

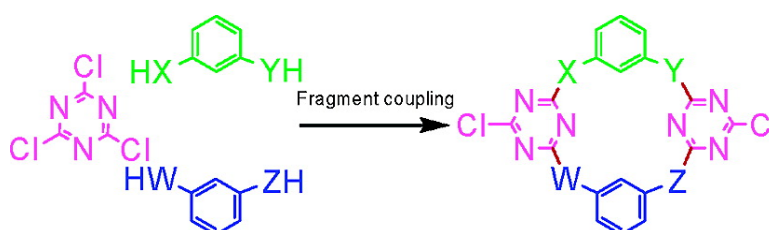
Article

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J. Am. Chem. Soc., **2004**, 126 (47), 15412-15422 • DOI: 10.1021/ja0465092 • Publication Date (Web): 06 November 2004

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A General and High Yielding Fragment Coupling Synthesis of Heteroatom-Bridged Calixarenes and the Unprecedented Examples of Calixarene Cavity Fine-Tuned by Bridging Heteroatoms

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Abstract: A number of aza- and/or oxo-bridged calix[2]arene[2]triazines have been synthesized through an unusually high yielding and efficient fragment coupling approach starting from cyanuric chloride and resorcinol, 3-aminophenol, *m*-phenylenediamine, and *N,N'*-dimethyl-*m*-phenylenediamine. These novel macrocycles, which belong to the next generation of calixarenes or cyclophanes, form a unique cavity that is resulted from two isolated benzene planes and two bis-heteroatom-conjugated triazine planes in a 1,3-alternate fashion. The nature of the bridging heteroatoms, i.e., combination of the electronic, conjugative, and steric effects of the nitrogen and oxygen atoms, strongly regulates the cavity size, generating a set of fine-tuned cavities in which the distance between two benzene rings at the upper rim ranges from 5.011 to 7.979 Å. The multiple intermolecular hydrogen bond interactions among *N,N'*-dimethylated tetraazacalix[2]arene[2]triazines and among tetraazacalix[2]arene[2]triazines lead to the formation of infinite one-dimensional chain structure and two-dimensional zigzag layered structure, respectively, in the solid state. The ease of preparation and further chemical manipulations, and the readily tunable cavity structures render these aza- and/or oxo-bridged calix[2]arene[2]triazines the unique platforms in the study of supramolecular chemistry.

Introduction

The sophistication of the design and synthesis of novel and functional macrocyclic host molecules has always been one driving force to promote the major advances in supramolecular chemistry. One of the recent examples is the explosive studies of calixarene chemistry¹ following Gutsche's pioneering work² of synthesis and structural elucidation of calix[*n*]arenes. Because of the easy availability, unique conformational and cavity structures, and recognition properties, calixarenes have been developed into an indispensable part of supramolecular chemistry.¹ While the effort to derivatize the fundamental calixarene skeletons is still increasing,³ one of the recent developments in this area is the construction of new calixarenes by replacing their phenol units with other heteroaromatics, to tune the cavity and therefore to improve their efficiency and selectivity toward recognizing various guest species including cations, anions, and neutral molecules. This has in fact resulted in a few intriguing macrocycles such as calixpyrroles,⁴ calixpyridines,⁵ and other calixheteroaromatics.⁶ In particular, calixpyrroles⁴ have been shown to be powerful anion receptors. In contrast to these

coarse-tuned macrocyclic molecules, construction of calixarenes with a fine-tuned cavity by substitution of the methylene bridges with heteroatoms has been scatteringly investigated⁷ because of synthetic obstacles except for thiacalixarenes.⁸ For example, reaction of 1,3-dichloro-4,6-dinitrobenzene with resorcinol gave

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13% yield of tetranitro-substituted tetraoxacalix[4]arene,⁹ while the Pd(0)-catalyzed amination of 3-bromo-*N*-methylaniline produced a mixture of azacalix[*n*]arenes (*n* = 3–8) in very low yields.¹⁰ Silicon-bridged calixarenes were synthesized by coupling phenol or 1,3-dibromobenzene with dichlorodimethylsilane in 16% or 12% yield, respectively.¹¹ By incorporating heteroatoms with heteroaromatics, a few heteroatom-bridged calix-heteroaromatics have also been prepared.⁷ Among them, silicon-bridged calix[*n*]phosphaarenes are noticeable because they act as ligands with strong π -acceptor properties.¹² In almost all cases, however, very low and unpractical chemical yields (<20%) were obtained for heteroatom-bridged macrocyclic compounds.^{7–13} As a consequence of difficulty of synthesis and functionalization, the structures and recognition properties of these appealing heteroatom-bridged calix(hetero)aromatics have remained largely unexplored.

We envisioned that the introduction of oxygen and/or nitrogen atoms as the bridge linkages in calix(hetero)aromatics would result in a wide variety of fine-bridge-tuned macrocyclic cavities because oxygen and, particularly, nitrogen atoms might adopt sp^3 and/or sp^2 hybrid configurations with and/or without forming conjugation with the neighboring (hetero)aromatics. Very recently, we have established a fragment coupling approach to synthesize azacalix[*m*]arene[*n*]pyridines (*m* = *n* = 2, 4) in a total yield of 48%.¹⁴ The nitrogen-bridged calix[4]arene[4]-pyridine prepared has been shown to exhibit indeed intriguing structural property and remarkable capability to recognize [60]- and [70]-fullerenes.¹⁴ Herein, we report a general, efficient, and convenient synthesis of oxo- and/or azacalix[2]arene[2]triazines based on the fragment coupling strategy. We will also show that the bridging heteroatoms play indeed an important part in determining the structural and spectroscopic properties of these novel macrocycles.

Triazine is a valuable element in molecular recognition and self-assembly because triazine-based molecules including melamine derivatives can act as both hydrogen bond donor and acceptor to bind guest molecules such as carbohydrates, cyanuric acid, and uracil derivatives through multiple hydrogen bond interactions.¹⁵ Besides, recent theoretical calculations¹⁶ and single-crystal molecular structure of a copper(II)–triazine complex¹⁷ have indicated a potential application of triazine as an electron-deficient π -aromatic component to interact with anion species. Although a triazine element has been incorporated into a few macrocyclic molecules,^{18–21} construction of calixarene scaffolds utilizing triazine as the skeleton building blocks has been underestimated.^{20,21} Having considered the high

reactivity of a cyanuric halide toward nucleophilic reagents in a controlled fashion, we envisioned the synthetic advantages of cyanuric halides in the construction of desired heteroatom-bridged calix(hetero)aromatics.

Experimental Section

Melting points are uncorrected. Elemental analyses were performed at the Analytical Laboratory of the Institute. All chemicals were dried or purified according to standard procedures prior to use.

1,3-Bis(dichloro-*s*-triazinyloxy)benzene (3). To an ice-bath cooled solution of cyanuric chloride **2** (5.55 g, 30 mmol) in tetrahydrofuran (100 mL) was added dropwise a mixture of resorcinol **1** (1.65 g, 15 mmol) and diisopropylethylamine (4.48 g, 37.5 mmol) in tetrahydrofuran (75 mL) during 2 h. The reaction mixture was stirred for another 2.5 h. After removal of diisopropylethylamine hydrochloride salt through filtration, the filtrate was concentrated and chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate as the mobile phase to give pure 1,3-bis(dichloro-*s*-triazinyloxy)benzene **3** (4.77 g, 78.3%) as a white solid: mp 140–142 °C (lit.²² mp 141–143 °C); IR (KBr) ν 1536, 1505, 1406 cm^{-1} ; ¹H NMR (300 MHz, CDCl₃) δ 7.57 (t, *J* = 8.2 Hz, 1H), 7.21 (dd, *J* = 8.2 Hz, *J* = 2.3 Hz, 2H), 7.11 (t, *J* = 2.2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 173.3, 170.7, 151.4, 130.9, 119.8, 115.0; MS (EI) *m/z* (%) 410 (4) (*M*⁺ + 6), 408 (14) (*M*⁺ + 4), 406 (18) (*M*⁺ + 2), 404 (26) (*M*⁺). Anal. Calcd for C₁₂H₆Cl₂N₆O₂: C, 35.50; H, 0.99; N, 20.70. Found: C, 35.49; H, 1.18; N, 20.57.

***N,N'*-Bis(dichloro-*s*-triazinyl)-*m*-phenylenediamine (11).** Following the procedure for the preparation of **3**, the reaction of *m*-phenylenediamine **5** (1.08 g, 10 mmol) with **2** (3.69 g, 20 mmol) in the presence of diisopropylethylamine (3.23 g, 25 mmol) gave pure *N,N'*-bis(dichloro-*s*-triazinyl)-*m*-phenylenediamine **11** (3.34 g, 82.7%) as a white solid: mp 244–245 °C (lit.²³ mp 230–231 °C); IR (KBr) ν 3251, 3135, 1583, 1541, 1389 cm^{-1} ; ¹H NMR (300 MHz, DMSO-*d*₆) δ 11.25 (s, 2H), 7.89 (t, *J* = 1.8 Hz, 1H), 7.42–7.46 (m, 3H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 169.7, 168.8, 163.8, 137.3, 129.2, 118.2, 114.6; MS (EI) *m/z* (%) 408 (5) (*M*⁺ + 6), 406 (37) (*M*⁺ + 4), 404 (100) (*M*⁺ + 2), 402 (68) (*M*⁺). Anal. Calcd for C₁₂H₆Cl₂N₆: C, 35.67; H, 1.50; N, 27.73. Found: C, 35.44; H, 1.39; N, 27.70.

