Tetrahedron 68 (2012) 9464–9477

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Syntheses and conformational structures of functionalized tetraoxacalix[2]arene[2]triazines

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ARTICLE INFO

Article history:
Received 6 July 2012
Received in revised form 21 August 2012
Accepted 23 August 2012
Available online 4 September 2012

ABSTRACT

The syntheses and conformational structures of various functionalized tetraoxacalix[2]arene[2]triazines were studied. Applying the fragment coupling approach and the post-macrocyclization chemical manipulations, a number of tetraoxacalix[2]arene[2]triazines that contain, on the lower rim, one or two aldehyde, ester, carboxylic acid, hydroxymethyl, and aminomethyl functional groups were prepared in moderate to high chemical yields from cheap and commercially available materials. On the basis of X-ray crystallography and NMR spectroscopy, all tetraoxacalix[2]arene[2]triazines containing electron-withdrawing group(s) adopted 1,3-alternate conformation both in solution and in the solid state, while tetraoxacalix[2]arene[2]triazines bearing hydroxymethyl and aminomethyl substituent(s) existed as pinched or distorted partial cone conformers due to the formation of intramolecular hydrogen bond between hydroxyl or amino group and triazine ring.

1. Introduction

Heteroatom-bridged calixaromatics, also known as heteracalixaromatics, are a new generation of macrocyclic host molecules in supramolecular chemistry.[1–5] Being different from the methylene linkages in conventional calixarenes,[6] the bridging heteroatoms, such as nitrogen can adopt different electronic configurations between sp^2 and sp^3 and form various conjugation systems with their adjacent aromatic rings.[1,3,7] As a consequence, heteracalixaromatics exhibit intriguing structural characteristics and versatile molecular recognition properties.[1–5] The self- and fine-tuning cavities of varied electronic features render heteracalixaromatics powerful macrocyclic hosts in the interactions with neutral organic guests[8–10] and with positively[11–15] and negatively charged species.[16–19]

The parent heteracalixaromatics, the macrocyclic compounds that contain no functional groups, are easily prepared from simple and commercially available aromatic compounds. Starting from aromatic bisnucleophiles and biselectrophiles, the fragment coupling approach[1–3] has been established as a powerful methodology for the construction of a large number of heteracalixarenes,[1–3,20] pyridines,[9a–c] pyrazines,[15] pyrimidines[9d,21] and triazines.[22] Remarkably, this stepwise protocol provides rapid accesses to both symmetrical and unsymmetrical heteracalixaromatics of varied macrocyclic ring sizes. In addition, one-pot reaction strategy under thermodynamically controlled reaction conditions works straightforwardly and efficiently for the synthesis of a few symmetrically substituted heteracalixaromatics.[1–3,23]

While some parent heteracalixaromatics, such as azacalix[*n*]pyridines show binding ability toward guest species ranging from metal ions,[11–13,15] organometallic clusters[14] to neutral organic molecules,[8–10] tailor-made functionalized heteracalixaromatics, which are not widely available, are however much more demanded for the recognition of specific guests and molecular self-assembly in supramolecular chemistry study. One of the synthetic methods is based on post-macrocyclization chemical manipulations.[1,3] Using parent heteracalixaromatics as platforms, selective chemical modifications on aromatic rings by means of electrophilic[21,24] and nucleophilic aromatic substitution reactions[22,25] and arene C–H bond transformations[26] have led to the generation of (multi)functionalized macrocycles. Functional groups have been introduced readily into the bridging nitrogen atoms through N-alkylation[24] and N-arylation,[22d] yielding uniquely functionalized azacalixaromatics. It is noteworthy that post-macrocyclization functionalizations in controllable manners enable the fabrication of higher level and sophisticated molecular architectures including heteracalixcrowns and molecular cages.[22c,f,g] The other route to functionalized heteracalixaromatics comprises the stepwise fragment coupling reactions employing pre-functionalized aromatic reactants.[1,3,10] The value of the method has been demonstrated, for

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http://dx.doi.org/10.1016/j.tet.2012.08.069

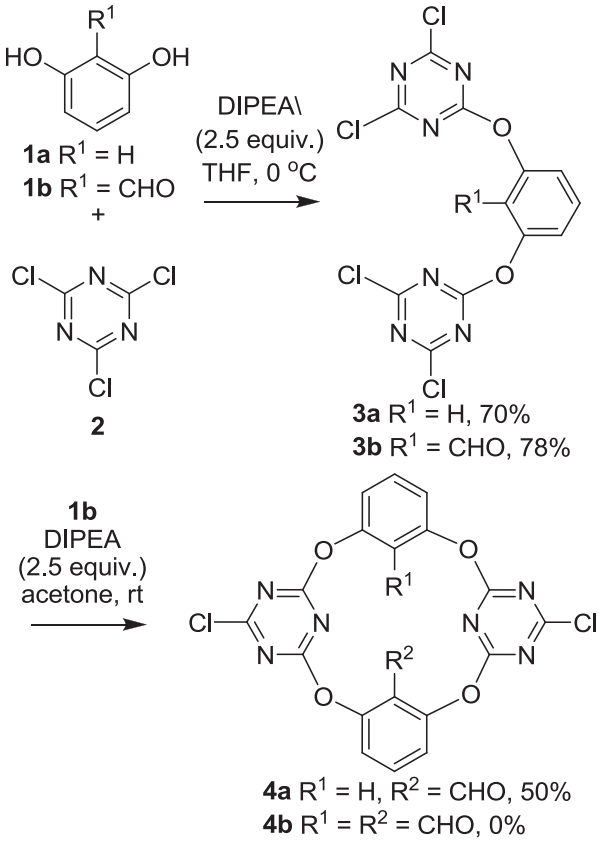
example, in the synthesis of functionalized inherently chiral heteracalixaromatics.[22b]

One of the salient structural features of heteracalix[4]aromatics is their conformational preference for a 1,3-alternate conformation.[1–3] Only in the case of synthesis under kinetic controlled conditions, products of a pinched partial core conformation are obtained in low yields.[22e] The predominant formation of 1,3-alternate conformation of heteracalix[4]aromatics is mainly attributable to the dipole–dipole repulsions among aromatic rings,[27] which is in stark contrast to conventional calix[4]arenes, which adopt core conformation mainly because of intramolecular circular hydrogen bond interactions.[6] To construct other conformational structures, we attempted previously the replacement of benzene rings in tetraoxacalix[2]arene[2]triazines with phenol moieties.[10] Although two phenolic hydroxyl groups are present in the lower rim positions, the resulting dihydroxylated tetraoxacalix[2]arene [2]triazines still give 1,3-alternate conformation. It is most probably that no effective intramolecular hydrogen bonds are formed between phenolic hydroxyl groups and triazine rings because of unfavorable hydrogen bond angles, yielding therefore no regulating effect on conformations of macrocycles. Nevertheless, we envisioned that the effective intramolecular hydrogen bonding between approximal aromatic rings or between groups attached on two approximal aromatic rings would enable the generation of conformational structures other than a 1,3-alternate conformer. To test our hypothesis of tuning conformational structures by means of intramolecular hydrogen bonding, and also to construct novel and functional heteracalixaromatics, we undertook the current study. We report herein the synthesis of tetraoxacalix[2]arene[2] triazines in which benzene ring contains a hydrogen bond donor on the lower rim position. We demonstrate for the first time the regulation of 1,3-alternate conformation to designed partial cone structure of heteracalix[2]arene[2]triazines through the formation of intramolecular hydrogen bond of the triazine moiety with its neighboring benzylic alcohol.

2. Results and discussion

Because of the unfavorable intramolecular hydrogen bond interactions, 1,3-alternate dihydroxy-substituted tetraoxacalix[2] arene[2]triazines form *intermolecular* hydrogen bonds between phenolic hydroxyl and triazine nitrogen moieties, yielding a tetrameric aggregator in the solid state. To facilitate the formation of *intramolecular* hydrogen bonds between hydroxyl and its adjacent triazine ring, we decided to replace the phenol segment by a hydroxymethylbenzene (benzylic alcohol) and an aminomethylbenzene (benzylamine) unit.[10] To obtain the desired products, we started with the synthesis of tetraoxacalix[2]arene[2] triazines **4** that bear versatile formyl group(s) at the lower rim position of the benzene ring(s). The fragment coupling strategy,[1] which works nicely for the synthesis of unsymmetrically substituted heteracalixaromatics, was employed. As depicted in Scheme 1, a linear trimer **3a**,[22a] obtained conveniently from the reaction between resorcinol **1a** and cyanuric chloride **2**, underwent macrocyclization reaction with 2,6-dihydroxybenzaldehyde **1b** at ambient temperature in acetone to afford target macrocycle **4a** in 50% yield. Surprisingly, the reaction between **3b** and **1b** under identical conditions led to oligomers rather than macrocyclic compound **4b**. The aldehyde **4a** was found not soluble in most of the organic solvents, prohibiting its chemical transformations into other functional groups.

To circumvent solubility problems, we then introduced dipropylamino group into the triazine ring. In the presence of diisopropylethylamine (DIPEA) as an acid scavenger, two aromatic nucleophilic substitution reaction of resorcinol **1a** or 2,6-dihydroxybenzaldehyde **1b** with 4,6-dichloro-2-dipropylamino-

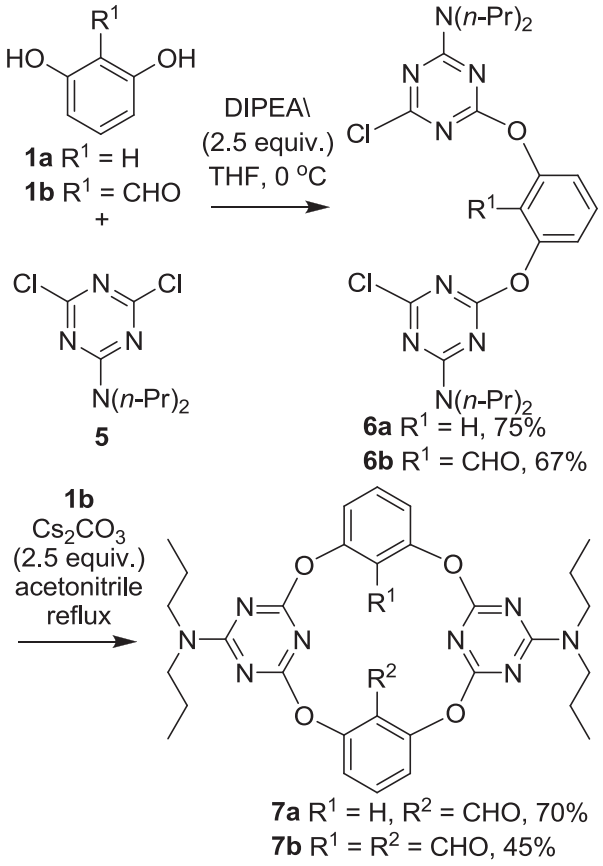


Scheme 1. Synthesis of formyl-substituted tetraoxacalix[2]arene[2]triazine **4a**.

1,3,5-triazine **5** at 0 °C resulted in the formation of a linear trimer **6a** in 75% yield of **6b** in 67% yield. Being slightly less reactive than **3**, higher temperature was necessary to promote the reaction of **6** with **1b**. To our delight, refluxing a mixture of **6** and **1b** with Cs_2CO_3 in acetonitrile gave rise to the formation of macrocyclic products. The monoformyl-substituted tetraoxacalix[2]arene[2]triazine **7a** was isolated in 70% yield while a yield of 45% was obtained for bis-aldehyde product **7b** (Scheme 2). The symmetrically diformylated macrocycle **7b** was also prepared from a one-pot reaction between **1b** and **5**, and the chemical yield was around 30%. As we expected, both products **7a** and **7b** were soluble in common organic solvents.

