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Synthesis and Structure of Functionalized Homo Heteracalix[2]arene[2]triazines: Effect of All Heteroatom Bridges on Macrocyclic Conformation

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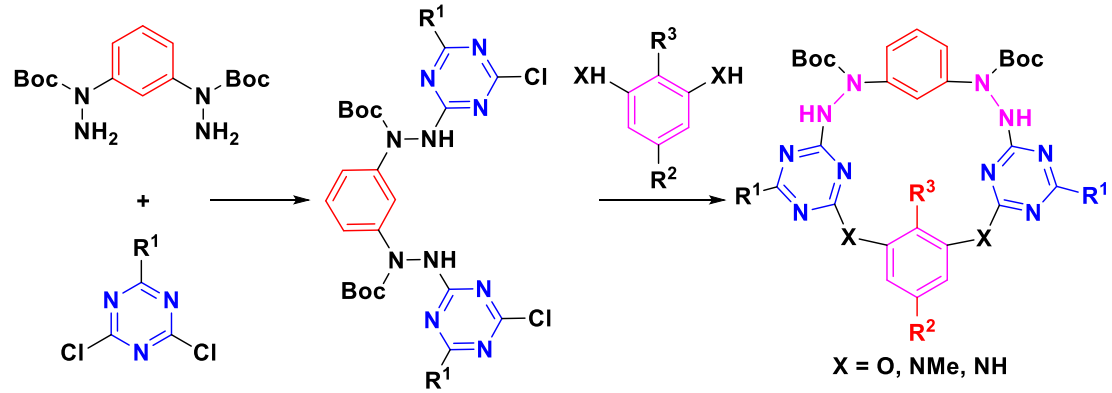


ABSTRACT: A number of unprecedented homo heteracalix[2]arene[2]triazines were synthesized by means of a fragment coupling approach. Two directional nucleophilic substitution reactions of *N*-Boc-protected 1,3-dihydrazobenzene with cyanuric acid chloride and 2-butoxy-4,6-dichloro-1,3,5-triazine led to hydrazo-linked trimers which underwent efficient macrocyclic condensation reaction with functionalized resorcinol derivatives to afford $(NHNBoc)_2,O_2$-calix[2]arene[2]triazine macrocycles which contain a functional group either on the upper rime or the lower rim. The use of 1,3-phenylenediamines instead of resorcinol in the reaction produced $(NR)_2,(NHNBoc)_2$-calix[2]arene[2]triazines. Post-macrocyclization modifications such as nucleophilic substitution reaction of chloro on triazine by amines and removal of Boc from hydrazo moieties produced homo calix[2]arene[2]triazine derivatives. In the solid state, $(NHNR)_2,O_2$-bridged calix[2]arene[2]triazines with and without a substituent on the upper rim position, and $(NMe)_2,(NHNBoc)_2$-calix[2]arene[2]triazine adopted a typical partial cone conformation while the heavily twisted 1,3-alternate conformational

structures were observed for both $(NHNBoc)_2,O_2$-calix[2]arene[2]triazines bearing a functional group on the lower rim position and $(NH)_2,(NHNBoc)_2$-calix[2]arene[2]triazine. In solution, all synthesized homo heteracalix[2]arene[2]triazines existed as the mixture of different macrocyclic conformers which underwent slow inter-conversions at room temperature relative to the NMR time scale.

INTRODUCTION

Heteracalixaromatics[1-4] are synthetic macrocycles which are composed of heteroatoms and *meta*-(het)arylene in an alternative manner. Being different from conventional calix[4]arenes, nitrogen and oxygen bridged calix[4]aromatics reported to date adopt generally 1,3-alternate conformational structures both in crystalline state and in solution.[5] One of the salient structural features is that the bridging heteroatoms participate in the formation of conjugation with their adjacent aromatic rings to various degrees leading to the variable bond lengths and angles. As a consequence, the macrocyclic cavities and, more significantly, the electronic features of 1,3-alternate heteracalix[4]aromatics are amenable to regulation by means of the interplay between different heteroatoms and diverse aromatic subunits.[6] The unique structural advantages along with the easy availability render heteracalix[4]aromatics powerful and versatile macrocyclic host molecules in supramolecular chemistry.[1-3] For example, azacalix[4]pyridines interact selectively with both the electron neutral organic molecules such as fullerenes[7] and the charged species including transition metal ions[8] while oxacalix[2]arene[2]triazines form complexes with anions of different geometries, shapes and volumes owing to non-covalent anion-π interactions.[9] Applications of heteracalix[4]aromatics in the fabrication of metal organic frameworks,[10] CO_2-absorbents,[11] anion responsive vesicles,[12] liquid crystals,[13] stationary phase[14] and organic catalysts[15] have also been demonstrated. Moreover, as a member of heteracalix[4]aromatics, azacalix[1]arene[3]pyridines are able to form structurally well-defined high valent arylcopper organometallic complexes, providing unique

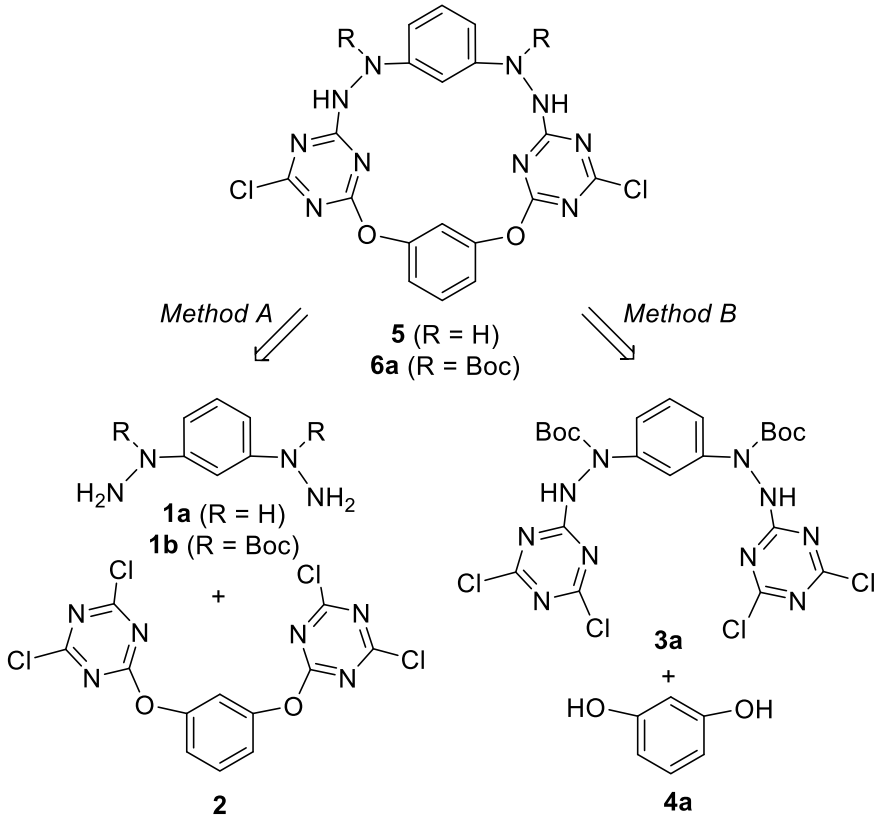
molecular tools to investigate the mechanism of Cu(II)-catalyzed arene C-H bond activation and functionalization.[16]

To fully exploit the applications of heteracalix[4]aromatics in molecular recognition and self-assembly, endeavor to construct macrocyclic conformers other than 1,3-alternate one has been reported. One of the strategies is to introduce functional groups in order to create non-covalent bond interactions intramolecularly. Unfortunately, fixation of two hydroxy or carboxylic groups at the lower rim positions does not induce the formation of other conformational oxacalix[2]arene[2]triazines as no effective intramolecular hydrogen bonds are formed between the hydrogen bond donors and triazine moieties.[17] Steric effect offers another approach to control the conformation. Installation of very bulky substituents on the aromatic subunits for instance leads indeed to flattened partial cone oxacalix[2]arene[2]triazines. However, as minor and the kinetically favored products, the flattened partial cone oxacalix[2]arene[2]triazines are generated only in very low yields from the crucial macrocyclization reaction step,[18] which limits the exploration of their applications in host-guest chemistry. Several years ago, we designed and prepared -CH_2O- and -CH_2NR- bridged homo heteracalix[2]arene[2]triazine host molecules with the purpose of enlarging the macrocyclic cavity at the expense of regulation of electronic characteristics of phenylene by heteroatoms. It was discovered that insertion of extra methylene units into the linking positions of typical heteracalix[2]arene[2]triazines generates new macrocycles which adopt surprisingly various conformational structures.[19] The dipole-dipole interaction between proximal aromatic rings was rationalized to play a dominant role in determining the conformational structures. To decrease such dipole-dipole interaction by increasing the distance of two neighboring aromatic rings, we have very recently devised all hydrazo-bridged homo calix[2]pyridine[2]triazines, and found all resulting macrocycles give cone conformers.[20] Inspired by the previous observations,[19a,20] we undertook the current study to construct all heteroatom linked homo X_2,$(NHNR)_2$-calix[4]aromatics (X = O or NR'). We envisioned that the replacement of two of the four single heteroatom linkages in X_4-calix[4]aromatics (X

= O or NR') with hydrazo moieties would generate different conformers and particularly the partial cone conformers of homo heteracalix[4]aromatics. We report herein the synthesis of a number of functionalized O_2,$(NHNR)_2$- and $(NR')_2$,$(NHNR)_2$-bridged calix[2]arene[2]triazines by means of a convenient fragment coupling method. The influence of the bridging heteroatoms and the substituents on the macrocyclic conformations was examined. X-ray crystallography showed the all acquired compounds did not adopt typical 1,3-alternate conformation. Gratifyingly, most of homo calix[2]arene[2]triazines gave predominantly partial cone conformers in which hydrazo formed conjugation with both benzene and triazine rings.