***N*-(Dichloro-*s*-triazinyl)-3-(dichloro-*s*-triazinyloxy)aniline (15).** Following the procedure for the preparation of **3**, the reaction of 3-aminophenol **4** (1.1 g, 10 mmol) with **2** (3.7 g, 20 mmol) in the presence of diisopropylethylamine (3.23 g, 25 mmol) gave pure *N*-(dichloro-*s*-triazinyl)-3-(dichloro-*s*-triazinyloxy)aniline **15** (3.03 g, 74.8%) as a white solid: mp 205–207 °C (lit.²⁴ mp 199–200 °C); IR (KBr) ν 3289, 1610, 1575, 1536, 1510 cm^{-1} ; ¹H NMR (300 MHz, CDCl₃) δ 7.62–7.64 (m, 2H), 7.49 (t, *J* = 8.1 Hz, 1H), 7.41–7.44 (m,

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1H), 7.03–7.06 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.2, 170.9, 164.1, 151.4, 137.4, 130.5, 119.3, 118.1, 114.0; MS (EI) m/z (%) 409 (7) ($\text{M}^+ + 6$), 407 (26) ($\text{M}^+ + 4$), 405 (59) ($\text{M}^+ + 2$), 403 (47) (M^+). Anal. Calcd for $\text{C}_{12}\text{H}_5\text{Cl}_4\text{N}_7\text{O}$: C, 35.58; H, 1.24; N, 24.21. Found: C, 35.65; H, 1.47; N, 24.04.

***N,N'*-Bis(dichloro-*s*-triazinyl)-*N,N'*-dimethyl-*m*-phenylenediamine (17).** Following the procedure for the preparation of **3**, the reaction of *N,N'*-dimethyl-*m*-phenylenediamine **6** (0.41 g, 3 mmol) with **2** (1.33 g, 7.2 mmol) in the presence of diisopropylethylamine (0.93 g, 7.2 mmol) gave pure *N,N'*-bis(dichloro-*s*-triazinyl)-*N,N'*-dimethyl-*m*-phenylenediamine **17** (1.0 g, 77.2%) as a white solid: mp 200–202 °C; IR (KBr) ν 1611, 1556, 1492, 1441, 1404 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.55 (t, $J = 8.2$ Hz, 1H), 7.24–7.30 (m, 3H), 3.61 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.6, 170.1, 165.1, 142.8, 130.3, 125.2, 124.3, 39.1; MS (EI) m/z (%) 436 (6) ($\text{M}^+ + 6$), 434 (27) ($\text{M}^+ + 4$), 432 (64) ($\text{M}^+ + 2$), 430 (53) (M^+). Anal. Calcd for $\text{C}_{14}\text{H}_{10}\text{Cl}_4\text{N}_8$: C, 38.92; H, 2.33; N, 25.93. Found: C, 38.92; H, 2.40; N, 25.71.

General Procedure for the Preparation of Oxo- and/or Aza-Bridged Calix[2]arene[2]triazines. At room temperature, both solutions of resorcinol, or diamine or 3-aminophenol (1 mmol), in acetone (90 mL) and the trimer **3**, **11**, **15**, or **17** (1 mmol) in acetone (90 mL) were added dropwise at the same time and the same rate to a solution of diisopropylethylamine (0.31 g, 2.4 mmol) in acetone (200 mL). In the case of synthesis of **12** and **18**, a mixture of K_2CO_3 (0.331 g, 2.4 mmol), water (40 mL), and acetone (160 mL) was used instead of diisopropylethylamine solution in acetone. After addition of two reactants, which took about 3–10 h depending on the structure of substrates, the resulting mixture was stirred for another 12–48 h until the starting materials were consumed. The solvents were removed, and the residue was chromatographed on a silica gel column to give pure product.

Tetraoxocalix[2]arene[2]triazine 7: 3 + 36 h; yield 46.5%; mp > 300 °C (colorless prisms from *n*-hexane/ethyl acetate) (Figure 1); IR (KBr) ν 1551, 1440, 1387 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.32 (t, $J = 8.2$ Hz, 2H), 6.92 (dd, $J = 8.2$ Hz, $J = 2.1$ Hz, 4H), 6.72 (t, $J = 2.1$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.5, 172.4, 151.6, 130.8, 119.5, 115.9; MS (EI) m/z (%) 446 (9) ($\text{M}^+ + 4$), 444 (43) ($\text{M}^+ + 2$), 442 (66) (M^+), 409 (34), 407(100). Anal. Calcd for $\text{C}_{18}\text{H}_8\text{Cl}_2\text{N}_6\text{O}_4$: C, 48.78; H, 1.82; N, 18.96. Found: C, 48.97; H, 1.64; N, 18.80.

Azatetraoxocalix[2]arene[2]triazine 8: 8 + 12 h; yield 62%; mp > 300 °C (colorless needles from *n*-hexane/dichloromethane) (Figure 2); IR (KBr) ν 3252, 1571, 1542, 1459, 1415 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 10.66 (s, 1H, NH), 7.40 (t, $J = 8.2$ Hz, 1H), 7.35 (t, $J = 8.0$ Hz, 1H), 7.29 (t, $J = 2.2$ Hz, 1H), 7.25 (t, $J = 2.1$ Hz, 1H), 7.00–7.09 (m, 3H), 6.91–6.93 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.5, 171.8, 170.9, 170.6, 170.4, 165.7, 151.6, 151.3, 150.8, 137.3, 130.7, 130.1, 122.7, 119.3, 119.2, 118.5, 118.4, 116.6; MS (EI) m/z (%) 445 (14) ($\text{M}^+ + 4$), 443 (69) ($\text{M}^+ + 2$), 441 (100) (M^+), 408 (18), 407 (27), 406 (40), 405 (49). Anal. Calcd for $\text{C}_{18}\text{H}_9\text{Cl}_2\text{N}_7\text{O}_3$: C, 48.89; H, 2.05; N, 22.17. Found: C, 48.95; H, 2.05; N, 22.27.

Diazatetraoxocalix[2]arene[2]triazine 9: 10 + 12 h; yield 79%; mp > 300 °C (colorless needles from *n*-hexane/ethyl acetate) (Figure 3); IR (KBr) ν 3383, 3275, 1569, 1550, 1420 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 10.56 (s, 2H, NH), 7.36–7.44 (m, 3H), 7.25 (t, $J = 8.0$ Hz, 1H), 7.05 (dd, $J = 8.2$ Hz, $J = 2.2$ Hz, 2H), 6.83 (dd, $J = 8.0$ Hz, $J = 1.9$ Hz, 2H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 170.8, 170.2, 164.8, 151.6, 137.1, 130.7, 129.1, 120.2, 118.9, 118.4, 117.4; MS (EI) m/z (%) 444 (13) ($\text{M}^+ + 4$), 442 (68) ($\text{M}^+ + 2$), 440 (100) (M^+), 406 (17), 405 (25), 404 (38). Anal. Calcd for $\text{C}_{18}\text{H}_{10}\text{N}_8\text{O}_2\text{Cl}_2$: C, 49.00; H, 2.28; N, 25.40. Found: C, 48.93; H, 2.13; N, 25.15.

Dimethylazadiazatetraoxocalix[2]arene[2]triazine 10: 5 + 12 h; yield 57%; mp > 300 °C (colorless prisms from dichloromethane/acetone) (Figure 4); IR (KBr) ν 1574, 1508, 1386 cm^{-1} ; ^1H NMR (300 Hz,

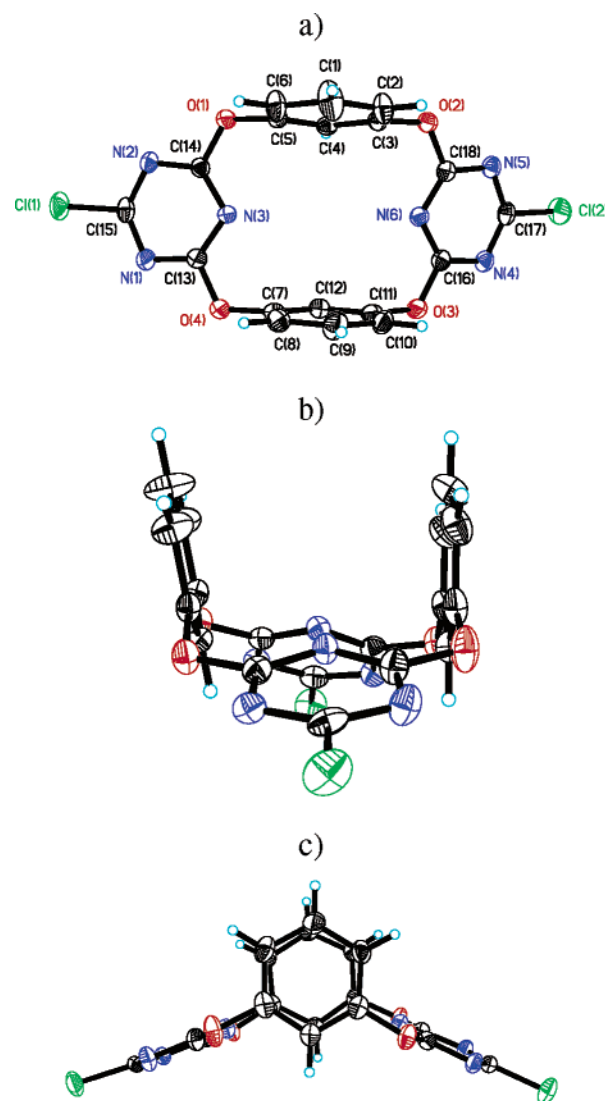


Figure 1. Crystal structure of tetraoxocalix[2]arene[2]triazine **7**: (a) top view and (b and c) side views. Distances between C(1) and C(9), C(4) and C(12), N(3) and N(6), and C(15) and C(17) are 5.011, 4.441, 4.460, and 9.489 Å, respectively.

$\text{DMSO-}d_6$) δ 7.39 (t, $J = 8.0$ Hz, 1H), 7.27 (t, $J = 8.3$ Hz, 1H), 7.15 (dd, $J = 7.9$ Hz, $J = 1.6$ Hz, 2H), 7.06 (d, $J = 1.7$ Hz, 1H), 6.89–6.92 (m, 3H), 5.76 (s, 0.5H, CH_2Cl_2), 3.36 (s, 6H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 170.4, 169.9, 165.8, 151.7, 143.3, 130.7, 130.1, 126.5, 125.7, 118.9, 116.4, 54.9 (CH_2Cl_2), 38.8; MS (EI) m/z (%) 472 (13) ($\text{M}^+ + 4$), 470 (65) ($\text{M}^+ + 2$), 468 (100) (M^+), 435 (26), 433(71). Anal. Calcd for $\text{C}_{20}\text{H}_{14}\text{Cl}_2\text{N}_8\text{O}_2 \cdot (0.5\text{CH}_2\text{Cl}_2)$: C, 48.11; H, 2.95; N, 21.90. Found: C, 48.47; H, 2.90; N, 21.72.