Having had aldehyde compounds **7** in hand, the synthesis of hydroxymethyl-substituted tetraoxacalix[2]arene[2]triazines was conducted. The reduction of aldehyde **7a** into alcohol was not trivial at all. When $NaBH_4$ was used as a reducing agent in methanol, macrocyclic ring opening along with the reduction of aldehyde was always observed even when the reaction was performed at −10 °C. At room temperature, treatment of **7a** with $NaBH_4$ in methanol afforded linear product **8** in <15% yield (Scheme 3). To avoid macrocyclic ring opening reaction due to the nucleophilic attack of methanol at triazine ring, tetrahydrofuran (THF) was employed as solvent. Unfortunately, reaction gave a mixture of very polar and not separable compounds. A small amount of products **10** and **11** were isolated after work-up and silica gel column chromatography. The structures of the products **10** and **11**, which were confirmed unambiguously by single crystal X-ray crystallography (see Supplementary data), indicated a hydrolytic macrocyclic ring opening process followed by reductive amination and further hydrolysis (Scheme 3).

Fortunately, reduction of **7** using borane as a reducing agent in dry THF gave satisfactory results. For example, in the presence of 2 equiv of BH_3·THF, aldehyde **7a** was converted quantitatively into **12a** within 0.5 h at −20 °C. Pure product **12a** was obtained in 25%



Scheme 2. Synthesis of soluble formyl-functionalized tetraoxacalix[2]arene[2]triazines **7**.

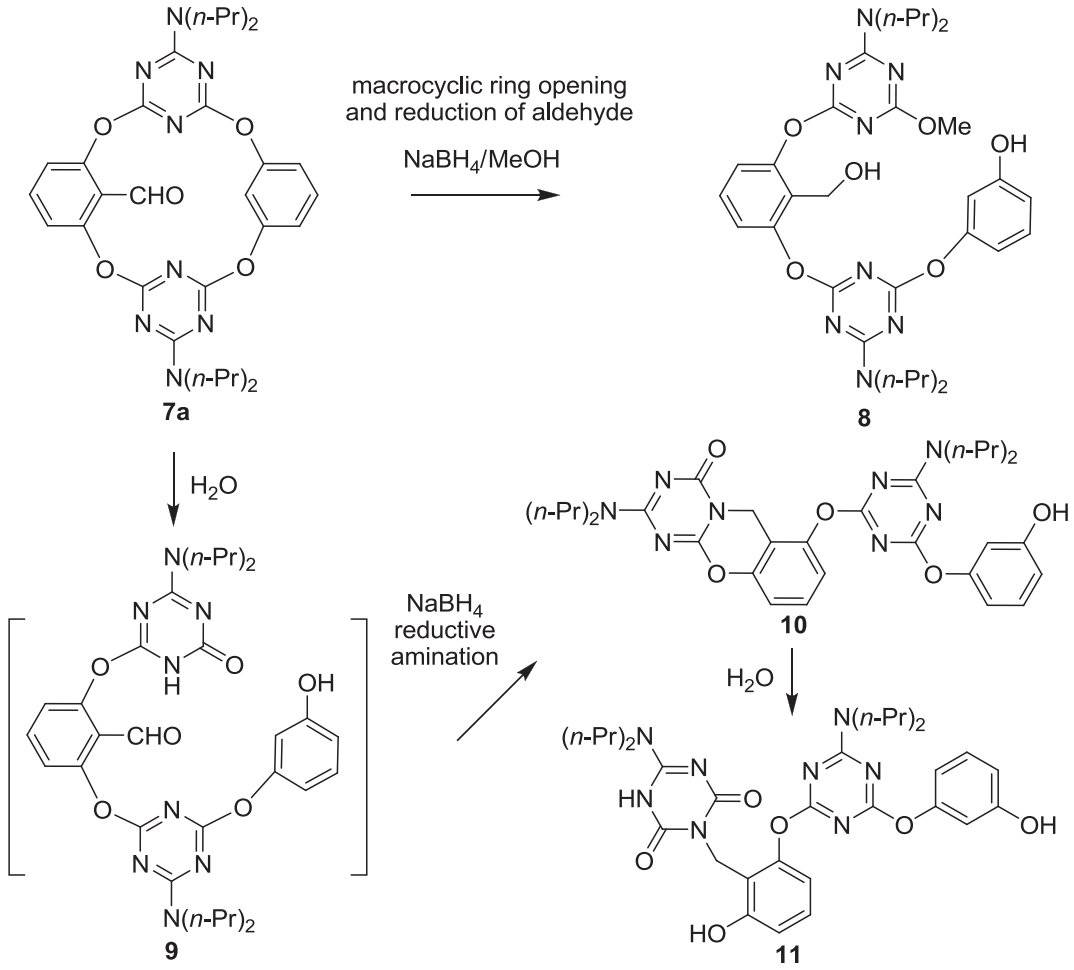
isolated yield after silica gel column chromatography, since it underwent decomposition during purification process. Similar reduction of **7b** with BH_3·THF at room temperature afforded diol product **12b** in 90% isolated yield (Scheme 4).

To synthesize aminomethyl-substituted tetraoxacalix[2]arene[2]triazine **13**, reductive amination of **7a** was investigated. Under various reaction conditions, such as using NH_4Cl and $NH_2OH·HCl$ as nitrogen sources and $NaBH_4$, $NaBH(OAc)_3$, borane and H_2/Pd/C as reducing agents at different temperatures, no desired product was obtained (see Supplementary data). Finally, interaction of **7a** with a mixture of NH_3 solution in 2-propanol (2 M), acetic acid (2 equiv) and $NaBH(OAc)_3$ (4 equiv) in dry THF gave product **13**, albeit in 20% yield (Scheme 5).

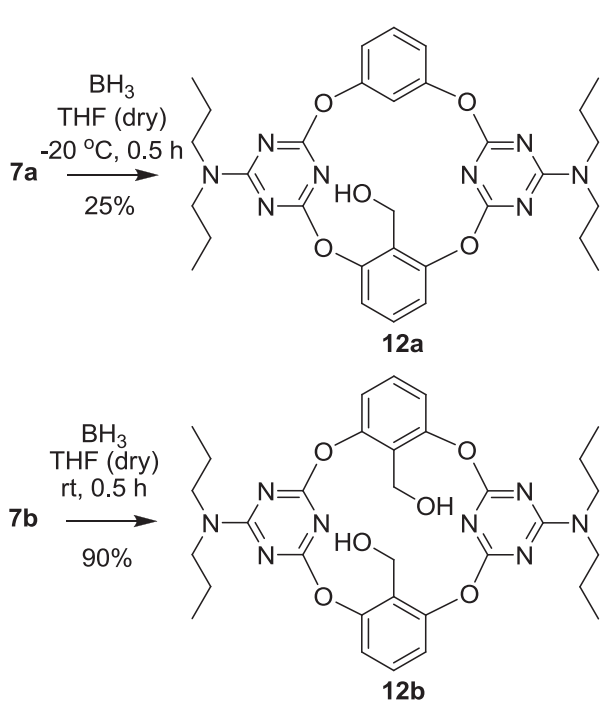
In addition to hydroxyl and amino groups that may function as intramolecular hydrogen bond donors, carboxylic acid was also considered in our study. Scheme 6 illustrates the synthesis of tetraoxacalix[2]arene[2]triazines that contain one and two carboxylic acid groups. Thus, macrocyclic condensation reaction between a linear trimer **14** and benzyl or methyl 2,6-dihydroxybenzoate **15** in hot acetonitrile with the aid of K_2CO_3 yielded macrocycle **17a** or **17c** efficiently. Good yields were also obtained for the synthesis of bis-ester-bearing tetraoxacalix[2]arene[2]triazines **17b** and **17d** from **15** and 4,6-dichloro-2-methoxy-1,3,5-triazine **16** in one-pot reaction fashion. Debenzylation reaction of **17a** and **17b**, which was achieved efficiently by means of catalytic hydrogenolysis, furnished mono- and bis-carboxylic acid products **18a** and **18b** in 90% and 78% yields, respectively (Scheme 6).

The structures of all functionalized tetraoxacalix[2]arene[2]triazine products were established on the basis of spectroscopic data and microanalyses. To assign the structures without ambiguity, and also to understand the conformational behaviors in the solid state, single crystals of products were grown. Slow evaporation of solvent from solution of **7b** or **12b** in a mixture of acetone and petroleum ether and from solution of **17d** or **18b** in acetonitrile gave X-ray quality single crystals. Molecular structures of symmetrically bis-substituted macrocyclic products **7b**, **12b**, **17d** and **18b** were then determined by X-ray diffraction analysis. As shown in Figs. 1–3, tetraoxacalix[2]arene[2]triazines containing two aldehyde (**7b**), ester (**17d**) or carboxylic acid (**18b**) groups adopt 1,3-alternate conformation. In all cases, two benzene rings are nearly face-to-face paralleled with the distances between upper rim carbons and between lower rim carbons being around 4.2–4.4 Å and 5.1–5.8 Å, respectively. Two triazine rings, on the other hand, tend to be procumbent relative to the plain defined by four bridging oxygen atoms, giving the upper-rim and lower rim distances around 9.0–9.4 Å and 4.6 Å, respectively. Careful scrutiny of the bond lengths and angles of bridging oxygen atoms (see captions of Figs. 1–3) revealed the formation of conjugation of bridging oxygen atom with its neighboring triazine ring rather than benzene ring. Bishydroxymethyl-substituted macrocycle **12b**, however, gives the flattened pinched cone conformation. Two triazine rings are edge-to-edge aligned on the same plain as four bridging oxygen atoms while two benzene rings, which are anti-paralleled each other, are almost perpendicular to the plain (Fig. 4). Distances of a hydroxyl oxygen atom to each lower rim nitrogen atom of two triazine rings are 3.306 Å and 3.156 Å, respectively, indicating weak O–H···N interactions.

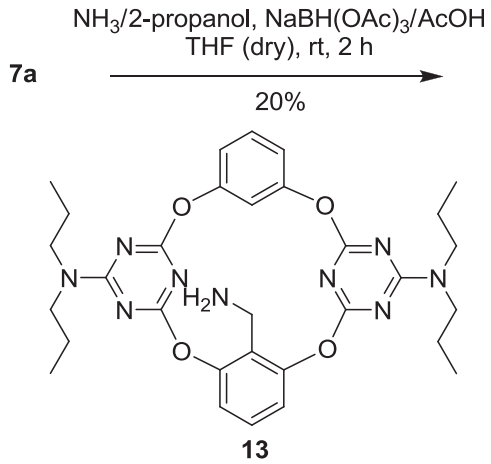
To get deep insight into the conformational structures of functional tetraoxacalix[4]aromatics in solution phase, ^1H NMR and ^{13}C NMR spectra were carefully examined. In agreement to parent tetraoxacalix[2]arene[2]triazines,[1,22a] each symmetrically bis-substituted tetraoxacalixarene, such as **7b**, **17b**, **17d** or **18b** gave a simple and single set of proton and carbon resonance signals in ^1H and ^{13}C NMR spectra, respectively (Figs. 5 and 6, see Supplementary data). Since the substituents on both benzene and triazine rings prohibit the rotation of each aromatic ring around the annulus, the outcomes of NMR study suggested the predominant adoption of symmetric 1,3-alternate conformation of these macrocycles. While functional tetraoxacalix[2]arene[2]triazines substituted by only one formyl (**7a**), benzyl ester (**17a**), methyl ester (**17c**) or carboxylic acid (**18a**) group exhibit analogously the single set of proton and carbon signals as compounds **7b**, **17b**, **17d** and **18b** (Figs. 5 and 6, see Supplementary data), mono-hydroxymethylated and mono-aminomethylated tetraoxacalix[2]arene[2]triazines **12a** and **13** give NMR spectra in which two different sets of signals corresponding to two different triazine rings within a macrocycle were observed (Figs. 5 and 6). In different solvents, such as in $CDCl_3$, CD_3COCD_3, even in the presence of a small amount of D_2O, similar ^1H NMR spectra were observed for compound **12a**. Desymmetrization of molecular structures or the broken of symmetric relationship of two triazine rings, which were evidenced by NMR spectroscopic data, was best explained by the formation of intramolecular hydrogen bond between hydroxyl or amino group and one of the triazine rings of macrocyclic compounds. Gratifyingly, the intramolecular hydrogen bonding was validated by the variable temperature ^1H NMR spectra of **12a** and **13**. As illustrated in Fig. 7, the proton signal of benzylic alcohol of **12a** shifted gradually from 7.2 ppm to 8.3 ppm when the temperature decreased from 25 °C to −60 °C. Similar downfield shift of the signal of hydroxyl proton of **12b** was also observed albeit with a lower degree (see Supplementary data). It should be noted that the chemical shift of the hydroxyl proton signal of bis-hydroxymethylated compound **12b** varied dramatically from that of mono-hydroxymethylated analog **12a**. While the former compound gave a hydroxyl proton signal at 2.41 ppm, the hydroxyl proton of the later compound resonated at 8.30 ppm at 213 K. The huge difference in chemical shift between two compounds is the reflection of different conformational structures (vide infra).



