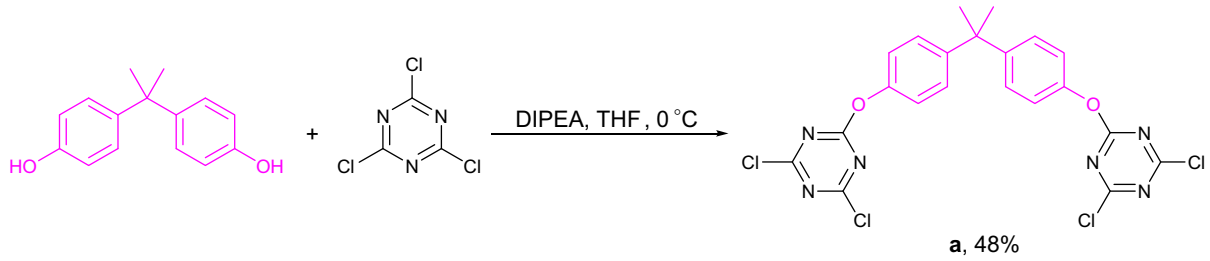
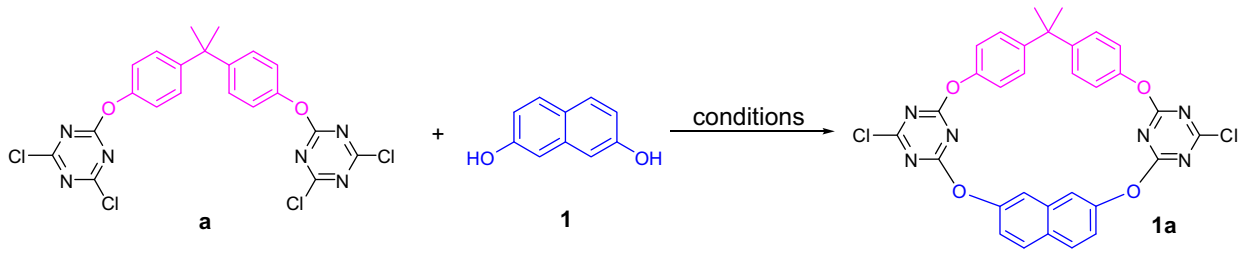


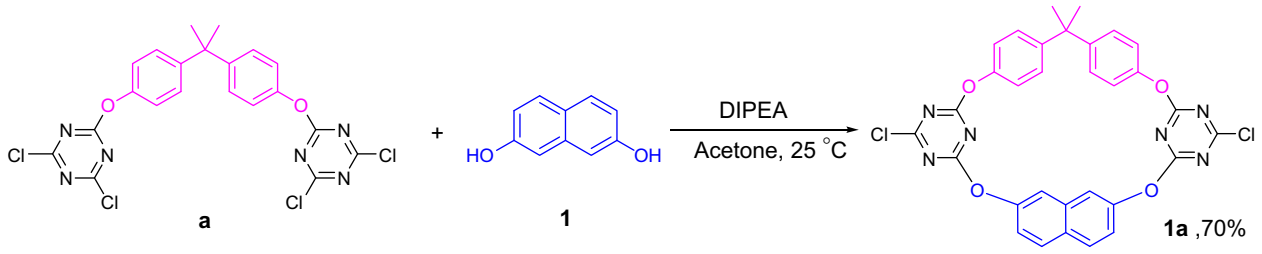
Scheme 1. Synthesis of the molecular fragment **a**.

Table 1
Synthesis of tetraoxocalix[2](propane-2,2-diyldibenzene,naphthalene)[2]triazine **1a**[a]



Entry	Solvent	Base	Temp. (°C)	Time (h)	**1a** Yield[b]
1	Acetone	DIPEA	25	20	66%
2	THF	DIPEA	25	20	17%
3	1,4-Dioxane	DIPEA	25	20	<10%
4	DMF	DIPEA	25	20	0
5	CH_3CN	DIPEA	25	20	<10%
6	Acetone	Na_2CO_3	25	20	0
7	Acetone	K_2CO_3	25	20	0
8	Acetone	Et_3N	25	20	0

[a] Reaction was carried out with 1.0 equiv of fragment **a**, 1.0 equiv **1** (naphthalene-2,7-diol) and 2.5 equiv of base.
[b] Isolated yields.