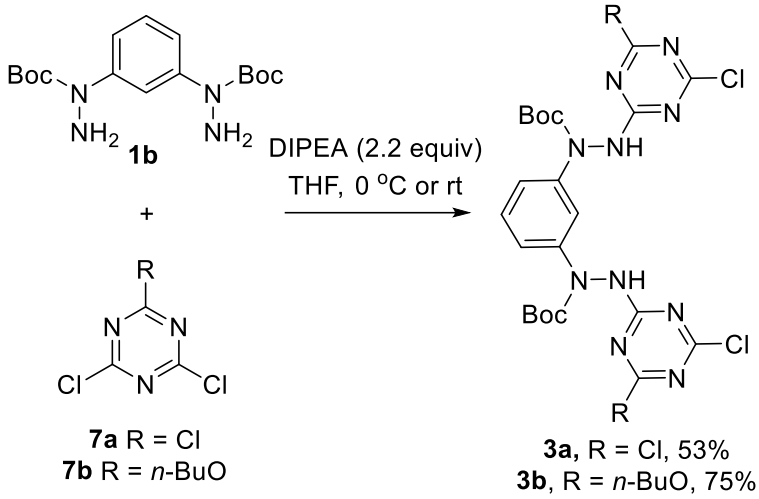
RESULTS AND DISCUSSION

We commenced our study with the synthesis of O_2,$(N_2H_2)_2$-bridged calix[2]arene[2]triazine **5** (R = H). Retro-synthetically, macrocycle **5** could be constructed via two distinct fragment coupling approaches. One involves the macrocyclic condensation between 1,3-dihydrazobenzene **1a** (R = H) and 1,3-bis((4,6-dichloro-1,3,5-triazin-2-yl)oxy)benzene **2**, which is readily obtained from the two directional nucleophilic aromatic substitution of resorcinol with two equivalents of cyanuric acid chloride. The other synthetic route comprises the reaction of a di-tert-butyl 1,1'-(1,3-phenylene)bis(2-(4,6-dichloro-1,3,5-triazin-2-yl)hydrazine intermediate **3a** with resorcinol **4** (Scheme 1). For convenience, compounds **1a** and **3a** and their analogs are referred roughly to as the trimers or trimeric intermediates throughout this article.



Scheme 1. Two distinct fragment coupling approaches to $(NHNR)_2,O_2$-calix[2]arene[2]triazines

Since 1,3-dihydrazobenzene **1a** (R = H) was found to undergo spontaneous decomposition under ambient conditions, *N*-Boc-protected 1,3-dihydrazobenzene **1b** (R = Boc), which was prepared from copper-mediated cross coupling reaction between 1,3-diiodobenzene and *tert*-butyl hydrazinecarboxylate[21] (see Supporting Information), was employed in the synthesis. Under the various conditions tested, the reaction of **1b** and **2** did not produce desired macrocyclic compound (Method A). Instead, in all cases, the reaction gave a mixture of polar and inseparable oligomers. We then turned our attention to the synthesis of **6a** from the reaction of **3a** with resorcinol **4a**. The trimeric intermediate **3a** was obtained straightforwardly by treating *N*-Boc-protected 1,3-dihydrazobenzene **1b** with an excess amount of cyanuric acid chloride **7a** (3 equiv) at 0 ^{o}C in the presence of DIPEA as an acid scavenger. Under the identical conditions, trimer **3b** was prepared analogously in 75% when 2-butoxy-4,6-dichloro-1,3,5-triazine **7b** was applied (Scheme 2).

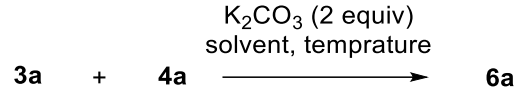


Scheme 2. Preparation of hydrazo-linked trimers **3a** and **3b**

In contrast to the efficient construction of heteracalix[2]arene[2]triazines reported previously,[6a] the synthesis of homo heteracalix[2]arene[2]triazines **6a** was not trivial. Trimer **3a** exhibited great reactivity toward resorcinol **4a** in most common organic solvents when tertiary amines such as Et_3N and DIPEA were used as an acid scavenger. Disappointingly, however, no macrocyclic products were obtained under the optimal conditions which worked nicely for the synthesis of heteracalix[2]arene[2]triazines.[6a] In all cases, after reactant **3a** was consumed within 6 h, a mixture of highly polar and inseparable oligomers was yielded. Only when an inorganic base such as Cs_2CO_3 or K_2CO_3 was used, the reaction between **3a** and **4a** in acetone at room temperature afforded target macrocycle **6a** in 8% or 19%, respectively, in addition to a large amount of oligomers (Table S1 in Supporting Information). Using K_2CO_3 as a base, other reaction parameters were further investigated. Notably, the reaction outcomes were strongly dependent on the solvent system used. The results compiled in Table S2 showed clearly that nonpolar and less polar solvents including CCl_4, toluene, ether and THF appeared not beneficial to the reaction as more than 50% to nearly a quantitative yield of the starting trimer **3a** were recovered after reaction. It should also be pointed out that the reaction was inhibited completely in water whereas oligemerization took place exclusively in acetonitrile. Comparable chemical yields (13% - 19%) were

obtained for **6a** when the reaction was conducted in 1,4-dioxane, DMF and DMSO. Accidently, we observed the slight increase of chemical yield of **6a** from 19% to 25% when a mixture of acetone and water (v : v = 9 : 1) was used as the reaction media (entries 1 and 2 in Table 1). Slight increase of reaction temperature to 40 ^{o}C led to a further improvement to 39% yield (entry 4, Table 1). Either a higher or a lower temperature resulted in no satisfactory results (entries 3 and 5, Table 1). Finally, after optimization of the mixed solvent systems (Table S3 and entries 6 - 8, Table 1), we were pleased to discover that, in the presence of K_2CO_3, macrocyclic condensation between **3a** and **4a** proceeded smoothly at 40 ^{o}C in a mixture of acetonitrile and water (v : v = 5 : 1 – 9 : 1) to afford product **6a** in 46% yield (entry 7, Table 1). Although the exact reason why the reaction of **3a** with **4a** differed from that of **1b** and **2** remained unknown at this stage, the linear tetramer precursors derived from two reactions may probably adopt different conformations which were amenable to macrocyclization and oligomerization, respectively.

Table 1. Development of the synthesis of **6a** from the reaction of **3a** with **4a**

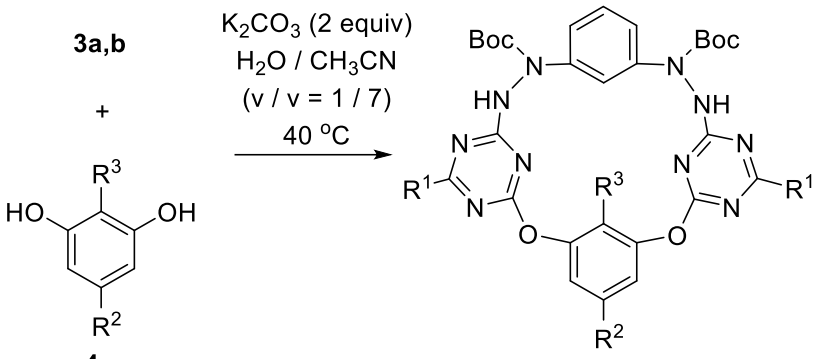


entry	solvent	temp (^{o}C)	yield of **6a** (%)
1	acetone	25	19
2	acetone / H_2O (9 / 1)	25	25
3	acetone / H_2O (9 / 1)	-15	15
4	acetone / H_2O (9 / 1)	40	39
5	acetone / H_2O (9 / 1)	50	33
6	acetonitrile / H_2O (9 / 1)	40	42
7	acetonitrile / H_2O (7 / 1)	40	46
8	acetonitrile / H_2O (5 / 1)	40	43