Scheme 3. Reduction of **7a** with $NaBH_4$ in methanol.

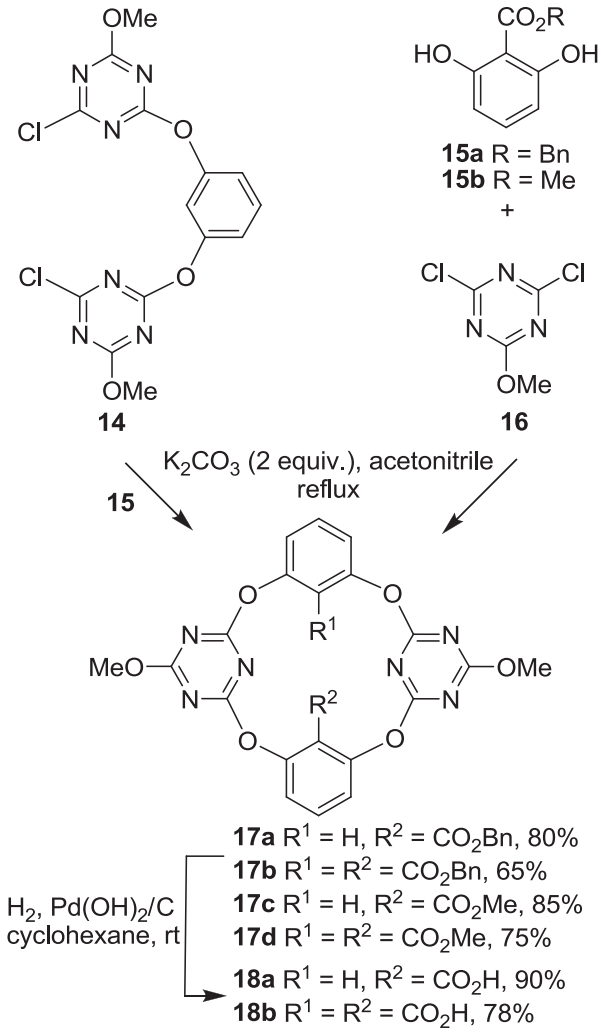


Scheme 4. Synthesis of hydroxymethylated tetraoxacalix[2]arene[2]triazines **12**.



Scheme 5. Synthesis of aminomethylated tetraoxacalix[2]arene[2]triazine **13**.

To shed further light on the three dimensional structures of formyl-substituted compounds **7a** and **7b**, and hydroxymethyl-substituted compounds **12a** and **12b** in solution, nuclear Overhauser effect spectroscopy (NOESY) was studied. At room temperature, no nuclear Overhauser effect (NOE) was found for all compounds (see Supplementary data). When the probe temperature was decreased to 193 K, the NOE was clearly evidenced



Scheme 6. Synthesis of ester and acid-functionalized tetraoxacalix[2]arene[2]triazines **17** and **18**.

between aldehyde proton and the lower rim proton of the distal benzene ring for monoformyl-substituted tetraoxacalix[2]arene[2]triazine **7a** (Fig. 8 and Supplementary data), while bisformyl-substituted analog **7b** did not show spacial correlation between formyl and benzene ring (see Supplementary data). The outcomes are in agreement with their 1,3-alternate conformational structures. In other words, tetraoxacalix[2]arene[2]triazines that are substituted by one and two electron-withdrawing groups, such as aldehyde (**7a** and **7b**), ester (**17a**–**d**) and carboxylic acid (**18a** and **18b**) at the lower rim position adopt in solution 1,3-alternate conformation, the structure that is similar to the X-ray crystal structures observed for **7b**, **17d** and **18b** (Figs. 1–3). In the case of bis-hydroxymethylated tetraoxacalix[2]arene[2]triazine **12b**, NOESY spectrum at 193 K shows correlation between all protons of hydroxymethyl substituent and aromatic protons of the distal benzene ring (Fig. 9), reflecting the proximity of two moieties. In solution, the macrocycle **12b** adopts therefore most likely the pinched partial cone conformation that is similar to its structure in the solid state (Fig. 4). The pinched partial cone also best explains the strong shielding effect of hydroxyl proton experienced, as hydroxyl proton is positioned above the centroid of the other benzene ring (see Fig. 4 and Supplementary data). Interestingly, as indicated by low temperature NOESY spectrum (Fig. 10), only hydroxyl proton (δ=8.30 ppm), which is hydrogen bonded to one of the triazine ring within macrocycle **12a**, was found to interact with H^c of the other benzene ring. Taking the unsymmetric structure reflected by ^1H and ^{13}C NMR spectra (Figs. 5 and 6), the deshielding effect of hydroxyl proton and the NOE between hydroxyl proton and H^c of the other benzene ring into account, it was proposed that tetraoxacalix[2]arene[2]triazine **12a** adopts a heavily distorted partial cone conformation in solution (Fig. 10, inset). It should be noted that, in the case of tetraoxacalix[2]arene[2]triazines **18a** and **18b** that were substituted by one and two carboxylic acid groups, respectively, 1,3-alternate conformational structure was found exclusively in solution and in the crystalline state. This was probably attributable to the unfavorable geometry of the rigid carboxylic acid group at the lower rim position to form hydrogen bond with the nitrogen atom of the adjacent triazine ring.

3. Conclusion

Utilizing the fragment coupling approach and the post-macrocyclization chemical manipulation protocol, a number of tetraoxacalix[2]arene[2]triazines functionalized on the lower rim position with one or two aldehyde, ester, carboxylic acid, hydroxymethyl and aminomethyl substituents have been synthesized from cheap and commercially available starting materials. While all tetraoxacalix[2]arene[2]triazines containing electron-withdrawing group(s) adopt 1,3-alternate conformation both in solution and in the solid state, bis-hydroxymethyl-, mono-hydroxymethyl- and mono-aminomethyl-substituted tetraoxacalix[2]arene[2]triazines exist as pinched or distorted partial cone conformers due to the intramolecular hydrogen bond interactions between hydroxyl or amino group and triazine ring. Our study has provided the first example to regulate the conformational structures of heteracalixaromatics through the intramolecular hydrogen bond interactions. It is anticipated that enhancement of rationally designed intramolecular non-covalent bond interactions on the skeleton of heteracalixaromatics would lead to the generation of desired conformers other than 1,3-alternate conformational structures.

4. Experimental part

4.1. Synthesis of 4a

To a stirred solution of DIPEA (2.4 mmol) in acetone (120 mL) at room temperature was added simultaneously both solutions of **3a**[22a] (1 mmol) in acetone (50 mL) and **1b** (1 mmol) in acetone (50 mL) through two dropping funnels at the same rate. After addition (ca. 10 h), the mixture was kept stirring for another 14 h. The solvent was removed using a rotary evaporator, and the residue was chromatographed on a silica gel column eluted with a mixture of acetone and petroleum ether (1:2) to give product **4a**. Recrystallization in ethanol gave pure product as a pale yellow solid. Compound **4a** (236 mg, 50%): mp 285–286 °C; ^1H NMR (300 MHz, acetone-d_6) δ 9.90 (s, 1H), 7.75 (t, J=8.3 Hz, 1H), 7.42 (t, J=8.2 Hz, 1H), 7.24 (d, J=8.2 Hz, 2H), 7.04 (dd, J=8.2, 1.9 Hz, 2H), 6.94 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 186.7, 172.7, 171.9, 171.7, 151.6, 151.1, 136.8, 130.9, 121.5, 119.8, 119.6, 115.9; IR (KBr) IR (KBr) ν 1699, 1550 cm^{-1}; MS (MALDI-TOF) m/z 471.1 $[M+H]^+$ (100%), 473.1 $[M+H+2]^+$ (40), 493.1 $[M+Na]^+$ (52), 495.1 $[M+Na+2]^+$ (20). Anal. Calcd for $C_{19}H_8Cl_2N_6O_5\cdot C_2H_5OH$: C, 48.76; H, 2.73; N, 16.25. Found: C, 48.62; H, 2.36; N, 16.36.

4.2. General procedure for the synthesis of 6

After a mixture of **5**[28] (4 mmol) and Cs_2CO_3 (5 mmol) in acetonitrile (40 mL) was heated to 60 °C, compound **1** (2 mmol) dissolved in acetonitrile (20 mL) was added drop-wise. The resulting mixture was kept stirring at 60 °C for another 6 h. After removal of precipitate through filtration and solvent using a rotary evaporator, the residue was chromatographed on a silica gel column eluted