Oxotriazacalix[2]arene[2]triazine 12: 12 + 48 h; yield 46%; mp > 300 °C (white powder from *n*-hexane/tetrahydrofuran); IR (KBr) ν 3266, 1591, 1572, 1523, 1421, 1396 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 10.57 (s, 1H, NH), 10.07 (s, 1H, NH), 9.95 (s, 1H, NH), 7.62 (s, 1H), 7.53 (s, 1H), 7.34 (t, $J = 8.0$ Hz, 1H), 7.24 (t, $J = 8.0$ Hz, 1H), 6.97 (dd, $J = 8.1$ Hz, $J = 1.3$ Hz, 1H), 6.90 (d, $J = 8.1$ Hz, 1H), 6.80 (d, $J = 7.4$ Hz, 2H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 170.1, 170.0, 168.3, 165.2, 164.9, 164.2, 151.1, 138.0, 137.9, 137.1, 129.8, 129.0, 122.0, 120.6, 119.9, 119.2, 118.4, 117.9; MS (EI) m/z (%) 443 (3) ($\text{M}^+ + 4$), 441 (14) ($\text{M}^+ + 2$), 439 (23) (M^+), 405 (4), 403 (10). Anal. Calcd for $\text{C}_{18}\text{H}_{11}\text{Cl}_2\text{N}_9\text{O} \cdot (0.25\text{C}_4\text{H}_8\text{O})$: C, 49.80; H, 2.86; N, 27.51. Found: C, 49.79; H, 2.70; N, 27.30.

Tetraazacalix[2]arene[2]triazine 13: 8 + 48 h; yield 58%; mp > 300 °C (colorless prisms obtained from the diffusion of diethyl ether to DMF solution of product) (lit.²⁰ mp > 300 °C) (Figure 5); IR (KBr)

(24) Harayama, T.; Sekiguchi, S.; Matsui, K. *J. Heterocycl. Chem.* **1970**, *7*, 975.

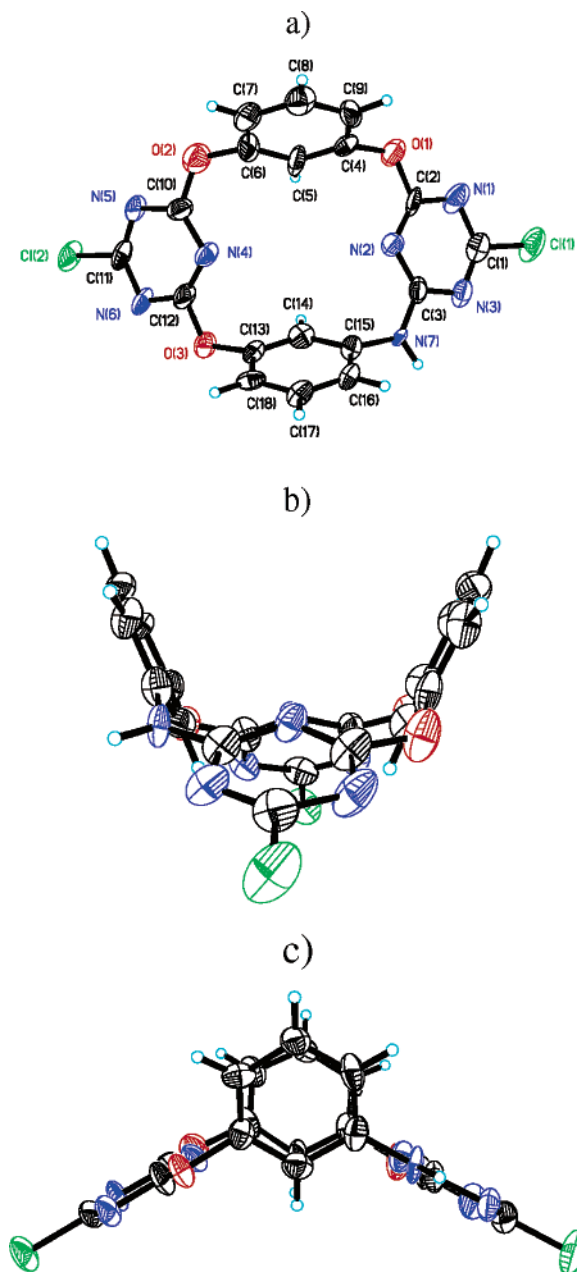


Figure 2. Crystal structure of azatrioxocalix[2]arene[2]triazine **8**: (a) top view and (b and c) side views. Distances between C(8) and C(17), C(5) and C(14), N(2) and N(4), and C(1) and C(11) are 6.533, 4.328, 4.619, and 9.200 Å, respectively.

ν 3246, 1596, 1576, 1558, 1388 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 10.02 (s, 4H, NH), 7.78 (s, 2H), 7.23 (t, $J = 8.0$ Hz, 2H), 6.81 (dd, $J = 8.0$ Hz, $J = 1.8$ Hz, 4H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 168.0, 164.2, 137.9, 128.9, 118.7, 118.0; MS (MALDI-TOF) m/z 443 ($M^+ + 1 + 4$), 441 ($M^+ + 1 + 2$), 439 ($M^+ + 1$). Anal. Calcd for $\text{C}_{18}\text{H}_{12}\text{Cl}_2\text{N}_{10}$: C, 49.22; H, 2.75; N, 31.89. Found: C, 49.25; H, 2.91; N, 31.69.

Diazadimethylazacalix[2]arene[2]triazine 14: 10 + 12 h; yield 55%; mp > 300 °C (colorless prisms from *n*-hexane/tetrahydrofuran) (Figure 6); IR (KBr) ν 3237, 3073, 1575, 1541, 1514, 1405 cm^{-1} ; ^1H NMR (300 MHz, $\text{C}_4\text{D}_8\text{O}$) δ 8.85 (s, 2H, NH), 7.51 (d, $J = 1.8$ Hz, 1H), 7.37 (t, $J = 8.1$ Hz, 1H), 7.30 (s, 1H), 7.03–7.08 (m, 3H), 7.62 (dd, $J = 8.1$ Hz, $J = 2.1$ Hz, 2H), 3.42 (s, 6H); ^{13}C NMR (75 MHz, $\text{C}_4\text{D}_8\text{O}$) δ 167.2, 164.5, 161.9, 143.0, 136.9, 128.6, 126.5, 126.4, 123.1, 115.8, 114.8, 36.2; MS (EI) m/z (%) 470 (12) ($M^+ + 4$), 468 (69) ($M^+ + 2$), 466 (100) (M^+), 431 (18). Anal. Calcd for $\text{C}_{20}\text{H}_{16}\text{Cl}_2\text{N}_{10}$

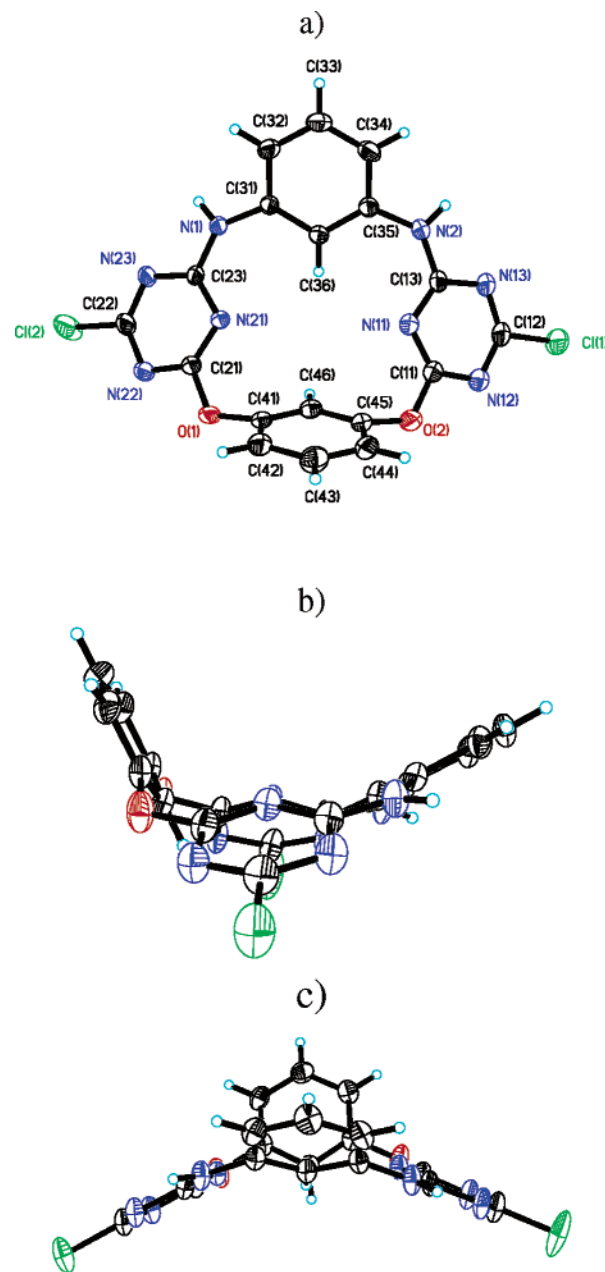


Figure 3. Crystal structure of diazadioxocalix[2]arene[2]triazine **9**: (a) top view and (b and c) side views. Distances between C(33) and C(43), C(36) and C(46), N(11) and N(21), and C(12) and C(22) are 7.979, 4.213, 4.544, and 9.328 Å, respectively.

(0.25 $\text{C}_4\text{H}_8\text{O}$): C, 51.97; H, 3.74; N, 28.86. Found: C, 51.90; H, 3.64; N, 28.70.