Under the optimized conditions, the hydrazo-linked trimer **3a** underwent effective

macrocyclic condensation reaction with resorcinol derivatives **4b-g** to produce functionalized $(NHNBoc)_2,O_2$-calix[2]arene[2]triazine macrocycles. As summarized in Table 2, the reaction of 3,5-dihydroxybenzaldehyde **4b**, ethyl 3,5-dihydroxybenzoate **4c**[22] and 5-(4-nitrophenoxy)benzene-1,3-diol **4d**[23] with **3a** afforded the corresponding macrocyclic products **6b-c** in good yields, permitting therefore the functionalization of $(NHNBoc)_2,O_2$-calix[2]arene[2]triazine with an aldehyde, ester and 4-nitrophenoxy group at the upper rim position (entries 2-4, Table 2). The lower-rim-functionalized $(NHNBoc)_2,O_2$-calix[2]arene[2]triazine macrocycles **6e-g** were readily accessible by the same fragment coupling method. The employment of 2,6-dihydroxybenzonitrile **4e**[24] and 2-nitrobenzene-1,3-diol **4f** in the reaction with **3a** thus furnished the formation of cyanided and nitrated homo calix[2]arene[2]triazines **6e** and **6f**, respectively (entries 5 and 6, Table 2). When **3a** was treated with 2,6-dihydroxybenzaldehyde **4g**,[25] the lower-rim-formylated $(NHNBoc)_2,O_2$-calix[2]arene[2]triazine **6g**, a positional isomer of **6b** was also generated albeit in a low yield due to the formation of oligomers under the identical macrocyclization reaction conditions. The hydrazo-connected trimer **3b**, which was derived from 2-butoxy-4,6-dichloro-1,3,5-triazine (*supra vide*), was also able to undergo macrocyclic condensation with resorcinol. Because of the presence of an electron-donating *n*-butoxy on the terminal triazine ring, trimer **3b** was less electrophilic than trimer **3a**. Nevertheless, under more forcing conditions such to use Cs_2CO_3 as a base and boiling acetonitrile as media, the reaction proceeded efficiently to give a high yield of $(NHNBoc)_2,O_2$-calix[2]arene[2]triazine **6h** (entry 8, Table 2). Trimer **3b** also reacted smoothly with 2-nitrobenzene-1,3-diol **4f** to produce the corresponding nitro-bearing macrocycle **6i** (entry 9, Table 2).

Table 2. Synthesis of functionalized $(NHNBoc)_2,O_2$-calix[2]arene[2]triazines **6a-h**

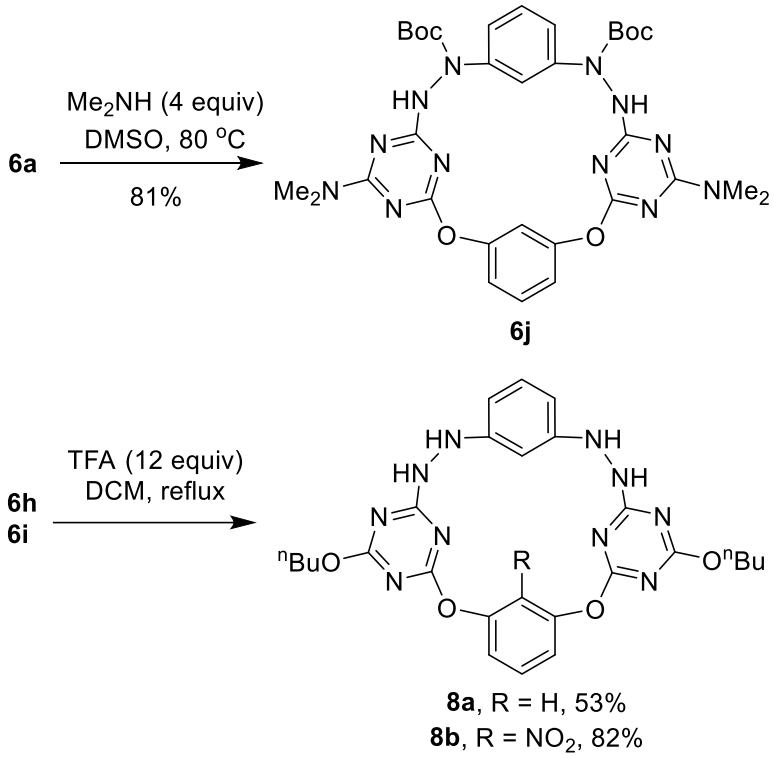


entry	**3**	**4**	**6**	%[a]
1	**3a** (R^1 = Cl)	**4a** (R^2 = R^3 = H)	**6a**	46
2	**3a** (R^1 = Cl)	**4b** (R^2 = CHO, R^3 = H)	**6b**	34
3	**3a** (R^1 = Cl)	**4c** (R^2 = CO_2Et, R^3 = H)	**6c**	57
4	**3a** (R^1 = Cl)	**4d** (R^2 = 4-NO_2-C_6H_4O, R^3 = H)	**6d**	43
5	**3a** (R^1 = Cl)	**4e** (R^2 = H, R^3 = CN)	**6e**	30
6	**3a** (R^1 = Cl)	**4f** (R^2 = H, R^3 = NO_2)	**6f**	41
7	**3a** (R^1 = Cl)	**4g** (R^2 = H, R^3 = CHO)	**6g**	15
8	**3b** (R^1 = *n*-BuO)	**4a** (R^2 = R^3 = H)	**6h**	77[b]
9	**3b** (R^1 = *n*-BuO)	**4f** (R^2 = H, R^3 = NO_2)	**6i**	47[b]

[a] Isolated yield. [b] Cs_2CO_3 (2.2 equiv) was used as a base. The reaction was performed in refluxing CH_3CN for 6 h.

It is worth addressing that the resulting (NHNBoc)$_2$,O_2-calix[2]arene[2]triazine compounds **6** would provide a useful and versatile platform for the fabrication of high-ordered and sophisticated molecular architectures based on a wide variety of well-known functional group transformations. In addition, the chlorotriazine components would constitute invaluable handles allowing direct functionalization on the upper rim of triazine through nucleophilic aromatic substitution reaction. As a demonstration, the displacement of chloro substituents on triazine rings by dimethylamine occurred easily at 80 °C in DMSO to afford *N*,*N*-dimethyl-substituted macrocycle **6j** in 81% (Scheme 3). Moreover, the chemical manipulations on the hydrazo linkages would further enrich the molecular diversity of homo heteracalix[2]arene[2]triazines. Scheme 3 illustrates

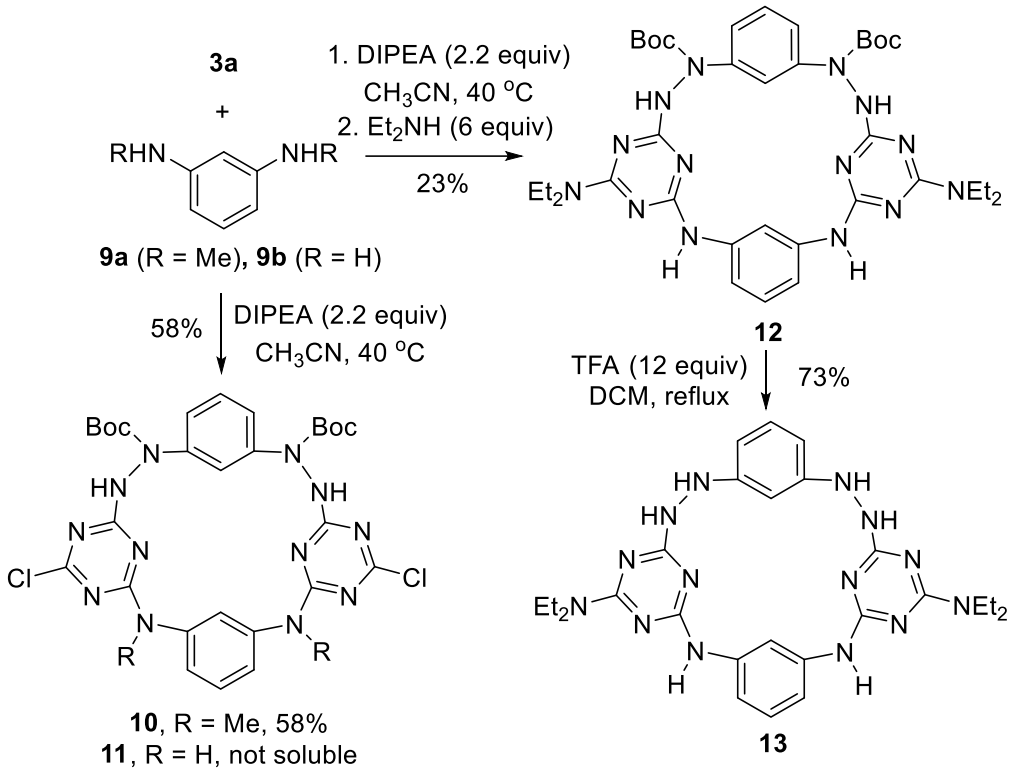
for example the synthesis of $(N_2H_2)_2$,O_2-calix[2]arene[2]triazines **8a** and **8b** which were not accessible by the fragment coupling synthesis starting with 1,3-dihydrazobenzene (*vide supra*). In the presence of TFA, the Boc groups on hydrazo moieties were removed nicely under very mild conditions, affording product **8** in good yields.