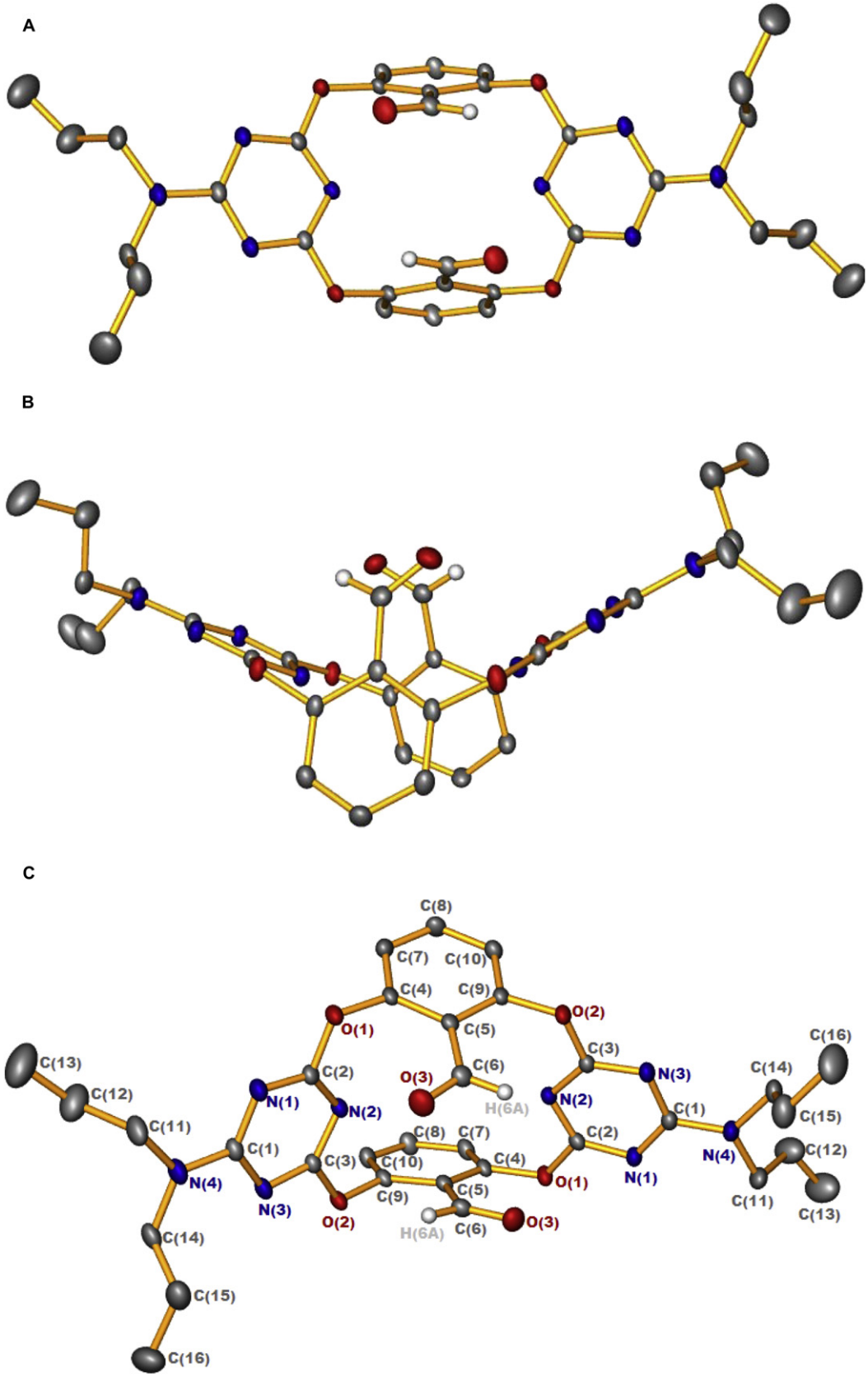


Fig. 1. X-ray molecular structure of **7b** with top view (A, C) and side view (B). Selected bond lengths [Å]: C2–O1 1.354, O1–C4 1.396, C3–O2 1.348, O2–C9 1.399. Selected angles: ∠C5–C4–O1 121.5°, ∠C4–O1–C2 119.6°, ∠O1–C2–N2 117.8°. The probability is 25%. Some hydrogen atoms were omitted for clarity.

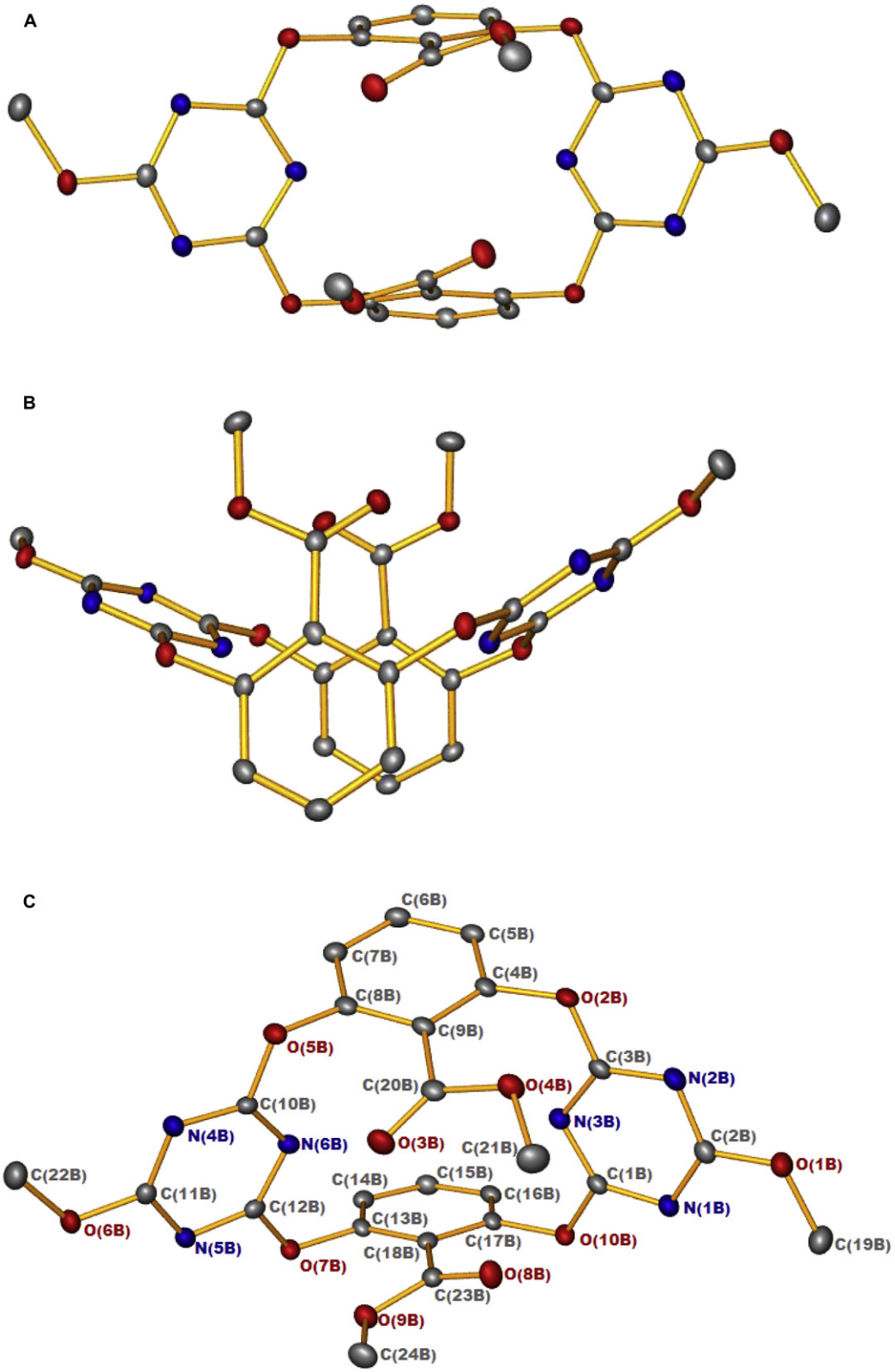


Fig. 2. X-ray molecular structure of **17d** with top view (A, C) and side view (B). Selected bond lengths [Å]: C3B–O2B 1.334, O2B–C4B 1.402, C8B–O5B 1.400, O5B–C10B 1.338, C12B–O7B 1.347, O7B–C13B 1.406, C17B–O10B 1.403, O10B–C1B 1.349. Selected angles: ∠C9B–C4B–O2B 121.4°, ∠C4B–O2B–C3B 118.4°, ∠O2B–C3B–N3B 118.8°. The probability is 25%. Hydrogen atoms were omitted for clarity.

with a mixture of ethyl acetate and petroleum ether (1:8) to give product **6**.

Compound **6a** (800 mg, 75%): white solid: mp 115–116 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (t, J=8.1 Hz, 1H), 7.08–7.05 (m, 3H), 3.49 (t, J=7.5 Hz, 4H), 3.26 (t, J=7.5 Hz, 4H), 1.61 (h, J=7.5 Hz, 4H), 1.45 (h, J=7.5 Hz, 4H), 0.91 (t, J=7.4 Hz, 6H), 0.73 (t, J=7.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.2, 165.5, 152.4, 129.2, 119.1, 115.9, 49.6, 49.5, 20.8, 20.5, 11.2, 11.0; IR (KBr) ν 1578, 1507 cm^{-1};

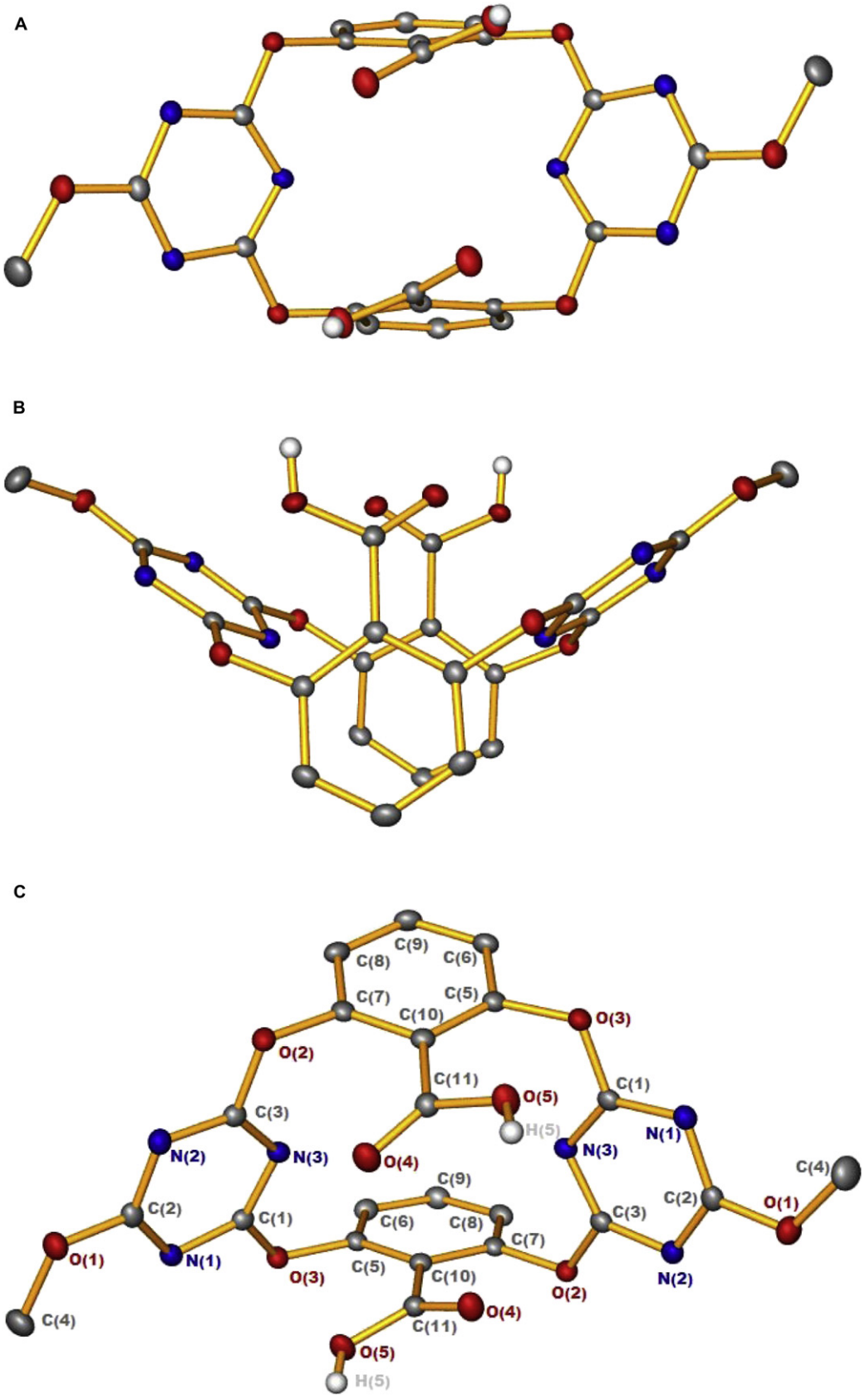


Fig. 3. X-ray molecular structure of **18b** with top view (A, C) and side view (B). Selected bond lengths [Å]: C1–O3 1.346, O3–C5 1.407, C7–O2 1.407, O2–C3 1.342. Selected angles: ∠C8–C7–O2 116.2°, ∠C7–O2–C3 117.4°, ∠O2–C3–N3 118.5°. The probability is 25%. Some hydrogen atoms were omitted for clarity.