Azadimethylazaoxocalix[2]arene[2]triazine 16: 8 + 48 h; yield 34%; mp > 300 °C (colorless prisms from dichloromethane/acetone) (Figure 7); IR (KBr) ν 3225, 1576, 1514, 1405, 1373 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 9.75 (s, 1H, NH), 7.39 (t, $J = 7.9$ Hz, 1H), 7.11–7.26 (m, 4H), 7.05 (t, $J = 1.9$ Hz, 1H), 6.85 (dd, $J = 7.9$ Hz, $J = 1.9$ Hz, 1H), 6.79 (d, $J = 8.0$ Hz, 1H), 3.38 (s, 3H), 3.32 (s, 3H); ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 170.3, 168.9, 168.5, 166.0, 165.4, 164.2, 151.1, 144.4, 143.3, 138.2, 130.7, 129.5, 127.1, 125.6, 124.9, 122.1, 119.6, 117.7, 39.4, 38.4; MS (EI) m/z (%) 471 (12) ($M^+ + 4$), 469 (66) ($M^+ + 2$), 467 (100) (M^+), 434 (17), 432 (51). Anal. Calcd for $\text{C}_{20}\text{H}_{15}\text{Cl}_2\text{N}_9\text{O}$: C, 51.40; H, 3.23; N, 26.92. Found: C, 51.34; H, 3.26; N, 26.50.

Tetramethylazacalix[2]arene[2]triazine 18: 4 + 36 h; yield 46%; mp > 300 °C (colorless prisms from *n*-hexane/dichloromethane) (Figure

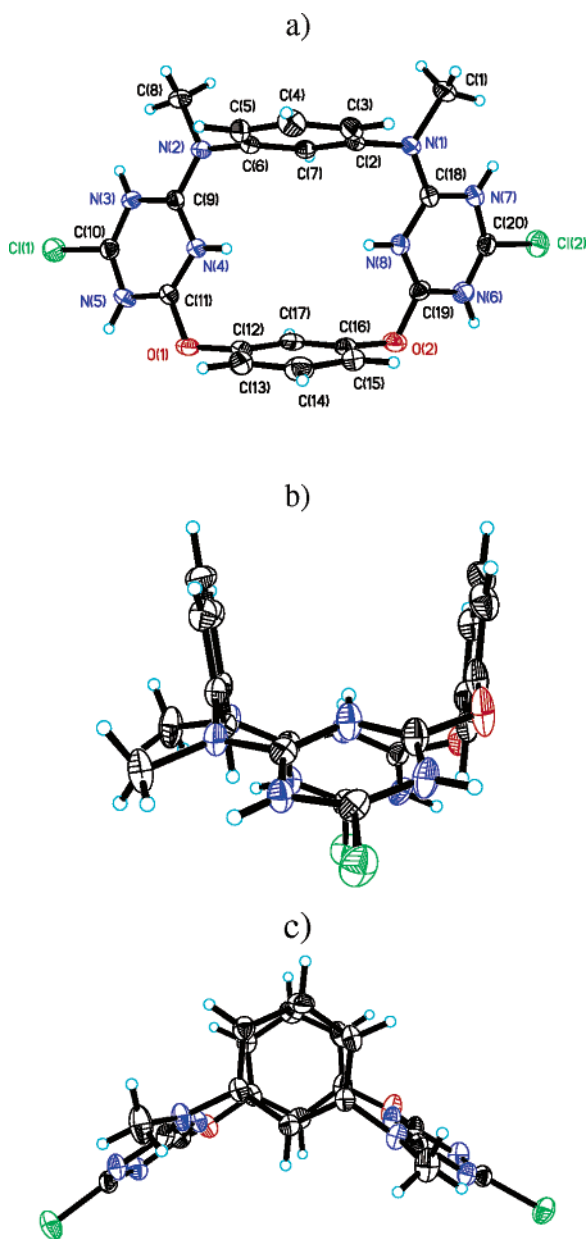


Figure 4. Crystal structure of dimethylazadioxocalix[2]arene[2]triazine **10**: (a) top view and (b and c) side views. Distances between C(4) and C(14), C(7) and C(17), N(4) and N(8), and C(10) and C(20) are 5.175, 4.449, 4.665, and 9.032 Å, respectively.

8); IR (KBr) ν 1573, 1559, 1485, 1398 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.19 (t, $J = 8.0$ Hz, 2H), 6.84 (dd, $J = 7.9$ Hz, $J = 2.0$ Hz, 4H), 6.71 (t, $J = 1.9$ Hz, 2H), 3.36 (s, 12H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.5, 165.3, 145.1, 130.1, 127.0, 125.8, 38.0; MS (EI) m/z (%) 498 (13) ($\text{M}^+ + 4$), 496 (68) ($\text{M}^+ + 2$), 494 (100) (M^+), 459 (22). Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{Cl}_2\text{N}_{10}$: C, 53.34; H, 4.07; N, 28.27. Found: C, 53.39; H, 4.11; N, 28.12.

Reaction of Diazadioxocalix[2]arene[2]triazine 9 with Diethanolamine: A mixture of diethanolamine (1 mmol) and diisopropylethylamine (2.2 mmol) in THF (20 mL) was stirred at 70 °C for 30 min. A solution of diazadioxocalix[2]arene[2]triazine **9** (0.5 mmol) in THF (20 mL) was then added during 30 min. The reaction mixture was refluxed for 36 h. After removal of the solvent, the residue was subjected to silica gel column chromatography with a mixture of acetone, petroleum ether, and methanol (30:15:2) as an eluent to give product **19** (0.208 g, 72%) as a white solid: mp 233–235 °C; IR (KBr) ν 3427, 1584 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 9.23 (s, 2H), 7.37 (d, $J = 1.6$ Hz, 1H), 7.31 (t, $J = 8.1$ Hz, 1H), 7.15 (s, 1H), 7.09

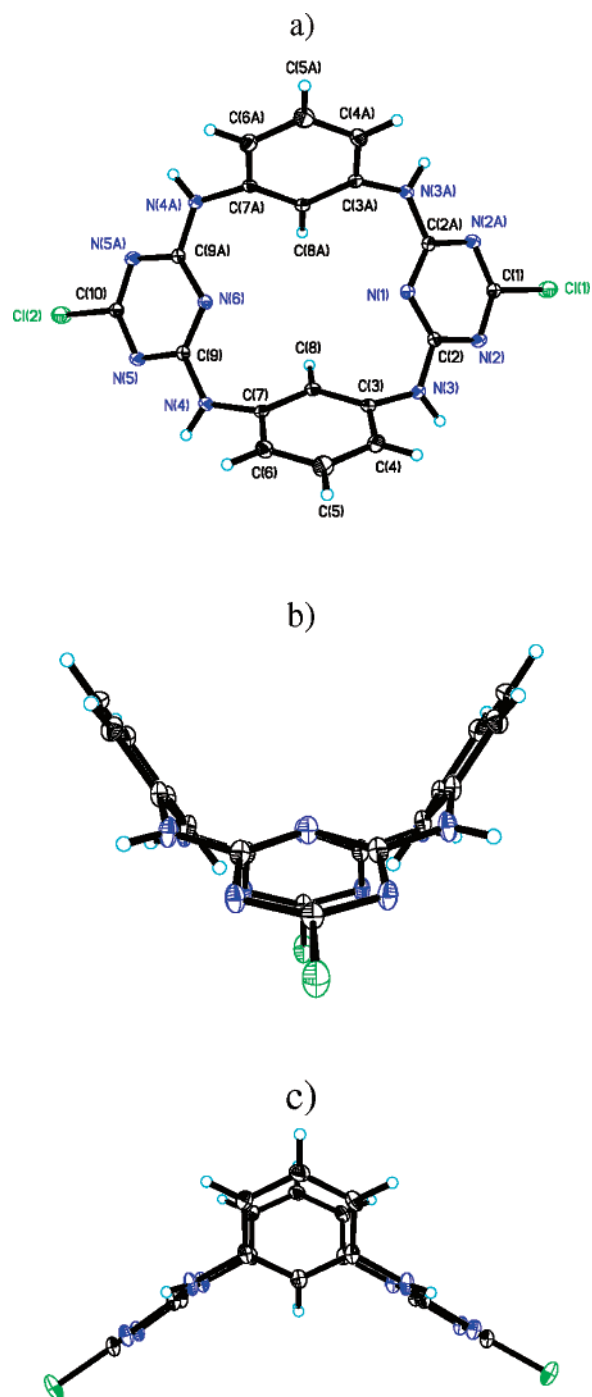


Figure 5. Crystal structure of tetraazacalix[2]arene[2]triazine **13**: (a) top view and (b and c) side views. Distances between C(5) and C(5A), C(8) and C(8A), N(1) and N(6), and C(1) and C(10) are 7.392, 4.217, 4.648, and 9.035 Å, respectively.

(t, $J = 8.0$ Hz, 1H), 6.89 (dd, $J = 8.1$ Hz, $J = 2.2$ Hz, 2H), 6.67 (dd, $J = 8.0$ Hz, $J = 1.8$ Hz, 2H), 4.75–4.84 (m, 4H), 3.63–3.70 (m, 16H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ 170.7, 166.1, 164.8, 164.7, 152.2, 138.9, 138.8, 130.0, 128.4, 118.2, 118.1, 117.7, 117.2, 117.0, 58.9, 58.7, 50.0; MS (MALDI-TOF) m/z 579.3 ($\text{M}^+ + 1$), 601.2 ($\text{M}^+ + 23$), 617.1 ($\text{M}^+ + 39$). Anal. Calcd for $\text{C}_{28}\text{H}_{30}\text{N}_{10}\text{O}_6 \cdot 0.5\text{H}_2\text{O}$: C, 53.15; H, 5.32; N, 23.84. Found: C, 53.04; H, 5.14; N, 23.62.