Scheme 2. Synthesis of unsymmetrical O-bridged calixarene derivatives **1a** via fragment coupling strategy.

(Scheme 3). With the carbonyl group linking the two benzenes, we envision it may not only remodel the molecule, but also enlarge the size of the cavity.

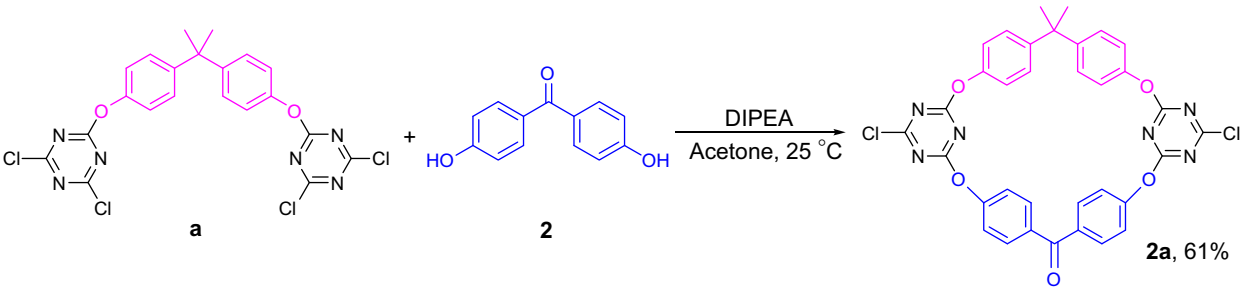
In order to obtain more molecules with tunable conformations and cavities, a series of aromatic diamines (**3**–**6**) were also investigated, under the prior condition. To our delight, **3a**, **4a**, **5a**, **6a** could be obtained in 58%, 64%, 70% and 55% yields, respectively, and the diverse aromatic diamines have little influence on the overall reaction efficiency (Scheme 4).

Given the diversity of our research system and the orderliness of the conformations of the macrocycles, fragment **b** (*N*,*N*′-bis(dichloro-*s*-triazinyl)-4,4′-methylenedianiline) was obtained by condensation of 4,4′-methylenedianiline (**3**) (1.98 g, 10 mmol) with cyanuric chloride (3.69 g, 20 mmol) in the presence of DIPEA (3.25 g, 25 mmol) using THF (100 ml) in an ice bath (Scheme 5).