Scheme 3. Post-macrocyclization functionalizations

The established fragment coupling strategy was applied successfully in the construction of $(NR)_2$,$(NHNBoc)_2$-calix[2]arene[2]triazines. This has been exemplified in the synthesis of macrocycles **10** and **12**. As depicted in Scheme 4, in the presence of DIPEA, the reaction of trimer **3a** with N,N'-dimethyl-1,3-phenylenediamine **9a** in warm acetonitrile produced all nitrogen atom bridged homo calix[2]arene[2]triazine compound **10**. The reaction between **3a** and 1,3-phenylenediamine **9b** took place similarly. Being sparingly soluble in common organic solvents, purification of **11** was difficult. To circumvent the solubility problem, the compound was transformed in situ into macrocycle **12** taking the advantage of the reactivity of chlorotriazine toward

nucleophile diethylamine. The one-pot two-step synthesis therefore yielded the desired macrocycle in 23% yield. Deprotection of Boc groups resulted in the formation of homo $(NH)_2$,$(NHNH)_2$-calix[2]arene[2]triazine **13** (Scheme 4).



Scheme 4. Synthesis of $(NR)_2$,$(NHNBoc)_2$-calix[2]arene[2]triazines **10**, **12** and **13.**

The structure of all homo heteracalix[2]arene[2]triazine products was in agreement with the spectroscopic data. The constitution of products for example was supported by both mass spectra and microanalysis while the variable temperature NMR spectra revealed macrocyclic ring structures (see Supporting Information). To put the structure beyond ambiguity, and also to shed light on the conformation of these novel macrocycles, high quality single crystals of products **6a**, **6c**, **6e**, **6f**, **8a, 8b, 10, 12** and **13** were obtained and their structures were determined by X-ray diffraction analysis. As we anticipated, the structures depicted in Figure 1 – 6 show that most of the homo $(NHNR)_2$,O_2-calix[2]arene[2]triazine macrocycles adopt the similar partial cone conformations in the solid state. The presence of both a substituent at the low-rim position of benzene ring and two Boc groups on hydrazo moieties, however, caused the

deformation of the partial cone structure due to probably the steric effect. For example, in the case of compounds **6a** and **6c,** the phenylene connected to hydrazo linkers and two triazine rings orientate toward the same direction whereas the other phenylene in between two oxygen atoms positions to the opposite direction, yielding the typical partial cone conformation with a mirror plane that bisects the phenylene moieties. Introduction of a cyano and a nitro group into the lower-rim position resulted in the twisted 1,3-alternate conformations of macrocycles **6e** and **6f**, respectively. In comparison to **6a** and **6c**, it was evident that two N-Boc groups in **6e** and **6f** are almost anti-parallelly aligned. After removal of two Boc groups from hydrazo bridges, the resulting $(N_2H_2)_2$,O_2-calix[2]arene[2]triazines **8a** and **8b**, with and without a substituent on the lower-rim, resumed typical partial cone structures again. The bond lengths and bond angles (Figures S5, S6, S9, and S10 in Supporting Information) indicated that in partial cone conformers such as **6a**, **6c**, **8a** and **8b** all bridging oxygen atoms form stronger conjugation with their adjacent triazine rings. Two pairs neighboring lone-pair electrons on a hydrazo moiety appeared orthogonal to each other, forming conjugation with triazine and benzene rings, respectively. Careful analysis of the bond lengths and angles (Figures S7 and S8 in Supporting Information) of twisted 1,3-alternate conformers of **6e** and **6f** revealed however a strong conjugational system of carbamate. In other word, one of the lone-pair electrons on hydrazo conjugate with the Boc group rather than the phenylene ring. It seemed that, in addition to steric effect, competition of the Boc substituents with the phenylene ring in conjugating with nitrogen lone-pair electrons imposed perturbation on the macrocyclic conformation.

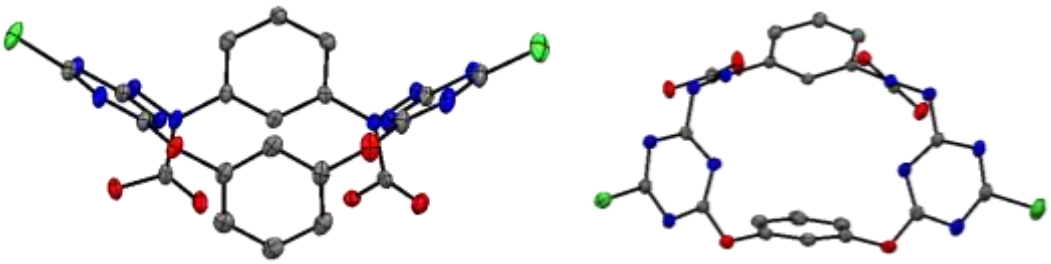


Figure 1. X-ray molecular structure of **6a** (25% probability) with side (left) and top (right) views. Alkyl substituents and hydrogen atoms were omitted for clarity.

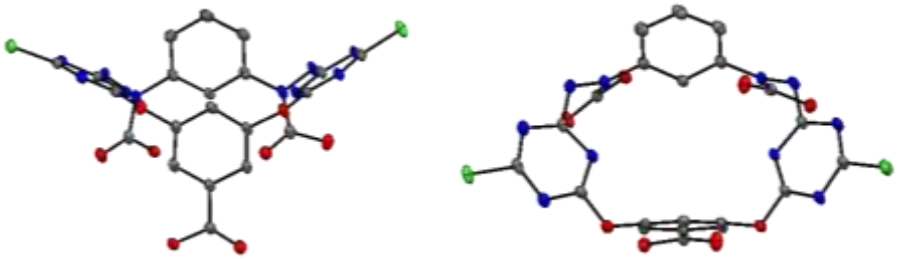


Figure 2. X-ray molecular structure of **6c** (25% probability) with side (left) and top (right) views. Alkyl substituents and hydrogen atoms were omitted for clarity.

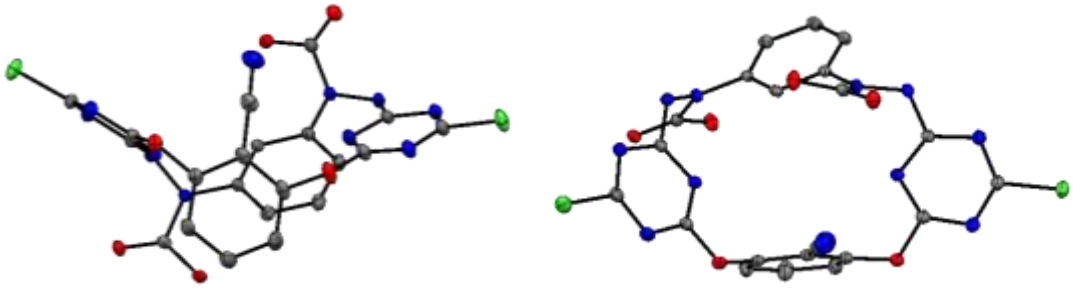


Figure 3. X-ray molecular structure of **6e** (25% probability) with side (left) and top (right) views. Alkyl substituents and hydrogen atoms were omitted for clarity.

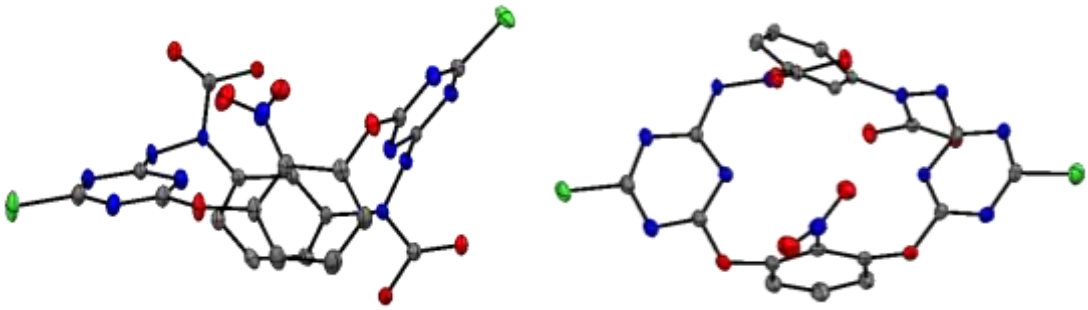


Figure 4. X-ray molecular structure of **6f** (25% probability) with side (left) and top (right) views. Alkyl substituents and hydrogen atoms were omitted for clarity.

Figure 5. X-ray molecular structure of **8a** (25% probability) with side (left) and top (right) views. Alkyl substituents and hydrogen atoms were omitted for clarity.

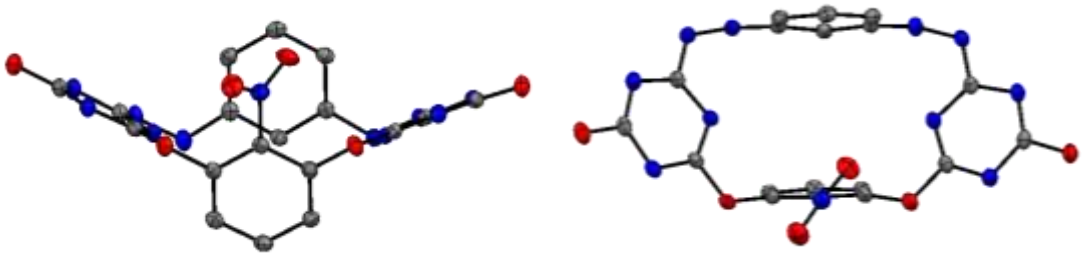


Figure 6. X-ray molecular structure of **8b** (25% probability) with side (left) and top (right) views. Alkyl substituents and hydrogen atoms were omitted for clarity.