Results and Discussion

The synthesis of tetraoxo-bridged calix[2]arene[2]triazine **7** was first attempted by directly reacting resorcinol **1** with 1 equiv

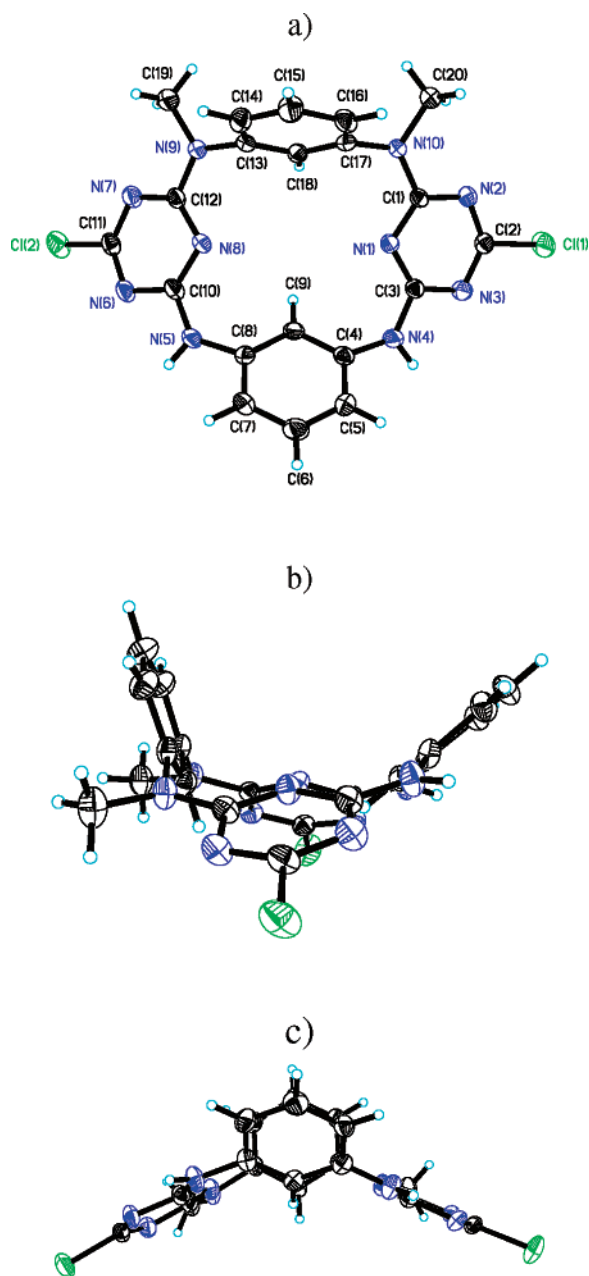


Figure 6. Crystal structure of *N,N'*-dimethylated tetraazacalix[2]arene[2]triazine **14**: (a) top view and (b and c) side views. Distances between C(6) and C(15), C(9) and C(18), N(1) and N(8), and C(2) and C(11) are 7.393, 4.356, 4.677, and 9.467 Å, respectively.

of cyanuric chloride **2**. Under various conditions examined, however, the maximum chemical yield of desired product **7** was only 11%. In many cases, the reaction produced a mixture of oligomers. A stepwise strategy, the fragment coupling approach, was then investigated. We found by trial and error that, in the presence of diisopropylethylamine (DIPEA) as an acid scavenger, the reaction between resorcinol and 2 equiv of cyanuric chloride in tetrahydrofuran proceeded smoothly and efficiently at 0 °C to afford linear trimer product, 1,3-bis(dichloro-*s*-triazinyloxy)benzene **3**²² in 78%. The chemical yield can be improved slightly when a large excess amount of cyanuric chloride was employed. It should be noted that the use of acetone or a mixture of acetone and water as the solvent and the use of NaOH, Na₂CO₃, triethylamine, and collidine instead of DIPEA had detrimental effects on the formation of **3**, yielding

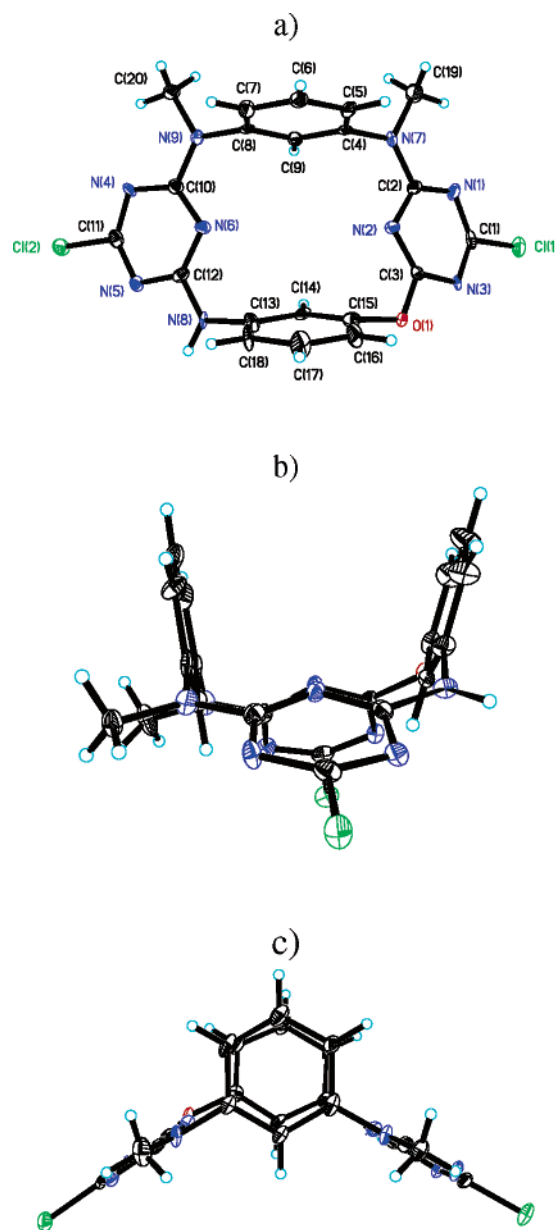


Figure 7. Crystal structure of *N,N'*-dimethylated oxotriazacalix[2]arene[2]triazine **16**: (a) top view and (b and c) side views. Distances between C(6) and C(17), C(9) and C(14), N(2) and N(6), and C(1) and C(11) are 5.559, 4.421, 4.681, and 9.135 Å, respectively.

either oligomers or other byproducts. The macrocyclizative coupling reaction between resorcinol **1** and the linear trimer **3** took place effectively at room temperature, and tetraoxocalix[2]arene[2]triazine **7** was obtained in 46.5% yield in acetone solution with DIPEA as a base (Scheme 1). A one-pot synthesis of tetraoxocalix[2]arene[2]triazine **7** by the room-temperature macrocyclic coupling reaction of resorcinol with the linear trimer **3**, which was resulted initially from the condensation of resorcinol with cyanuric chloride at 0 °C without isolation and purification, gave an overall chemical yield of 18%. Because of the ease of preparation and purification of the linear trimer **3** and its high reactivity toward other annulation reagents in the construction of heteroatom-bridged calix(hetero)aromatics (vide infra) and because of good chemical yields of individual coupling reactions, the stepwise fragment coupling approach to desired macrocyclic molecules appears more advantageous and practical.

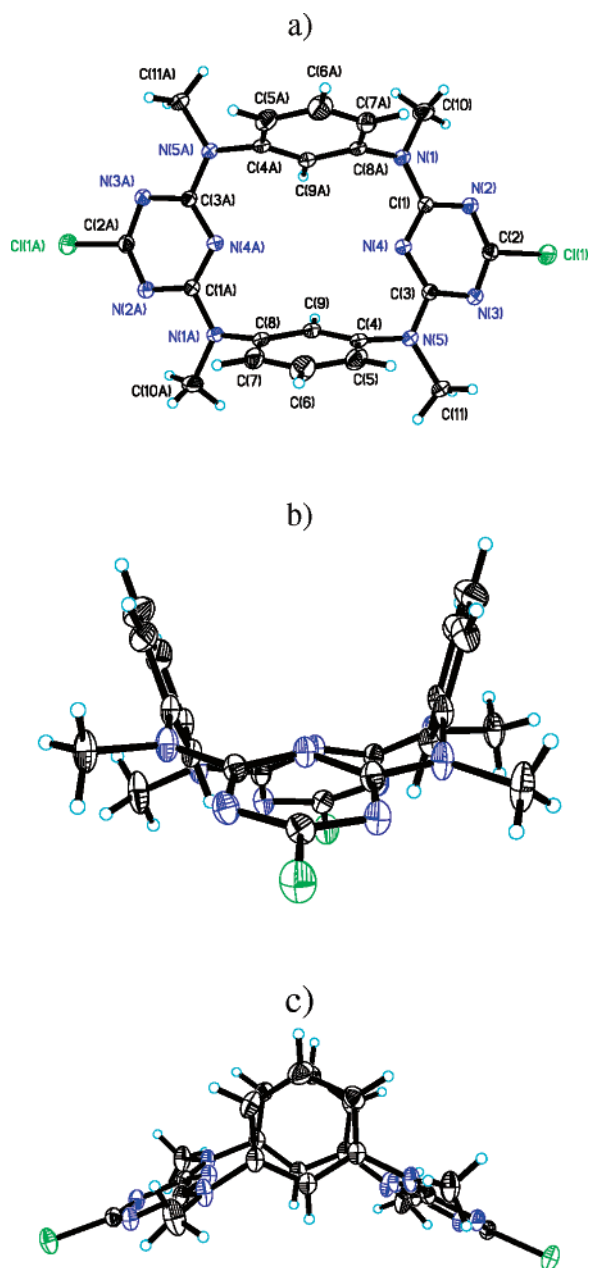
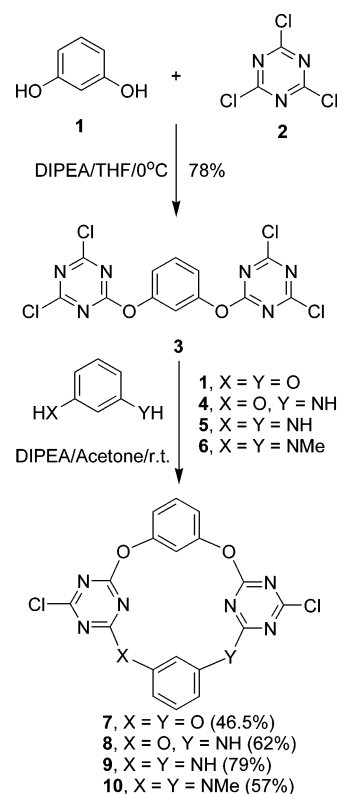


Figure 8. Crystal structure of tetramethylazacalix[2]arene[2]triazine **18**: (a) top view and (b and c) side views. Distances between C(6) and C(6A), C(9) and C(9A), N(4) and N(4A), and C(2) and C(2A) are 6.046, 4.289, 4.721, and 9.465 Å, respectively.