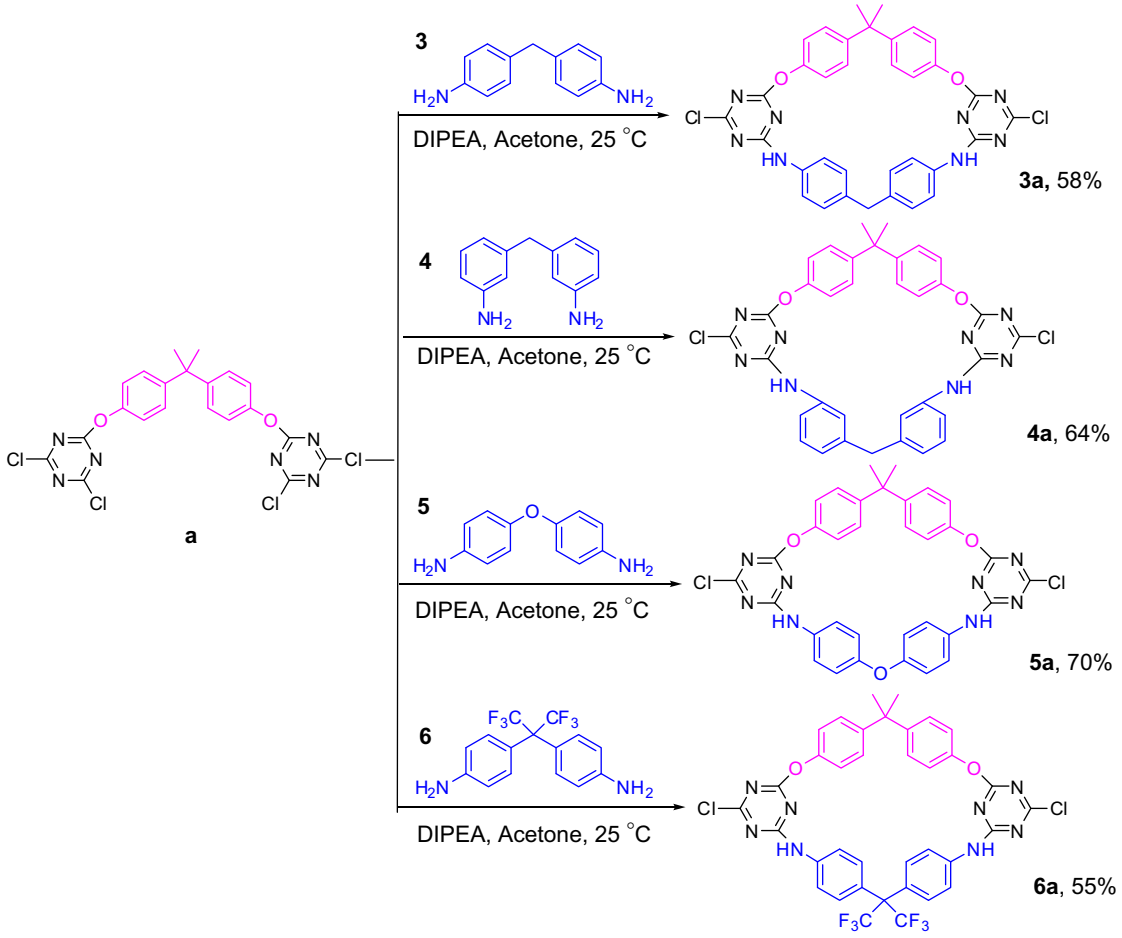
Compounds **2b** and **5b** were prepared by the fragment **b** (494 mg, 1 mmol) condensing with bis(4-hydroxyphenyl)methanone (**2**) (214 mg, 1 mmol) and 4,4′-oxydianiline (**5**) (200 mg, 1 mmol) in the presence of DIPEA (322.5 mg, 2.5 mmol) in acetone (100 ml) at room temperature (25 °C) (Scheme 6).

Fortunately, crystal of unsymmetrical O-bridged calixarene derivatives **1a**[7] was obtained from slow evaporation of chloroform solvent. The crystal structure of **1a** adopts a twisted 1,3-alternate conformation (Fig. 1). The cavity of **1a** can be regarded as being constructed by one naphthalene ring, propane-2,2-diyldibenzene segments and two triazine rings.

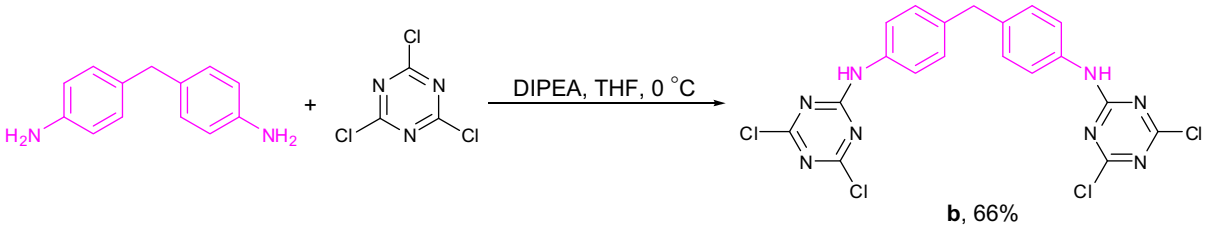
X-ray structure analysis also showed that two molecules of **1a** can form a dimer by C–H···N ($d_{N\cdots H}$ = 2.645 Å, $\theta_{C-H\cdots N}$ = 165.72°) and C–H···O ($d_{O\cdots H}$ = 2.664 Å, $\theta_{C-H\cdots O}$ = 154.81°) quadruple hydrogen bonds in the direction of face-to-face (Fig. 2). Subsequently, it