Being very similar to $(NHNBoc)_2$,O_2-calix[2]arene[2]triazine **6a**, an all nitrogen atom-linked homo calix[2]arene[2]triazine, namely, $(NHNBoc)_2$,$(NMe)_2$-calix[2]arene[2]triazine **10**, adopted a symmetric partial cone conformation in the solid state (Figure 7). Evidenced by the bond lengths and angles (Figure S11), each triazine ring formed conjugation with its two linking nitrogen atoms while two planar *tert*-butoxycarbonylamino moieties were not coplanar with the *meta*-phenylene in between. As illustrated in Figure 8, replacement of two NMe bridges and chloro substituents in **10** with NH and diethylamino units, respectively, led macrocycle **12** to give unexpectedly a heavily distorted conformation. After further removal of Boc groups from the linking hydrazine moieties, $(NH)_2$,$(NHNH)_2$-calix[2]arene[2]triazine **13** afforded a twisted partial conformation (Figure 9). It seems that the presence of *N*,*N*-diethylamino group on the upper-rim position of the triazine ring had a marked effect on the conformational structure of all nitrogen atom-linked homo calix[2]arene[2]triazines. Revealed by the bond lengths (Figures S12 and S13 in Supporting Information) of bridging nitrogen atoms to the carbons of aromatic rings and by the bond angles (Figures S12 and S13 in Supporting Information) around linking units, both benzene and triazine rings formed varied conjugation systems with their neighboring nitrogen atoms.

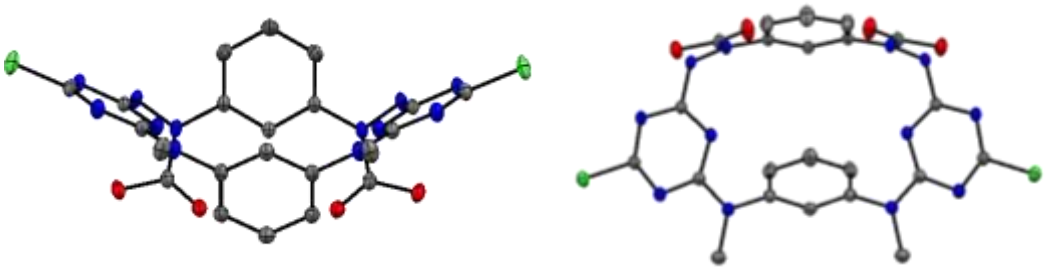


Figure 7. X-ray molecular structure of **10** (25% probability) with side (left) and top (right) views. Alkyl substituents and hydrogen atoms were omitted for clarity.

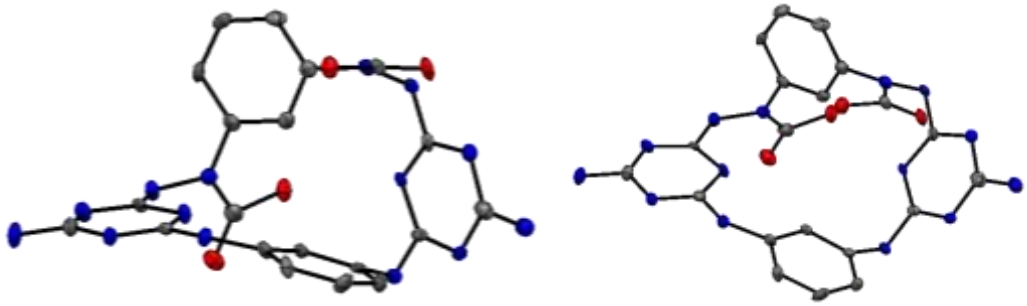


Figure 8. X-ray molecular structure of **12** (25% probability) with side (left) and top (right) views. Alkyl substituents and hydrogen atoms were omitted for clarity.

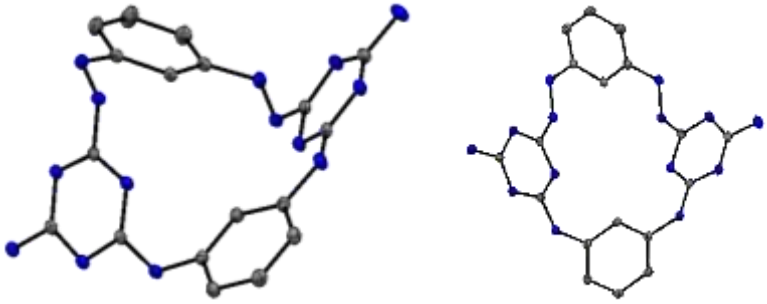


Figure 9. X-ray molecular structure of **13** (25% probability) with side (left) and top (right) views. Alkyl substituents and hydrogen atoms were omitted for clarity.

It should be noted that the partial cone and the distorted 1,3-alternate conformers observed in the crystalline state may not retain in solution. As shown by ^{1}H and ^{13}C NMR spectra of all aforementioned products at and below room temperature (Figures S2-S4), which gave very broad resonance proton and carbon signals, homo calix[2]arene[2]triazines existed most likely as a mixture of conformers in solution. The signals became sharpened with the increase of measuring temperature (Figure 10). As shown in Supporting Information, for macrocycles without *N*-Boc substituents, decent

^{1}H and ^{13}C NMR spectra with well-resolved signals were obtained at 80 ^{o}C - 100 ^{o}C. In the case of products **10** and **12**, a probe temperature as high as to 146 ^{o}C was required to assure the quality of spectra. The outcomes of variable temperature ^{1}H NMR spectra (Figures 10 and S2-S4), suggested clearly that different conformers in equilibria in solution were able to undergo very fast inter-conversion at a high temperature relative to the NMR time scale.

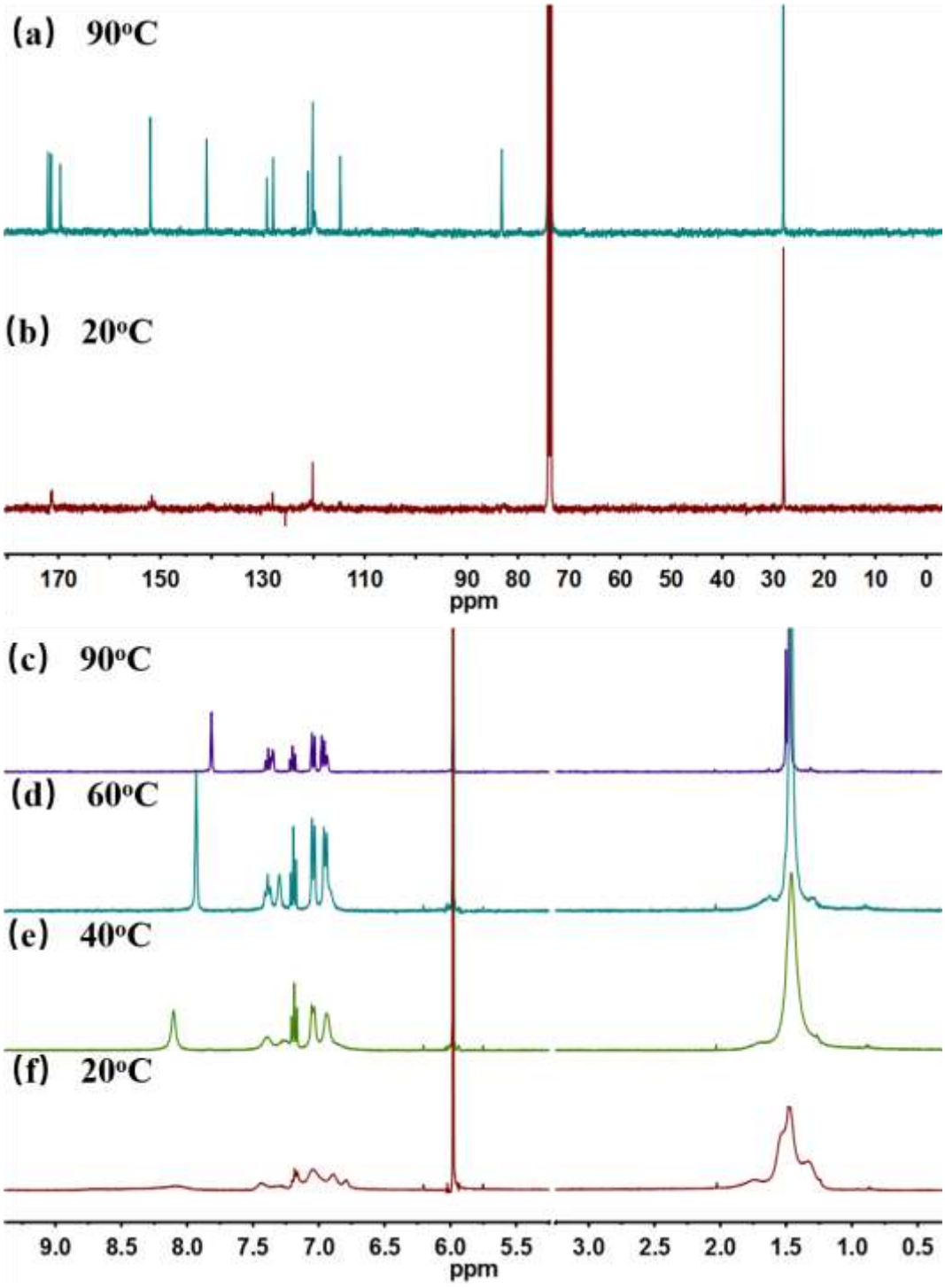


Figure 10. Partial variable temperature ^{1}H and ^{13}C NMR spectra of **6a** in d_2-$CDCl_2CDCl_2$.