At ambient temperature, the linear trimer **3** underwent equally efficient macrocyclizative coupling reactions with 3-aminophenol **5**, *m*-phenylenediamine **6**, and *N,N'*-dimethyl-*m*-phenylenediamine **7**, respectively, to produce the corresponding azatrioxocalix[2]arene[2]triazine **8**, diazadioxocalix[2]arene[2]triazine **9**, and dimethylazadioxocalix[2]arene[2]triazine **10** in the chemical yields ranging from 57% to 79% (Scheme 1).

To further examine the generality of the fragment coupling approach and also to prepare oxo-triaza-, tetraaza-, and tetramethylaza-bridged calix[2]arene[2]triazine analogues, other linear trimeric fragments were synthesized. Similar to the synthesis of **3**, *N,N'*-bis(dichloro-*s*-triazinyl)-*m*-phenylenediamine **11**,²³ *N,O*-bis(dichloro-*s*-triazinyl)-3-aminophenol **15**,²⁴ and *N,N'*-bis(dichloro-*s*-triazinyl)-*N,N'*-dimethyl-*m*-phenylenediamine **17** were readily and high yieldingly prepared from the coupling reaction

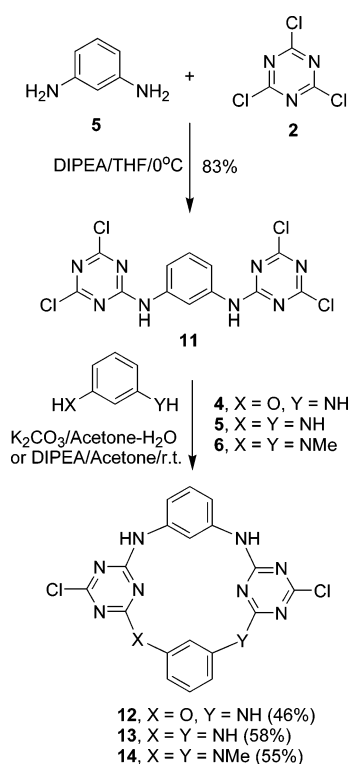
Scheme 1



between cyanuric chloride **2** and *m*-phenylenediamine **5**, 3-aminophenol **4**, and *N,N'*-*m*-phenylenediamine **6**, respectively. Being a reactive intermediate, *N,N'*-bis(dichloro-*s*-triazinyl)-*m*-phenylenediamine **11** underwent macrocyclizative coupling reactions with 3-aminophenol **4** and *m*-phenylenediamines **5** and **6** to produce the desired heteroatom-bridged calix[2]arene[2]triazines **12**, **13**,²⁰ and **14** in 46–58% yields (Scheme 2). Both linear trimeric fragments **15** and **17** were found analogously reactive to interact with *N,N'*-*m*-phenylenediamine **6**, yielding *N,N'*-dimethylated oxotriazacalix[2]arene[2]triazine **16** and tetramethylazacalix[2]arene[2]triazine **18**, albeit in lower chemical yield in the former case (Schemes 3 and 4). In the cases of synthesis of oxotriazacalix[2]arene[2]triazine **12** and tetramethylazacalix[2]arene[2]triazine **18**, however, the best results were obtained when K_2CO_3 was applied as a base and a mixture of water and acetone (1:4) was used as the reaction media (Schemes 2 and 4). It is particularly worth noting that the stepwise fragment coupling approach is practically applicable in the multigram scale synthesis of aza- and/or oxo-bridged calix[2]arene[2]triazines. For example, the macrocyclizative coupling reaction between **3** and resorcinol **1** in 2 L of reaction medium gave 2.6 g of pure tetraoxocalix[2]arene[2]triazine **7**.

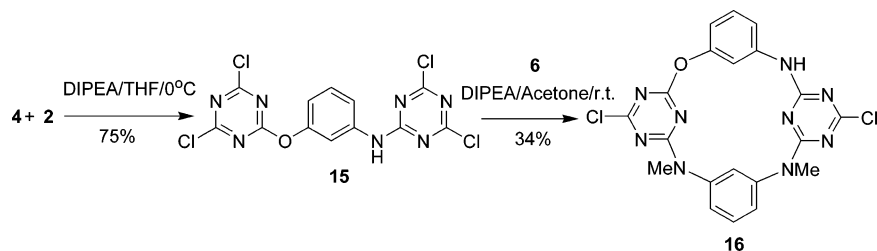
The structures of all oxo- and/or aza-bridged calix[2]arene[2]triazines synthesized were confirmed on the basis of spectroscopic data and elemental analysis. It was noticeable that all macrocyclic molecules exhibit only one set of signals in both 1H and ^{13}C NMR spectra. For example, both tetraoxocalix[2]arene[2]triazine **7** and tetraazacalix[2]arene[2]triazine **13** give three types of proton signals in 1H NMR and six carbon resonance peaks in ^{13}C NMR, the results being in agreement to a highly symmetric structure having two *meta* disubstituted benzene and *s*-triazine moieties. In the case of tetramethylazacalix[2]arene[2]triazine **18**, in addition to the proton signals of a *meta*

Scheme 2

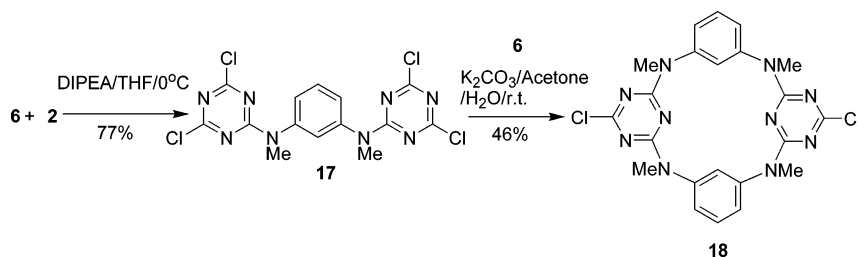


disubstituted benzene moiety, there is only one sharp singlet peak at 3.36 ppm corresponding to 12 protons of four bridging methylamino groups. Only one sharp singlet peak of two methyl protons was also observed in the range 3.36–3.42 ppm for dimethylazadioxocalix[2]arene[2]triazine **9** and dimethylated tetraazacalix[2]arene[2]triazine **14**. No peak split or other changes were observed when ^1H NMR spectra of dimethylazadioxocalix[2]arene[2]triazine **10**, *N,N'*-dimethylated tetraazacalix[2]arene[2]triazine **14**, and tetramethylazacalix[2]arene[2]triazine **18** were recorded at -50°C . The spectroscopic characteristics observed suggest that either these macrocyclic molecules adopt stable symmetric conformations or these macrocycles are conformationally flexible and all conformations interconvert rapidly on the NMR time scale above -50°C .

Scheme 3



Scheme 4



Except for tetraoxo- and azatrioxocalix[2]arene[2]triazines **7** and **8**, all of the heteroatom-bridged calix[2]arene[2]triazines have low solubility in most common polar and nonpolar solvents. Surprisingly, however, most of them dissolve very well in tetrahydrofuran. It is also worth noting that, for calix[2]arene[2]triazines bearing more than three oxygen bridging atoms, such as **7** and **8**, no absorption band was observed in their UV–vis spectra, while the rest of calix[2]arene[2]triazine compounds absorbed UV light in the range 239–279 nm (Figure S11). More interestingly, calix[2]arene[2]triazines bridged by more than two methylaza (MeN) groups displayed an absorption band at around 240 nm. With the increase of aza (NH) bridges from 2 to 4, the absorption band shifted bathochromically from 239 to 279 nm. The outcomes of UV–vis absorption spectra reflected the conjugation state of the bridging heteroatoms with their neighboring aromatic rings. In other words, the electron-donating nature and less steric hindrance rendered the aza (NH) linkage conjugate easily with the aromatic rings, leading to a bathochromic effect in the UV–vis spectrum. The presence of a methyl group on the bridging nitrogen atom (MeN), on the other hand, might cause the macrocyclic ring to be more folded to release the steric hindrance around the bridging nitrogen and, therefore, preclude methylaza (MeN) from effectively conjugating with the aromatics.