Scheme 3. Synthesis of unsymmetrical O-bridged calixarene derivatives **2a** via fragment coupling strategy.

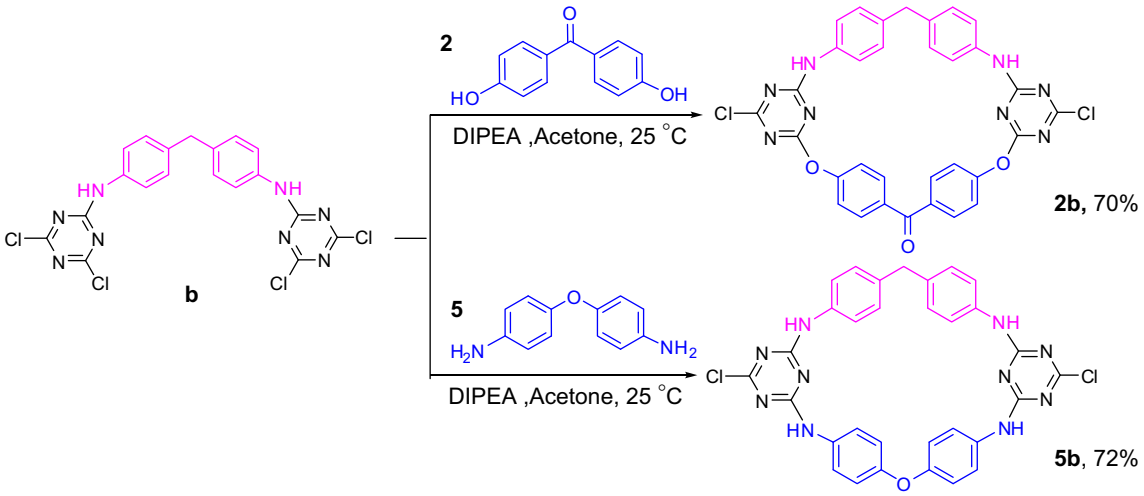


Scheme 4. Synthesis of unsymmetrical N, O-bridged calixarene derivatives **3a**, **4a**, **5a**, **6a** via fragment coupling strategy.



Scheme 5. Synthesis of the molecular fragment **b**.

is worth noting that a molecular capsule can be shaped by two dimers through one pair of C–H···O hydrogen bonds ($d_{O\cdots H}$ = 2.526 Å, $\theta_{C-H\cdots O}$ = 164.69°) and one pair of C–H···π interactions ($d_{H\cdots\pi}$ = 2.866 Å, $\theta_{C-H\cdots\pi}$ = 32.73°). And one chloroform molecule was encapsulated in the cavity (Fig. 3). Finally, along the direction of *c*-axis, an infinite molecular chain also can be viewed, which



Scheme 6. Synthesis of unsymmetrical N, O-bridged calixarene derivatives **2b** and **5b** via fragment coupling strategy.