CONCLUSION

We have presented the efficient and convenient synthesis of a series of functionalized homo heteracalixaromatics, namely, $(NHNR)_2$,O_2-calix[2]arene[2]triazines and $(NR)_2$,$(NHNR')_2$-calix[2]arene[2]triazines by means of a fragment coupling strategy. The unprecedented homo heteracalix[4]arenes adopt predominantly partial cone conformation in the solid state. In solution, the novel macrocycles exist as a mixture of conformers which undergo very fast inter-conversion at high temperatures relative to the NMR time scale. Our study has demonstrated an alternative approach to engineer the macrocyclic conformation and cavity structures. Through the formation of varied conjugations with the neighboring aromatic components, hydrazo moiety was able to tune the electronic feature of heteracalixaromatics. Studies on the construction of stable macrocyclic conformers and their applications in molecular recognition and self-assembly are being actively pursued in this laboratory and results will be disclosed in due course.

Experimental Section

General Information. Unless otherwise noted, all reactions were carried out in oven-dried glassware. Anhydrous solvents were purified and dried following standard procedures. All commercially available reagents were used as received. TLC analysis was performed on pre-coated, glass-backed silica gel plates and visualized with UV light. Unless otherwise noted, flash column chromatography was performed on silica gel (200 - 300 mesh). Melting points were uncorrected. The ^{1}H NMR, ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometer. ^{1}H and ^{13}C NMR chemical shifts were reported relative to the signals of residual of chloroform (7.26 ppm, 77.16 ppm), DMSO (2.50 ppm, 39.52 ppm), $CDCl_2CDCl_2$ (5.98 ppm, 73.80 ppm) and that of

internal standard of TMS (0.0 ppm), respectively. Abbreviations are used in the description of NMR data as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dt = doublet of triplets, m = multiplet), coupling constant (*J*, Hz). The electron spray ionization mass spectra (ESI-MS) were recorded on a MASS spectrometer. Infrared spectra were recorded with KBr pellets in the 4000-400 cm^{-1} region. Compounds **1b**,[21] **4c**,[22] **4d**,[23] **4e**,[24] **4g**[25] and **7b**[26] were prepared following the reported procedures.

Preparation of 3a. To an ice-bath cooled solution of cyanuric chloride **7a** (552 mg, 3 mmol) in tetrahydrofuran (20 mL) was added dropwise a mixture of substituted *N*-Boc-protected 1,3-dihydrazobenzene **1b** (338 mg, 1.0 mmol) and diisopropylethylamine (324 mg, 2.5 mmol) in tetrahydrofuran (10 mL) during 1 h. The reaction mixture was stirred for 3h. After removal of diisopropylethylamine hydrochloride salt through filtration, the filtrate was mixed with saline (100 mL) and extracted with ethyl acetate (3 x 50 mL). After drying (Na_2SO_4) and then removing the solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate (v / v = 8 / 1) as the mobile phase to give pure **3a** (336 mg, 53%): white solid, mp 198-199 °C; ^{1}H NMR (400 MHz, $CDCl_2CDCl_2$, 100°C) δ 8.02 (s, 2H), 7.59 (s, 1H), 7.33 (s, 3H), 1.47 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 100°C) δ 171.3, 168.2, 152.08, 141.5, 128.7, 122.0, 120.1, 83.7, 27.9; IR (KBr, cm^{-1}) ν 3283, 2974, 1700, 1561,1511. HRMS (ESI-ion trap) calcd. for $C_{22}H_{24}Cl_4N_{10}O_4Na$: $[M+Na]^+$ 657.0604. Found: 657.0594.

Preparation of 3b. Following the procedure for the preparation of **3a**, **3b** was synthesized from the reaction of 2-butoxy-4,6-dichloro-1,3,5-triazine **7b** (666 mg, 3 mmol) with **1b** (338 mg, 1.0 mmol) at room temperature in the presence of diisopropylethylamine (324 mg, 2.5 mmol). Pure **3b** was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 5 / 1) (532 mg, 75% yield): white solid, mp 95-97 °C; ^{1}H NMR (400 MHz, $CDCl_2CDCl_2$, 120°C) δ 7.69 (br, 3H), 7.47-7.15 (m, 3H), 4.39 (t, J = 6.6 Hz, 4H), 1.79-1.70 (m, 4H), 1.47 (s, 22H), 0.98 (t, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 120°C) δ 171.5, 171.2, 169.2, 152.4, 141.9, 128.1, 120.9, 118.5, 82.8, 68.7, 30.4, 27.9, 18.7, 13.2; IR

(KBr, cm^{-1}) v 3233, 2966, 1730, 1566,1447. HRMS (ESI-ion trap) calcd. for $C_{30}H_{42}Cl_2N_{10}O_6Na$: $[M+Na]^+$ 731.2558. Found: 731.2554.

General procedure for the synthesis of homo heteracalix[2]arene[2]triazines 6a-g. At 40 °C, both solutions of resorcinol or its derivatives (1 mmol) in acetonitrile (25 mL) and **3a** (1 mmol) in acetonitrile (25 mL) were added dropwise at the same time and the same rate to a solution of K_2CO_3 (276 mg, 2.0 mmol) in a mixture of acetonitrile (175 mL) and water (25 mL). After addition of two reactants, which took about 1 h, the resulting mixture was stirred for another 6 h. The solvents were removed, and the residue was mixed with saline (100 mL) and extracted with ethyl acetate (3 x 50 mL) and then dried with anhydrous Na_2SO_4. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate as the mobile phase to give products.

6a was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 8 / 1) (309 mg, 46% yield): white solid, mp 220 °C (decomposed); ^1H NMR (400 MHz, $CDCl_2CDCl_2$, 90°C) δ 7.82 (s, 2H), 7.41-7.35 (m, 2H), 7.20 (t, J = 8.0 Hz, 1H), 7.05-6.93 (m, 5H), 1.48 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 90°C) δ 175.4, 174.8, 173.0, 155.4, 155.3, 144.3, 132.5, 131.3, 124.5, 123.5, 123.1, 118.2, 86.5, 31.3; IR (KBr, cm^{-1}) v 3232, 2981, 1726, 1563. HRMS (ESI-ion trap) calcd. for $C_{28}H_{28}Cl_2N_{10}O_6Na$: $[M+Na]^+$ 693.1468. Found: 693.1458. Elemental analysis calcd. (%) for $C_{28}H_{28}Cl_2N_{10}O_6$: C, 50.08; H, 4.20; N, 20.86. Found: C, 49.85; H, 4.21; N, 20.62. A high quality single crystal for X-ray diffraction analysis was obtained by diffusing *n*-hexane vapor into the solution of **6a** in ethyl acetate.

6b was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 3 / 1) (238 mg, 34% yield): white solid, mp 226 °C (decomposed); ^1H NMR (400 MHz, $CDCl_2CDCl_2$, 90°C) δ 9.95 (s, 1H), 7.96 (s, 2H), 7.54 (d, J = 2.4Hz, 2H), 7.33 (s, 1H) 7.21-7.16 (m, 2H), 6.96 (d, J = 8.4 Hz, 2H) 1.46 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 90°C) δ 191.9, 175.6, 174.5, 172.8, 155.9, 155.2, 144.2, 141.6, 131.4, 124.3, 123.8, 123.6, 122.3, 86.9, 31.4; IR (KBr, cm^{-1}) v 3236, 3101, 2979, 1729, 1566. HRMS (ESI-ion trap) calcd. for $C_{29}H_{28}Cl_2N_{10}O_7Na$: $[M+Na]^+$ 721.1412. Found: 721.1408. Elemental analysis calcd. (%) for

$C_{29}H_{28}Cl_2N_{10}O_7$: C, 49.79; H, 4.03; N, 20.02. Found: C, 49.65; H, 4.06; N, 19.67.

6c was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 3 / 1) (424 mg, 57% yield): white solid, mp 218-219 °C; ^{1}H NMR (400 MHz, CD_3CN, 80°C) δ 8.85 (s, 2H), 7.84 (s, 2H), 7.37-7.27 (m, 3H), 7.14 (d, J = 7.6 Hz, 2H), 4.45 (q, J = 6.8 Hz, 2H) 1.54-1.45 (m, 21H); ^{13}C NMR (100 MHz, CD_3CN, 80°C) δ 173.2, 173.0, 171.2, 165.7, 153.8, 153.5, 142.8, 134.8, 129.9, 123.5, 122.7, 121.3, 120.7, 84.0, 63.0, 28.8, 14.9; IR (KBr, cm^{-1}) ν 3226, 2982, 1729, 1562. HRMS (ESI-ion trap) calcd. for $C_{31}H_{32}Cl_2N_{10}O_8Na$: $[M+Na]^+$ 765.1674. Found: 765.1670. Elemental analysis calcd. (%) for $C_{31}H_{32}Cl_2N_{10}O_8$: C, 50.08; H, 4.34; N, 18.84. Found: C, 50.03; H, 4.35; N, 18.97. A high quality single crystal for X-ray diffraction analysis was obtained by diffusing *n*-hexane vapor into the solution of **6c** in ethyl acetate.