To investigate the solid-state structures of heteroatom-bridged calix[2]arene[2]triazines and also to examine the effect of a bridging heteroatom on the conformational structures of the macrocycles, single-crystal molecular structures of **7–10**, **12**, **13**, **16**, and **18** were determined (Table 1). Some intriguing structural features are noticed. First, all heteroatom-bridged calix[2]arene[2]triazines adopt a *1,3-alternate* conformation in the solid state (Figures 1–8). This is different from calixarene,² calixpyridine,⁵ and calixpyrroles.⁴ Second, four bridging atoms are located nearly in the same plane with the deviation of less than 0.2395 Å. Additionally, it is always a pair of benzene rings that stand up to form a cliplike conformation, while a pair of opposite triazine rings always tends to be roughly coplanar and edge-to-edge orientated and is well separated. Furthermore, both the bond lengths between heteroatom and its connecting (hetero)aromatic carbons and bond angles of bridging atoms

Table 2. X-ray Crystallographic Data of Heteroatom-Bridged Calix[2]arene[2]triazines

compound	7	9	10-0.5CH ₂ Cl ₂	13	14-0.25C ₄ H ₈ O	16-1.5H ₂ O	18
empirical formula	C ₁₈ H ₈ Cl ₂ N ₆ O ₄	C ₁₈ H ₁₀ Cl ₂ N ₈ O ₂	C ₃₀ H ₁₄ Cl ₂ N ₈ O ₂ •0.5CH ₂ Cl ₂	C ₁₈ H ₁₂ Cl ₂ N ₁₀	C ₃₀ H ₁₆ Cl ₂ N ₁₀ •0.25C ₄ H ₈ O	C ₃₀ H ₁₆ Cl ₂ N ₉ O •1.5H ₂ O	C ₂₂ H ₂₀ Cl ₂ N ₁₀
M _r	443.2	441.24	511.8	439.28	485.35	445.34	495.38
crystal size (mm ³)	0.42 × 0.11 × 0.09	0.38 × 0.26 × 0.17	0.30 × 0.25 × 0.15	0.53 × 0.51 × 0.10	0.36 × 0.30 × 0.24	0.18 × 0.15 × 0.06	0.26 × 0.22 × 0.18
crystal system	orthorhombic	monoclinic	trigonal	orthorhombic	orthorhombic	monoclinic	monoclinic
space group	P2(1)2(1)2(1)	C2/c	P-1	Pnma	P2(1)2(1)2(1)	P2(1)/c	C2/c
a [Å]	8.8228(7)	21.2008(9)	8.8051(1)	10.127(2)	15.95(2)	18.444(1)	20.305(7)
b [Å]	12.032(1)	8.2713(3)	11.2289(5)	12.040(2)	9.169(1)	18.767(1)	9.995(4)
c [Å]	18.167(2)	21.339(1)	11.8862(6)	15.569(3)	20.89(3)	13.677(2)	12.001(4)
α [deg]	90	90	87.871(6)	90	90	90	90
β [deg]	90	95.009(2)	72.449(3)	90	90	104.276(4)	107.289(5)
γ [deg]	90	90	78.862(4)	90	90	90	90
V [Å ³]	1928.5(3)	3727.7(3)	1099.12(8)	1898.2(7)	3055(7)	4587.9(7)	2325.5(1)
d [g/cm ³]	1.527	1.572	1.565	1.537	1.055	1.434	1.415
Z	4	8	2	4	4	4	4
T [K]	293(2)	293(2)	293(2)	293(2)	293(2)	293(2)	293(2)
R1, wR2	0.0288, 0.0228	0.0465, 0.1173	0.0554, 0.1350	0.0429, 0.1185	0.0830, 0.2269	0.0543, 0.0676	0.0412, 0.1053
I > 2σ(I)	0.0703, 0.0256	0.0740, 0.1313	0.1384, 0.1564	0.0532, 0.1226	0.1104, 0.2588	0.2293, 0.0868	0.0615, 0.1159
R1, wR2 (all data)							
quality of fit	0.554	1.015	0.876	1.003	1.205	0.601	1.033

indicate that heteroatoms form conjugation with a triazine ring rather than with a benzene ring. The cavity of heteroatom-bridged calix[2]arene[2]triazines can therefore be viewed as resulting from a cyclic array of two isolated benzene rings and two conjugated 2,6-diaza-, 2,6-dioxo-, or 2-aza-6-oxo-substituted triazine segments in a *1,3-alternate* fashion. Finally, the nature of the bridging units influences the inclined angles of both benzene and triazine rings to the plane of the four linking heteroatoms. In other words, the cavity of the heteroatom-bridged calix[2]arene[2]triazines was controlled by the nature of the bridging heteroatoms. For example, two benzene rings in tetraoxocalix[2]arene[2]triazine **7** are almost perpendicular to the plane formed by four bridging oxygen atoms, with the inclined angles being 89.3° and 77.4°, respectively (Figure 1). The distance of two face-to-face paralleled benzene rings ranges from 4.441 Å at the low rim to 5.011 Å at the upper rim, suggesting a weak π - π stacking interaction. A similar heavily folded *1,3-alternate* conformation was also observed for dimethylazadioxocalix[2]arene[2]triazine **16**, in which the distance between two benzene rings is from 4.449 Å (low rim) to 5.175 Å (upper rim) and the inclined angles of two benzene rings are 83.6° and 81.2°, respectively (Figure 7). Replacement of oxygen linkages by methylaza (MeN) or aza (NH) groups led to the opening of the upper rim of two paralleled benzene rings. This was exemplified by the extreme case of molecule **9** in which the inclined angles of diaza-linked and dioxo-linked benzene rings were 27.8° and 63.7°, respectively, and the distance of the upper rim of two benzene rings spanned 7.979 Å (Figure 3). The inclined angles of triazine rings remain in a narrow range between 20.5° and 36°, and the distance between two triazines rings at the upper rim ranges from 9.032 to 9.489 Å (Figures 1–8).

The crystal structural features of heteroatom-bridged calix[2]arene[2]triazines are most probably resulted from the combination of electronic and steric effects of both bridging heteroatoms and (hetero)aromatics. Because of the lack of intramolecular hydrogen bonds that exist in calixarene,² all heteroatom-bridged calix[2]arene[2]triazines synthesized do not adopt the corn conformation. Moreover, to avoid possible steric hindrance arisen from the corn conformation, heteroatom-bridged calix[2]arene[2]triazines adopt a *1,3-alternate* conformation. This is the same for the situation of azacalix[2]arene[2]pyridine¹⁴ which adopts the *1,3-alternate* as the most energetically stable conformation. The strong electron-withdrawing nature of triazinyl and less steric repulsion between triazinyl and the bridging moiety, methylaza (NMe) in particular, may be responsible for the favored formation of conjugation of a bridging heteroatom with a triazine ring rather than with a benzene ring. Therefore the cavity of all heteroatom-bridged calix[2]arene[2]triazines are resulted from four planar segments, two isolated benzene rings, and two diheteroatom-conjugated triazine rings, in a *1,3-alternate* pattern. Since a triazine ring is a π -deficient aromatic ring with a positive charge,¹⁶ two opposite triazine rings in all calix[2]arene[2]triazines tend to be roughly coplanar and keep apart from each other. In contrast, however, two opposite benzene rings tend to align in parallel, such as those observed in **7** (Figure 1) and **10** (Figure 4), that might bring in extra stabilization of the molecule due to weak π - π stacking interaction. The combined steric and electronic effects of bridging heteroatoms and (hetero)aromatics result in the

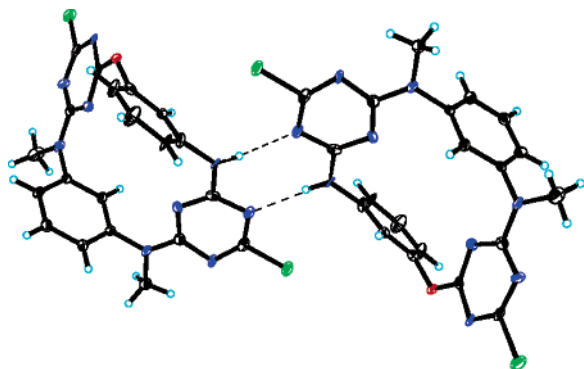


Figure 9. Intermolecular hydrogen bond formation of **16** in the solid state. $d_{(D-H)} = 0.860$ Å, $d_{(H\cdots A)} = 2.094$ Å, $\angle D-H\cdots A = 173.7^\circ$, $d_{(D\cdots A)} = 2.950$ Å.

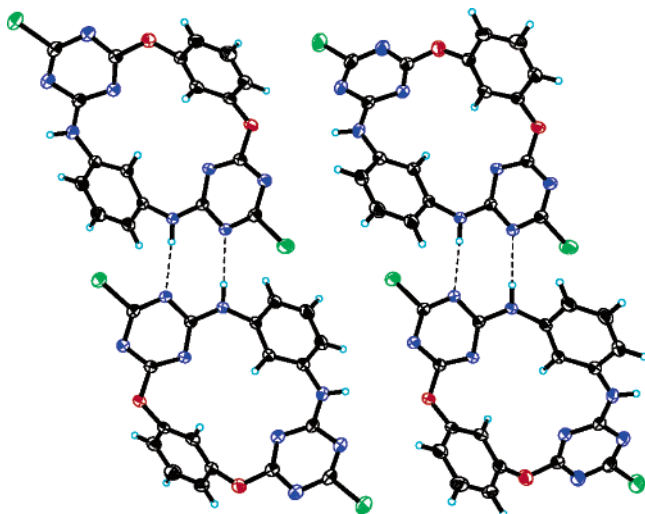
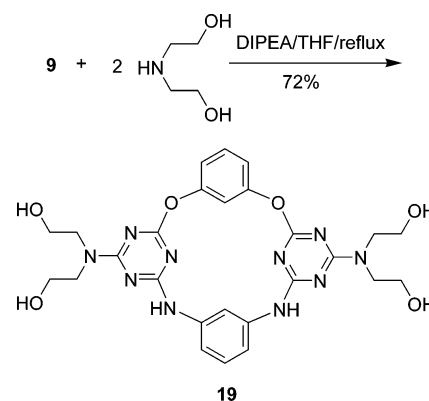


Figure 10. Intermolecular hydrogen bonding between two molecules of **9** in a layered structure. $d_{(D-H)} = 0.860$ Å, $d_{(H\cdots A)} = 2.211$ Å, $\angle D-H\cdots A = 161.2^\circ$, $d_{(D\cdots A)} = 3.038$ Å.

formation of a set of calix[2]arene[2]triazines of varied cavities in which the distances between two benzene rings at the upper rim span from 5.011 to 7.979 Å (Figures 1–8).