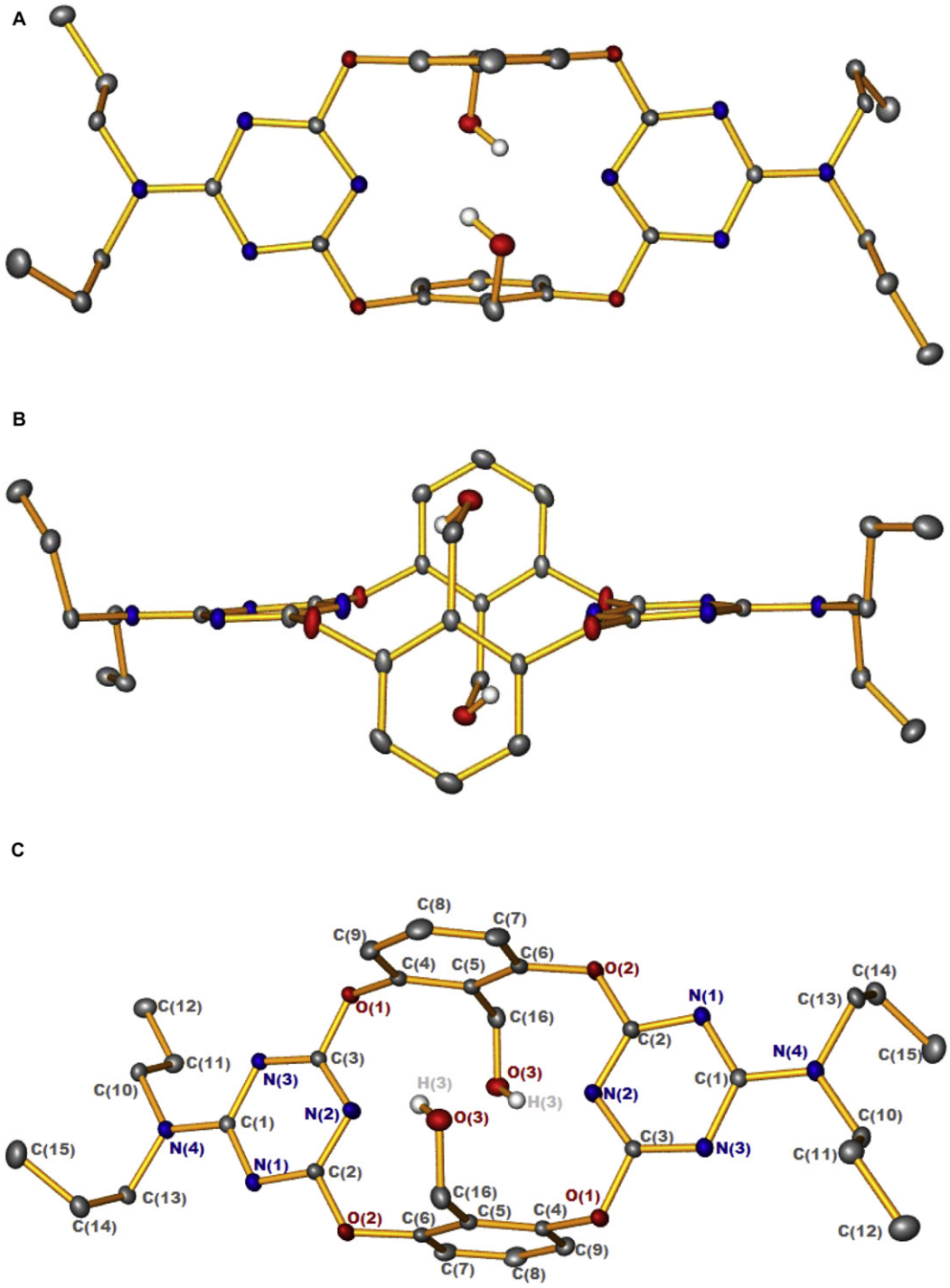


Fig. 4. X-ray molecular structure of **12b** with top view (A, C) and side view (B). Selected bond lengths [Å]: C4–O1 1.407, O1–C3 1.358, C2–O2 1.362, O2–C6 1.409. Selected angles: ∠C9–C4–O1 117.0°, ∠C4–O1–C3 115.9°, ∠O1–C3–N2 117.3°. The probability is 25%. Some hydrogen atoms were omitted for clarity.

MS (MALDI-TOF) *m*/*z* 535.1 $[M+H]^+$ (50), 537.1 $[M+H+2]^+$ (20), 557.0 $[M+Na]^+$ (100%), 559.0 $[M+Na+2]^+$ (50). Anal. Calcd for $C_{24}H_{32}Cl_2N_8O_2$: C, 53.83; H, 6.02; N, 20.93. Found: C, 53.94; H, 6.00; N, 20.66.

Compound **6b** (783 mg, 67%): pale yellow solid: mp 130–131 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.19 (s, 1H), 7.87 (t, *J*=8.3 Hz, 1H), 7.38 (d, *J*=8.3 Hz, 2H), 3.54 (t, *J*=7.5 Hz, 4H), 3.33 (t, *J*=7.5 Hz, 4H), 1.64 (h, *J*=7.5 Hz, 4H), 1.49 (h, *J*=7.5 Hz, 4H), 0.90 (t, *J*=7.4 Hz, 6H), 0.73 (t, *J*=7.4 Hz, 6H); ^{13}C NMR (75 MHz, acetone) δ 187.2, 171.6, 171.5, 166.5, 154.1, 136.1, 122.7, 122.4, 50.4, 50.2, 21.4, 21.1, 11.4, 11.3; IR (KBr) ν 3431, 2965, 2874, 1698, 1589, 1502, 1362 cm^{-1}; MS (MALDI-TOF) *m*/*z* 585.0 $[M+H]^+$ (100%), 586.0 $[M+2]^+$ (20), 587.0 $[M+H+2]^+$ (60), 588.0 $[M+4]^+$ (10). Anal. Calcd for $C_{25}H_{32}Cl_2N_8O_3$: C, 53.29; H, 5.72; N, 19.89. Found: C, 53.39; H, 5.81; N, 19.75.

4.3. Synthesis of 7a

To a boiling solution of Cs_2CO_3 (2.5 mmol) in acetonitrile (250 mL) was added simultaneously both solutions of **6a**[22a] (1 mmol) in acetonitrile (50 mL) and **1b** (1 mmol) in acetonitrile

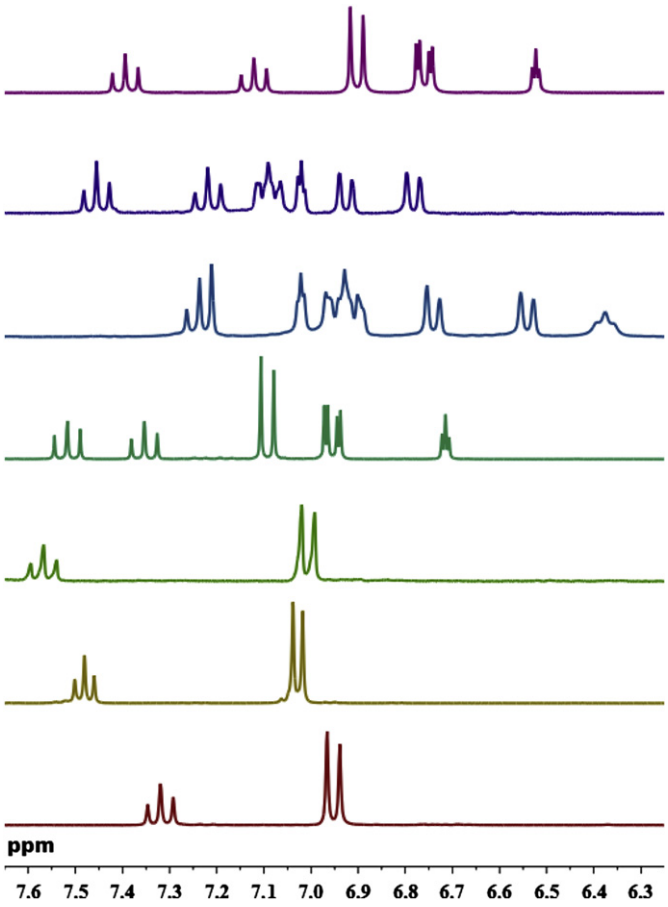


Fig. 5. Partial ^{1}H NMR spectra of compounds **7a**, **12a**, **13**, **18a**, **7b**, **12b** and **18b** (from top to bottom).

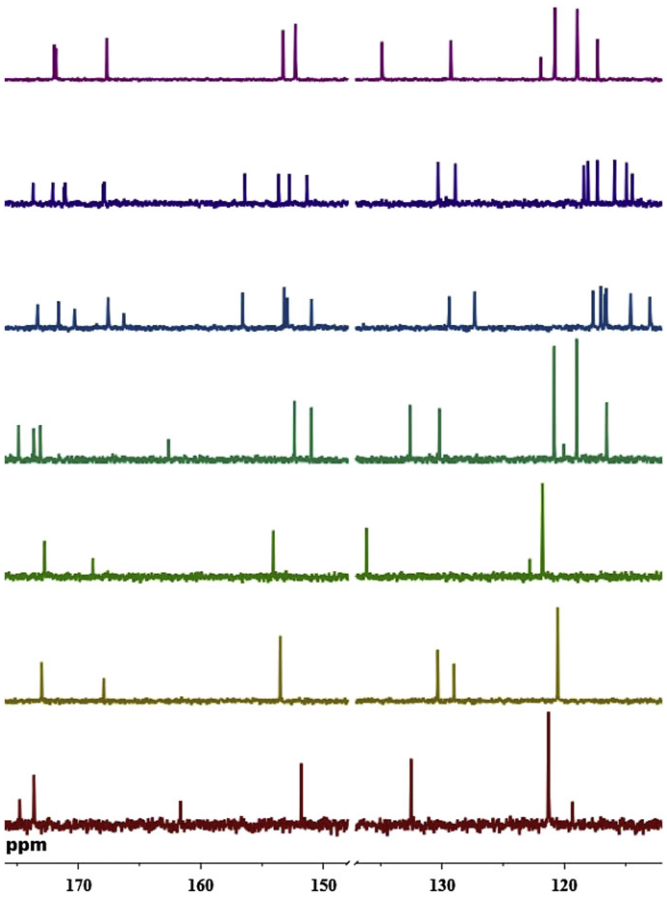


Fig. 6. Partial ^{13}C NMR spectra of compounds **7a**, **12a**, **13**, **18a**, **7b**, **12b** and **18b** (from top to bottom).

(50 mL) through two dropping funnels at the same rate. After addition (ca. 1 h), the mixture was kept stirring for another 1 h. The solvent was removed using a rotary evaporator, and the residue was chromatographed on a silica gel column eluted with a mixture of acetone and petroleum ether (1:4) to give product **7a** (421 mg, 70%) as a white solid. Compound **7a**: mp 120–121 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.90 (s, 1H), 7.39 (t, J=8.2 Hz, 1H), 7.12 (t, J=8.1 Hz, 1H), 6.90 (d, J=8.2 Hz, 2H), 6.76 (dd, J=8.1, 2.2 Hz, 2H), 6.52 (t, J=2.2 Hz, 1H), 3.70–3.52 (m, 8H), 1.77–1.66 (m, 8H), 0.98 (t, J=7.4 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.2, 172.0, 171.8, 167.7, 153.3, 152.3, 134.9, 129.3, 121.9, 120.8, 119.0, 117.3, 49.3, 20.8, 11.3; IR (KBr) ν 1699, 1605 cm^{-1}; MS (MALDI-TOF) m/z 601.4 $[M+H]^+$ (100%). Anal. Calcd for $C_{31}H_{36}N_8O_5$: C, 61.99; H, 6.04; N, 18.65. Found: C, 62.29; H, 6.32; N, 18.90.