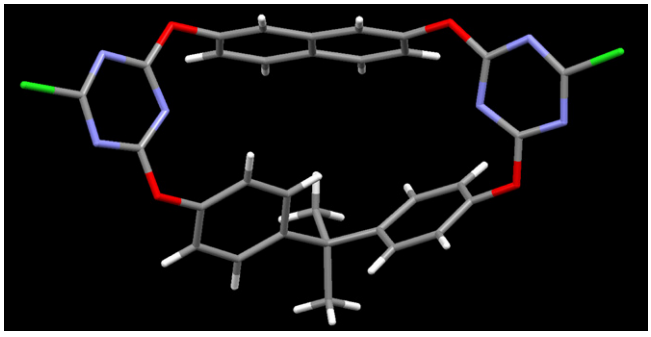


Figure 1. Crystal structure of unsymmetrical O-bridged calixarene derivatives **1a** (top view).

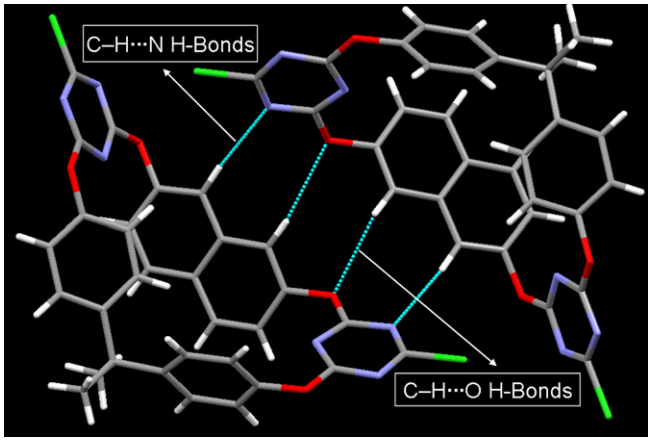


Figure 2. The structure of dimer formed by two **1a** molecules.

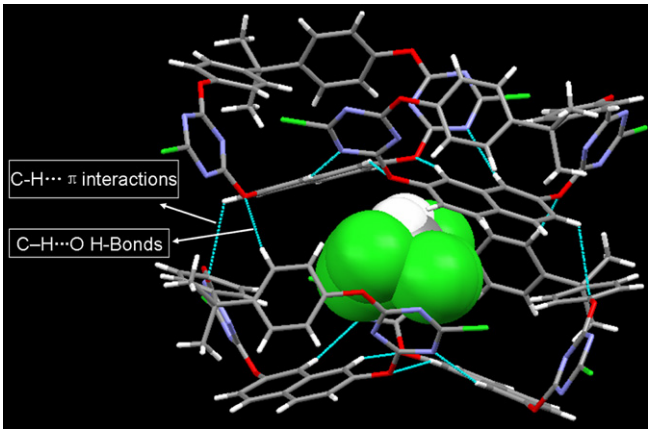


Figure 3. The molecular encapsule of **1a** formed by two dimers and solvent molecule $CHCl_3$.

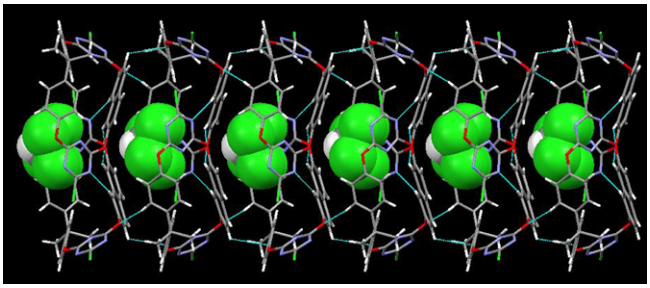


Figure 4. The infinite molecular chain formed by the molecular capsules of **1a** linking with each other along the direction of *c*-axis.

was formed by the molecular capsules linking with each other (Fig. 4). Furthermore, in the crystal structure, the solvent molecule $CHCl_3$ exists the phenomenon of symmetrical disorder. Due to the unsymmetrical structure and the inclusion mechanics of **1a**, we suppose that these molecules will unfold engaging conformations and develop to be the potential powerful host molecules with excellent inclusion ability in supramolecular system.