Being amino-substituted triazine species, it was not surprising to observe the intermolecular hydrogen bonding effect of the aza (NH)-bridged calix[2]arene[2]triazines in the solid state. However, the formation of intermolecular hydrogen bond(s) was strongly influenced by intrinsic structure of the rest heteroatoms, and different intermolecular hydrogen bond formation affected dramatically molecular packing patterns yielding various solid

Scheme 5



structures. For example, a pair of intermolecular hydrogen bonds were evidenced in *N,N'*-dimethylated oxotriazacalix[2]arene[2]triazine **16** (Figure 9), whereas no intermolecular interaction was observed at all in the crystal structure of azatrioxocalix[2]arene[2]triazine **8**. In the case of diazadioxocalix[2]arene[2]triazine **9**, there was only one pair of intermolecular hydrogen bonds formed, leading to a layered structure consisting of an intermolecular hydrogen bonded dimer repeating unit (Figure 10). In contrast, one *N,N'*-dimethylated tetraazacalix[2]arene[2]triazine molecule **14** formed two pairs of hydrogen bonds intermolecularly with its neighboring two molecules, yielding a one-dimensional infinite chain structure (Figure 11). The perfect and multiple, i.e., four pairs or eight, hydrogen bonds were formed for each of the tetraazacalix[2]arene[2]triazine molecules **13** with its neighboring four molecules and, therefore, produced a two-dimensional zigzag layered structure (Figure 12).

All heteroatom-bridged calix[2]arene[2]triazines can serve as versatile platforms for the construction of more sophisticated and functionalized host molecules, since the chlorine substituents on both triazine rings can be readily displaced by a variety of nucleophiles. In the presence of diisopropylethylamine, for example, diazadioxocalix[2]arene[2]triazine **9** underwent an efficient nucleophilic substitution reaction with diethanolamine to furnish product **19** in 72% yield. Having being functionalized with four hydroxy groups, the new macrocyclic molecule **19** shows dramatically improved solubility in methanol (Scheme 5).

Conclusion

We have developed an efficient and convenient stepwise fragment coupling approach to the synthesis of aza- and/or oxo-

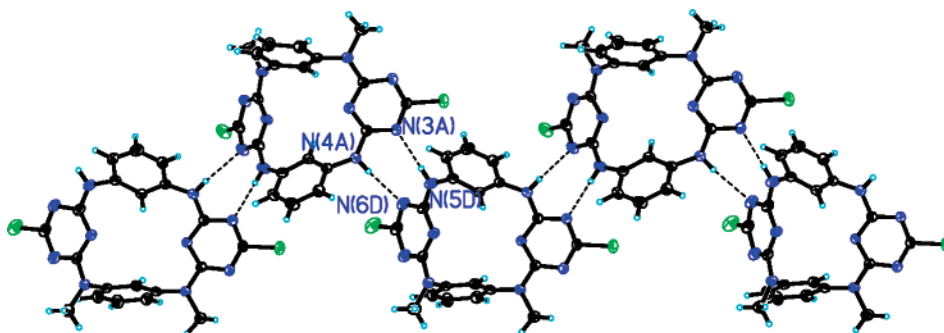


Figure 11. One-dimensional chain structure of **14** formed through intermolecular hydrogen bonds in the solid state. $d_{[N(5D)-H(5D)]} = 0.860$ Å, $d_{[H(5D)\cdots N(3A)]} = 2.164$ Å, $\angle N(5D)-H(5D)\cdots N(3A) = 173.5^\circ$, $d_{[N(5D)\cdots N(3A)]} = 3.020$ Å, $d_{[N(4A)-H(4A)]} = 0.860$ Å, $d_{[H(4A)\cdots N(6D)]} = 2.425$ Å, $\angle N(4A)-H(4A)\cdots N(6D) = 160.8^\circ$, $d_{[N(4A)\cdots N(6D)]} = 3.250$ Å.

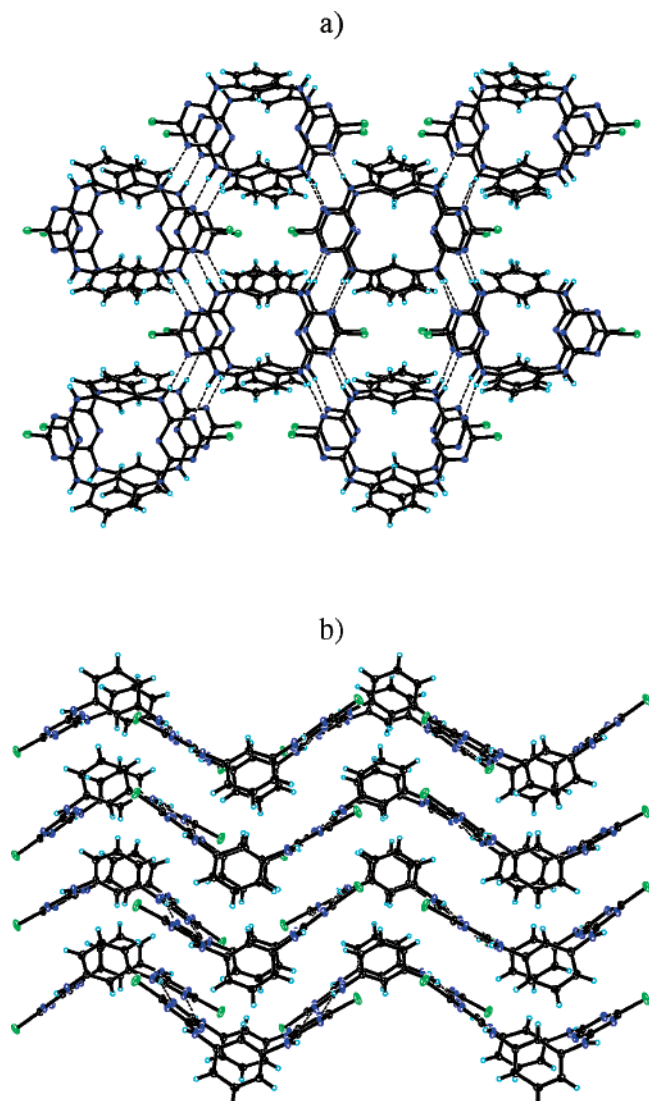


Figure 12. Two-dimensional zigzag layered structure of **13** formed through multiple intermolecular hydrogen bonds in the solid state: (a) along *a* axis and (b) along *b* axis. $d_{(D-H)} = 0.860$ Å, $d_{(H...A)} = 2.284$ Å, $\angle D-H...A = 159.0^\circ$, $d_{(D...A)} = 3.103$ Å.

bridged calix[2]arene[2]triazines. In the presence of diisopropylethylamine in tetrahydrofuran at 0 °C, resorcinol **1**, *m*-phenylenediamine **5**, 3-aminophenol **4**, and *N,N'*-dimethyl-*m*-phenylenediamine **6** underwent, respectively, a coupling reaction with cyanuric chloride **2** to give the corresponding linear trimers **3**, **11**, **15**, and **17** in the chemical yields ranging from 75% to 83%. Macrocyclizative coupling reaction of the linear trimers **3**, **11**, **15**, and **17** with respective resorcinol **1**, *m*-phenylenediamine **5**, 3-aminophenol **4**, and *N,N'*-dimethyl-*m*-phenylenediamine **6** proceeded smoothly and efficiently in acetone at room temperature to afford good yields of heteroatom-bridged calix[2]arene[2]triazines. The high yielding fragment coupling approach established in this study should be generally applicable in the preparation of various heteroatom-bridged calix(hetero)-aromatics when substituted (hetero)aromatic diamine, diphenol, and aminophenol derivatives are employed. The method should also have potential in the synthesis of unsymmetric heteroatom-

linked calix(hetero)aromatics if different fragments are used. In addition, the aza- and/or oxo-bridged calix[2]arene[2]triazines are versatile macrocyclic platforms for the construction of more sophisticated and functionalized molecular architectures because of the ease of elaboration of benzene rings and chloro-substituted triazine rings. This has been exemplified by the efficient conversion of the parent diazadioxocalix[2]arene[2]triazine **9** into its bis(dihydroxyethylamino)-substituted derivative **19**.

Aza- and/or oxo-bridged calix[2]arene[2]triazines obtained adopt a 1,3-*alternate* conformation, with a pair of triazine rings being roughly coplanar while a pair of benzene rings were perpendicular to the plane defined by four bridging heteroatoms. Because of the electronic and steric effects, the bridging heteroatoms tend to form conjugation with a triazine ring rather than a benzene ring, and the cavity of heteroatom-bridged calix[2]arene[2]triazines can therefore be viewed as being resulted from two isolated benzene planes and two bis-heteroatom-conjugated triazine planes in a 1,3-*alternate* fashion. The cavity of the heteroatom-bridged calix[2]arene[2]triazines, such as the distances between two opposite (hetero)aromatic rings and the inclined angles of (hetero)aromatic rings to the plane of four bridging heteroatoms, is determined strongly by the nature of the bridging heteroatoms. The upper rim distances between two benzene rings range widely from 5.011 to 7.979 Å when heteroatoms varied from four oxygen atoms to two oxygen and two nitrogen atoms. To our knowledge, this is probably the first example that the cavity of calixarene species is regulated by the bridge linkages. That might open an avenue for one to coarse- and fine-regulate the cavity of these macrocycles by modifying not only the (hetero)aromatic rings but also the bridging heteroatoms as well. In the solid state, different patterns of intermolecular hydrogen bonds were observed. The multiple intermolecular hydrogen bond interactions among *N,N'*-dimethylated tetraazacalix[2]arene[2]triazine **14** and among tetraazacalix[2]arene[2]triazine **13** led to the formation of an infinite one-dimensional chain structure and a two-dimensional zigzag layered structure, respectively. The readily tunable cavity structures and the unique electronic feature of the surface of the cavity, i.e., 1,3-*alternate* electron-rich and electron-deficient π -aromatics, should render heteroatom-bridged calix[2]arene[2]triazines and their derivatives intriguing macrocyclic host molecules in the study of molecular recognition.

Acknowledgment. The work was partially supported by funds from the National Natural Science Foundation of China, Ministry of Science and Technology of China (Grant No. 2002CCA03100) and Chinese Academy of Sciences. We thank Dr. H.-W. Ma for determining the crystal structures of products and Q.-Q. Wang, B.-Y. Hou, and M.-H. Huang for their technical assistance.

Supporting Information Available: ^1H and ^{13}C NMR spectra and UV-vis spectra of aza- and/or oxo-bridged calix[2]arene[2]triazines. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA0465092