4.4. Synthesis of 7b

To a refluxing solution of **6b** (1 mmol) and Cs_2CO_3 (2.5 mmol) in acetonitrile (120 mL) was added drop-wise a solution of **1b** (1 mmol) in acetonitrile (50 mL). After addition (ca. 0.5 h), the reaction was finished. The solvent was removed using a rotary evaporator, and the residue was chromatographed on a silica gel column eluted with a mixture of acetone and petroleum ether (1:2) to give product **7b** (283 mg, 45%) as a white solid. Compound **7b**: mp 215–216 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 9.72 (s, 2H), 7.57 (t, J=8.2 Hz, 2H), 7.01 (d, J=8.2 Hz, 4H), 3.73–3.54 (m, 8H), 1.82–1.70 (m, 8H), 0.98 (t, J=7.4 Hz, 12H); ^{13}C NMR (75 MHz, acetone-d_6) δ 186.3, 172.7, 168.8, 154.1, 136.2, 122.9, 121.8, 50.1, 21.5, 11.5; IR (KBr) ν 1699, 1606 cm^{-1}; MS (MALDI-TOF) m/z 629.3

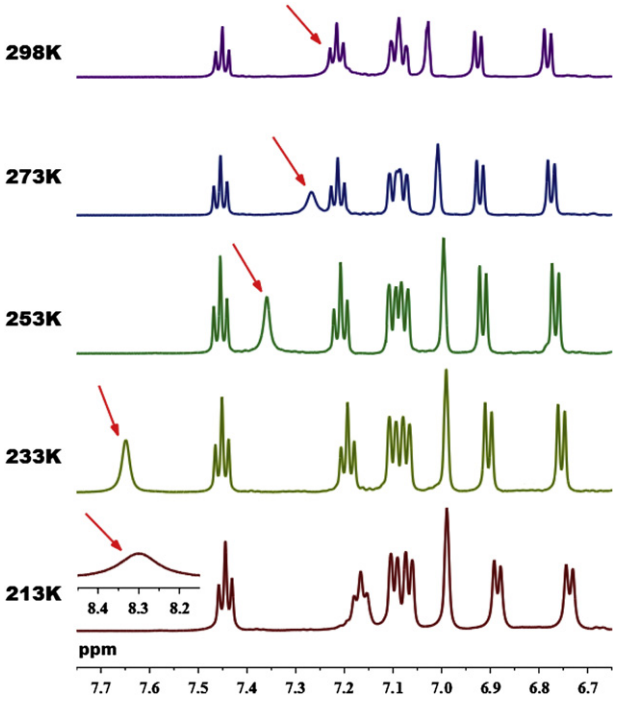


Fig. 7. Partial variable temperature ^{1}H NMR spectra of **12a**.

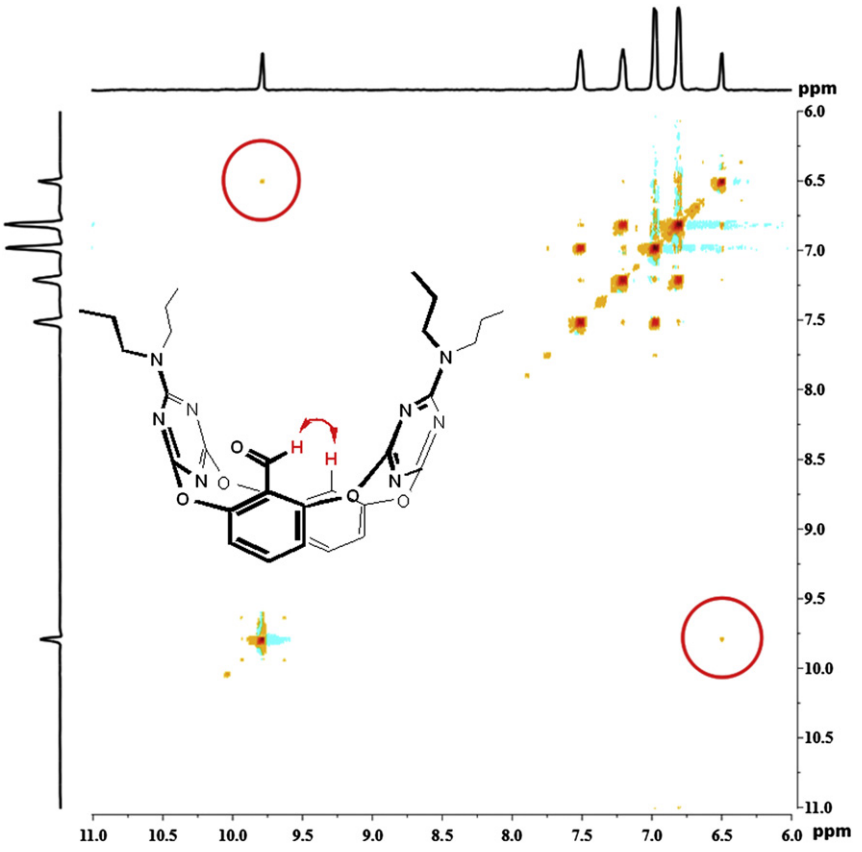


Fig. 8. NOESY spectra of **7a** at 213 K.

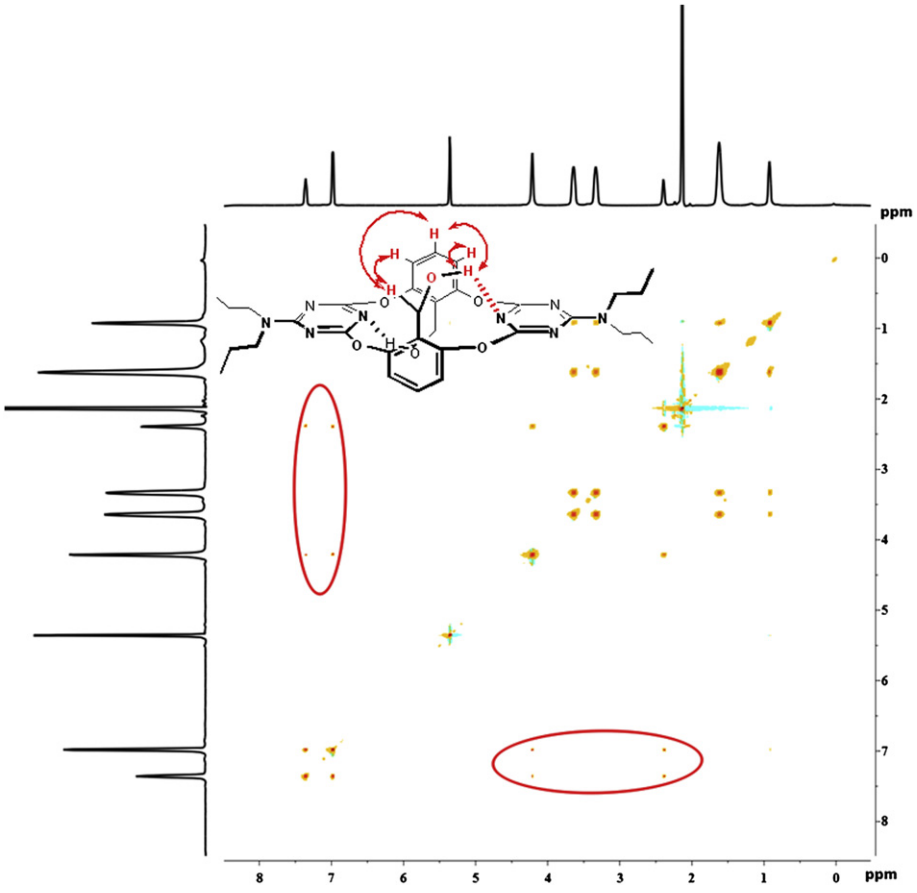


Fig. 9. NOESY spectra of **12b** at 193 K.

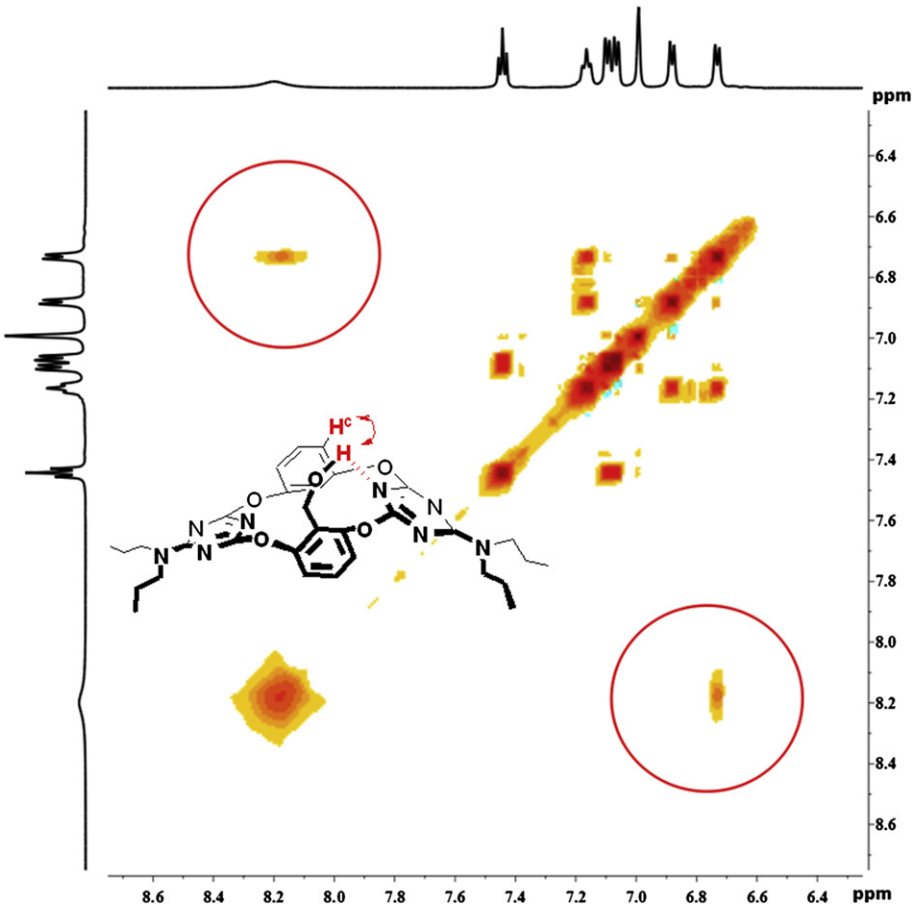


Fig. 10. NOESY spectra of **12a** at 213 K.

$[M+H]^+$ (100%), 651.2 $[M+Na]^+$ (80), 667.2 $[M+K]^+$ (20). Anal. Calcd for $C_{32}H_{36}N_8O_6$: C, 61.13; H, 5.77; N, 17.82. Found: C, 60.97; H, 5.78; N, 17.58.

4.5. Reduction of 7a with $NaBH_4$ in methanol

To a solution of **7a** (1 mmol) in methanol (10 mL) at room temperature was added portion-wise $NaBH_4$ (1 mmol). After stirring for additional 2 h, a saturated aqueous solution of NH_4Cl (10 mL) was added, and the resulting mixture was extracted with ethyl acetate (3×10 mL). Organic layers were combined and dried with anhydrous $MgSO_4$. After filtration, the filtrate was concentrated under reduced pressure, and the residue was chromatographed on a silica gel column eluted with a mixture of acetone and petroleum ether (1:2) to give product **8** (ca. 98 mg, <15%) as a white solid: mp 150–151 °C; ^1H NMR (300 MHz, acetone-d_6) δ 11.40 (s, 1H), 8.63 (s, 1H), 7.48 (t, J=8.1 Hz, 1H), 7.26–7.10 (m, 4H), 6.81 (d, J=8.1 Hz, 1H), 6.65 (d, J=8.0 Hz, 1H), 4.51 (s, 2H), 3.50–3.31 (m, 8H), 3.27 (s, 3H), 1.64–1.43 (m, 8H), 0.93–0.63 (m, 12H); ^{13}C NMR (75 MHz, acetone-d_6) δ 173.4, 172.9, 167.7, 158.4, 153.8, 153.0, 152.9, 130.1, 129.7, 120.1, 119.7, 117.7, 117.0, 114.5, 113.8, 65.6, 58.1, 50.7, 50.1, 50.0, 49.7, 21.8, 21.5, 21.4, 11.4, 11.3, 11.2; IR (KBr) ν 3429, 1591, 1559, 1530 cm^{-1}; MS (MALDI-TOF) m/z 657.4 $[M+Na]^+$ (100). Anal. Calcd for $C_{32}H_{42}N_8O_6$: C, 60.55; H, 6.67; N, 17.65. Found: C, 60.41; H, 6.70; N, 17.54.