In order to study conformation of the molecules in solution, we further carried out the variable-temperature ^1H NMR experiments of compounds **1a**, **3a**, **4a**, **5a,** and **6a** in $CDCl_3$ solution, and found that no significant changes for compounds **1a**, **3a**, **5a,** and **6a** at 298, 308, and 318 K. This indicated that these compounds might have a rigid conformation at this temperature range. However, significant spectral changes appeared for compound **4a** when temperature was changed from 298 to 318 K. So we dissected these changes once again from 298 to 319 K for every 3 K (Fig. 5).

From the spectrum of **4a**, we predicated the phenylene proton signal H_a of **4a** appeared as a singlet at $\delta = 7.46$ ppm in $CDCl_3$

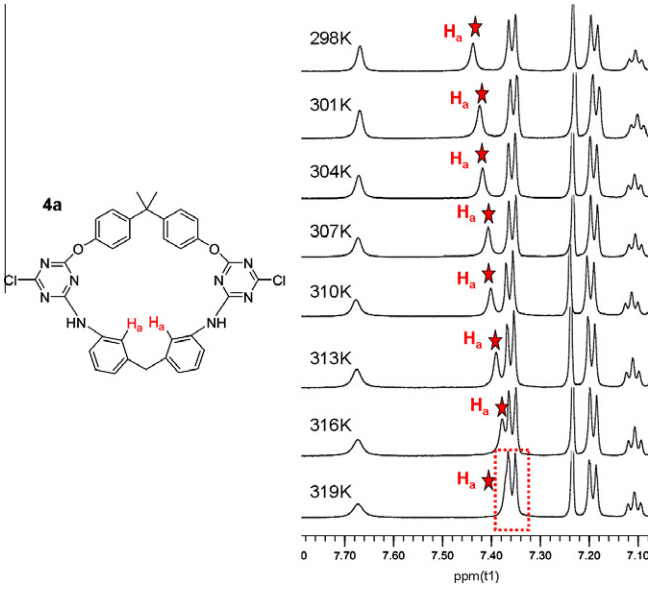


Figure 5. Variable-temperature ^{1}H NMR experiments of compound **4a** in $CDCl_3$ solution.

solution at 298 K. When temperature was elevated from 298 to 319 K for every 3 K, the proton signal moved upfield gradually and finally was enfolded into the neighboring doublet. This phenomenon might attribute to the conformational conversion of compound **4a** in solution (See S10–S14 of Supplementary data for details).

In summary, a number of unsymmetrical N and/or O-bridged calixarene derivatives have been synthesized via general and good-yield fragment coupling strategy. And we obtained the crystal structure of **1a** which can form a molecular capsule by two dimers with C–H···N and C–H···O quadruple hydrogen bonds. And it has the inclusion ability toward solvent molecules. Variable-temperature ^{1}H NMR experiments of compound **4a** in $CDCl_3$ solution have been carried out, and the chemical shift of phenylene proton signal H_a of **4a** might demonstrate the conformational conversion of compound **4a** in solution. Progress in the recognition ability of these compounds is still underway. The work will be reported in due course.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.12.099.

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7. Crystal structure data for compound **1a**: CCDC 850834. $C_{63}H_{41}Cl_7N_{12}O_8$, chemical formula weight: 1342.23, tetragonal space group *I4(1)cd*, a = 28.8658 (2), b = 28.8658 (2), c = 14.754 (2) Å; α = 90.000°, β = 90.000°, γ = 90.000°, U = 12294(2) Å^3, T = 298 (2) K, Z = 8, DC = 1.450 mg/m^3, μ = 0.390 mm^{-1}, λ = 0.71073 Å, F(000) 5488, crystal size 0.20 × 0.20 × 0.10 mm^3, 5374 independent reflections [R(int) = 0.1147], reflections collected 31488, refinement method: full-matrix least-squares on F^2: goodness-of-fit on F^2 1.104, final R indices [$I > 2\sigma(I)$], $R1$ = 0.0647, $wR2$ = 0.1392, largest diff. peak and hole 0.191 Å^{-3} and −0.193 e Å^{-3}.