6d was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 5 / 1) (348 mg, 43% yield): white solid, mp 219-220 °C; ^{1}H NMR (400 MHz, CD_3CN, 80°C) δ 8.71 (s, 2H), 8.19 (d, J = 8.4 Hz, 2H), 7.42 (s, 1H), 7.26 (t, J = 8.4 Hz, 1H), 7.09-7.04 (m, 4H), 6.91 (s, 2H), 6.82 (s, 1H) 1.37 (s, 18H); ^{13}C NMR (100 MHz, CD_3CN, 80°C) δ 173.2, 172.9, 171.3, 163.5, 157.3, 154.7,153.5, 145.1, 142.9, 129.9, 127.5, 123.1, 121.4, 119.3, 114.6, 113.4, 84.0, 28.8; IR (KBr, cm^{-1}) ν 3234, 2979, 1730, 1563. HRMS (ESI-ion trap) calcd. for $C_{34}H_{31}Cl_2N_{11}O_9Na$: $[M+Na]^+$ 830.1573. Found: 830.1568. Elemental analysis calcd. (%) for $C_{34}H_{31}Cl_2N_{11}O_9$: C, 50.50; H, 3.86; N, 19.06. Found: C, 50.17; H, 3.76; N, 18.75.

6e was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 3 / 1) (209 mg, 30% yield): white solid, mp 197-198 °C; ^{1}H NMR (400 MHz, $CDCl_2CDCl_2$, 90°C) δ 7.82 (s, 2H) , 7.59 (t, J = 8.0 Hz, 1H), 7.24-7.15 (m, 4H), 6.97 (dd, J = 8.4 Hz, J = 2.4 Hz, 2H), 1.48 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 90°C) δ 175.9, 174.2, 173.1, 156.8, 155.2, 144.2, 136.3, 131.5, 124.5, 123.2, 122.4, 113.5, 106.2, 86.8, 31.4; IR (KBr, cm^{-1}) ν 3235, 2979, 1734, 1691, 1572. HRMS (ESI-ion trap) calcd. for $C_{29}H_{27}Cl_2N_{11}O_6Na$: $[M+Na]^+$ 718.1412. Found: 718.1408. Elemental analysis calcd. (%) for $C_{29}H_{27}Cl_2N_{11}O_6$: C, 50.01; H, 3.91; N, 22.12. Found: C, 49.88; H, 3.99; N, 21.81. A high quality single crystal for X-ray

diffraction analysis was obtained by diffusing *n*-hexane vapor into the solution of **6e** in ethyl acetate.

6f was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 2 / 1) (294 mg, 41% yield): white solid, mp 232 ^{o}C (decomposed); ^{1}H NMR (400 MHz, $CDCl_2CDCl_2$, 120^{o}C) δ 7.93 (s, 2H) , 7.59 (t, J = 8.0 Hz, 1H), 7.28-7.15 (m, 4H), 7.00-6.98 (m, 2H), 1.49 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 120^{o}C) δ 175.7, 174.0, 173.0, 155.2, 147.4, 144.3, 140.6, 134.5, 131.1, 125.7, 122.9, 122.8, 86.8, 31.4; IR (KBr, cm^{-1}) ν 3220, 2976, 1720, 1701, 1573. HRMS (ESI-ion trap) calcd. for $C_{28}H_{27}Cl_2N_{11}O_8Na$: $[M+Na]^+$ 738.1311. Found: 738.1306. A high quality single crystal for X-ray diffraction analysis was obtained by diffusing *n*-hexane vapor into the solution of **6f** in ethyl acetate.

6g was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 3 / 1) (105 mg, 15% yield): white solid, mp 192 ^{o}C (decomposed); ^{1}H NMR (400 MHz, $CDCl_2CDCl_2$, 120^{o}C) δ 10.13 (s, 1H), 7.79 (s, 2H), 7.56 (t, J = 8.4 Hz, 1H), 7.25 (s, 1H) 7.18 (t, J = 8.0 Hz, 1H), 7.11 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 7.2 Hz, 2H), 1.48 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 120^{o}C) δ 188.3, 175.6, 174.7, 173.2, 155.5, 155.2, 144.3, 137.0, 131.2, 125.1, 125.0, 123.3, 122.6, 86.7, 31.3; IR (KBr, cm^{-1}) ν 3349, 3229, 2982, 1717, 1700 1569. HRMS (ESI-ion trap) calcd. for $C_{29}H_{28}Cl_2N_{10}O_7Na$: $[M+Na]^+$ 721.1412. Found: 721.1410.

General procedure for the synthesis of homo heteracalix[2]arene[2]triazines 6h-i. Both solutions of resorcinol **4**, or its derivative **4f** (1 mmol), in acetonitrile (25 mL) and **3b** (1 mmol) in acetonitrile (25 mL) were added dropwise at the same time and the same rate to a solution of Cs_2CO_3 (717 mg, 2.2 mmol) in boiling acetonitrile (200 mL). After addition of two reactants, which took about 1 h, the resulting mixture was stirred for another 6 h. The solvents were then removed, and the residue was mixed with saline (100 mL) and extracted with ethyl acetate (3 x 50 mL) and dried with anhydrous Na_2SO_4. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate as the mobile phase to give products.

6h was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 4 / 1) (575 mg, 77% yield): white solid, mp 236-237 ^{o}C; ^{1}H

NMR (400 MHz, $CDCl_2CDCl_2$, 90°C) δ 7.72 (s, 2H), 7.41 (s, 1H), 7.31 (t, J = 8.4 Hz, 1H), 7.17-7.12 (m, 1H),7.00-6.92 (m, 5H), 4.44 (t, J = 6.4 Hz, 4H), 1.79-1.75 (m, 4H), 1.52-1.45 (m, 22H), 0.99 (t, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 90°C) δ 176.02, 175.97, 174.1, 155.8, 155.7, 144.9, 132.0, 130.7, 124.9, 123.3, 123.1, 118.6, 85.7, 71.4, 33.9, 31.4, 22.2, 16.8; IR (KBr, cm^{-1}) v 3228, 2960, 1719, 1597, 1570. HRMS (ESI-ion trap) calcd. for $C_{36}H_{46}N_{10}O_8Na$: $[M+Na]^+$ 769.3392. Found: 769.3389. Elemental analysis calcd. (%) for $C_{36}H_{46}N_{10}O_8$: C, 57.90; H, 6.21; N, 18.76. Found: C, 57.74; H, 6.25; N, 18.53.

6i was obtained from flash column chromatographed on a silica gel column (petroleum ether and ethyl acetate = 5 / 1) (372 mg, 47% yield): white solid, mp 234-235 °C; ^{1}H-NMR (400 MHz, $CDCl_2CDCl_2$, 100°C) δ 7.61 (s, 2H), 7.41 (t, J = 8.2 Hz, 2H), 7.23-7.05 (m, 3H), 6.98 (d, J = 7.8 Hz, 2H), 4.57-4.35 (m, 4H), 1.92-1.70 (m, 4H), 1.64-1.28 (m, 22H), 1.14-0.92 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 100°C) δ 172.7, 171.8, 170.6, 152.4, 144.3, 141.4, 137.7, 130.6, 127.2, 122.2, 120.2, 119.8, 82.8, 68.4, 30.6, 28.0, 18.8, 13.4; IR (KBr, cm^{-1}) v 3230, 2965, 1722, 1610, 1599, 1419. HRMS (ESI-ion trap) calcd. for $C_{36}H_{46}N_{11}O_{10}$: $[M+H]^+$ 792.3424. Found: 792.3409.

Synthesis of 6j. To a solution of **6a** (201 mg, 0.3 mmol) in DMSO (6 mL) was added dimethylamine (2 M in THF, 0.6 mL, 1.2 mmol) at 80 °C. The mixture was stirred at 80 °C for another 0.5 h. After **6a** was consumed, the mixture was mixed with saline (100 mL) and extracted with ethyl acetate (3 x 50 mL). After drying (Na_2SO_4) and then removing the solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate (v /v = 3 /1) as the mobile phase to give **6j** (168 mg, 81% yield): white solid, mp 202-204 °C; ^{1}H-NMR (400 MHz, $CDCl_2CDCl_2$, 90°C) δ 7.44 (s, 1H), 7.35 (s, 2H), 7.23 (t, J = 7.8 Hz, 1H), 7.12 (t, J = 7.8 Hz, 1H), 7.05-6.74 (m, 5H), 3.21 (s, 12H), 1.44 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 90°C) δ 171.2, 169.2, 166.5, 152.9, 152.6, 142.0, 128.2, 126.9, 121.8, 120.2, 119.8, 115.5, 82.0, 36.5, 28.0; IR (KBr, cm^{-1}) v 3236, 2961, 1586, 1415. HRMS (ESI-ion trap) calcd. for $C_{32}H_{40}N_{12}O_6Na$: $[M+Na]^+$ 711.3086. Found: 711.3085.