4.6. Reduction of 7a with $NaBH_4$ in THF

To a solution of **7a** (1 mmol) in THF (10 mL) at room temperature was added portion-wise $NaBH_4$ (1 mmol). After stirring for additional 2 h, a saturated aqueous solution of NH_4Cl (10 mL) was added, and the resulting mixture was extracted with ethyl acetate (3×10 mL). Organic layers were combined and dried with anhydrous $MgSO_4$. After filtration, the filtrate was concentrated under reduced pressure, and the residue was chromatographed on a silica gel column eluted with a mixture of acetone and petroleum ether (1:4) to give very small amount of products **10** and **11**. Slow evaporation of the solvent from different fractions that contained **10** and **11** gave single crystals of **10** and **11**, respectively.

4.7. General procedure for the synthesis of 12

To an argon protected solution of **7** (0.5 mmol) in dry THF (10 mL) at −20 °C (**7a**) or at room temperature (**7b**) was added BH_3·THF solution in THF (1 M, 1 mL). The resulting mixture was stirred at −20 °C (**7a**) or at ambient temperature (**7b**) for another 0.5 h. The reaction was quenched by adding a saturated NH_4Cl solution in water (20 mL), and the mixture was extracted with ethyl acetate (3×20 mL). The organic layers were combined and dried with anhydrous $MgSO_4$. After removal of drying agent by filtration and of solvent by evaporation under a reduced pressure, the residue was chromatographed on a silica gel column eluted with a mixture of ethyl acetate and petroleum ether (1:6) to afford product **12**.

Compound **12a** (75 mg, 25%): oil; ^1H NMR (600 MHz, CD_2Cl_2) δ 7.45 (t, J=8.2 Hz, 1H), 7.22 (t, J=8.1 Hz, 2H), 7.09 (t, J=8.2 Hz, 2H), 7.03 (s, 1H), 6.93 (d, J=8.1 Hz, 1H), 6.78 (d, J=8.3 Hz, 1H), 5.52 (s, 2H), 3.58–3.37 (m, 8H), 1.72–1.52 (m, 6H), 0.96 (t, J=7.4 Hz, 9H), 0.82 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 173.7, 172.1, 171.2, 171.1, 168.0, 167.9, 156.4, 153.6, 152.8, 151.3, 130.3, 128.9, 118.4, 118.1, 117.3, 115.9, 115.0, 114.5, 64.7, 50.1, 49.8, 49.6, 49.5, 21.2, 21.0, 11.4, 11.3; IR (KBr) ν 3432, 1592, 1523 cm^{-1}; MS (MALDI-TOF) m/z 603.3 $[M+H]^+$

(100%), 625.3 $[M+Na]^+$ (50). Anal. Calcd for $C_{31}H_{39}N_8O_5$: *m/z*: 603.3038. FT-ICRMS: 603.3025 $[M+H]^+$.

Compound **12b** (285 mg, 90%): white solid; mp 235–236 °C; ^1H NMR (300 MHz, CD_2Cl_2) δ 7.32 (t, *J*=8.1 Hz, 2H), 6.95 (d, *J*=8.1 Hz, 4H), 4.27 (d, *J*=5.8 Hz, 4H), 3.74–3.54 (m, 8H), 1.84–1.70 (m, 10H), 1.03 (t, *J*=7.4 Hz, 12H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 173.0, 167.9, 153.5, 130.3, 129.0, 120.6, 50.0, 21.1, 11.5; IR (KBr) ν 3484, 1609, 1579, 1518 cm^{-1}; MS (MALDI-TOF) *m/z* 633.4 $[M+H]^+$ (30), 655.4 $[M+Na]^+$ (100%), 671.4 $[M+K]^+$ (22). Anal. Calcd for $C_{32}H_{40}N_8O_6$: C, 60.75; H, 6.37; N, 17.71. Found: C, 60.62; H, 6.45; N, 17.44.

4.8. Synthesis of 13

NH_3 solution in a mixture of 2-propanol and THF was prepared by mixing commercially available NH_3 solution in 2-propanol (2 M, 0.5 mL) with dry THF (1.5 mL), while acetic acid solution was obtained by dissolving glacial acetic acid (60 mg, 1 mmol) in dry THF (2 mL). Under argon protection and at room temperature, both solutions were added simultaneously through two syringes at the same rate using a syringe pump to the solution of **7a** (0.5 mmol) in dry THF (10 mL). After stirring for 0.5 h, $NaBH(OAc)_3$ (2 mmol) was added and the resulting mixture was kept stirring for another 1.5 h. The reaction was quenched by adding hydrochloric acid (1 M, 5 mL) and water (20 mL). The aqueous mixture was extracted with ethyl acetate (3×20 mL), and organic layers were combined and dried with anhydrous $MgSO_4$. After filtration, the filtrate was concentrated under reduced pressure and residue was chromatographed on a silica gel column eluted with a mixture of ethyl acetate and petroleum ether (1:8) to give pure compound **13**. **13** (60 mg, 20%): oil; ^1H NMR (300 MHz, acetone-d_6) δ 7.42 (t, *J*=8.2 Hz, 1H), 7.24 (s, 1H), 7.18 (t, *J*=8.2 Hz, 1H), 7.01 (dt, *J*=8.0, 2.1 Hz, 1H), 6.94 (d, *J*=8.4 Hz, 1H), 6.82 (d, *J*=7.6 Hz, 1H), 6.82 (d, *J*=7.6 Hz, 1H), 4.60 (d, *J*=4.8 Hz, 2H), 3.47–3.24 (m, 8H), 1.62–1.37 (m, 8H), 0.86 (t, *J*=7.4 Hz, 9H), 0.68 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 171.6, 170.3, 167.6, 167.5, 166.3, 156.3, 153.2, 152.9, 151.0, 129.4, 127.3, 117.7, 117.0, 116.7, 116.6, 114.6, 113.0, 48.7, 37.5, 20.8, 20.7, 11.2, 11.1; IR (KBr) ν 3424, 2963, 1589, 1527, 1379 cm^{-1}; MS (MALDI-TOF) *m/z* 603.3 $[M+H]^+$ (100%), 625.3 $[M+Na]^+$ (50). Anal. Calcd for $C_{31}H_{39}N_9O_4$: *m/z*: 602.3198. FT-ICRMS: 602.3191 $[M+H]^+$.

4.9. General procedure for the synthesis of 17a and 17c

To a boiling solution of K_2CO_3 (2 mmol) in acetonitrile (120 mL) was added simultaneously both solutions **14** (1 mmol) in acetonitrile (50 mL) and of **15a** or **15b**[29,30] (1 mmol) in acetonitrile (50 mL) through two dropping funnels at the same rate. After addition (ca. 2 h), the resulting mixture was refluxed for another 4 h. The solvent was removed using a rotary evaporator, and the residue was chromatographed on a silica gel column eluted with a mixture of acetone and petroleum ether (1:5) to give crude product. Pure compound **17a** or **17c** was obtained from recrystallization from methanol.

Compound **17a** (455 mg, 80%): white solid; mp 158–159 °C; ^1H NMR (300 MHz, acetone-d_6) δ 7.51 (d, *J*=8.2 Hz, 1H), 7.34 (dd, *J*=4.9, 1.7 Hz, 3H), 7.28 (d, *J*=8.2 Hz, 1H), 7.19 (dd, *J*=6.4, 3.2 Hz, 2H), 7.06 (d, *J*=8.2 Hz, 2H), 6.88 (dd, *J*=8.2, 2.2 Hz, 2H), 6.29 (t, *J*=2.2 Hz, 1H), 5.03 (s, 2H), 4.06 (s, 6H); ^{13}C NMR (75 MHz, acetone-d_6) δ 174.8, 173.4, 173.0, 161.8, 152.3, 150.9, 135.2, 133.0, 130.1, 129.0, 128.6, 128.6, 121.0, 119.0, 118.9, 116.5, 67.1, 55.3; IR (KBr) ν 1725, 1570, 1427 cm^{-1}; MS (ESI) *m/z* 569.5 $[M+H]^+$ (100%). Anal. Calcd for $C_{28}H_{20}N_6O_8$: C, 59.16; H, 3.55; N, 14.78. Found: C, 59.22; H, 3.73; N, 14.71.

Compound **17c** (418 mg, 85%): white solid; mp 141–142 °C; ^1H NMR (300 MHz, acetone-d_6) δ 7.53 (t, *J*=8.2 Hz, 1H), 7.34 (t, *J*=8.2 Hz, 1H), 7.09 (d, *J*=8.2 Hz, 2H), 6.94 (dd, *J*=8.2, 2.2 Hz, 2H), 6.73 (t, *J*=2.2 Hz, 1H), 4.08 (s, 6H), 3.56 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 175.8, 174.5, 174.0, 163.3, 153.3, 151.9, 133.9, 131.1, 121.8, 119.9, 119.7, 117.5, 56.2, 52.7; IR (KBr) ν 1728, 1590, 1564 cm^{-1}; MS (ESI) *m/z* 514.9 $[M+Na]^+$ (100%). Anal. Calcd for $C_{22}H_{16}N_6O_8 \cdot CH_3OH$: C, 52.67; H, 3.84; N, 16.02. Found: C, 52.98; H, 3.55; N, 15.94.

4.10. General procedure for the synthesis of 17b and 17d

A mixture of **15a** (1 mmol) or **15b** (1 mmol), **16** (1 mmol) and K_2CO_3 (2 mmol) in acetonitrile (100 mL) was refluxed for 1 h. After removal of solvent under reduced pressure, the residue was chromatographed on a silica gel column eluted with a mixture of acetone and petroleum ether (1:3) to give crude product. Recrystallization from ethanol gave pure compound **17b** or **17d**.

Compound **17b** (456 mg, 65%): white solid; mp 160–161 °C; ^1H NMR (300 MHz, acetone-d_6) δ 7.52 (t, *J*=8.2 Hz, 2H), 7.35 (s, 10H), 7.05 (d, *J*=8.2 Hz, 4H), 5.08 (s, 4H), 3.94 (s, 6H); ^{13}C NMR (75 MHz, acetone-d_6) δ 174.6, 173.4, 161.2, 151.9, 135.6, 133.3, 128.5, 128.3, 128.1, 121.6, 118.5, 67.0, 55.1; IR (KBr) ν 1723, 1598, 1563 cm^{-1}; MS (MALDI-TOF) *m/z* 725.0 $[M+Na]^+$ (100%). Anal. Calcd for $C_{36}H_{26}N_6O_{10}$: C, 61.54; H, 3.73; N, 11.96. Found: C, 61.69; H, 3.87; N, 11.87.

Compound **17d** (413 mg, 75%): white solid; mp 135–136 °C; ^1H NMR (300 MHz, acetone-d_6) δ 7.53 (t, *J*=8.2 Hz, 2H), 7.06 (d, *J*=8.2 Hz, 4H), 4.10 (s, 6H), 3.56 (s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.1, 172.9, 161.0, 151.3, 133.9, 121.7, 116.8, 55.8, 52.1; IR (KBr) ν 1723, 1597, 1572, 1425, 1359 cm^{-1}; MS (MALDI-TOF) *m/z* 573.2 $[M+Na]^+$ (100%). Anal. Calcd for $C_{19}H_8Cl_2N_6O_8 \cdot C_2H_5OH$: C, 52.35; H, 4.06; N, 14.09. Found: C, 52.57; H, 3.82; N, 13.90.

4.11. General procedure for the synthesis of 18a and 18b

Under H_2 atmosphere with a balloon, a mixture of **17a** (0.5 mmol) or **17b** (0.5 mmol) and $Pd(OH)_2/C$ (20%, 200 mg) in cyclohexane (20 mL) was stirred at room temperature for 12 h. The catalyst was removed by filtration through a Celite pad, and the filtrate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column eluted with a mixture of acetone and petroleum ether (2:1) to give crude product. Pure compound **18a** or **18b** was obtained from recrystallization from ethanol.

Compound **18a** (215 mg, 90%): white solid; mp 196–197 °C; ^1H NMR (300 MHz, acetone-d_6) δ 7.52 (t, *J*=8.2 Hz, 1H), 7.35 (t, *J*=8.2 Hz, 1H), 7.09 (d, *J*=8.2 Hz, 2H), 6.95 (dd, *J*=8.2, 2.2 Hz, 2H), 6.71 (t, *J*=2.2 Hz, 1H), 4.08 (s, 6H); ^{13}C NMR (75 MHz, acetone-d_6) δ 174.9, 173.6, 173.1, 162.6, 152.4, 151.0, 132.6, 130.2, 120.8, 120.1, 119.0, 116.6, 55.2; IR (KBr) ν 3429, 1725, 1593, 1574, 1362 cm^{-1}; MS (ESI) *m/z* 479.1 $[M+H]^+$ (100%). Anal. Calcd for $C_{21}H_{14}N_6O_8 \cdot CH_3OH$: C, 51.77; H, 3.55; N, 16.47. Found: C, 52.00; H, 3.41; N, 16.18.

Compound **18b** (204 mg, 78%): white solid; mp 227–228 °C; ^1H NMR (400 MHz, acetone-d_6) δ 7.48 (t, *J*=8.2 Hz, 2H), 7.03 (d, *J*=8.2 Hz, 4H), 4.05 (s, 6H); ^{13}C NMR (100 MHz, acetone-d_6) δ 174.8, 173.6, 161.7, 151.8, 132.5, 121.3, 119.3, 55.1; IR (KBr) ν 3428, 1727, 1598, 1571 cm^{-1}; MS (MALDI-TOF) *m/z* 544.9 $[M+Na]^+$ (100%), 558.9 $[M+K]^+$ (20). Anal. Calcd for $C_{28}H_{20}N_6O_8 \cdot C_2H_5OH$: C, 50.82; H, 4.26; N, 3.68. Found: C, 51.34; H, 4.30; N, 13.59.

Acknowledgements

We thank the National Natural Science Foundation of China (21132005, 21121004, 20972161), Ministry of Science and Technology (2011CB932501), Tsinghua University and the Chinese Academy of Sciences for financial support.

Supplementary data

^{1}H and ^{13}C NMR spectra of products, X-ray structures of **7b**, **10**, **11**, **12b**, **17d**, **18b** (CIFs). Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.08.069.

References and notes

1. (a) Wang, M.-X. *Acc. Chem. Res.* **2012**, *45*, 182; (b) Wang, M.-X. *Chem. Commun.* **2008**, 4541.
2. Maes, W.; Dehaen, W. *Chem. Soc. Rev.* **2008**, *37*, 2393.
3. Tsue, H.; Ishibashi, K.; Tamura, R. *Top. Heterocycl. Chem.* **2008**, *17*, 73.
4. Morohashi, N.; Narumi, F.; Iki, N.; Hattori, T.; Miyano, S. *Chem. Rev.* **2006**, *106*, 5291.
5. König, B.; Fonseca, M. H. *Eur. J. Inorg. Chem.* **2000**, 2303.
6. Gutsche, C. D. *Calixarenes: an Introduction*; The Royal Society of Chemistry: 2008.
7. Gong, H.-Y.; Zhang, X.-H.; Wang, D.-X.; Ma, H.-W.; Zheng, Q.-Y.; Wang, M.-X. *Chem.—Eur. J.* **2006**, *12*, 9262.
8. Gong, H.-Y.; Wang, D.-X.; Xiang, J.-F.; Zheng, Q.-Y.; Wang, M.-X. *Chem.—Eur. J.* **2007**, *13*, 7791.
9. (a) Wang, M.-X.; Zhang, X.-H.; Zheng, Q.-Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 838; (b) Liu, S.-Q.; Wang, D.-X.; Zheng, Q.-Y.; Wang, M.-X. *Chem. Commun.* **2007**, 3856; (c) Zhang, E.-X.; Wang, D.-X.; Zheng, Q.-Y.; Wang, M.-X. *Org. Lett.* **2008**, *10*, 2565; (d) Wang, L.-X.; Zhao, L.; Wang, D.-X.; Wang, M.-X. *Chem. Commun.* **2011**, 9690.
10. Wang, Q.-Q.; Wang, D.-X.; Yang, H.-B.; Huang, Z.-T.; Wang, M.-X. *Chem.—Eur. J.* **2010**, *16*, 7265.
11. (a) Gong, H.-Y.; Zheng, Q.-Y.; Zhang, X.-H.; Wang, D.-X.; Wang, M.-X. *Org. Lett.* **2006**, *8*, 4895; (b) Gong, H.-Y.; Wang, D.-X.; Zheng, Q.-Y.; Wang, M.-X. *Tetrahedron* **2009**, *65*, 87; (c) Zhang, E.-X.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *J. Org. Chem.* **2009**, *74*, 8589.
12. Yang, H.-B.; Wang, D.-X.; Wang, Q.-Q.; Wang, M.-X. *J. Org. Chem.* **2007**, *72*, 3757.
13. Ma, M.-L.; Li, X.-Y.; Wen, K. *J. Am. Chem. Soc.* **2009**, *131*, 8338.
14. (a) Gao, C.-Y.; Zhao, L.; Wang, M.-X. *J. Am. Chem. Soc.* **2011**, *133*, 8448; (b) Gao, C.-Y.; Zhao, L.; Wang, M.-X. *J. Am. Chem. Soc.* **2012**, *134*, 824.
15. Wu, J.-C.; Zhao, L.; Wang, D.-X.; Wang, M.-X. *Inorg. Chem.* **2012**, *51*, 3860.
16. Wang, D.-X.; Zheng, Q.-Y.; Wang, Q.-Q.; Wang, M.-X. *Angew. Chem., Int. Ed.* **2008**, *47*, 7485.
17. Wang, D.-X.; Wang, Q.-Q.; Han, Y.; Wang, Y.; Huang, Z.-T.; Wang, M. −X. *Chem.—Eur. J.* **2010**, *16*, 13053.
18. Li, S.; Fa, S.-X.; Wang, Q.-Q.; Wang, D.-X.; Wang, M.-X. *J. Org. Chem.* **2012**, *77*, 1860.
19. Chen, Y.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *Chem. Commun.* **2011**, 8112.
20. (a) Tsue, H.; Ono, K.; Tokita, S.; Ishibashi, K.; Matsui, K.; Takahashi, H.; Miyata, K.; Takahashi, D.; Tamura, R. *Org. Lett.* **2011**, *13*, 490; (b) Tsue, H.; Takahashi, H.; Ishibashi, K.; Inoue, R.; Shimizu, S.; Takahashi, D.; Tamura, R. *CrystEngComm* **2012**, *14*, 1021.
21. Wang, L.-X.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *J. Org. Chem.* **2010**, *75*, 741.
22. (a) Wang, M.-X.; Yang, H.-B. *J. Am. Chem. Soc.* **2004**, *126*, 15412; (b) Hou, B.-Y.; Zheng, Q.-Y.; Wang, D.-X.; Wang, M.-X. *Tetrahedron* **2007**, *63*, 10801; (c) Hou, B.-Y.; Wang, D.-X.; Yang, H.-B.; Zheng, Q.-Y.; Wang, M.-X. *J. Org. Chem.* **2007**, *72*, 5218; (d) Wang, Q.-Q.; Wang, D.-X.; Ma, H.-W.; Wang, M.-X. *Org. Lett.* **2006**, *26*, 5967; (e) Wang, Q.-Q.; Wang, D.-X.; Zheng, Q.-Y.; Wang, M.-X. *Org. Lett.* **2007**, *9*, 2847; (f) Hou, B.-Y.; Zheng, Q.-Y.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *Chem. Commun.* **2008**, 3864; (g) Naseer, M. M.; Wang, D.-X.; Zhao, L.; Huang, Z.-T.; Wang, M.-X. *J. Org. Chem.* **2011**, *76*, 1804.
23. For added examples, see: (a) Katz, J. L.; Geller, B. J.; Conry, R. R. *Org. Lett.* **2006**, *8*, 2755; (b) Van Rossom, W.; Robeyns, K.; Ovaere, M.; Van Meervelt, L.; Dehaen, W.; Maes, W. *Org. Lett.* **2011**, *13*, 126; (c) Zhu, Y.; Yuan, J.; Li, Y.; Gao, M.; Cao, L.; Ding, J.; Wu, A.-X. *Synlett* **2011**, 52; (d) Katz, J. L.; Tschaen, B. A. *Org. Lett.* **2010**, *12*, 4300; (e) Capici, C.; Gattuso, G.; Notti, A.; Parisi, M. F.; Bruno, G.; Nicolo, F.; Pappalardo, S. *Tetrahedron Lett.* **2011**, *52*, 1351; (f) Van Rossom, W.; Kishore, L.; Robeynes, K.; Van Meervelt, L.; Dehaen, W.; Maes, W. *Eur. J. Org. Chem.* **2010**, 4122; (g) Akagi, S.; Yasukawa, Y.; Kobayashi, K.; Konishi, H. *Tetrahedron* **2009**, *65*, 9983; (h) Lawson, K. V.; Barton, A. C.; Spence, J. D. *Org. Lett.* **2009**, *11*, 895; (i) Chen, C.-F. *Chem. Commun.* **2011**, 1674 and references cited therein; (j) Katz, J. L.; Geller, B. J.; Foster, P. D. *Chem. Commun.* **2007**, 1026; (k) Raimundo, J. M.; Chen, Z.; Siri, O. *Chem. Commun.* **2011**, 10410; (l) Haddoub, R.; Touil, M.; Raimundo, J. M.; Siri, O. *Org. Lett.* **2010**, *12*, 2722; (m) Zuo, C.-S.; Wiest, O.; Wu, Y.-D. *J. Phys. Org. Chem.* **2011**, *12*, 1157.
24. Yao, B.; Wang, D.-X.; Gong, H.-Y.; Huang, Z.-T.; Wang, M.-X. *J. Org. Chem.* **2009**, *74*, 5361.
25. Van Rossom, W.; Maes, W.; Kishore, L.; Ovaere, M.; Van Meervelt, L.; Dehaen, W. *Org. Lett.* **2008**, *10*, 585.
26. (a) Yao, B.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *Chem. Commun.* **2009**, 2899; (b) Yao, B.; Wang, Z.-L.; Zhang, H.; Wang, D.-X.; Zhao, L.; Wang, M.-X. *J. Org. Chem.* **2012**, *77*, 3336; (c) Wang, Z.-L.; Zhao, L.; Wang, M.-X. *Org. Lett.* **2011**, *13*, 6560; (d) Wang, Z.-L.; Zhao, L.; Wang, M.-X. *Org. Lett.* **2012**, *14*, 1472.
27. Chen, Y.; Wang, D.-X.; Huang, Z.-T.; Wang, M.-X. *J. Org. Chem.* **2010**, *76*, 3786.
28. Hiroyoshi, O.; Nobumasa, I. .; Tetsuo, T. *Agric. Biol. Chem.* **1987**, *51*, 2563.
29. (a) Firoj, A.; Kumar, S. S.; Takashi, O.; Masami, I.; Amina, K. *Heterocycles* **2010**, *80*, 477; (b) Guo, W.; Li, J.-F.; Fan, N.-J.; Wu, W.-W.; Zhou, P.-W.; Xia, C.-Z. *Synth. Commun.* **2005**, *35*, 145.
30. Cesare, G.; Francesco, M.; Umberto, P.; Marcella, B. *Tetrahedron* **1990**, *46*, 7289.