General procedure for the synthesis of homo heteracalix[2]arene[2]triazines 8a and 8b. To a solution of **6h** or **6i** (0.3 mmol) in boiling DCM (6 mL) was added

trifluoroacetic acid (268 μL, 3.6 mmol). The mixture was refluxed for 6 h. The mixture was cooled to room temperature, and water was added. The aqueous layer was adjusted to pH = 7 - 8 with a saturated aqueous solution of $NaHCO_3$, then the mixture was extracted with EtOAc (10 mL × 3), the combined organic phase was dried over anhydrous Na_2SO_4. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of chloroform and ethyl acetate as the mobile phase to afford products.

8a was obtained from flash column chromatographed on a silica gel column (chloroform and ethyl acetate = 4 / 1) (87 mg, 53% yield): white solid, mp >300 °C; ^{1}H-NMR (400 MHz, CD_3CN-DMSO, 80 °C) δ 8.91 (s, 2H), 7.43 (t, J = 8.0 Hz, 1H), 7.07 (d, J = 8.2 Hz, 2H), 6.84 (t, J = 8.0 Hz, 1H), 6.67 (s, 1H), 6.17 (br, 4H), 5.75 (s, 1H), 4.35 (t, J = 6.6 Hz, 4H), 1.84-1.63 (m, 4H), 1.57-1.32 (m, 4H), 0.97 (t, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 60°C) δ 173.0, 172.7, 170.2, 153.0, 149.5, 130.2, 128.4, 120.4, 115.4, 106.3, 100.1, 68.3, 31.0, 19.2, 13.8; IR (KBr, cm^{-1}) ν 3237, 2961, 1591. HRMS (ESI-ion trap) calcd. for $C_{26}H_{31}N_{10}O_4$: $[M+H]^+$ 547.2524. Found: 547.2510. Elemental analysis calcd. (%) for $C_{26}H_{30}N_{10}O_4$: C, 57.13; H, 5.53; N, 25.63. Found: C, 57.39; H, 5.79; N, 25.76. A high quality single crystal for X-ray diffraction analysis was obtained by diffusing *n*-hexane vapor into the solution of **8a** in DCM.

8b was obtained from flash column chromatographed on a silica gel column (chloroform and ethyl acetate = 20 / 1) (145 mg, 82% yield): white solid, mp 273-274 °C; ^{1}H-NMR (400 MHz, $CDCl_2CDCl_2$, 100°C) δ 7.43 (s, 1H), 7.23 (s, 2H), 7.12 (d, J = 7.3 Hz, 2H), 6.91 (t, J = 7.8 Hz, 1H), 6.20 (d, J = 7.3 Hz, 2H), 5.84 (s, 1H), 5.05-3.96 (br, 6H), 1.96-1.67 (m, 4H), 1.60-1.45 (m, 4H), 1.02 (t, J = 7.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 100°C) δ 172.4, 171.5, 169.7, 144.2, 137.6, 130.2, 129.5, 121.7, 120.2, 105.5, 98.9, 68.4, 30.6, 18.8, 13.4; IR (KBr, cm^{-1}) ν 3242, 2961, 1594, 1422. HRMS (ESI-ion trap) calcd. for $C_{26}H_{30}N_{11}O_6$: $[M+H]^+$ 592.2375. Found: 592.2366. A high quality single crystal for X-ray diffraction analysis was obtained by diffusing *n*-hexane vapor into the solution of **8b** in THF.

Preparation of 10. Both solutions of *N*,*N'*-dimethyl-*m*-phenylenediamine **9a** (136 mg, 1 mmol) in acetonitrile (25 mL) and **3a** (634 mg, 1 mmol) in acetonitrile (25 mL) were

added dropwise at the same time and the same rate to a solution of diisopropylethylamine (284 mg, 2.2 mmol) in acetonitrile (200 mL) at 40 °C. After addition of two reactants, which took about 1 h, the resulting mixture was stirred for another 6 h. The solvents were removed, and the residue was mixed with saline (100 mL) and extracted with ethyl acetate (3 x 50 mL) and then dried with anhydrous Na_2SO_4. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate (v /v = 5 / 1) as the mobile phase to give products **10** (405 mg, 58% yield): white solid, mp 260 °C decomposed; ^{1}H NMR (400 MHz, $CDCl_2CDCl_2$, 146°C) δ 7.49 (s, 1H), 7.33 (br, 3H), 7.16-6.94 (m, 6H), 3.51 (s, 6H), 1.51 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 146°C) δ 170.2, 168.1, 166.4, 152.8, 144.7, 142.0, 129.0, 127.4, 126.7, 123.6, 121.0, 119.3, 82.6, 38.2, 28.4; IR (KBr, cm^{-1}) ν 3228, 2977, 1725, 1578. HRMS (ESI-ion trap) calcd. for $C_{30}H_{34}Cl_2N_{12}O_4Na$: $[M+Na]^+$ 719.2095. Found: 719.2082. A high quality single crystal for X-ray diffraction analysis was obtained by diffusing *n*-hexane vapor into the solution of **10** in THF.

Preparation of 12. Both solutions of *m*-phenylenediamine **9b** (108 mg, 1 mmol) in acetonitrile (25 mL) and **3a** (634 mg, 1 mmol) in acetonitrile (25 mL) were added dropwise at the same time and the same rate to a solution of diisopropylethylamine (284 mg, 2.2 mmol) in acetonitrile (200 mL) at 40 °C. After addition of two reactants, which took about 1 h, the resulting mixture was kept stirring at 40 °C for another 6 h. After the mixture was heated to reflux, diethylamine (438 mg, 6 mmol) was added dropwise, and the resulting reaction mixture was refluxed for another 3 h. The solvents were then removed, and the residue was mixed with saline (100 mL) and extracted with ethyl acetate (3 x 50 mL), and dried with anhydrous Na_2SO_4. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of petroleum ether and ethyl acetate (v /v = 10 / 1) as the mobile phase to give products **12** (171 mg, 23% yield): white solid, mp 220-221 °C; ^{1}H NMR (400 MHz, $CDCl_2CDCl_2$, 146°C) δ 8.23 (br, 2H), 7.18-7.14 (m, 4H), 6.89 (s, 2H), 6.74 (s, 2H), 6.60 (s, 2H), 3.62-3.58 (m, 8H), 1.41 (s, 18H), 1.21 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 146°C) δ 167.9, 166.1, 165.3, 153.9, 143.5, 140.0, 128.4, 127.5, 121.2, 119.0, 81.8, 41.3, 28.3, 13.3; IR (KBr, cm^{-1}) ν 3270, 2976, 1725, 1587, 1572. HRMS (ESI-ion trap) calcd. for $C_{36}H_{51}N_{14}O_4$:

$[M+H]^+$ 743.4194. Found: 743.4212. It should be noted that the product **12** did not give satisfactory ^{13}C NMR spectra even at very high temperatures (146 °C) probably because of the high energy barrier for inter-conversion of various conformers. A high quality single crystal for X-ray diffraction analysis was obtained by diffusing *n*-hexane vapor into the solution of **12** in DCM at 0 °C.

Preparation of 13. To a solution of **12** (0.3 mmol) in boiling DCM (6 mL) was added trifluoroacetic acid (268 μL, 3.6 mmol). The mixture was refluxed for 6 h. The mixture was cooled to room temperature, and water was added. The aqueous layer was adjusted to pH = 7 - 8 with a saturated aqueous solution of $NaHCO_3$, then the mixture was extracted with $CHCl_3$ (10 mL x 3), the combined organic phase was dried over anhydrous Na_2SO_4. After removal of solvent, the residue was chromatographed on a silica gel column with a mixture of chloroform and ethyl acetate (v /v = 10 / 1)as the mobile phase to afford products **13** (119 mg, 73% yield): white solid, mp 290 °C decomposed; ^1H NMR (400 MHz, $CDCl_2CDCl_2$, 100°C) δ 7.20 (t, J = 8.0 Hz, 1H), 7.05 (t, J = 7.8 Hz, 1H), 6.61 (br, 4H), 6.41-6.19 (m, 5H), 6.05 (s, 2H), 5.97 (s, 1H), 3.57 (q, J = 7.0 Hz, 8H), 1.15 (t, J = 6.8 Hz 12H); ^{13}C NMR (100 MHz, $CDCl_2CDCl_2$, 100°C) δ 168.3, 165.2, 164.9, 150.6, 139.6, 129.5, 128.3, 105.6, 41.1, 13.0; IR (KBr, cm^{-1}) ν 3320, 3272, 2974, 1526, 1497. HRMS (ESI-ion trap) calcd. for $C_{26}H_{35}N_{14}$: $[M+H]^+$ 543.3164. Found: 543.3158. It should be noted that the product **13** did not give satisfactory ^{13}C NMR spectra even at very high temperatures (146 °C) probably because of the high energy barrier for inter-conversion of various conformers. A high quality single crystal for X-ray diffraction analysis was obtained by diffusing *n*-hexane vapor into the solution of **13** in 1,4-dioxane at 0 °C.

ASSOCIATED CONTENT

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Notes

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Supporting Information. ^{1}H and ^{13}C NMR spectra of all products, and X-ray structures of **6a**, **6c**, **6e**, **6f**, **8a, 8b, 10, 12** and **13** (CIFs). This material is available free of charge via the Internet at http://pubs.acs.org.

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